



Faculty of Medicine and Health Sciences

**Methylated DNA Damage Repair Genes: RRM2 and GAPDH are
Prognostic Biomarkers and Correlate with Immunotherapy in Lung
Adenocarcinoma**

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**Doctor of Philosophy
2025**

Methylated DNA Damage Repair Genes: RRM2 and GAPDH are Prognostic
Biomarkers and Correlate with Immunotherapy in Lung Adenocarcinoma

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A thesis submitted

In fulfillment of the requirements for the degree of Doctor of Philosophy

(Medical Sciences)

Faculty of Medicine and Health Sciences
UNIVERSITI MALAYSIA SARAWAK

2025

DECLARATION

I declare that the work in this thesis was carried out in accordance with the regulations of Universiti Malaysia Sarawak. Except where due acknowledgements have been made, the work is that of the author alone. The thesis has not been accepted for any degree and is not concurrently submitted in candidature of any other degree.

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Date : 5 Oct 2025

ACKNOWLEDGEMENT

I would like to take this opportunity to those who have contributed directly or indirectly to this thesis.

My sincere gratitude to the Centre for Graduate Studies, for the advice and support given during my period of study in Universiti Malaysia Sarawak.

Finally, I would like to thank the management of the Universiti Malaysia Sarawak for making it possible for me to complete my study here in Sarawak. Thank you all.

ABSTRACT

Background: Mounting evidence indicated that aberrant DNA methylation is particularly important in the pathogenesis of lung adenocarcinoma (LUAD). Systematic screening of methylated DNA damage-repair-related genes (DDRGs) with a bioinformatic approach can establish methylated DDRGs-based prognostic biomarker. Nevertheless, limited previous studies identify methylated DDRGs as prognostic biomarker. In this study, the aim was to assess the prognostic value of methylated DDRGs in LUAD.

Methods: LUAD-related datasets were obtained from public databases. In the TCGA-LUAD dataset, differential expression analysis was used to identify differentially expressed genes (DEGs) and differentially expressed methylated genes (DE-MGs). Next, methylated DE-DDRGs were identified by combining up-regulated DEGs with demethylated DE-MGs as well as down-regulated DEGs with hypermethylated DE-MGs. Then, univariate and multivariate cox analyses were done using methylated DE-DDRGs to identify prognostic biomarkers and build risk-prognostic models. Independent prognostic analysis was performed using risk scores and clinical features to identify independent prognostic parameters for nomogram development. Finally, the study examined response to immunotherapy responses.

Results: One high-confidence gene, CLU, was hypermethylated and hyperexpressed in LUAD tissues. In addition, eight hypomethylated and highly expressed genes have been identified (BUB1B, SHCBP1, RRM2, RPL39L, TRIP13, GAPDH, ENO1, and CENPM). Among them, RRM2 and GAPDH were identified by univariate and multivariate analyses as significantly associated with shorter overall survival. Meanwhile, the risk score based on the prognostic signature was also identified as an independent prognostic factor for LUAD.

Moreover, the high-risk group associated with the poor prognosis of LUAD showed lower immune/stromal scores and immune infiltration characteristics. Ultimately, TIDE, a tool to predict immunotherapy response, analysis revealed that patients in the low-risk group may be more sensitive to immune checkpoint inhibitor therapy.

Conclusion: RRM2 and GAPDH could serve as promising prognostic and immunotherapeutic biomarkers in LUAD and can contribute to novel drug strategy for LUAD treatment.

Keywords: Lung adenocarcinoma; DNA methylation; DNA damage repair; Prognosis; Immune checkpoint; Immunotherapy;

Gen Pembaikan Kerosakan DNA yang dimetilasi : RRM2 dan GAPDH adalah penanda ramalan (prognostik) dan Berkorelasi dengan Imunoterapi dalam Adenokarsinoma Paru-paru

ABSTRAK

Latar Belakang: Kebelakangan ini, bukti yang semakin banyak menunjukkan bahawa metilasi DNA yang luar biasa adalah sangat penting dalam patogenesis adenokarsinoma paru-paru (LUAD). Penapisan secara sistematik terhadap gen yang berkaitan dengan pembaikan kerosakan DNA yang dimetilasi (DDRG) dengan pendekatan bioinformatik boleh membina penanda ramalan (prognostik) berasaskan DDRG. Walau bagaimanapun, kajian-kajian mengenai DDRG yang dimetilasi sebagai penanda ramalan adalah terhad. Dalam kajian ini, kami mencadangkan gen yang berkaitan dengan DDR yang dimetilasi dalam LUAD akan memberi impak secara ramalan.

Kaedah: Dataset yang berkaitan dengan LUAD telah diperolehi daripada pangkalan data awam. Dalam dataset TCGA-LUAD, analisis ekspresi pembezaan digunakan untuk mengenal pasti gen yang diekspresikan secara berbeza (DEG) dan gen yang dimetilasi secara berbeza (DE-MG). Seterusnya, DDRG yang dimetilasi (DE-DDRG) telah dikenalpasti dengan menggabungkan DEG yang meningkat dengan DE-MG yang demetilasi, serta DEG yang menurun dengan DE-MG yang hipermetilasi. Kemudian, analisis univariat dan multivariat Cox dilaksanakan dengan menggunakan DE-DDRG yang dimetilasi untuk mengenal pasti penanda ramalan dan membina model ramalan risiko. Analisis ramalan bebas dilakukan dengan menggunakan skor risiko dan ciri klinikal untuk menentukan parameter ramalan bebas bagi pembangunan nomogram. Akhirnya, tindakbalas imunoterapi dan titik pemeriksaan imunologi digambarkan.

Keputusan: Satu gen berkeyakinan tinggi, CLU, telah hipermetilasi dan hiperekspresi dalam tisu LUAD. Di samping itu, lapan gen hypomethylated dan sangat dinyatakan telah dikenal pasti (BUB1B, SHCBP1, RRM2, RPL39L, TRIP13, GAPDH, ENO1, dan CENPM). Antaranya, RRM2 dan GAPDH telah dikenal pasti oleh analisis univariat dan multivariate sebagai secara signifikan dikaitkan dengan kelangsungan hidup keseluruhan yang lebih pendek. Sementara itu, skor risiko berdasarkan tandatangan prognostik juga dikenal pasti sebagai faktor prognostik bebas untuk LUAD. Selain itu, kumpulan berisiko tinggi yang dikaitkan dengan prognosis buruk LUAD menunjukkan skor imun / stromal yang lebih rendah dan ciri penyusupan imun. Akhirnya, analisis TIDE mendedahkan bahawa pesakit dalam kumpulan berisiko rendah mungkin lebih sensitif terhadap terapi perencat pusat pemeriksaan imun.

Kesimpulan: Dalam kajian ini, RRM2 dan GAPDH didapati berpotensi sebagai penanda-penanda ramalan dan imunoterapi dalam LUAD dan boleh menyumbang kepada strategi ubat baru untuk rawatan LUAD.

Kata kunci: *Adenokarsinoma paru-paru; metilasi DNA; Pembaikan kerosakan DNA; Prognostik, Titik pemeriksaan imun, Imunoterapi*

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LIST OF ABBREVIATIONS

alt-EJ	Alternative end joining
AML	Acute myeloid leukemia
ANOVA	Analysis of Variance
APE1	Apurinic/apyrimidinic endonuclease 1
ARID1A	AT-rich interaction domain 1A
ATR	Ataxia telangiectasia and Rad3-related protein
AURK	Aurora
AURKA	Aurora A
AURKB	Aurora B
AURK	Aurora kinase
AUC	Area under the curve
BC	Breast Cancer
BER	Base excision repair
BUB1B	BUB1 Mitotic Checkpoint Serine/Threonine Kinase B
CDK	Cyclin-dependent kinase??
CDK4/6	Cyclin-dependent kinases 4/6
CENPM	Centromere Protein M
CHK	Checkpoint kinase
CI	Confidence intervals
CLU	Clusterin
CP	Carboplatin/paclitaxel
CPD	Cyclobutane pyrimidine dimers
CR	Complete response

CRT	Chemo-Radiotherapy
CTLA4	Cytotoxic T-lymphocyte associated protein 4
DCR	Disease control rate
DCs	Dendritic cells
DDR	DNA damage and repair
DDRGs	DNA damage-repair-related genes
DEGs	Differentially expressed genes
DE-MCS	Differentially expressed methylated CpG sites
DE-MGs	Differentially expressed methylated genes
DE-DDRGs	Differential-expression DNA damage-repair-related genes
DNA-PK	DNA-dependent protein kinase
DNMT3A	DNA Methyltransferase 3 Alpha
DNMTi	DNA methyltransferase inhibitors
DLBCL	Diffuse large B cell lymphoma
dMMR	MMR deficiency
DNA	Deoxyribonucleic Acid
DRR	Direct Reversal Repair
DSBs	DNA double strand breaks
EFS	Event-free survival
EGFR	Epidermal growth factor receptor
EGFR-TKI	Epidermal growth factor receptor tyrosine kinase inhibitor
ELF3	Early Flowering 3
EMT	Epithelial-mesenchymal transition
ENO1	Enolase 1
ERCC1	Excision repair cross-complementation group 1

ERK1/2	Extracellular signal-regulated kinase 1/2
ESTIMATE	Estimation of STromal and Immune cells in MAlignant Tumor tissues using Expression data
FA	Fanconi anemia
GAPDH	Glyceraldehyde-3-Phosphate Dehydrogenase
GEO	Gene Expression Omnibus
HNSCC	Head and neck squamous cell carcinoma
HR	Hazard ratio
HRD	Homologous recombination deficiency
HRR	Homologous recombination repair
ICI	Immune Checkpoint Inhibitor
ICLs	Interstrand crosslinks
iDCs	Immature dendritic cells
JAK2	Janus Kinase 2
KM	Kaplan-Meier
KMT2C/D	Lysine N-methyltransferase 2C/D
KRAS	Kristen Rat Sarcoma Viral oncogene homolog
LC	Lung cancer
LCC	Large cell carcinoma
LDCT	Low-dose CT scan
LOH	Loss of heterozygosity
LUSC	Squamous cell carcinoma
LUAD	Lung adenocarcinoma
mCRC	Metastatic colorectal cancer
mCRPC	Metastatic Castration-Resistant Prostate Cancer

MGMT	Methylguanine methyl transferase
MMR	Mismatch repair
MR	Minor response
MSI	Microsatellite instability
MTAP	Methylthioadenosine phosphorylase
mTOR	Mechanistic Target Of Rapamycin Kinase
NCI	National Cancer Institute
NER	Nucleotide excision repair
NES	Normalized ssGSEA score
NHEJ	Non-homologous DNA end joining
NK	Natural killer
NSCLC	Non-small cell lung cancer
nsqNSCLC	nsqNSCLC
OC	Ovarian Cancer
OGG	Enzyme 8-oxoguanine DNA N-glycosylase
8-OHdG	8-oxo-7,8-dihydro-2'-deoxyguanosine
ORR	Overall response
OS	Overall survival
PALB2	Partner And Localizer Of BRCA2
PARP	Poly ADP-ribose Polymerase
PARPi	Poly (ADP-ribose) polymerase inhibitors
PD1/PDL1	Programmed death (ligand) 1
PDAC	Pancreatic ductal adenocarcinoma
PDX	Patient-derived xenograft
PFR-4	Progression free rate at 4 months

PFS	Progression-free survival
PIKK	Phosphatidylinositol 3-kinase-related kinase
PNET	Pancreatic neuroendocrine tumour
(6-4)PP	Pyrimidine-pyrimidone (6-4) photoproducts
PPP2R2A	Protein Phosphatase 2 Regulatory Subunit B alpha
PR	Partial response
PRMT	Protein arginine methyltransferase 1
RNA	Ribonucleic Acid
ROC	Receiver operating characteristic curve
RPL39L	Ribosomal Protein L39 Like
RRM2	Ribonucleotide reductase M2
RSK	Ribosomal s6 kinase
RT-PCR	Real-time PCR
SABR	Stereotactic ablative radiotherapy
SCCs	Squamous cell cancers
SCLC	Small cell lung cancer
SD	Stable disease
SHCBP1	SHC Binding And Spindle Associated 1
SLFN11	Schlafen family member 11
SoC	Standard of care
SSB	Single-strand break
ssDNA	Single-stranded DNA
ssGSEA	Single sample gene set enrichment analysis
STK11	Serine/threonine kinase 11
SubMap	Subclass mapping

TCGA	The Cancer Genome Atlas
TFH	T follicular helper
TIDE	Tumour immune dysfunction and exclusion
TMB	Tumour mutational burden
TME	immunosuppressive tumor microenvironment
TNBC	Triple-negative breast cancer
TPS	Tumour Proportion Score
TRIP13	Thyroid Hormone Receptor Interactor 13
UCSC	UC Santa Cruz
UV	Ultraviolet
VEGFR2	Vascular endothelial growth factor receptor 2
WBRT	Whole brain radiation therapy

CHAPTER 1

INTRODUCTION

1.1 Study Background

Lung cancer is the main cause of cancer deaths, accounting for an estimated 1.8 million deaths annually and representing the highest global cancer burden in terms of disability - adjusted life years lost (Sung et al., 2021). Its incidence demonstrates significant geographical and demographic variation, strongly correlated with historical patterns of tobacco consumption, while rates are declining in high income countries due to successful smoking cessation programs, they are rising in many parts of Asia and Africa (Sung et al., 2021). The 5-year survival and prognostication of lung cancer is based on the tumor (T), lymph node (N), distant metastasis (M) staging classification, wherein long-term survival rate concomitantly declines with advancing disease stage (Goldstraw et al., 2016; J. K. Hwang et al., 2020; Woodard et al., 2016). Non-small cell lung cancer (NSCLC) accounts for approximately 80% of primary lung cancer, with lung adenocarcinoma (LUAD) as the predominant NSCLC subtype, particularly among women, non-smokers, and younger populations (Bray et al., 2024; H. Chen et al., 2019; Testa et al., 2018).

The primary aetiological factor for LUAD is tobacco smoking, responsible for a vast majority of cases (Alberg et al., 2013). However, other significant risk factors include exposure to radon gas, asbestos, air pollution, and second-hand smoke (Houston et al., 2014; S. Sun et al., 2007). Notably, a growing number of LUAD cases occur in never-smokers, where genetic carcinogens are believed to play a more prominent role (Chen et al., 2020; S. Sun et al., 2007). The pathogenesis of LUAD is a multi-step process driven by the accumulation of genetic and epigenetic alterations. The activation of oncogenes like

EGFR, KRAS, BRAF, ALK alterations promotes uncontrolled cell proliferation and survival (Collisson et al., 2014). Inactivation of tumor suppressor genes such as TP53, STK11/LKB1 via mutation or deletion removes critical barriers to tumorigenesis (Herbst et al., 2018). Tumors develop mechanisms to evade the immune system, often through upregulation of immune checkpoint proteins like PD-L1 (Chen & Mellman, 2017).

The management of LUAD stage dependent. Early-stage LUAD is typically managed with surgery, radiotherapy, and chemotherapy (Ettinger et al., 2023). However, relapse is common even after complete surgical resection (Dziedzic et al., 2016). For advanced metastatic disease, treatment has been revolutionized by targeted therapies against specific oncogenic driver and immunotherapy using immune checkpoint inhibitors (ICIs) such as anti-PD-1/PD-L1 antibodies (Chaft et al., 2021). Although advances in targeted therapy and immunotherapy have improved outcomes for metastatic LUAD, the long-term survival rate, risk of metastasis, and recurrence rates remain suboptimal (Dziedzic et al., 2016; Siegel et al., 2023). Thus, identifying novel biomarkers and therapeutic targets is critical to enhancing the diagnosis and overall prognosis of LUAD.

DNA methylation is an epigenetic mechanism that regulates proper gene expression and stable gene silencing (Moore et al., 2013). Aberrant DNA methylation is a key regulatory mechanism in early stages of carcinogenesis (Sharma et al., 2010). Given that DNA methylation is reversible, it presents a promising therapeutic target (Kulis & Esteller, 2010). Numerous studies have explored the role of DNA methylation as diagnostic biomarker for cancer detection (Cai et al., 2020; Tsou et al., 2002; Yang et al., 2019). In addition, DNA methylation can also be used as biomarkers to predict clinical outcomes and treatment responses. DNA methylation patterns are different between lung cancer histological subtypes, while methylation rates of ANK1, APC, CCND2, CDH13, KCNH5,

RAR β , and RUNX3 are distinctly higher in LUAD than other subtypes (Hawes et al., 2010; Tessema et al., 2017; Toyooka et al., 2003). In LUAD, decreased methylation of FAM83A leads to gene upregulation, which demonstrates a poor prognosis (Yu et al., 2020), while a nine-gene methylation pattern (including C20orf56, BTG2, C13orf16, DNASE1L1, ZDHHC3, FHDC1, ARF6, ITGB3, and ICAM4) can predict the survival and recurrence (R. Wang et al., 2019). Thus, studies of DNA methylation are promising in identifying predictive biomarkers for treatment and offering individualized treatment strategies.

DNA damage plays an important role in tumorigenesis of various tumors, including LUAD (Burgess et al., 2020; Dizdaroglu, 2015; Jeggo et al., 2016; Papalouka et al., 2023; Tufail, 2023). Five major DNA repair pathways are identified to maintain genetic stability: base excision repair (BER), nucleotide excision repair (NER), mismatch repair (MMR), homologous recombination repair (HRR), and non-homologous DNA end joining (NHEJ) as well as two specific damage repair pathways (direct chemical reversal and interchain crosslinking repair) are important supplements (Chatterjee & Walker, 2017; Tufail, 2023). Defects in these pathways can drive tumorigenesis by allowing the accumulation of mutations. Conversely, these altered defects can be exploited therapeutically. Multiple studies have shown that DNA repair is related to tumor progression and therapeutic response in different cancers (Gavande et al., 2016; Groelly et al., 2023; Lima et al., 2019; Mei et al., 2019; Tessoulin et al., 2018).

In lung cancer, DNA damage signalling and repair pathways significantly influence prognosis and treatment outcomes (Burgess et al., 2020; Mao et al., 2024). DNA repair genes are critical for maintaining genomic stability. When their promoters are methylated and silenced, cells accumulate unrepaired DNA lesions, leading to increased genomic instability and sensitization to DNA-damaging therapies. For instance, methylation of DNA

repair genes can predict the response to chemotherapy and target therapies, such as PARP inhibitors (Asakawa et al., 2010; Bartkova et al., 2005; Gao et al., 2016; Gkatzamanidou et al., 2014; Kang et al., 2012). For example, PARP1 inhibitors have been approved for the treatment of ovarian, breast, and other DNA-repair deficient tumors (Ray Chaudhuri & Nussenzweig, 2017). In LUAD, the five major DNA repair pathways significantly impact tumorigenesis (via the accumulation of mutations resulting from repair defects) and therapy response (influencing the efficacy of chemotherapy, PARP inhibitors, and immunotherapy), forming the basis for biomarker discovery and precision treatment strategies. These pathways are crucial for understanding the development of LUAD, tailoring therapies, and overcoming resistance to enhance patient outcomes.

1.2 Problem Statement

Despite the rapid advancement in targeted therapy and immunotherapy that have attributed improved outcomes for metastatic LUAD, long-term survival rate, metastasis risk, and recurrence rates remain unsatisfactory.

A key opportunity to address this gap lies in the understudied role of DNA damage-repair (DDR) genes. While DDR gene alterations are widespread in LUAD, alterations of DNA repair genes are diverse in LUAD. To the best of current knowledge, fewer than 10 published studies have investigated aberrant DNA methylation of these genes as prognostic factors. Notably, none have integrated methylation patterns across multiple DDR pathways to develop a prognostic signature in LUAD cohorts for LUAD. Systematically identifying DDR genes silenced by hypermethylation or activated by hypomethylation could reveal novel biomarkers for prognosis, immune infiltration, and response to therapy, ultimately guiding more personalized and effective treatment strategies.

1.3 Objectives

Understanding the expression patterns and mechanisms of DNA damage and repair genes in LUAD is of great significance for the prognosis and treatment improvement of LUAD. DNA methylation modification is considered to be a key gene regulation mechanism in epigenetics, and it has been confirmed to be a reversible process and a potential therapeutic target (Kulis & Esteller, 2010).

This study hypothesize that a distinct subset of DDR genes is aberrantly methylated in LUAD, and that a prognostic signature derived from these methylated DE-DDRGs can effectively stratify patients into high and low risk groups with distinct overall survival and tumor immune microenvironments. To test this hypothesis, the study employed publicly available data for gene expression and DNA methylation profiles of the LUAD cohort from The Cancer Genome Atlas (TCGA) to perform various bioinformatics analyses. And these findings were validated using an independent stage I-II LUAD cohort (GSE31210 and GSE68465 datasets).

This study aims to investigate the prognostic implications of aberrant regulation of DDR-related genes in LUAD. This can be achieved through the following set of objectives:

- i. To identify methylated differential expression DNA damage-repair-related genes (methylated DE-DDRGs)
- ii. To develop and validate a prognostic signature based on methylated DE-DDRGs
- iii. To analyse association between methylated DE-DDRGs with immune infiltration and immunotherapy

1.4 Chapter Summary

This study is based on bioinformatics methods to screen and study the prognostic biomarkers of DNA damage and repair-related methylation regulation in LUAD, and provide basis and ideas for the improvement of the prognosis of the disease, clinical immunotherapy and early diagnosis.

CHAPTER 2

LITERATURE REVIEW

2.1.1 DNA Damage and genomic instability in NSCLC

In recent decades, lung cancer (LC) research has shown significant advancements in screening, diagnosis, and treatment, thanks to the rapid development of technologies such as low-dose CT scan (LDCT), minimally invasive techniques (Rijavec et al., 2019), stereotactic ablative radiotherapy (SABR), new targeted therapy, and new immunotherapy. These advancements have improved the survival rate of LC patients by 56% in men and 32% in women (Siegel et al., 2022). Despite this progress, LC remains the leading cause of cancer death, with an estimated 2.2 million new cases and 1.8 million deaths in 2020 (Sung et al., 2021) .

LC has two major pathological subtypes: non-small cell lung cancer (NSCLC), which accounts for approximately 85% of all LC cases, and small cell lung cancer (SCLC), comprising the remaining 15%. NSCLC can be further divided into three subtypes relative to all NSCLC cases: lung adenocarcinoma (LUAD, 50%), squamous cell carcinoma (LUSC, 30-40%), and large cell carcinoma (LCC, 10-20%).

Maintenance of genomic integrity is critical for cellular homeostasis and the prevention of tumorigenesis. Friedberg et al. reported that the human body is subject to around 10,000 to 1,000,000 instances of DNA damage per day (Friedberg, 2019). DNA damage caused by endogenous (for example, free radicals) (Gupta et al., 2020; Owiti et al., 2021) or exogenous (for example, ionizing radiation) factors (Maremonti et al., 2020; Mavragani et al., 2019; Pariset et al., 2021) can lead to genome instability and diseases such

as cancer. DNA double-strand breaks (DSBs) are the most severe type of damage, as accumulation of incorrectly repaired or unrepaired DSBs can cause mutation, genomic instability, or induce cell death (Bröckelmann et al., 2020).

LC generally exhibits a distinct genomic profile compared with other tumors, with high somatic mutational burden (Chalmers et al., 2017). Smoking is the main cause of LC, as tobacco carcinogens like benzo[a]pyrene damage DNA and create specific mutations—such as G→T changes in TP53 and mutations in KRAS—that drive LC development, accounting for 90% of cases. However, approximately 20% of newly diagnosed lung adenocarcinoma cases are non- or light-smokers in developed countries now. Smokers have a higher somatic mutational burden than non-smokers (Govindan et al., 2012) and smokers show additional genomic instability process likely contributes to tumor progression (de Bruin et al., 2014). Non-small cell lung cancer (NSCLC) primary tumors display high genomic diversity, characterized by heterogeneous tumor driver mutations. Since not all clones within the tumor carry the same mutations, this variability means patients may not benefit from targeted therapies.

DNA damage is repaired by specific cellular pathways during the normal cell cycle. When DNA damage fails to be repaired or excised, the mutations will eventually trigger carcinogenesis. For instance, EGFR exon 19 deletion corrected with decreased expression of ERCC1 but also impacted ERCC1 foci formation in response to DNA cross-link damage, contributing to DNA damage and repair (DDR) deficiency (L. Zhang et al., 2020). Germline mutations in ATM, TP53, BRCA2, EGFR, and PARK2 are implicated in cancer predisposition syndromes (Parry et al., 2017). Chromosomal instability may cause tumor heterogeneity and drug resistance. For instance, over 60% NSCLC cases present aneuploidy.

Chromosomal instability elevates in the NSCLC patients with ROS1 fusion treated with crizotinib (Soca-Chafre et al., 2019). The AURK family is involved in mitosis and chromosomal segregation. Abnormalities in AURK proteins can be associated with genomic instability. Overexpression of AURKA (A. S. K. Al-Khafaji et al., 2017; Kuang et al., 2017; N. Liu et al., 2019; Schneider et al., 2017; Xu et al., 2014; Zhang et al., 2018) or AURKB (Hayama et al., 2007; Takeshita et al., 2013; Vischioni et al., 2006) was correlated with poor prognosis of overall survival in NSCLC. Some research revealed that AURKA and AURAB were associated with resistance of EGFR-TKI (Bertran-Alamillo et al., 2019; Shah et al., 2019; Wu et al., 2011), chemotherapy (A. S. Al-Khafaji et al., 2017; Linardopoulos, 2007; C. Sun et al., 2007; Y. Wang et al., 2025), and/or radiotherapy (J. B. Liu et al., 2019; N. Liu et al., 2019; Orth et al., 2018) in lung cancer in pre-clinical models.

Targeted therapy and ICIs-based treatment with/without chemotherapy have been widely used in NSCLC. Despite a number of inhibitors having been developed for targeting EGFR, ALK, ROS1, KRAS, MET, NTRK, HER2, RET, LUSC and LCC rarely present mutations in tyrosine kinase receptors compared with LUAD.

2.1.2 DNA Repair in NSCLC

Various DNA repair pathways, including Direct Reversal Repair (DRR), Base Excision Repair (BER), Nucleotide Excision Repair (NER), Mismatch Repair (MMR), Non-Homologous End Joining (NHEJ), Homologous Recombination repair (HRR), and interchain crosslinking repair, can circumvent DNA damage.

DNA damage caused by various agents such as alkylation, oxidation, UV radiation, and cross-linking requires different repair mechanisms. The mechanism of DRR is involved

in reversing the O-alkylated DNA damage caused by methylguanine methyl transferase (MGMT) (Soll et al., 2017). DRR also removes photolesions caused by UV radiation with DNA-photolyase (Kavakli et al., 2019; Sancar, 2016). The activity of the DNA repair enzyme 8-oxoguanine DNA N-glycosylase (OGG), is associated with lung cancer (Paz-Elizur et al., 2003). BER can repair small base lesion damage such as the damage on 8-oxo-7,8-dihydro-2'-deoxyguanosine (8-OHdG) by radicals with DNA glycosylase, AP endonuclease, DNA polymerase and DNA ligase (Robertson et al., 2009; Vechtomova et al., 2021). The BER pathway repairs, which is one component of the larger DNA damage repair system and works with other pathways.

The nucleotide excision repair (NER) mechanism is responsible for repairing Cyclobutane pyrimidine dimers (CPD) and pyrimidine-pyrimidone (6-4) photoproducts ((6-4)PP) caused by UV radiation (Vechtomova et al., 2021). There is a group of proteins (XPA-XPG, RPA, CSA, CSB, ERCC6 and RAD23B, etc.) that are involved in NER process (Schärer, 2013). In LC, Lys751Gln (Li et al., 2014) and ERCC2-rs13181 (Li et al., 2019) polymorphism pose significant risk in allele, heterozygote, and dominant comparisons.

Mismatch repair (MMR) corrects base mismatch pairs and small loops. MMR does it with MSH2, MSH6, MLH1, PCNA and RPA proteins by identifying the site of the insertion-deletion loop, removing the lesion site and replacing it with newly synthesized DNA (Li et al., 2016). These repair mechanisms have been associated with different cancers, including LC. MMR deficiency (dMMR) leads to multiple mutations at repetitive DNA sequence stretches known as microsatellite instability (MSI). MSI-high/dMMR varies widely among different cancer types. In LUAD, it accounted for 0.53~1% while 0.6% in LUSC respectively (Zhao et al., 2019)

Up to the present time, Immune Checkpoint Inhibitors (ICIs) had been approved for MSI-high/dMMR in solid tumors. The deficiency of expression of MSH2 or MLH1 in LUAD has been associated with resistance to immunotherapy (Zhao et al., 2019). A study had reported MSI-high/dMMR group demonstrated greater survival and responded to ICIs in NSCLC (Olivares-Hernández et al., 2022). The high tumor mutational burden (TMB) corrected with DDR gene mutations and mutations of DNMT3A and DDR pathway-related genes increased tumor-infiltrating lymphocytes (Chang et al., 2018) and were important predictive markers for overall survival (OS) in NSCLC (H. Zhang et al., 2020).

While BER, NER and MMR fix single-strand break (SSB) repair, DSB repair requires HRR, NHEJ and alternative end joining (alt-EJ) pathways. Homologous recombinant repair (HRR) is a complicated process pathway to repair DSB in S and G2 phases of the cell cycle. HRR faithfully duplicates the genome by providing the critical support for DNA replication and telomere maintenance due to its dependence on the existence of sister chromatids. For instance, in homologous recombinant repair (HRR), RAD51 is the core mechanism of RAD51 filament formation and DNA strand invasion. This repair also plays a role in the repair of DNA interstrand crosslinks (ICLs) with the collaboration of NER. The NHEJ pathway is essential for repairing DSBs throughout the cell cycle, while alt-EJ assists in repairing the residual DSBs when NHEJ and HRR are unavailable. The tumor suppressor gene TP53 plays an important role in cell cycle regulation, and frequent TP53 mutations may cause DNA damage, leading to tumorigenesis and metastasis. The repair of interstrand crosslinking requires Fanconi anemia (FA) active proteins. 49.6% NSCLC patients identified having deleterious DDR mutations and associated with improved clinical outcomes of ICIs (Biagio Ricciuti et al., 2020). The

understanding of these repair mechanisms can help in the development of more effective therapies for LC and other cancers.

Targeting DDR pathways can be exploited as cancer therapy. In the following sections, several DDR inhibitors will be discussed, including the application as monotherapy or in combination with chemotherapy, radiotherapy and immunotherapy and their current landscape of research in NSCLC for clinical use will be demonstrated. Potential predictive biomarkers of response in the pre-clinical or clinical trials will also be discussed. The list of DDR inhibitors is presented in **Figure2.1** and **Table 2.1**.

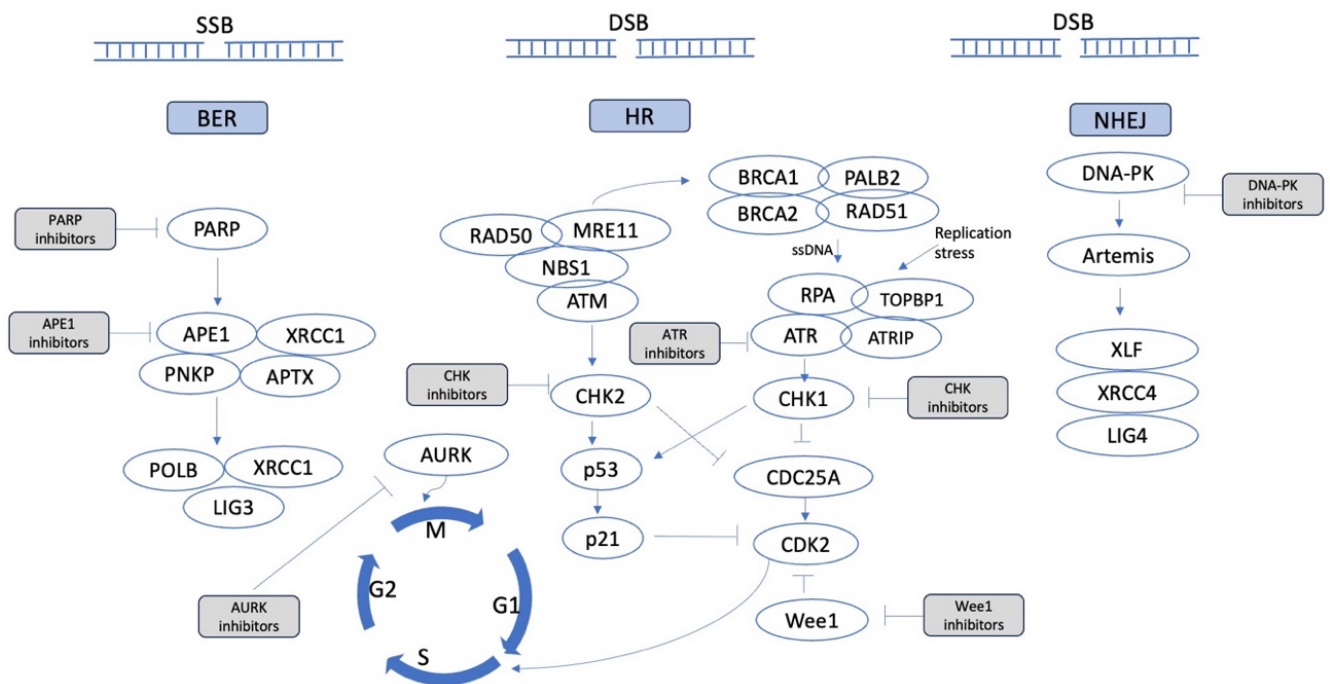


Figure 2.1: Targeting DNA damage and response in NSCLC.

DNA damage types have been reported as single-strand DNA breaks (SSBs) or double-strand DNA breaks (DSBs). While base excision repair (BER) fixes SSBs repair, DSBs repair requires homologous recombination repair (HRR), non-homologous end joining (NHEJ) and alternative end joining (alt-EJ) pathways. Poly(ADP-ribose) polymerase (PARP) enzymes and apurinic/apyrimidinic endonuclease 1 (APE1) are key proteins involved in the base excision repair (BER) pathway of DNA lesions. Ataxia telangiectasia-mutated (ATM) checkpoint kinase 2 (CHK2) and ataxia telangiectasia and Rad3-related (ATR) checkpoint kinase 1 (CHK1) signals are two key pathways in HRR. CHK1 and CHK2 regulate cell cycle control checkpoints. WEE1 is a distinct nuclear kinase that regulates G2/M checkpoint transition in coordination with DDR. Aurora kinases play a regulatory role of G2/M phase, being involved in mitotic chromosomal segregation. The key role of DNA-PK kinase is in NHEJ repair. polynucleotide kinase 3'-phosphatase (PNKP) ;XRCC1, X-ray repair cross complementing 1; POLB, DNA polymerase- β ; LIG3, DNA ligase 3; ssDNA, single-strand DNA; MRN complex, MRE11-RAD50-NBS1; ATRIP, ATR-interacting protein; RPA, replication protein A; TOPBP1, DNA topoisomerase 2-binding protein; XRCC4,X-ray cross complementing protein 4; XLF, XRCC4-like factor; LIG4, DNA ligase 4.

Table 2.1: DDR inhibitors under clinical investigation for NSCLC and other cancers

Type	Inhibitor	selectivity/specificity	Status
PARP inhibitor	Niraparib	PARP1/2 (IC ₅₀ =3.8 nM/2.1 nM)	approved in OC
	Olaparib	PARP1/2 (IC ₅₀ =5 nM/1 nM)	approved in OC, BC, mCRPC and Pancreatic cancer
	Talazoparib	PARP1/2 (K _i : 1.2/0.85 nM)	approved in mCRPC and BC
	Rucaparib	PARP 1, 2 and 3 (IC ₅₀ =0.8, 0.5 and 28 nM)	approved in mCRPC and OC
	Veliparib	PARP1/2 (K _i =5.2 nM/2.9 nM)	phase 3 NSCLC
	RP12146	PARP1/2 (IC ₅₀ =0.62nM/0.44nM)	phase 1 solid tumors
	AZD5305	PARP1/2 (IC ₅₀ =3 nM/1400 nM)	phase 1/2 solid tumors
	IMP4297	PARP1/2 (IC ₅₀ =6.27nM/1.57nM)	phase 1 SCLC
	Parimparib	PARP1/2 (IC ₅₀ =0.83/0.11 nM)	approved in OC in China
ATR inhibitor	Ceralasertib (AZD6738)	ATR (IC ₅₀ =1nM)	phase 3 NSCLC; phase 2 SCLC; phase 2 solid tumors; phase 2 Ovarian Cancer; phase 1 HNSCC;
	M6620 (VX970, Berzosertib, VE822)	ATR (IC ₅₀ =0.2 nM); >100-fold ATR vs ATM/DNA-PK	phase 2 SCLC; phase 1 solid tumors; phase 1 OC;
	BAY1895344 (Elimusertib, NSC#810486)	ATR (IC ₅₀ =7 nM); >60 fold selectivity to ATR compared to PI3K/AKT/mTOR pathway	phase 1 solid tumors;
	Gartisertib (M4344, YX-803)	ATR (IC ₅₀ < 0.2 nM); >100 fold selectivity PI3K	phase 1 solid tumors;
ATR inhibitor	M1774 (Tuvusertib)	ATR (IC ₅₀ = 5 nM)	phase 1/2 SCLC; phase1 solid tumors;

Table 2.1: continued

ATR inhibitor	ATRN-119	ATR (IC ₅₀ =4 nM), ATM (>600-fold), DNA-PK (>2000-fold) and mTOR (>2000-fold).	phase1 solid tumors;
ATR inhibitor	RP-3500 (Camonsertib)	ATR (IC ₅₀ =1nM);30-fold selectivity for ATR over mTOR (IC ₅₀ =120 nM) and >2,000-fold selectivity over ATM, DNA-PK, and PI3K α kinases.	phase1/2 solid tumors;
ATR inhibitor	ART-0380	ATR	phase1/2 solid tumors;
ATR inhibitor	ATG-018	ATR	phase1/2 solid tumors and Hematologic Malignancies
ATR inhibitor	IMP9064	ATR	phase1/2 solid tumors;
AURKA inhibitor	AS703569 (R763)	ATR (IC ₅₀ = 0.5 nM)	phase 1 solid tumors;
AURKA inhibitor	Alisertib (MLN8237)	Aurora A(IC ₅₀ = 1.2 nM), >200-fold higher selectivity for Aurora A than Aurora B	phase 3 Peripheral T-Cell Lymphoma; phase 2 SCLC; phase 2 OC; phase 2 AML; phase 2 DLBCL; phase1/2 NSCLC;
AURKA inhibitor	ENMD2076	Aurora A (IC ₅₀ = 14 nM), B(IC ₅₀ = 290 nM); Flt3 (IC ₅₀ = 3 nM); VEGFR2(IC ₅₀ = 36 nM); KIT (IC ₅₀ = 120 nM); Abl (IC ₅₀ = 295 nM); Abl (T315I)(IC ₅₀ = 81 nm)	phase 2 OC; phase 2 TNBC; phase 1 Hepatocellular Carcinoma; phase 1 Multiple Myeloma;
AURKA inhibitor	MK5108	Aurora A(IC ₅₀ = 0.084 nM), B (IC ₅₀ = 27 nM), C (IC ₅₀ = 19 nM)	phase 1 solid tumors;
AURKA inhibitor	VIC-1911	Aurora A(IC ₅₀ = 0.4 nm)	Phase 1 Hepatocellular Carcinoma Phase 1 NSCLC

Table 2.1: continued

AURKA inhibitor	LY3295668	Aurora A(IC ₅₀ =0.8nm),B (IC ₅₀ = 1038 nm)	Phase ½ NSCLC Phase1 SCLC
	TAS-119	Aurora A(IC ₅₀ =1.0 nm),B (IC ₅₀ = 95 nM)	phase 1 solid tumors;
AURKB inhibitor	Barasertib (AZD1152)	Aurora A(IC ₅₀ = 1 nm), B(IC ₅₀ = 1100 nm)	phase 2/3 AML;
pan-AURK inhibitor	Danuserib (PHA739358)	Aurora A(IC ₅₀ = 13 nm), B(IC ₅₀ = 79 nm), C (IC ₅₀ = 61 nm); Abl (IC ₅₀ = 25 nm); VEGFR3 (IC ₅₀ = 161 nm)	phase 2 Multiple Myeloma; phase 2 Leukemia; phase 2 Prostate Cancer;
	AMG900	Aurora A/B/C (IC ₅₀ =5 nM/4 nM /1 nM); >10-fold selective for Aurora kinases than p38α, Tyk2, JNK2, Met and Tie2.	phase 1 Hematologic Malignancies; phase 1 solid tumors;
	AT9283	Aurora A, B (IC ₅₀ = 3 nm); JAK2 (IC ₅₀ = 1.2 nm); Abl (T315I)(IC ₅₀ = 4 nm); Flt3 (IC ₅₀ = 10 nm)	phase 2 Hematologic Malignancies;
APE1 inhibitor	Methoxyamine (TRC-102)	APE1 (IC ₅₀ =~50 mM)	phase 2 NSCLC; phase1/2 solid tumors;
	Lucanthone	APE1 (IC=5 μM)	phase 2 Glioblastoma;
	E3330 (APX3330)	APE1 (IC=5 μM)	phase 1 solid tumors;
	Gossypol (AT-101)	APE1 (IC ₅₀ =2.5 μM)	phase 2 NSCLC; phase 2 Hematologic Malignancies; phase 2 Glioblastoma; phase 2 Prostate Cancer;
DNA-PK inhibitor	Nedisertib (Peposertib, M3814, MSC2490484A)	DNA-PK (IC ₅₀ < 3 nM)	phase 1/2 Rectal Cancer. phase 1/2 SCLC;
	VX-984 (M9831)	DNA-PK (IC ₅₀ =88±64 nM)	phase 1 solid tumors;

Table 2.1: continued

DNA-PK inhibitor	CC-115	DNA-PK (IC ₅₀ = 0.013 μ M); mTOR (IC ₅₀ =0.021 μ M)	phase 1 solid tumors;
	AZD7648	DNA-PK (IC ₅₀ =0.6 nM), > 100-fold selective against 396 other kinases.	phase 1/2 solid tumors;
	LY3023414 (Samotolisib)	DNA-PK (IC ₅₀ =4.24 nM); mTOR (IC ₅₀ =165 nM); PI3K α , PI3K β , PI3K δ , PI3K γ (IC ₅₀ =6.07 nM, 77.6 nM, 38 nM, 23.8 nM).	phase 2 NSCLC; phase 2 solid tumors; phase 2 Prostate Cancer; phase 2 Endometrial Cancer; phase 2 PDAC; phase 2 TNBC;
	Voxtalisib (XL765, SAR245409)	DNA-PK (IC ₅₀ =150 nM); mTOR (IC ₅₀ =157 nM); PI3K (IC ₅₀ s=39, 113, 9 and 43 nM for p110 α , p110 β , p110 γ and p110 δ)	phase 2 OC; phase 1/2 BC; phase 2 Lymphoma; phase 1 NSCLC; phase 1 Glioblastoma;
	XRD-0394	ATM and DNA-PK	phase 1 solid tumors;
WEE1 inhibitor	ZN-c3 (NCT04158336)	WEE1 (IC ₅₀ =3.9 nM)	phase 2 Pancreatic Cancer; phase 2 OC; phase 2 Uterine Serous Carcinoma; phase 1/2 AML;
	Debio0123 (NCT03968653)	WEE1 (IC ₅₀ =0.8 nM)	phase 1 solid tumors; phase 1 SCLC; phase 1/2 Glioblastoma;
	AZD1775 (Adavosertib, MK1775)	WEE1 (IC ₅₀ =5.2 nM)	phase 2 Pancreatic Cancer; phase 2 OC; phase 2 Uterine Serous Carcinoma; phase 2 TNBC; phase 2 SCLC; phase 2 NSCLC;
	IMP7068	WEE1	phase 1 solid tumors;
	SY-4835	WEE1	phase 1 solid tumors;
CHK1/C HK2 inhibitor	Prexasertib (LY2606368)	CHK1 (IC ₅₀ <1 nM); CHK2 (IC ₅₀ =8 nM); RSK1 (IC ₅₀ =9 nM).	phase 2 OC; phase 2 SCLC;

Table 2.1: continued

CHK1/C HK2 inhibitor	MK8776 (SCH900776)	CHK1 (IC ₅₀ =3 nM), 500-fold selectivity against CHK2	phase 2 Hematologic Malignancies;
	GDC-0575 (ARRY-0575, RG774)	CHK1 (IC ₅₀ =1.2 nM)	phase 1 solid tumors;
	GDC-0425	CHK1 (IC ₅₀ =3 µM)	phase 1 solid tumors;
	PHI-101	CHK2	Phase 1 ovarian cancer
	BBI-355	CHK1	phase 1/2 solid tumors;
	PEP07	CHK1 (IC ₅₀ =1 nM); CHK2 (IC ₅₀ = 1630)	phase 1 solid tumors;
	SRA737	CHK1(IC ₅₀ =1.4 nM),>1,000-fold selectivity against CHK2 and CDK1	phase 1 solid tumors;
	LY2603618 (Rabusertib)	CHK1(IC ₅₀ =7 nM); CHK2 (IC ₅₀ = 12,000 nM)	phase 1 NSCLC;
	LY2880070	CHK1(IC ₅₀ < 0.001 µM)	phase 1 solid tumors;

2.2 Strategies for targeting the DDR in NSCLC

2.2.1 Single Agent Activity and Determinants of Sensitivity

A. PARP inhibitor

The poly (ADP-ribose) polymerase (PARP) is a family of nuclear protein enzymes that are activated upon binding to damage DNA and involved in DDR. Inhibition of PARP impair repair of SSBs that leads to synthetic lethality in homologous recombination deficiency (HRD) (such as deleterious of BRCA1/2) cells which unable accurately repair of DSBs. Several PARP inhibitors have been approved by FDA in different cancers with or

without HRD such as Olaparib, Niraparib, Rucaparib, Talazoparib (Mateo et al., 2019). The development of Veliparib is not very successful, which may as a result of Veliparib is less PARP trapping and is inactive (Murai et al., 2012).

These studies presented that PARP1/2 inhibitor as a monotherapy could represent a novel therapeutic strategy for NSCLC cells with ERCC1-deficient (Xie et al., 2021), or deficiencies in homologous recombination genes (loss of function of BRCA1 and BRCA2, ATM and elevated RAD54L expression) (Deraska et al., 2017), or KMT2C/D mutation (Chang et al., 2021), or ELF3 expression (Y. Wang et al., 2021), or AXL expression (Balaji et al., 2017). PPP2R2A is commonly downregulated in NSCLC cells, and loss of PPP2R2A may serve as a marker to predict sensitivity to PARP inhibitor (Kalev et al., 2012).

In advanced NSCLC, PARP inhibitors have demonstrated certain antitumor activity. However, their effectiveness remains limited. For instance, two trials tested Olaparib maintenance in NSCLC patients with chemosensitivity; compared with placebo, a trend toward longer progression-free survival (PFS: 16.6m vs 12.0m) and overall survival (OS: 59.4m vs 31.3 m) (Fennell et al., 2020); compared with standard of care (SoC), no significant PFS (2.7m vs 2.7 m) and OS (14.3m vs 14.1m) differences (Benjamin Besse et al., 2021). In the SAFIR02-lung trial, 2.1% (8/379) patients with pathogenic BRCA1/2 mutation indicated limited sensitivity to Olaparib (Barlesi et al., 2022). Antitumor activity of Niraparib single-agent was noted in NSCLC in the phase I dose -escalation trial; tumor shrinkage occurred in all 2 enrolled NSCLC patients, one BRCA2 mutation carrier had stable disease (SD) for 175 days, the other previous heavily treated patient maintained SD for 316 days (Sandhu et al., 2013). Talazoparib failed to show sufficient level of efficacy with 4% overall response (2/24 ORR) and 54% disease control rate (13/24 DCR) in LUSC with HRR deficiency (alteration

in ATM, ATR, BRCA1, BRCA2, or PALB2) in a phase 2 Lung-MAP subgroup S1400G (Owonikoko et al., 2021). In another subgroup S1900A of Lung-MAP, with Rucaparib, the study chose stage IV NSCLC patients with high genomic loss of heterozygosity (LOH) and/or BRCA1/2 mutated and progression on or after platinum base chemotherapy and/or programmed death (ligand) 1 (PD1/PDL1) antibody; the study showed activity with 7% ORR (4 patients: 3 BRCA1/2-mutated and 1 LOH-high) and 7.8 months OS (Riess et al., 2021).

In these EGFR-mutated lung cancer patients, low BRCA1 mRNA levels were associated with longer PFS in erlotinib-treated patients and acquired resistance of EGFR-TKI treatment could promote the sensitivity of PARP inhibitors (Marcar et al., 2019). A case report showed that Olaparib with Dacomitinib could prolong the survival of NSCLC patients with leptomeningeal metastasis (Zhang et al., 2022). When comparing Gefitinib plus Olaparib with Gefitinib, the combination did not provide a significant benefit (10.9m vs 12.8m) in a phase II trial (Garcia-Campelo et al., 2020); high BRCA1 mRNA expression and low mRNA expression of CtIP might impact the result (Karachaliou et al., 2021). The phase I study of Niraparib in combination with Osimertinib in EGFR-mutated advanced lung cancer is underway (NCT03891615) (**Table 2.2**).

AZD5305 is a second-generation, highly selective PARP1 inhibitor. It is currently in phase I/II trial as monotherapy and in combination with other treatments in solid tumors which include NSCLC (**Table 2.2**).

Collectively, these studies suggest that while PARP inhibitors show promise in NSCLC subpopulations with DDR defects, clinical efficacy remains modest outside BRCA-mutated cohorts.

B. ATR Inhibitors

ATR (Ataxia telangiectasia and Rad3 related protein) and ATM (Ataxia telangiectasia mutated protein) are the members of the phosphatidylinositol 3-kinase-related kinase (PIKK) family of serine/ threonine protein kinases. ATR is one of the two apical regulators of the DDR pathway that activate cellular response, including cell cycle checkpoints and DNA repair. ATM shares similar function and structure with ATR.

ATR and ATM are prime targets of DDR inhibitors. ATR inhibitors have demonstrated therapeutic potential in cancer treatment. Several compounds targeting ATR are moving to the clinical trial stage. M6620 (VX970/Berzosertib/VE822) was well tolerated, with preliminary antitumor responses observed in a patient with metastatic colorectal cancer (mCRC) harbouring ATM loss and ARID1A mutation reached complete response (CR) and 29 months PFS (Yap et al., 2020). Ceralasertib (AZD6738) monotherapy was well tolerated and resulted in confirmed PR and a high proportion of prolonged SD in advanced tumors of PATRIOT trial (Dillon et al., 2019). BAY1895344 (Elimusertib, NSC#810486) was tolerable and had antitumor activity in patients with various advanced solid tumors with certain DDR deficiency, including ATM loss (Yap, Tan, et al., 2021). M4344 (YX-803) is currently in a Phase I study single-agent or in combination with carboplatin to determine the safety and maximum tolerated dose (NCT02278250). The trial of M1774 as monotherapy and in combination with Niraparib is recruiting the patients with metastatic or locally advanced unresectable solid tumors including a group to explore the biomarker of loss-of-function mutations in the genes for ARID1A, ATM, or ATRX and/or DAXX (NCT04170153). There are no ongoing trials in NSCLC with ATR inhibitor monotherapy, but in combination with other anti-cancer treatments, M1774, M6620 and AZD6738 are currently on the development of phase II/III studies which are listed in **Table 2.2**.

Although ATR inhibitor have shown tolerability and efficacy in DDR-deficient tumors, their utility in NSCLC remains under investigation, particularly in combination settings.

C. Aurora kinase (AURK) inhibitor

Aurora kinase (AURK) belongs to a family (known as AURKA, AURKB and AURKC) of highly conserved serine and threonine kinases that function as key regulators of the mitosis process. AURKA and AURKB constitute potential targets in NSCLC. Several agents inhibited to AURK have been developed, AURKA inhibitors (TC-A2317, Alisertib/MLN8237, ENMD2076, MK5108, VIC1911, LY3295668, TAS-119), AURKB inhibitors (Quercetin, GSK 1070916, Barasertib/AZD1152) and pan-AURK inhibitors (Danusertib/PHA739358, AMG900, AT9283).

MK-5108 had proven anticancer activity in NSCLC in vitro as monotherapy or in combination with chemotherapies (Chinn et al., 2014). AT9283 is a multi-targeted kinase inhibitor of tyrosine and serine/threonine kinases including Aurora A and B, JAK2, and Abl. AT9283 was well tolerated and demonstrated antiproliferative and pro-apoptotic activity and SD (≥ 6 months) in esophageal cancer (n=1), NSCLC (n = 2) and colorectal cancer (CRC, n=1) in a phase I dose escalation study (Arkenau et al., 2012).

Danusertib (PHA-739358) is a small-molecule pan-aurora kinase inhibitor. A trial reported that Danusertib single-agent reached marginal anti-tumoral activity, the progression free rate at 4 months (PFR-4) was 10.4% (5/48) in NSCLC (all histotypes), 16.1% (5/31) in LUSC and 0% (0/14) in SCLC (Schöffski et al., 2015). Another phase II study evaluated the efficacy of Danusertib alone in advanced treated NSCLC in a Simon two-stage design; 3/19 patients were PFR-4 in stage I, the antitumor activity was superior in LUSC compared to

nsqNSCLC with a PFS of 6.4 months versus 2.2 months and an OS of 10.6 months versus 7.6 months; 5/31 evaluable squamous patients were PFR-4 in stage II (Gauler et al., 2013).

Previous study (Tanaka et al., 2021) discovered AURKB inhibitors as potent enhancers of Osimertinib-induced apoptosis and combined EGFR-TKI and AURKB inhibitor could overcome EGFR-TKI resistance. Alisertib (MLN8237) treatment restored the susceptibility of resistant cells to EGFR-TKIs and partially reversed the epithelial-mesenchymal transition (EMT) process (C. Y. Wang et al., 2021). The phase II trial tested single agent Alisertib in patients had undergone two or fewer previous cytotoxic regimens; it was noted that the objective response in ten of 48 participants with SCLC and one of 23 patients with NSCLC (Melichar et al., 2015). In patients with recurrent or metastatic EGFR wild-type NSCLC, the combination of Erlotinib and Alisertib was tolerable and effective (with one patient was PR >10 cycles and 5 patients were SD) in a phase I/II study (Godwin et al., 2016). The combination of Alisertib and Osimertinib was an acceptable safety profile and established 10% (1/10) ORR in patients with advanced EGFR mutated LUAD who experienced progression on Osimertinib monotherapy (Blakely et al., 2021). In a phase 1b study of Osimertinib plus Alisertib or Sapanisertib for Osimertinib-resistant EGFRm NSCLC, Osimertinib plus Alisertib (n = 20) showed median PFS was 1.9 months, ORR (5%) and DCR (40%) (Elamin et al., 2022). There are 2 ongoing clinical trials using AURKA inhibitors VIC-1911 or LY3295668 in combination with Osimertinib in EGFR mutant NSCLC (NCT05489731) (NCT05017025).

AURKA amplification is reported in NSCLC, and AURKA signaling may mediate adaptive resistance to KRAS inhibition. A study to research VIC-1911 combine with Sotorasib for treatment of KRAS mutant NSCLC is ongoing (NCT05374538).

D. APE1 inhibitor

Human apurinic/apyrimidinic endonuclease 1 (APE1) is an essential BER protein that is known to be processing of potentially cytotoxic abasic DNA damage site. The overexpression of APE1 was associated with DNA repair capacity and poor survival in solid tumors (Yuan et al., 2017). APE1 could serve as a potent target of antitumor drugs and several APE1 inhibitors have been developed. There are three types of APE1 inhibitors, including APE1 nuclease activity inhibitor (such as, Methoxyamine/TRC-102, lucanthone), APE1 redox activity inhibitor (E3330/APX3330) and inhibitors of the APE1/nucleophosmin (Gossypol/AT-101).

APE1 inhibitors induced DNA damage, apoptosis, pyroptosis, and necroptosis in NSCLC cell line A549 and NCI-H460 and impeded cancer progression in NCI-H460 mouse model (Long et al., 2021). E3330 (APX3330) is a highly selective inhibitor of Apurinic/apyrimidinic endonuclease 1/redox factor-1 (APE1/Ref-1). The anti-tumor effect of E3330 had been demonstrated in preclinical model in NSCLC (Manguinhas et al., 2020). CRT0044876, a selective APE1 endonuclease inhibitor, inhibited the AP endonuclease, 3'-phosphodiesterase, and 3'-phosphatase activities of APE1. CRT0044876 showed no cytotoxic effect in either NSCLC cell line A549 or NCI-H460 (Long et al., 2021).

Overexpression APE1 promoted chemotherapy and EGFR-TKI (Yang et al., 2018) resistance in NSCLC. Pre-clinical models suggested that AT-101 might serve a promise drug candidate for overcoming EGFR-TKIs resistance in H1975 cells harboring EGFR^{L858R/T790M} (Xu et al., 2019). A phase II trial of Erlotinib and AT-101 in advanced EGFR-mutated NSCLC patients found 1PR (partial response), 1 MR (minor response) and 3 SD in the enrolled 6 patients (NCT00988169).

APE1 is a clinically relevant target for NSCLC—especially in overcoming therapy resistance – but advancing APE1 inhibitors to the clinic requires focusing on effective inhibitor classes, scaling clinical trials, and using biomarkers to ensure these therapies reach patients most likely to benefit.

E. DNA-PKcs inhibitor

DNA-PK is a member of phosphatidylinositol 3-kinases-related kinases (PIKK) family, which consists of a catalytic subunit (DNA/PKcs) and a regulatory heterodimer Ku (Ku70/Ku80). DNA-PK plays a key role in repair of DSBs via NHEJ and it also involves in many other cellular processes. Reduced DNA-PK repair was associated with the risk of lung cancer.

AZD7648, a highly specific and potent DNA-PK inhibitor, had anti-tumor activity in A549 NSCLC cell lines and xenograft models derived from lung cancers (Cadogan et al., 2019). The best overall response of Nedisertib (Peposertib, M3814, MSC2490484A) was SD in a phase I trial including 2 NSCLC patients (I. Hwang et al., 2020). XRD-0394 is a dual kinase inhibitor of both ataxia-telangiectasia mutated (ATM) and DNA-dependent protein kinase (DNA-PK). CC-115, inhibition of mTOR kinase and DNA-PK, was tested *in vitro* across a panel of 123 cancer cell lines including 39 lung cancer cell lines and it potently inhibits proliferation and induces apoptosis in many cancer cell lines (Tsuji et al., 2017). In phase I trial, CC-115 showed clinical activity in endometrial carcinoma (CR, n=1, >4 years), head and neck squamous cell carcinoma (HNSCC), Ewing sarcoma, glioblastoma multiforme, CRPC, and Chronic lymphocytic leukemia (CLL) (PR, n=2 and SD, n=4), but it was found PD in NSCLC (n=1) (Munster et al., 2019).

In addition, as PIKKs have similar sequence to phosphatidylinositol-3 kinases (PI3Ks), the development of these inhibitors can base on small molecule inhibitors of PI3K. LY3023414 (Samotolisib), a dual PI3K/mTOR inhibitor, displayed PR of a patient with endometrial cancer harboring PIK3R1 and PTEN truncating mutations and 13 (28%) additional patients had a decrease in target lesions by up to 30%, but the all 3 patients of NSCLC were no response in the first-in human phase I trial (Bendell et al., 2018). XL765 (Voxtalisisb, SAR245409) is a new chemical entity that inhibits the kinases PI3K and mTOR. No partial response reported with XL765 and erlotinib in NSCLC patients treated with EGFR inhibitor previously in phase I trial (Jänne et al., 2014).

While DNA-PK is biologically relevant to NSCLC and shows preclinical potential, its inhibitors have yet to deliver meaningful clinical benefit in NSCLC. The future efforts should focus on combination strategies and larger, NSCLC-specific trials to unlock this target's value.

F. WEE1 inhibitor

WEE1 inhibitor, is a selective inhibitor of the WEE1 kinase, a key regulator of the G2/M and S phase cell-cycle checkpoints. AZD1775 (Adavosertib) is a highly selective, small molecule inhibitor of Wee1 kinase which allows cells with a deregulated G1 checkpoint to progress. AZD1775 single agent demonstrated efficacy and well well-tolerated in mouse xenograft model in the TP53-mutated subgroup of KRAS-mutated NSCLC (Ku et al., 2017). There are 61 clinical trials registered in CTG (<https://clinicaltrials.gov>) about AZD1775 from 2008. AZD1775 showed its antitumor activities especially in these cancers harbor DNA damage, such as mCRC with RAS and TP53 mutated (Seligmann et al., 2021). However, in a biomarker-driven phase 2 umbrella trial for patients with recurrent SCLC, no

patient had a partial response for ADZ1775 alone in 47 patients with different biomarkers in 4 groups (Park et al., 2020). Studies have not identified an effective strategy for launching this product, whether by identifying predictive biomarkers for response or exploring a combination with other anti-cancer agents.

Another four compounds, ZN-c3 (NCT04158336), Debio0123 (NCT03968653), IMP7068 (NCT04768868), and SY-4835 (NCT05291182), are currently in a Phase I trial in solid tumors, including NSCLC (**Table 2.2**).

WEE1 inhibitors have preclinical potential in genetically defined NSCLC subsets (for example, TP53/KRAS-mutated), but unlocking their clinical value requires validating predictive biomarkers and testing combination regimens.

G. CHK1 and CHK2 inhibitor

The cell cycles regulatory kinase, CHK1 and CHK2, coordinate with DDR pathways and immediate targets of the kinases ATM/ATR. CHK1/2 inhibitors have development for a long time, numerous compounds step towards slowly because of the complexity of optimizing dose and schedule selection and major questions mark over the efficacy. All clinical trials of the dual CHK1/CHK2 inhibitor XL-844 (EXEL-9844) were terminated in 2008. PF0047736 was terminated to develop in 2012 in advanced cancers. SNS-032 (BMS-387032), a potent inhibitor of cyclin-dependent kinases 2, 7 and 9, demonstrated limited clinical activity in solid tumors. Prexasertib (LY2606368) demonstrated activity in different cancers, including two (4.4%) patients with squamous cell cancers (SCCs) (Hong et al., 2016), four (20%) patients with SCCs (Hong et al., 2018), 3 (5.2%) patients with SCLC (Byers et al., 2021) and one (11.1%) BRCA wild type TNBC (Gatti-Mays et al., 2020), however, one NSCLC had no response (Hong et al., 2016).

Researchers consider how to combine CHK1 inhibitors with other compounds or to find proper biomarkers to get more encouraging data. In pre-clinical model, the low levels of POLA1, POLE, and POLE2 protein expression in NSCLC and CRC cells correlated with CHK1 inhibitor sensitivity (Rogers et al., 2020). UCN-01 (7-hydroxystaurosporine), the first CHK1/CHK2 inhibitor, contributed the antitumor activity in vitro and in vivo using A549 human lung adenocarcinoma cell line (Kawakami et al., 1996) and enhanced the effectiveness of radiation in cells with diminished TP53 activity (Mack et al., 2004; Xiao et al., 2002). CHK1 expression in lung adenocarcinomas correlated with poor tumor differentiation and worse patient outcome, and it could be a predictive marker for CHK1 inhibitor (MK-8776) sensitivity in vitro study (Grabauskiene et al., 2013). Two patients (6.7%) showed partial response (melanoma and cholangiocarcinoma) in MK8776 monotherapy or in combination with gemcitabine phase I trial, however, one lung adenocarcinoma only have 1.43 months PFS (Daud et al., 2015).

While CHK1/CHK2 inhibitors have shown promise in select cancers, their clinical value in NSCLC remains unproven. Advancing these agents will depend on pairing them with DNA damaging therapies and using validated biomarkers to select patients most likely to benefit.

2.2.2 Combinations with Chemotherapy Agents

As cytotoxic drug, chemotherapy distort the chemical structure of DNA leading to inhibition of normal DNA replication. There is a strong rationale for combining DDR inhibitors with chemotherapy to enhance the DNA-damaging effect in cancer cells.

A. PARP inhibitor with chemotherapy

The combination of DDR inhibitors (such as PARP inhibitor) in selected HRD tumors cause synthetic lethality, lead to genomic instability and cell death (Lord & Ashworth, 2017). Mechanistic studies indicated that PARP inhibitor plus cisplatin could lead to sustained DSBs, prolonged G2/M cell cycle arrest and more pronounced apoptosis preferentially in NSCLC cells with low ERCC1 expression (Cheng et al., 2013), or PTEN deficient (Minami et al., 2013).

Pre-clinical studies demonstrated antitumor efficacy of PARP inhibitor adding in different chemotherapy agents in NSCLC (Stolzenburg et al., 2022). In combination of Veliparib and carboplatin/paclitaxel (CP) confirmed safety and preliminary efficacy with 55% (6/11) ORR in a phase I Japanese NSCLC cohort (Mizugaki et al., 2015). In the following phase II trial of untreated advanced NSCLC, the veliparib-CP group showed favorable trend in ORR, PFS and OS versus CP alone (PFS: 5.8 vs 4.2 months, HR=0.72, p=0.17; OS: 11.7 vs 9.1 months, HR=0.80, p=0.27) in all evaluable patients; patients with squamous histology had better outcomes (PFS: HR=0.54, p=0.098; OS: HR=0.73, p=0.24) (Ramalingam et al., 2021). However, no therapeutic benefit of adding veliparib to first line chemotherapy in phase III trial, but risk of death was decreased by 34% in the LP521 population (Ramalingam et al., 2021), and history of recent smoking was most predictive factor for veliparib-CP (Reck et al., 2017). In another phase III trial, there was no significant improvement of OS with veliparib plus chemotherapy in patients with non-squamous NSCLC (nsqNSCLC), but improved OS in the LP52+ subgroup (Govindan et al., 2022).

The failure of Veliparib's phase III trials to replicate early-phase promising highlights the critical importance of biomarker-driven patient selection in developing PARP inhibitor combinations for NSCLC. Without validated biomarkers to select patients, broad

enrolment dilutes efficacy signals. Additionally, optimizing toxicity management treatment intensity may help better predict phase III success for future combinations treatment strategies in NSCLC.

B. ATR inhibitor with chemotherapy

Loss of ATM expression by immunohistochemistry with ab32420 antibody was found in 41%(61/147) cases in lung adenocarcinoma cells and may serve as a predictive biomarker for ATR inhibitor-cisplatin combinations (Villaruz et al., 2016). A phase I study, with AZD6738- carboplatin, observed 2 PRs with low ATM or SLFN11 protein expression and 8/34 (53%) SD patients; unconfirmed PR was found in a local advanced lung adenocarcinoma with four cycles of prior treatment (Yap, Krebs, et al., 2021).

Four (8.3%) patients (non-previously received gemcitabine) achieved PR with Berzosertib and gemcitabine including a patient present with lung adenocarcinoma with no response of prior multiple chemotherapies (Middleton et al., 2021). In the following phase Ib trial, Berzosertib with gemcitabine in advanced and pre-treated NSCLC, 4 patients reached PR(4/38, ORR10.5%) and 18 patients had SD; in the exploratory cohort, ORR was 30% (3/10) in high loss of heterozygosity (LOH) and 11% in low LOH, 33% (2/6) in high TMB, 12.5% (2/16) in intermediated TMB and 0% (0/3) in low TMB (Plummer et al., 2022).

Testing the addition of BAY1895344 to chemotherapy for advance solid tumors is ongoing (NCT04491942), which is listed in **Table 2.2**.

C. APE1 inhibitor with chemotherapy

The phase I study published that 15 out of 25 patients with TRC-102 and pemetrexed evaluate SD or better, including LUSC (n=3) and nsqNSCLC (n=1) (Gordon et al., 2013).

Two clinical trials indicated that TRC-102 with temozolomide had anti-tumor activities in advanced solid tumor, with PR in a pancreatic neuroendocrine tumor (PNET) and prolonged SD in a NSCLC patient (5.5 months) (Eads et al., 2021), and PR (n=4, 1 NSCLC, 2 OCs, 1 CRC) (Coyne et al., 2020).

D. WEE1 inhibitor with chemotherapy

WEE1 inhibition with TP53 mutation can disrupt both G1/S and G2/M, resulting in synthetic lethality and enhancing chemotherapy cytotoxicity. A phase II study of AZD1775 and carboplatin/pemetrexed in 1st line metastatic nsqNSCLC presented 4 (29%) patients reached PR (1 patient with AZD1775 alone for one year) and one patient had TP53 mutation. Another phase II study of AZD1775 plus docetaxel in recurrent NSCLC showed 3 (9%) patients evaluated PR (Spigel et al., 2016).

Some clinical trials use WEE1 inhibitor, but its clinical development hampered higher grade 3 toxicities when added to standard treatments and no effective predictive biomarkers. There are ongoing trials conducting WEE1 inhibitors with other agents, such as chemotherapy, radiation, PARP/ATR inhibitor (NCT02513563, NCT0333084, NCT02511795), anti-PD1/L1 inhibitor, which are listed in **Table 2.2**.

Overcoming these challenges of toxicity requires a multifaceted approach: optimizing dose/schedule to protect normal cells, using tumor-targeted delivery to reduce off-tumor exposure, stratifying patients with toxicity biomarkers, enhancing supportive care, and combining with normal cell-protective agents. Pairing these strategies with validated predictive biomarkers will be critical to unlocking the clinical potential of WEE1 inhibitor-chemotherapy combinations in NSCLC and other solid tumors.

E. CHK1/2 inhibitor with chemotherapy

Cancer Cells may activate compensatory pathways, limiting the efficacy of CHK1/2 inhibitors as monotherapy and suggesting the need for combination strategies.

LY2603618 (Rabusertib), a small molecule selective inhibitor CHK1 inhibitor, may enhance the effects of antimetabolites. LY2603618 with pemetrexed- cisplatin demonstrated that median PFS was significantly longer (4.7 vs 1.5 months, $P=0.022$) in phase II study in patient with advanced cancers (Wehler et al., 2017). With treatment GDC-0575 (ARRY-0575, RG774) and gemcitabine, four patients achieved confirmed partial responses with GDC-0575, including one NSCLC (593+ days on study), two sarcomas and TNBC with TP53 mutation (Italiano et al., 2018). To improve CHK1/2 inhibitor efficacy in NSCLC, biomarker-guided patient selection and rational combinations are critical.

2.2.3 Combinations with Radiotherapy and/or Chemo-Radiotherapy (CRT)

DDR inhibitors enhance radiosensitization by disrupting the repair of ionizing radiation induced double strand breaks and/or abrogating cell cycle checkpoints that enable repair. DDR inhibitors force cancer cells to accumulate irreparable DNA damage, leading to increased cell death and improved radiation efficacy. Radiotherapy induces targeted DNA damage, providing a rationale for combination it with DDR inhibitors and chemotherapy. This Strategy is currently under investigation in several ongoing clinical studies. Most advanced NSCLC patients may have brain metastasis and radiation therapy has been an available tool in that kind of patients, which causes the strategy about the combination of DDR inhibitors and whole brain radiation therapy (WBRT).

The result of phase I study was encouraging safety and preliminary efficacy of veliparib plus WBRT in NSCLC with brain metastases (Mehta et al., 2015), regrettably, no statistically significant differences in OS, intracranial response rate, and time to progression between the treatment arms were observed in the phase II randomization trial (Fan et al., 2018). Inhibition of AZD6738 could improve radiotherapy in preclinical models of NSCLC (Dunne et al., 2017). A parallel dose-escalation study of AZD6738 combined with palliative radiotherapy in solid tumors is underway (NCT02223923). These data will provide the basis to leverage the potential radio-sensitization properties of a DDR inhibitor in combination with radiation in a variety of therapeutic settings.

Two phase I studies evaluate PRAP inhibitors plus CRT in patients with stage III NSCLC; Veliparib-CRT demonstrated acceptable safety and antitumor activity with an PFS of 19.6 months (Kozono et al., 2021). A dose-finding study followed by a phase II randomization trial of CRT with or without veliparib (SWOG 1206); No significant difference in PFS between the two arms, while the OS was improved at 1 year 89% and 54%, respectively (Argiris et al., 2021). The combination strategy was proved well tolerated and encouraging response with 20% (3/15) CR, 80% (12/15) PR and 49% of 2-year PFS rate in stage III nsqNSCLC (Biswas et al., 2020) in the following phase I trial.

2.2.4 Combinations with Other Molecular Targeted Agents

A. DDR inhibitor-DDR inhibitor combination

Targeting enzymes in the same pathway also appears to have a synthetically lethal effect. Combining different DDR inhibitors may induce synthetic lethality and overcome resistance to monotherapy.

As these mutations (such as BRCA1, BRCA2, ATM) alter the HRR pathway, there is increased reliance on other DDR pathways. ATR inhibitors overcame the bypass of BRCA1/2 in fork protection and PARP inhibitor resistance of BRCA-deficient cancers cells (Kim et al., 2020). Studies disclosed that combination of PARP inhibitor and ATR inhibitor induced death for ATM-deficiency cells of lung adenocarcinoma (Jette et al., 2019). Tumor reduction was observed in breast, prostate, pancreatic and ampullary cancers in AZD6738-olaparib group in a phase I trial (Krebs et al., 2018). The signal of activity was seen with Ceralasertib plus Olaparib in recurrent platinum-resistant OC with BRCA1 mutation (Shah et al., 2021). In the pre-clinical models, KRAS-mutated NSCLC caused the increased levels of DNA damage and replication stress, which provided that inhibition of DDR was a promising strategy for Olaparib plus AZD1775 (Parsels et al., 2018). AZD7648 potentiated the activity of Olaparib in xenograft and PDX models in NSCLC (Fok et al., 2019), and this finding suggested a path toward clinical trial.

Some studies demonstrated replication fork arrest, ssDNA accumulation, replication collapse and synthetic lethal interaction between ATR inhibitor and other target inhibitors. The potential benefit of combination ATR inhibitor (VE-821) and CHK1 inhibitor (AZD7762) was seen in H460 lung tumor xenografts (Sanjiv et al., 2016). PPP2R2A deficiency provided a biomarker to treat NSCLC with ATR and CHK1 inhibitor in pre-clinical study (Qiu et al., 2020). The study confirmed the dependency on p53 mutation and ATM function for sensitivity to ATR inhibition by treating p53-mutated NSCLC cells with ATR inhibitor (VE-821) and ATM inhibitor (KU55933) (Weber et al., 2013). The effect of WEE1 inhibitor and ATR inhibitor was observed in NSCLC cell line (Rødland et al., 2021).

B. Combination of other target agents

Some actionable oncoproteins can directly or indirectly regulate DDR and cell cycle checkpoint pathways, raising possibility of combination strategy with DDR inhibitors and other target agents.

PARP inhibitors have a strong synergistic interaction with type I PRMT inhibition. PRIMA-1Met (APR-246) strongly synergized with Olaparib in NSCLC cell lines (Deben et al., 2016) and MTAP-negative NSCLC and certain cancer cells were resistant to PARP inhibitors (Dominici et al., 2021). DNA methyltransferase inhibitors (DNMTi) created a BRCAness phenotype through downregulating expression of HRR and NHEJ genes, led to combinatorial PARPi and DNMTi therapy robustly sensitize NSCLC cells to ionizing radiation in vitro and in vivo (Abbotts et al., 2019). Bloom syndrome protein (BLM) helicase inhibitor (ML216) with PARP inhibitor improved the radiosensitivity of Olaparib resistant NSCLC cell (Kong et al., 2021).

A phase 1b study, the Notch inhibitor Crenigacestat (LY3039478) in combination with LY3023414 in patients with advanced solid tumors, demonstrated poorly tolerated and response (0% ORR and 18.8% DCR) (Azaro et al., 2021). In metastatic LUSC, LY3023414 vs Necitumumab vs LY3023414 plus Necitumumab exhibited significant benefit with event-free survival (EFS: 14.2 and 32.4 vs 38.9 days) (Melchior et al., 2018). LY3214996 (ERK1/2 inhibitor) plus LY3023414 and additive Abemaciclib (CDK4/6 inhibitor) resulted in synergistic inhibition of tumor growth in PDX models of RAS-mutant lung cancer (Köhler et al., 2021).

However, these combination of doublet inhibitors are still in early exploratory phase. These approaches are supported by promising pre-clinical biology but are constrained by

incomplete mechanistic understanding, unproven human safety profiles, and limited clinical data.

2.2.5 Combinations with immunotherapy

Immune checkpoint inhibitors (ICIs) which target PD-1 and PD-L1 can enable the immune system to recognize and target cancer cells. Over recent decade, ICIs with single agent or combination of other therapy has dramatically expanded for the treatment of lung cancer from neoadjuvant to last line. However, ICIs vary in their activity across different cancer types. Several biomarkers are associated with increase ICI response are PD-L1 expression, tumor mutation burden (TMB), microsatellite instability (MSI) or MMR-deficient. It is also explored that alteration of DDR genes related to high TMB and response of ICIs improvement (Topalian et al., 2016). Unlike targeting genes mutation in cancer cells, the immune environment is complex, which lead future research shift to immune response effectiveness of combination therapy rather than identification biomarkers (Butterfield & Najjar, 2024; Yang et al., 2024). Genomic instability in cancer alters the tumor microenvironment, promoting neoantigen generation and potentially increasing response to ICIs (Mardis, 2019) and suggesting an effective therapeutic strategy to combine DDR inhibitors and immunotherapy.

Pre-clinical trial demonstrated PARP inhibitor potentiated IFN- γ -induced PD-L1 expression in NSCLC cell lines, enhanced in ERCC1-deficient contexts, promoted cellular immune response (Chabanon et al., 2019). Veliparib combined with nivolumab and platinum doublet CT was tolerated and had promising antitumor activity (confirmed objective response rate was 40%, and best overall response was 64%) in patients with advanced NSCLC in phase I dose escalation study (Clarke et al., 2021). Olaparib-Durvalumab

indicated an acceptable toxicity and response in breast cancers (Domchek et al., 2020) and mCRPC in the 2 phase II trials (Karzai et al., 2018). Olaparib plus PD1/PDL1 inhibitor demonstrated response in two NSCLC patients with germline BRCA2 S497* (Waddington et al., 2021) or BRCA2 G25085 (Chen et al., 2023). In the phase 2 JASPER trial, Niraparib-Pembrolizumab as first line therapy showed clinical activity; 56.3% (9/16) ORR and 8.4m PFS was found in cohort 1 (TPS $\geq$ 50%) ; 20% (4/20) ORR and 4.2m PFS was discovered in cohort 2 (TPS 1%–49%) in advanced NSCLC (Ramalingam et al., 2022).

As PARP inhibitor plus immunotherapy shows promising therapeutic strategy in NSCLC, ongoing investigations are underway to evaluate the efficacy and safety. A Phase I/II trial test Rucaparib-Pembrolizumab as maintenance therapy in stage IV nsqNSCLC after treatment of carboplatin, pemetrexed, and pembrolizumab (NCT03559049). A Phase III trial treat Pembrolizumab with concurrent chemoradiation therapy followed by pembrolizumab with or without Olaparib in stage III NSCLC (NCT04380636) and a phase II trial compare standard of care versus Olaparib-Durvalumab in relapsed stage III NSCLC pretreated with chemoradiotherapy and Durvalumab (NCT05568212). The phase III ZEAL-1L study is to compare the efficacy and safety of Niraparib-Pembrolizumab as maintenance therapy versus placebo-pembrolizumab in patients who had stable disease or response to pembrolizumab plus platinum-based first-line induction chemotherapy for advanced NSCLC without known driver mutation (NCT04475939). A Phase II Study take Talazoparib-Avelumab in stage IV or recurrent nsqNSCLC with pathogenic STK11 mutation (LUNG-MAP Sub-Study) (NCT04173507). Please refer **Table 2.2** for ongoing trial in lung cancer.

Besides PARP inhibitors, the ATR inhibitors in combination with ICIs have been in clinical development. In a phase 2 trial, AZD6738-Durvalumab had promising antitumor activity among patients with metastatic melanoma who had failed ICIs therapy (Kim et al.,

2022). Beyond melanoma, AZD6738-Durvalumab in advanced NSCLC of D5330C00004 trial also published encouraging data; 1 CR and 3 PRs (2 confirmed and 1 unconfirmed) out of 21 patients were found in advanced NSCLC (n=3) and HNSCC (n=1) irrespective of PD-L1 expression (Krebs et al., 2018). In HUDSON umbrella trial, AZD6738-Durvalumab provided effective activity compared with Durvalumab alone in ATM mutation tumors (n=18) with median ORR at 13.3% and a median PFS of 7.43 months and 100% of patients were followed through after 6 months (B. Besse et al., 2021).

Based on the previously studies result, more trials start to investigate the efficacy and safety of the combination of ATR inhibitors and immunotherapy (**Table 2.2**); a phase III study to evaluate AZD6738-Durvalumab versus Docetaxel in advanced NSCLC progressed prior treatment (NCT05450692); AZD6738-Durvalumab for advanced NSCLC patients with ICI resistance (NCT03833440); M1774 in combination with Cemiplimab in nsqNSCLC (NCT05882734); testing the addition of Berzosertib to Carboplatin and Gemcitabine and to Pembrolizumab for advanced LUSC (NCT04216316).

It is also interesting to combine WEE1 inhibitor with immunotherapy. Antitumor activity was observed with a DCR for the overall cohort of 36% in a phase I study to investigate preliminary activity of AZD1775-durvalumab in patients with advanced solid tumors (Patel et al., 2019).

A phase II trial of TRC102 in combination of pemetrexed, cisplatin and radiation therapy followed by Durvalumab in patients with stage III nsqNSCLC is underway (NCT05198830).

Table 2.2: Ongoing clinical trials of DDR inhibitor combination therapy in NSCLC

Drug	Indication	Title of the study	Combination	Phase	Biomarker	Identifier
AZD1775 (Adavosertib, MK1775)	sqNSCLC	AZD1775 Plus Carboplatin-Paclitaxel in Squamous Cell Lung Cancer	chemotherapy	2	NA	NCT02513563
Methoxyamine (TRC-102)	NSCLC	Methoxyamine Hydrochloride, Pemetrexed Disodium, Cisplatin, and Radiation Therapy in Treating Patients With Stage IIIA-IV Non-small Cell Lung Cancer	chemoradiotherapy	1	NA	NCT02535325
Ceralasertib (AZD6738)	NSCLC	National Lung Matrix Trial: Multi-drug Phase II Trial in Non-Small Cell Lung Cancer	Durvalumab	2	NA	NCT02664935
Niraparib	solid tumor; NSCLC	Study of Niraparib, TSR-022, Bevacizumab, and Platinum-Based Doublet Chemotherapy in Combination With TSR-042	TSR-042	1	NA	NCT03307785
Olaparib; Ceralasertib (AZD6738)	NSCLC	Phase II Umbrella Study of Novel Anti-cancer Agents in Patients With NSCLC Who Progressed on an Anti-PD-1/PD-L1 Containing Therapy	Durvalumab + AZD6738; Durvalumab + olaparib	2	NA	NCT03334617
Rucaparib	nsqNSCLC	Rucaparib and Pembrolizumab for Maintenance Therapy in Stage IV Non-Squamous Non-Small Cell Lung Cancer	Pembrolizumab	1/2	NA	NCT03559049
Olaparib	NSCLC	Study of Durvalumab+Olaparib or Durvalumab After Treatment With Durvalumab and Chemotherapy in Patients With Lung Cancer (ORION)	Durvalumab+chemotherapy	2	NA	NCT03775486
Ceralasertib (AZD6738)	NSCLC	Precision Immuno-Oncology for Advanced Non-small Cell Lung Cancer Patients With PD-1 ICI Resistance	Durvalumab	2	NA	NCT03833440
Niraparib	NSCLC	Niraparib in Combination With Osimertinib in EGFR-Mutated Advanced Lung Cancer	Osimertinib	1	EGFR-Mutated	NCT03891615

Table 2.2: continued

Olaparib	nsqNSCLC	Study of Pembrolizumab With Maintenance Olaparib or Maintenance Pemetrexed in First-line (1L) Metastatic Nonsquamous Non-Small-Cell Lung Cancer (NSCLC) (MK-7339-006, KEYLYNK-006)	Pembrolizumab	3	NA	NCT03976323
Olaparib	sqNSCLC	A Study of Pembrolizumab (MK-3475) With or Without Maintenance Olaparib in First-line Metastatic Squamous Non-small Cell Lung Cancer (NSCLC, MK-7339-008/KEYLYNK-008)	Pembrolizumab	3	NA	NCT03976362
Alisertib (MLN8237)	NSCLC	Alisertib in Combination With Osimertinib in Metastatic EGFR-mutant Lung Cancer	Osimertinib	1	EGFR-Mutated	NCT04085315
Talazoparib	sqNSCLC	Combination Treatment (Talazoparib Plus Avelumab) for Stage IV or Recurrent Non-Squamous Non-Small Cell Lung Cancer With STK11 Gene Mutation (A LUNG-MAP Treatment Trial)	Avelumab	2	STK11 Gene Mutation	NCT04173507
M6620 (VX970, Berzosertib, VE822)	NSCLC	Testing the Addition of an Anti-cancer Drug, Berzosertib (M6620, VX-970), to the Usual Treatments (Carboplatin and Gemcitabine) and to Pembrolizumab for Patients With Advanced Squamous Cell Non-small Cell Lung Cancer	Pembrolizuma+chemotherapy	1/2	NA	NCT04216316
Olaparib	NSCLC	Study of Pembrolizumab With Concurrent Chemoradiation Therapy Followed by Pembrolizumab With or Without Olaparib in Stage III Non-Small Cell Lung Cancer (NSCLC) (MK-7339-012/KEYLYNK-012)	Pembrolizumab+chemoradiotherapy	3	NA	NCT04380636
Niraparib	NSCLC	Placebo-controlled Study Comparing Niraparib Plus Pembrolizumab Versus Placebo Plus Pembrolizumab as Maintenance Therapy in Participants With Advanced/Metastatic Non-small Cell Lung Cancer	Pembrolizumab	3	NA	NCT04475939

Table 2.2: continued

Alisertib (MLN8237)	NSCLC	Osimertinib in Combination With Alisertib or Sapanisertib for the Treatment of Osimertinib-Resistant EGFR Mutant Stage IIIB or IV Non-Small Cell Lung Cancer	Osimertinib	1	EGFR-Mutated	NCT04479306
BAY1895344	solid tumor; NSCLC; SCLC	Testing the Addition of an Anti-cancer Drug, BAY 1895344, to the Usual Chemotherapy Treatment (Cisplatin, or Cisplatin and Gemcitabine) for Advanced Solid Tumors With Emphasis on Urothelial Cancer	chemotherapy	1	NA	NCT04491942
Olaparib	NSCLC; SCLC	Olaparib (LYNPARZA) Plus Durvalumab (IMFINZI) in EGFR-Mutated Adenocarcinomas That Transform to Small Cell Lung Cancer (SCLC) and Other Neuroendocrine Tumors	Durvalumab	2	EGFR-Mutated	NCT04538378
Olaparib	NSCLC	A Platform Study of Novel Agents in Combination With Radiotherapy in NSCLC	Radiotherapy	1	NA	NCT04550104
AZD5305	solid tumor; NSCLC; SCLC	Study of AZD5305 as Monotherapy and in Combination With Anti-cancer Agents in Patients With Advanced Solid Malignancies	AZD5305 Monotherapy; AZD5305 + Paclitaxel; AZD5305 + Carboplatin +- Paclitaxel; AZD5305 + Trastuzumab Deruxtecan; AZD5305 + Datopotamab Deruxtecan; AZD5305 + Camizestrant	1/2	NA	NCT04644068

Table 2.2: continued

Niraparib	MPM; NSCLC	UNITO-001- Study in HRR/PDL1 Positive MPM/NSCLC	Dostarlimab	2	HRR/PD L1	NCT049406 37
Methoxyami ne (TRC- 102)	nsqNSCLC	Testing the Addition of an Anti-Cancer Drug, TRC102, to the Usual Chemotherapy Treatment (Pemetrexed, Cisplatin) During Radiation Therapy for Stage III Non-Squamous NSCLC	Durvalumab+che moradiotherapy	2	NA	NCT051988 30
Ceralasertib (AZD6738)	NSCLC	A Phase III Study of Ceralasertib Plus Durvalumab Versus Docetaxel in Patients With NSCLC Whose Disease Progressed On or After Prior Anti PD (L)1 Therapy And Platinum Based Chemotherapy	Durvalumab	3	NA	NCT054506 92
Olaparib	NSCLC	Randomized Trial Comparing Standard of Care Versus Immune- Based Combination in Relapsed Stage III NSCLC Pretreated With Chemoradiotherapy and Durvalumab	Durvalumab+che motherapy	2	NA	NCT055682 12
Parimparib	NSCLC	Pamiparib (BGB-290) Was Used in EGFR-TkIs Resistant Non-small Cell Lung Cancer	chemotherapy	1	EGFR- Mutated	NCT055733 73
AZD5305	solid tumor; NSCLC	Phase I/IIa Study for AZD5335 as Monotherapy and in Combination With Anti-cancer Agents in Participants With Solid Tumors	AZD5335 + AZD5305	1/2	NA	NCT057971 68
M1774	nsqNSCLC	M1774 in Combination With Cemiplimab in Participants With Non-Squamous NSCLC (DDRiver NSCLC 322)	Cemiplimab	1/2	NA	NCT058827 34
Ceralasertib (AZD6738)	NSCLC	A Study to Investigate Efficacy and Safety of Ceralasertib Plus Durvalumab in Participants Aged ≥ 18 Years With Advanced or Metastatic Non-small Cell Lung Cancer Whose Disease Progressed on or After Prior Anti-PD-(L)1 Therapy and Platinum-based Chemotherapy	Durvalumab	2	NA	NCT059418 97

Table 2.2: continued

VIC-1911	NSCLC	Phase I Clinical Study of VIC-1911 Combined With Osimertinib in the Treatment of Advanced Non-small Cell Lung Cancer With EGRF- Mutation	Osimertinib	1	EGFR-Mutated	NCT05489731
VIC-1911	NSCLC	A Phase 1a/1b Study of Aurora Kinase A Inhibitor VIC-1911 Monotherapy and in Combination With Sotorasib for the Treatment of KRAS G12C-Mutant Non-Small Cell Lung Cancer	sotorasib	1	KRAS G12C-Mutant	NCT05374538
LY3295668	NSCLC	A Phase Ib/II Trial to Evaluate Safety, Tolerability and Efficacy of Aurora Kinase Inhibitor LY3295668 in Combination With Osimertinib for Patients With EGFR-Mutant Non-Small Cell Lung Cancer	Osimertinib	1	EGFR-Mutated	NCT05017025

2.3 Conclusions

Genomic profiling helps identify promising DDR targets of NSCLC, such as PARP, ATR, CHK1, CHK2, WEE1, AURK, DNA-PK, APE1. Medicine targeting these proteins are in various phase of preclinical or clinical development within different cancer types. The first approved DDR inhibitor, PARP inhibitors, have been used in certain patients with BRCA mutated. However, few DDR inhibitors run into phase 3 trial in NSCLC. Single agents of some DDR inhibitors show antitumor activity in NSCLC but limited. To improve the outcome, predictive biomarkers should be developed to optimize the response and an improve understanding of primary and acquired resistance mechanisms. The combination strategy of DDR inhibitors is usually chemotherapy and/or radiotherapy, which can enhance the effects. Combination of other target agents have demonstrated clinical potential and some of them step into clinical trials. Genomic instability of NSCLC influences innate and acquired immunity. Combination of DDR inhibitor and immunotherapy would be one of the most attractive future areas of research in NSCLC. While combine DDR inhibitor with different agents, their interactions should be considered. The appropriate dosing and scheduling of each agent to minimize toxicity adverse events and maximize benefits is critical factor for optimizing outcomes. In conclusion, it is believed that comprehensive preclinical research into biology of DDR and clinical study progress in the DDR target agents, will lead to great advances in the near future.

The future of DDR therapy lies in overcoming these hurdles through the development of predictive biomarkers, understanding resistance mechanisms, and designing intelligent combination strategies with chemotherapy, radiotherapy, targeted agents, and immunotherapy.

Despite this progress, a critical gap remains: the role of epigenetic regulation, specifically DNA methylation, in modulating the DDR pathway in NSCLC. Most research has focused on genetic mutation in DDR genes, but the expression and function of these gene are also profoundly regulated by reversible promoter methylation. This area is significantly underexplored. The systematic identification of aberrantly methylated DDR genes and their impact on the tumor immune microenvironment represents a major unmet need for biomarker discovery and novel therapeutic strategies.

This thesis directly addresses this gap. It was hypothesized that a distinct subset of DDR genes is silenced or activated by promoter methylation in LUAD, driving tumor progression and immune evasion. By integrating methylomic and transcriptomic data, the aim was to identify a novel signature of immunotherapy. This focus provides a crucial new dimension to the DDR field, moving beyond genetics to epigenetics, and offers a potential foundation for developing epigenetic biomarkers to guide the use of both existing and future DDR-targeted therapies.

CHAPTER 3

MATERIALS AND METHODS

3.1 Overview of the study design

The study design was illustrated in **Figure 3.1**. The study started with downloading transcriptome and methylome data, followed by screening paired samples. Then, it identified differentially expressed genes (DEGs) from the transcriptome and differentially methylated genes (DE-MGs) from the methylome. These data were integrated to find methylated DEGs, and combined with DNA damage repair-related genes (DDRGs) to obtain methylated DE-DDRGs. Prognosis-associated methylated DE-DDRGs were pinpointed via univariate and multivariate analyses to build a two-gene survival risk predictive model. The model was evaluated using TCGA-LUAD and independent cohort (GSE31210 and GSE 68465). Its prognostic value with clinical factors was assessed, and its relation to the tumor immune cell infiltration and immune checkpoint inhibitor response was explored. Finally, mRNA expression of specific genes in lung cancer and normal cells was analyzed by RT-PCR.

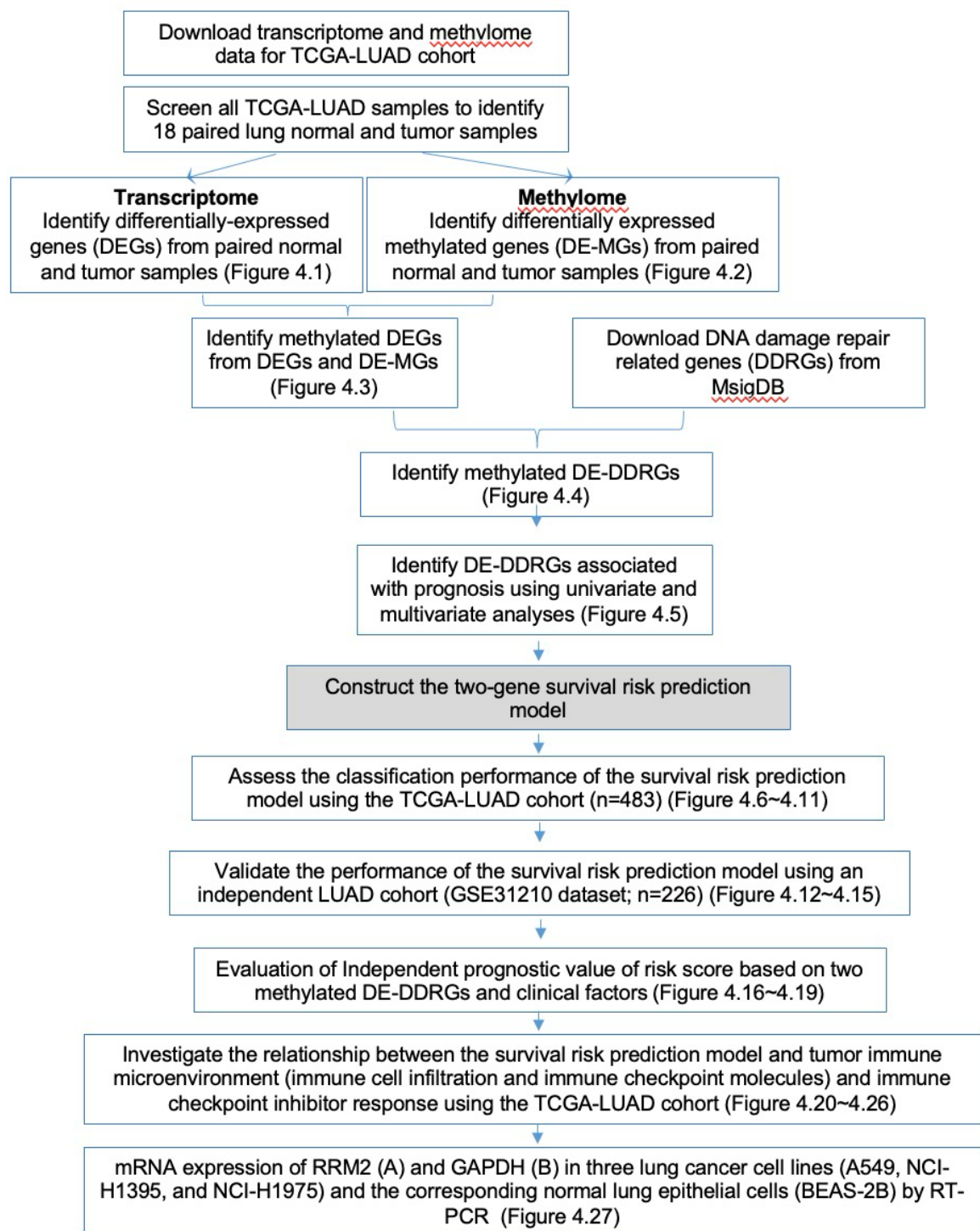


Figure 3.1: Flow chart of the study design

3.2 LUAD-related data source

The RNA sequencing (RNA-seq) data (FPKM) and DNA methylation used in this study were sourced from the TCGA (<https://portal.gdc.cancer.gov/>) and UCSC (<https://xena.ucsc.edu/public>) databases, respectively. After performing sample pairwise checks, RNA-seq and DNA methylation data were obtained for 18 normal and 18 tumor samples. The GSE31210 dataset was downloaded from the Gene Expression Omnibus (GEO) database (<http://www.ncbi.nlm.nih.gov/geo/>), while the GSE68465 dataset was retrieved from GPL96 (Affymetrix Human Genome U133A Array, [HG-U133A]). The GSE31210 dataset included 226 LUAD samples with complete survival time and status, while the GSE68465 dataset contained 442 LUAD cases with survival data, primarily used for validation of the constructed prognostic signature (Okayama et al., 2012; Yamauchi et al., 2012).

3.3 Collection of DNA damage-repair-related genes (DDRGs)

A total of 243 DNA damage-related genes (**Appendix C1**) and 387 DNA repair-related genes (**Appendix C2**) from the CancerSEA dataset (<http://biocc.hrbmu.edu.cn/CancerSEA/>). Additionally, 295 DNA damage & repair-related genes were retrieved from MSigDB (<https://www.gsea-msigdb.org/gsea/msigdb>) (**Appendix C3**). Subsequently, a de-duplication merge analysis was performed across the three gene lists, resulting a total of 696 (DDRGs; **Appendix C4**) for subsequent analysis.

3.4 Differential expression analysis

Differential expression genes (DEGs) between normal and tumor samples were identified using the R package limma (v 3.44.3) (Ritchie et al., 2015), applying the criteria

$|\log_2 \text{ fold change (FC)}| > 0.5$ and adjusted (adj.) $P < 0.05$. A $|\log_2 \text{FC}|$ cutoff of 0.5 is commonly applied in transcriptomic studies when the goal is to capture moderately but biologically relevant expression changes.

Differentially methylated CpG sites (DE-MCS) between 18 paired LUAD and normal samples were identified using the R package ChAMP, with a significance threshold of $|\text{deltaBeta}| > 0.2$ and $P < 0.05$, as a 20% methylation difference is generally considered biologically meaningful and has been adopted in prior genome-wide methylation studies. Genes annotated by DE-MCS were defined as differentially methylated genes (DE-MGs) for further analysis. DE-MGs with $\text{deltaBeta} > 0.2$ and $P < 0.05$ were considered hypermethylated genes; conversely, while those meeting $\text{deltaBeta} < -0.2$ and $P < 0.05$ were defined as hypomethylated genes.

3.5 Overlap analysis

Overlap analysis was performed to identify common factors across gene lists. Upregulated DEGs with hypomethylated genes were subjected to overlap analysis, with the shared genes termed hypomethylated upregulated genes. Similarly, downregulated DEGs with hypermethylated genes were designated as hypermethylated downregulated genes. The union of these two gene lists formed the set of methylated DEGs, which were then overlapped with the previously obtained DDRGs to identify methylated DE-DDRGs.

3.6 The construction, evaluation, and validation of risk model

To evaluate whether methylated DE-DDRGs were associated with the survival of patients with LUAD, the expression data of methylated DE-DDRGs were extracted from TCGA-LUAD dataset (n=483) and merged with clinical data, including survival follow up

information. These clinical expression data were used as the training set to construct the prognostic risk model, while two independent datasets, GSE31210 (n = 226) and GSE68465 (n=442), served as validation sets to verify the model's predictive accuracy.

In the training set, univariate Cox regression analysis merged with Kaplan-Meier (KM) (R: survival, v 3.2-3) (Ramsay et al., 2018) survival analysis for the identified methylated DE-DDRGs, with genes exhibiting a hazard ratio (HR) $\neq 1$ and $P < 0.05$ being identified as prognostic candidates. Multivariate Cox analysis with stepwise regression was performed for variables that met the conditions. The stepwise regression function was applied to optimize the model, using the Akaike Information Criterion (AIC) as the selection criterion to add or remove variables. The objective was to identify the most optimal regression model with the lowest AIC value.

Genes with $P < 0.05$ was considered as the significance threshold in terms of best prognostic value. Risk scores were subsequently calculated for each sample in both the training set and the independent external validation sets, based on the expression and regression coefficients (coef, output from multivariate Cox analysis) of the prognostic genes. The risk score of each sample was determined using the following formula:

$$\begin{aligned} \text{risk score} = & (\text{coef}_{\text{gene}_1} \times \text{expression value of gene}_1) \\ & + (\text{coef}_{\text{gene}_2} \times \text{expression value of gene}_2) \\ & + \dots (\text{coef}_{\text{gene}_n} \times \text{expression value of gene}_n) \end{aligned}$$

The LUAD samples from each dataset were divided into high- and low-risk groups based on the corresponding median value of the risk score. Samples with risk scores above the median value were classified into the high-risk group, while those with scores below the median were assigned to the low-risk group. The median the risk score value was calculated

by the MEDIAN function. Subsequently, differences in overall survival (OS) of LUAD patients between high- and low-risk groups in the training set and independent external validation set were assessed by K-M analysis and log-rank test, and $P < 0.05$ was considered statistically significant. Then, time-dependent (1, 2, and 3 years) ROC curves were plotted based on the risk scores, and the prognostic accuracy of the prognostic model was evaluated by calculating the area under the curve (AUC), where $AUC > 0.6$ was considered indicative of modest discriminatory power can provide valuable clinical insights (Çorbacıoğlu Ş & Aksel, 2023) .

3.7 Independent prognostic analysis of the risk score

Univariate and multivariate Cox regression analyses were performed to further examine the independence of the risk score to other clinical parameters including, age, gender, pathologic stage, pathologic T (tumor) stage, pathologic N (node) stage, and pathologic M (metastasis) stage as a prognostic factor for LUAD ($P < 0.05$). The final variable of $P < 0.05$ generated by multivariate Cox analysis was considered as an independent prognostic factor for LUAD patients.

3.8 Construction and evaluation of the nomogram model

All independent prognostic parameters were included in the construction of the nomogram(Iasonos et al., 2008) to predict 1-, 2-, and 3-year overall survival in the tumor samples in the TCGA-LUAD dataset. The performance of the model was evaluated via discrimination using Harrell's concordance index (C-index). The calibration curve of the nomogram was plotted to observe the nomogram prediction probabilities against the observed rates.

3.9 ESTIMATE and single sample gene set enrichment analysis (ssGSEA) of the LUAD samples

Estimation of STromal and Immune cells in MAlignant Tumor tissues using Expression data (ESTIMATE) is a tool for predicting tumor purity and presence of infiltrating stromal/immune cells in tumor samples (Yoshihara et al., 2013). The immune score (representing immune cell infiltration levels), stromal score (indicating stromal content), and ESTIMATE score (reflecting tumor purity) were calculated for each samples. The higher the respective score is, the larger the ratio of the corresponding component in the tumor immune microenvironment exists.

To further analyze immune cell infiltration, ssGSEA (Rooney et al., 2015) was performed to calculate the enrichment levels of 24 immune-associated gene sets for each LUAD sample using the gsva R package (v 1.36.3) (Wang et al., 2024). The significant differences in immune cell numbers were identified by analysis of variance (ANOVA).

3.10 TIDE and SubMap algorithms

The tumor immune dysfunction and exclusion (TIDE; <http://tide.dfci.harvard.edu/>) algorithm (Jiang et al., 2018) and subclass mapping (SubMap; <https://cloud.genepattern.org/gp>) (Hoshida et al., 2007) were utilized to predict the clinical response to immune checkpoint inhibitors of PD-1 and CTLA4 in the low- and high-risk score groups ($P < 0.05$).

3.11 Cell culture and reagents

The normal human lung epithelial cell line (BEAS-2B) and three human lung cancer cell lines (A549, NCI-H1975, and NCI-H1395) were purchased from American Type

Culture Collection (Manassas, VA, USA). These cell lines were selected to represent the key molecular heterogeneity observed in LUAD patients. The A549 cell line is classic model harbouring a activating KRAS_G12S mutation and is widely used for studying aggressive LUAD biology (Giard et al., 1973). The NCI-H1975 cell line contains a common treatment sensitive EGFR_L858R mutation and a resistance associated EGFR_T790M mutation, making it a model for EGFR mutated LUAD and tyrosine kinase inhibitor resistance (Gazdar et al., 2010). The NCI-H1395 cell line was derived from a lymph node metastasis and carries a loss-of-function RB1 mutation, representing a more advanced, metastatic disease context (Ghandi et al., 2019). All cells were seeded onto six-well plates containing RPMI-1640 supplemented with 10% fetal calf serum, L-glutamine (5 mmol/L), non-essential amino acids (5 mmol/L), penicillin (100 U/mL), and streptomycin (100 U/mL) (Invitrogen, Carlsbad, CA, USA), at 37 °C in a humidified 5% CO₂ atmosphere.

3.12 Validation of key gene expression levels

While nine methylated DE-DDRGs were initially identified, multivariate Cox regression analysis revealed that only the expression levels of RRM2 and GAPDH served as independent prognostic factors for constructing the most optimal risk prediction model. To clarify the expression of prognostic genes in both disease and normal samples, the Wilcoxon rank-sum test ($P < 0.05$) was employed to analyse the expression of two prognostic genes (RRM2 and GAPDH) across disease and normal samples in both training and validation sets. Based on this, the levels of two mRNAs (RRM2 and GAPDH) expressions were detected from three human lung cancer cell lines and the normal group. All cell lines were lysed with TRIzol Reagent (Life Technologies-Invitrogen, Carlsbad, CA, USA), and total RNA was isolated following the manufacturer's instructions. Then the concentration and purity of the

RNA solution were quantified using a NanoDrop 2000FC-3100 nucleic acid protein quantifier (Thermo Fisher Scientific, Waltham, MA, USA Life Real).

The extracted RNA was reverse-transcribed to cDNA using the SureScript-First-strand-cDNA-synthesis-kit (Genecopoeia, Guangzhou, China) prior to RT-PCR. The RT-PCR reaction consisted of 4 μ l of reverse transcription product, 2 μ l of 5 $\times$ BlazeTaq qPCR Mix (Genecopoeia, Guangzhou, China), 0.5 μ l each of forward and reverse primer, and 3 μ l nuclease-free water. PCR was performed in a BIO-RAD CFX96 Touch TM PCR detection system (Bio-Rad Laboratories, Inc., USA) under the following conditions: initial denaturation at 95°C for 30 s, followed by 40 cycles that each involved incubation at 95°C for 10 s, 60°C for 20 s, and 72°C for 30 s. The primers were as follows: RRM2 sense, 5'-CGGAGCCGAAACTAAAGCA-3' and anti-sense, 5'-ATGGGGAAGATGACAAAGCG-3'; GAPDH sense, 5'-CCTTCCGTGTTCTACCCC-3' and anti-sense, 5'-GCCCAAGATGCCCTTCAGT-3'; β -actin sense, 5'-TCCCTGGAGAAGAGCTATGA-3' and anti-sense, 5'-AGGAAGGAAGGCTGGAAAAG-3'. All primers were synthesized by Tsingke (Tsingke Biotechnology Co., Ltd., Beijing, China). The β -actin gene served as an internal control, and the relative expression of RRM2 and GAPDH was determined using the $2^{-\Delta\Delta C_t}$ method (Livak & Schmittgen, 2001).

The experiment was repeated in triplicate on independent occasions. Statistical differences of RRM2 and GAPDH between cell lines were detected by Analysis of Variance (ANOVA; ordinary one-way ANOVA), using GraphPad Prism V9 (GraphPad Software, La Jolla, CA, USA), and the level of statistical significance was tested and represented as * for $P < 0.05$ and ** for $P < 0.01$.

3.13 Statistical analysis

A heatmap illustrating the expression intensity of DEGs, DE-MCS, and prognostic genes was generated using the R package heatmap (v 0.7.7) (<https://CRAN.R-project.org/package=pheatmap>). The ROC curves were plotted based on the R package ROC. The nomogram was drawn based on the R package rms. The ESTIMATE algorithm was implemented with the R package ESTIMATE. Wilcoxon rank-sum test and Kruskal-Wallis test were used for subgroup differential analyses. The difference was considered statistically significant when $P < 0.05$ in all statistical analyses.

CHAPTER 4

RESULTS AND DISCUSSION

4.1 A Total of 5,425 Differentially Expressed Methylated Genes (DE-MGs) were Recognized

Utilized the RNA expression profiles of 18 pairs of paired samples after matching TCGA-RNA-seq and UCSC-methylation data as the basis for differential expression analysis. Differential expression analysis revealed a propound rewiring of the transcriptome in LUAD, with 1,778 DEGs identified between normal and LUAD samples. Compared to the normal group, 853 DEGs were up-regulated and a total of 925 were down-regulated in the LUAD group (**Figure 4.1; Appendix C5**).

USCS-methylation data from 18 pairs of paired samples were selected as the basis for DE-MCS analysis. With the ChAMP package, a total of 20,249 DE-MCS were obtained between LUAD and normal samples, indicating an even more widespread epigenomic disruption. Among them, a marked genome bias towards 12,977 hypermethylated sites and 7,272 hypomethylated sites was observed (**Figure 4.2**). Subsequently, a total of 5,425 differentially expressed methylated genes (DE-MGs) were obtained after annotation of these DE-MCSs, including 2,716 hypermethylated genes (**Appendix C6**) and 2,709 hypomethylated genes (**Appendix C7**).

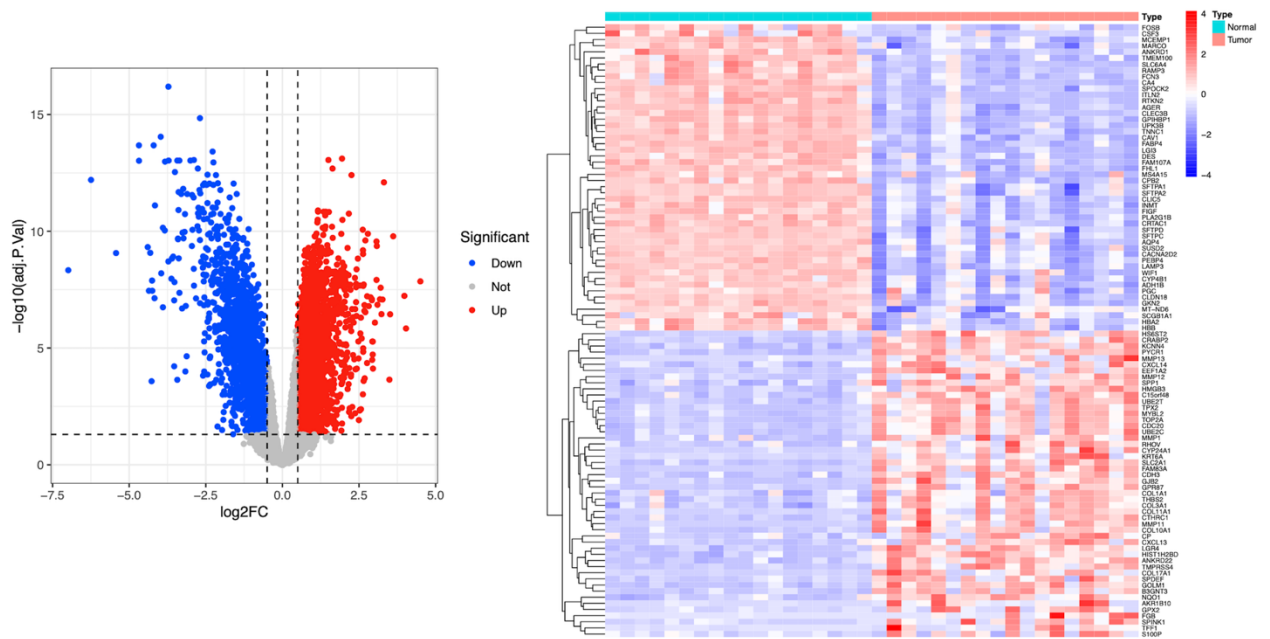


Figure 4.1: Volcano map depicting the distribution of the differentially expressed genes in LUAD samples.

The volcano map showed the distribution of the differentially expressed genes in LUAD samples as compared with paired normal tissue samples (n=18) : red dots represent upregulated genes, blue dots downregulated genes, and grey dots non-significant changes. Heatmap showing the gene expression pattern of the top 50 up-regulated genes and top 50 down-regulated genes in LUAD as compared with paired normal tissue samples (n=18) – indicating a coordinated transcriptional shift in LUAD.

The identification of 5,425 DE-MGs represents the cornerstone findings of the study, highlighting the universal role of epigenetic dysregulation in LUAD. This finding aligns with the established cancer hallmark of “genome instability and mutation”, now extended to the epigenetic field, where extensive methylation alterations drive transcriptional chaos (Hanahan, 2022). Hypermethylated genes were significantly enriched in key tumor suppressor pathways and developmental processes, suggesting their silencing may provide a selective advantage to the tumor (Jones & Baylin, 2007). Conversely, hypomethylated genes were associated with oncogenic signalling pathways and activation of pro-tumorigenic functions, potential leading to the overexpression of oncogenes and cancer-testis antigens (Ehrlich, 2009). This coordinated pattern of potential silencing of tumor suppressors via

hypermethylation and activation of oncogenes via hypomethylation provides a mechanistic link between the observed epigenomic changes and cancer development. Furthermore, this extensive epigenetic reprogramming may have significant implications for therapy, as it can influence response to both conventional chemotherapy and emerging immunotherapies (Hu et al., 2020).

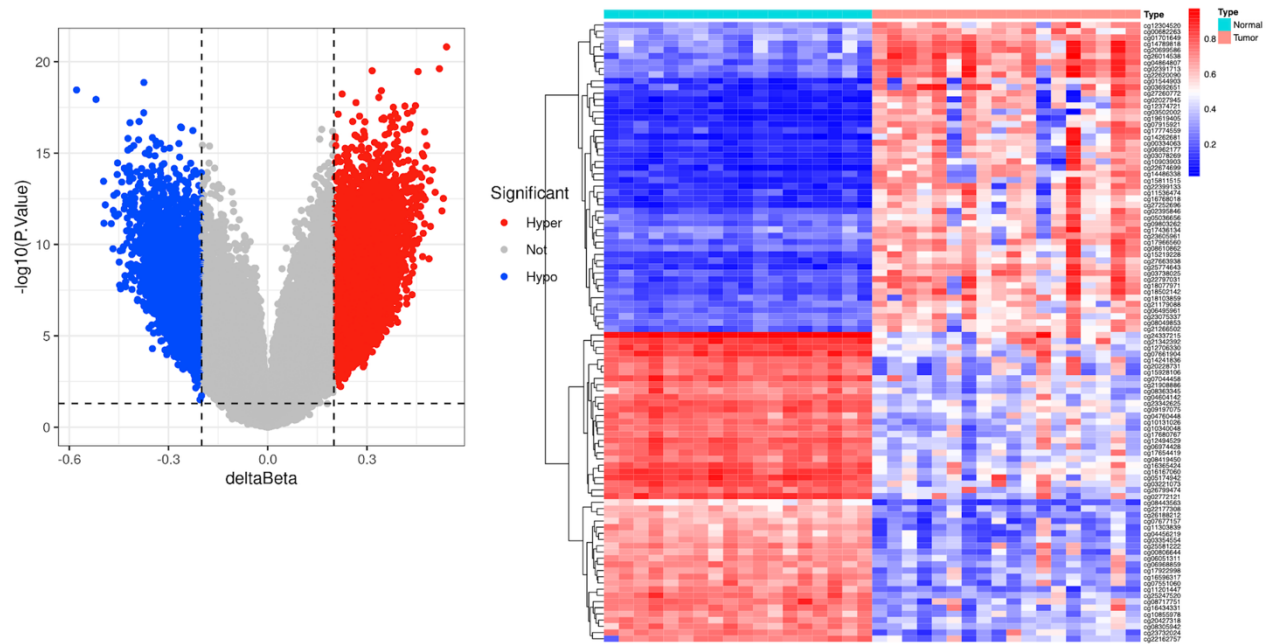


Figure 4.2: Volcano map depicting the distribution of the differentially expressed methylated CpG sites (DE-MCS) sites in LUAD.

The volcano map above showed the distribution of the differentially expressed methylated CpG sites (DE-MCS) in LUAD samples as compared with paired normal tissue samples (n=18) : red dots represent hypermethylated sites and blue dots hypomethylated sites. Heat map showing the DNA methylation pattern of the top 50 hypermethylated and top 50 hypomethylated CpG sites (D) in LUAD as compared with paired normal tissue samples (n=18) – with hypermethylation often silencing tumor suppressors and hypomethylation potentially activating oncogenes.

4.2 CLU, BUB1B, SHCBP1, RRM2, RPL39L, TRIP13, GAPDH, ENO1, and CENPM were identified as methylated DE-DDRGs

After identifying DEGs and DE-MGs from the above datasets, intersection analysis was performed to identify genes with hypomethylated high expression and hypermethylated low expression characteristics in LUAD. A total of 161 were identified by overlapping 2,709

hypomethylated and 853 highly expressed genes – suggesting epigenetic activation, while a total of 240 hypermethylated down-regulated genes were obtained by overlapping 2,716 hypermethylated and 925 low-expressed genes – suggesting epigenetic silencing (**Figure 4.3**). The hypomethylated-highly expressed and hypermethylated-lowly expressed genes were listed in **Appendix C8**, and these genes were defined as methylated DEGs. The scale of this overlap is biologically significant and aligns with established paradigms in cancer epigenetics, indicating that DNA methylation is a key, but not sole, regulator of gene expression in LUAD.

The link between DNA methylation and DNA damage repair systems is supported by increasing evidence (M. Wang et al., 2021). Notably, 696 DDRGs genes (**Appendix C4**) were collected from the CancerSEA database and MSigDB database and identified overlapping genes via intersection analysis with identified methylated DEGs. As shown in **Figure 4.4**, nine genes were common to both sets of genes, among which, CLU was a hypermethylated low-expression gene, whereas BUB1B, SHCBP1, RRM2, RPL39L, TRIP13, GAPDH, ENO1, and CENPM were hypomethylated high-expression genes, which were defined as methylated DE-DDRGs, representing a critical nexus between epigenetic regulation and genomic stability in LUAD. The nine methylated DE-DDRGs and their putative roles in LUAD pathogenesis are summarized **Table 4.1**

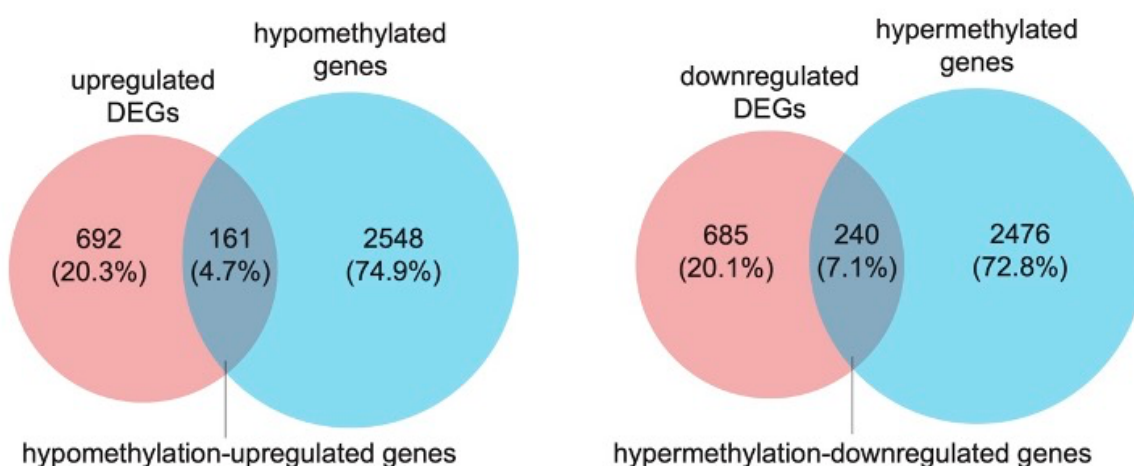


Figure 4.3: Venn Diagrams illustrating the intersection between up-regulated and hypomethylated genes and down-regulated and hypermethylated genes as methylated DEGs.

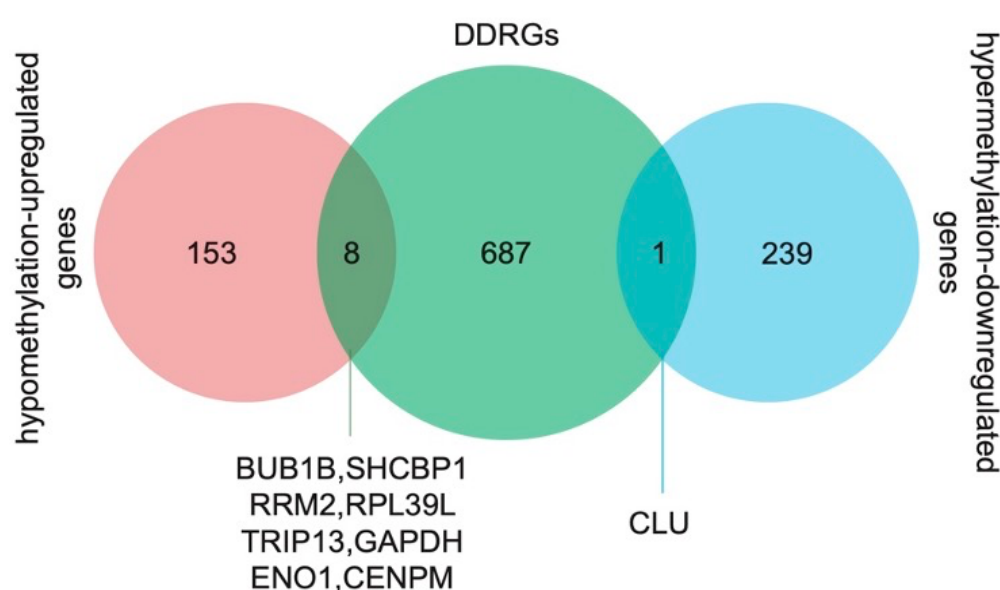


Figure 4.4: Venn Diagrams illustrating the intersection between methylated DEGs and DDR related genes (DDRGs) as methylated DE-DDRGs.

Subsequently, the expression profiles of nine methylated DE-DDRGs were extracted from the TCGA-LUAD dataset and calculated their correlation with DNA methylation data and found that all nine gene expressions were negatively correlated with DNA methylation (**Figure 4.5**). Among them, the expression of GAPDH showed the strongest negative correlation with methylation (cor = -0.79, P = 1.2e-08), suggesting its overexpression is not a passive consequence of increased metabolism but an actively driven event; followed by RRM2 (cor = -0.7, P = 2e-06), SHCBP1 (cor = -0.66, P = 1.1e-05), and ENO1 (cor = -0.63, P = 4e-05); the remaining RPL39L, TRIP13, CLU, and BUB1B had a cor range of -0.59 to -0.44 (all P < 0.05); however, the correlation between CENPM expression and methylation appeared to be less favorable (cor = -0.24, P = 0.16).

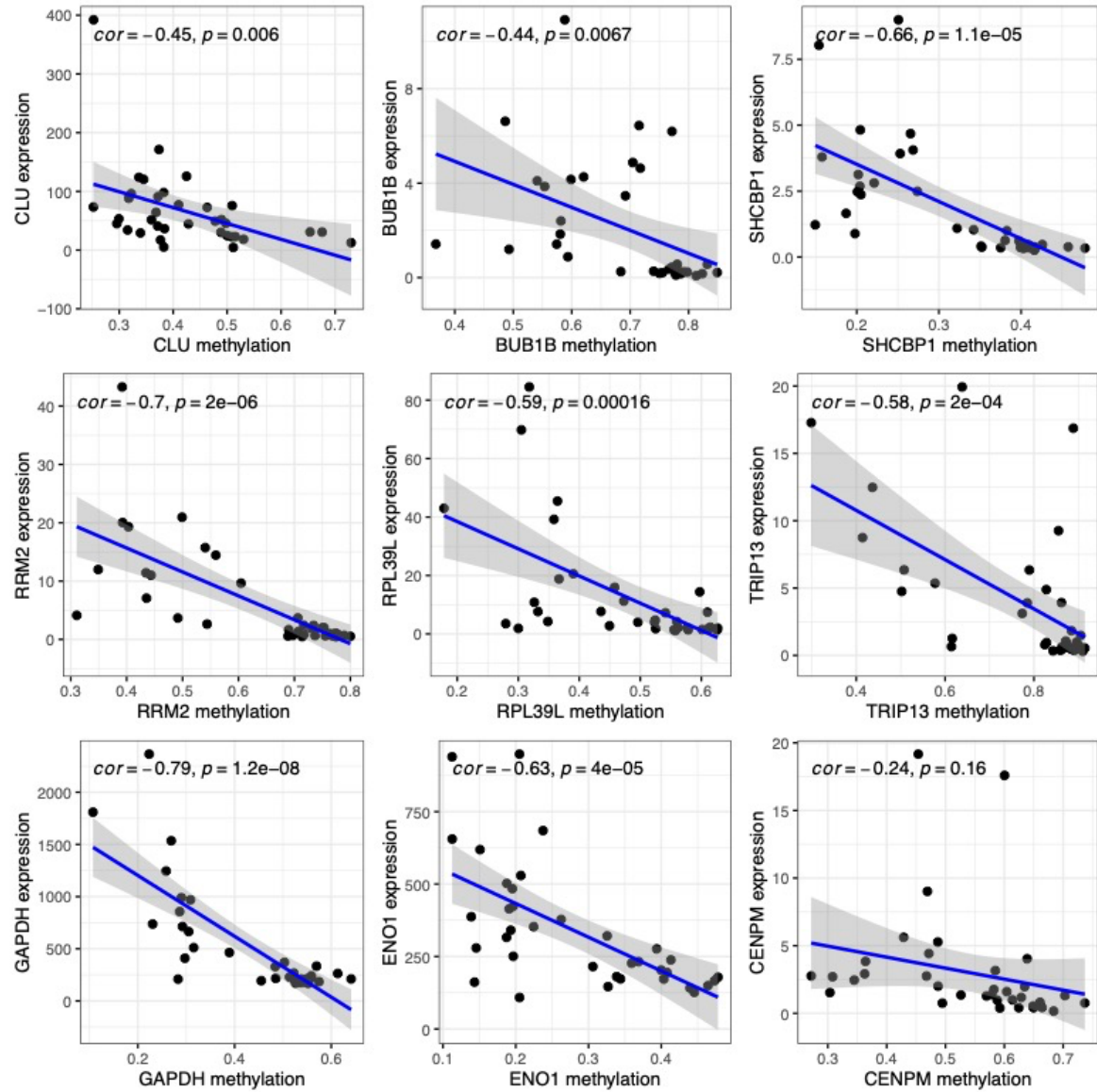


Figure 4.5: Scatter plots showing the Pearson correlation analysis between gene expression (y-axis) and DNA methylation (x-axis) levels of the 9 DDR-related methylated DE-DDRGs in paired normal and tumor samples (n=18).

Each dot in the scatter plot above depicted data points for each of the 36 samples. The blue line indicates the best fitting line. The grey shadow indicates the 95% confidence intervals (CI). The Pearson correlation coefficient and p-values were indicated for each gene.

Table 4.1: Functional Annotation of the Nine Methylated DE-DDRGs in LUAD

Gene	Full name	Methylation Expression /	Known Functions in DDR/Cancer	Relevance to LUAD
CLU	Clusterin	Hypermethylated / Low	Apoptosis regulator; promotes cell survival after DNA damage; putative tumor suppressor (Peng et al., 2019) (Shiota et al., 2011)	Epigenetic silencing may enhance cell survival and resistance to therapy-induced apoptosis(Park et al., 2006; Wang et al., 2014)
RRM2	Ribonucleotide Reductase M2 Subunit	Hypomethylated / High	Directly involve DNA repair by supplying nucleotides for lesion bypass. High RRM2 expression correlates with defective homologous recombination repair(Aye et al., 2015; Morikawa, Hino, et al., 2010)	Overexpression is a known oncogenic driver in LUAD, linked to proliferation and gemcitabine resistance. (Jin et al., 2020) (C. Ma et al., 2020)
GAPDH	Glyceraldehyde -3-Phosphate Dehydrogenase	Hypomethylated / High	Multifunctional protein; role in DDR includes regulating telomere integrity and apoptosis; key glycolytic enzyme. (Colell et al., 2009) (Nicholls et al., 2012)	Overexpression linked to poor prognosis in LUAD; drives metabolic reprogramming (Warburg effect) and proliferation. (Puzone et al., 2013) (Ouyang et al., 2023)
ENO1	Enolase 1	Hypomethylated / High	Glycolytic enzyme (enolase); also known to bind DNA and participate in DNA repair processes. (Huang et al., 2022)	Promotes glycolytic flux and biomass generation; overexpression associated with cancer progression. (H. J. Li et al., 2021)
BUB1B	BUB1 Mitotic Checkpoint Serine/Threonine Kinase B	Hypomethylated / High	Essential for mitotic spindle checkpoint activation, ensuring accurate chromosome segregation. (Kapanidou et al., 2015)	Overexpression can lead to chromosomal instability and aneuploidy, fueling tumor evolution. (Hao et al., 2025)
TRIP13	Thyroid Hormone Receptor Interactor 13	Hypomethylated / High	ATP-dependent chaperone involved in meiotic recombination and mitotic spindle assembly; resolving DNA-protein crosslinks (Z. H. Li et al., 2021) (Clairmont et al., 2020)	Overexpression can confer resistance to paclitaxel and is linked to poor prognosis in various cancers. (Zheng et al., 2025) (Cai et al., 2021)

Table 4.1: continued

SHCBP1	SHC SH2-Domain Binding Protein 1	Hypomethylated / High	Shc SH2-domain binding protein; involved in cell cycle progression, specifically mitosis. (H. Wang et al., 2025) (Zhou et al., 2018)	Promotes proliferation and is frequently overexpressed in cancers; potential oncogene. (F. Wang et al., 2019) (Xu et al., 2020)
CENPM	Centromere Protein M	Hypomethylated / High	Component of the kinetochore complex; essential for proper chromosome segregation. (Foltz et al., 2006)	Overexpression may contribute to chromosomal instability, a hallmark of cancer. (Qi et al., 2022)
RPL39L	Ribosomal Protein L39 Like	Hypomethylated / High	A ribosomal protein; specific role in DDR is less clear but may influence translation of DDR-related proteins. (Nadano et al., 2002)	Potential role in modulating the cellular stress response; requires further validation. (Tan et al., 2007)

In conclusion, the analysis moves beyond a simple listing of genes to provide a biologically grounded narrative. A panel of nine epigenetically deregulated DDR genes were identified, whose concerted actions likely create a permissive environment for genomic instability and tumor progression in LUAD.

4.3 LUAD patients in the low-risk group have better survival than those at high risk

To explore the relationship between methylated DE-DDRGs and survival of LUAD patients, clinical data were extracted from the TCGA-LUAD sample (n = 483) and identified the variables significantly associated with OS in LUAD patients by univariate Cox regression analysis incorporating K-M survival analysis. The results indicated that six (BUB1B, SHCBP1, RRM2, TRIP13, GAPDH, ENO1) of the nine methylated DE-DDRGs were significantly correlated with OS in patients with LUAD (all $P < 0.05$; **Figure 4.6; Appendix C9**). These six genes are functionally interconnected in processes critical for cancer aggressiveness: genomic instability (BUB1B, TRIP13) (Clairmont et al., 2020; Kapanidou et al., 2015), cell cycle and proliferation (SHCBP1, RRM2) (Aye et al., 2015; Xu et al., 2020), altered metabolism (GAPDH, ENO1) (Colell et al., 2009; Lu et al., 2025), and treatment resistance (RRM2, TRIP13) (Abuduhailili et al., 2025; Z. H. Li et al., 2021). Their methylation status likely alters their expression, thereby influencing these key pathways and ultimately patient survival in LUAD. Meanwhile, all of these variables were hypomethylated high-expression genes with hazard ratio (HR) > 1 (range: 1.1-1.5) for overall survival, indicating these patients faces 10%- 50% higher risk of death. Clinically, these genes may be pro-oncogenes in LUAD.

Further, multivariate Cox analysis with stepwise regression selected RRM2 ($P = 0.042$, HR = 1.179, 95% CI: 1.006-1.382) and GAPDH ($P = 0.003$, HR = 1.403, 95% CI:

1.125-1.750) as the optimal variables for constructing prognostic models for LUAD from the above six variables (**Figure 4.7; Appendix C10**). The risk score was calculated as follows:

$$\begin{aligned} \text{risk score} = & (0.164973625 \times \text{expression value of RRM2}) \\ & + (0.338623053 \times \text{expression value of GAPDH}) \end{aligned}$$

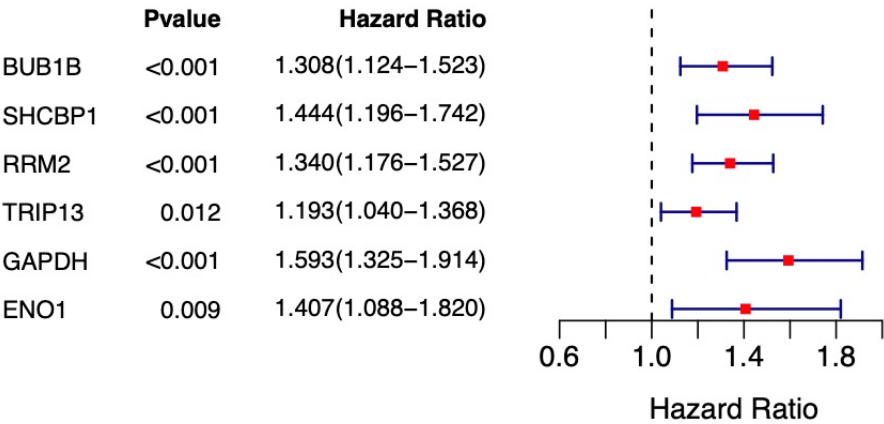


Figure 4.6: The Forest plot shows the result of univariate Cox regression analysis for the association between methylated DE-DDRGs' expression.

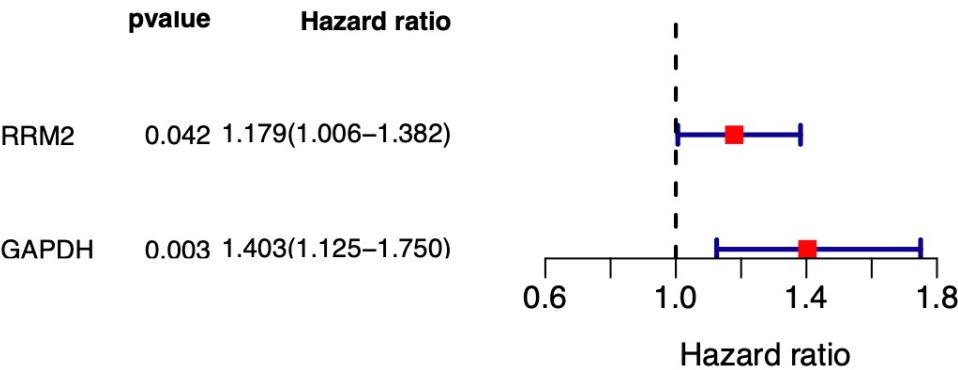


Figure 4.7: The Forest plot shows the result of multivariate Cox regression analysis for the association between methylated DE-DDRGs' expression.

TCGA-LUAD patients were divided into a high-risk group (n = 241) and a low-risk group (n = 242) according to the median value of the risk score (critical value = 3.724466) (**Appendix C11**). According to the risk curves, the mortality of patients appeared to increase successively with increasing risk scores (**Figure 4.8**). Consistently, K-M survival curves showed that LUAD patients in the high-risk group had significantly worse OS than the low-risk group ($P < 0.001$; **Figure 4.9**). To assess the predictive power of the risk signature based on methylated DE-DDRGs, the AUC was calculated. The AUC of the ROC curve for 1-year OS was 0.665, 0.672 for 2 years, and 0.681 for 3 years (**Figure 4.10**), indicating that the risk score had an acceptable validity in predicting OS in LUAD patients. A heatmap further revealed that both RRM2 and GAPDH exhibited high expression in the high-risk group (**Figure 4.11**).

In summary, this RRM2/GAPDH signature effectively identified a high-risk LUAD patients whose tumors are likely driven by hyper-proliferation (RRM2) and metabolic adaptation (GAPDH). Its true value will be realized when integrated with standard clinical staging to improve risk assessment and when tested as a biomarker for selecting patients for more aggressive or targeted therapies.

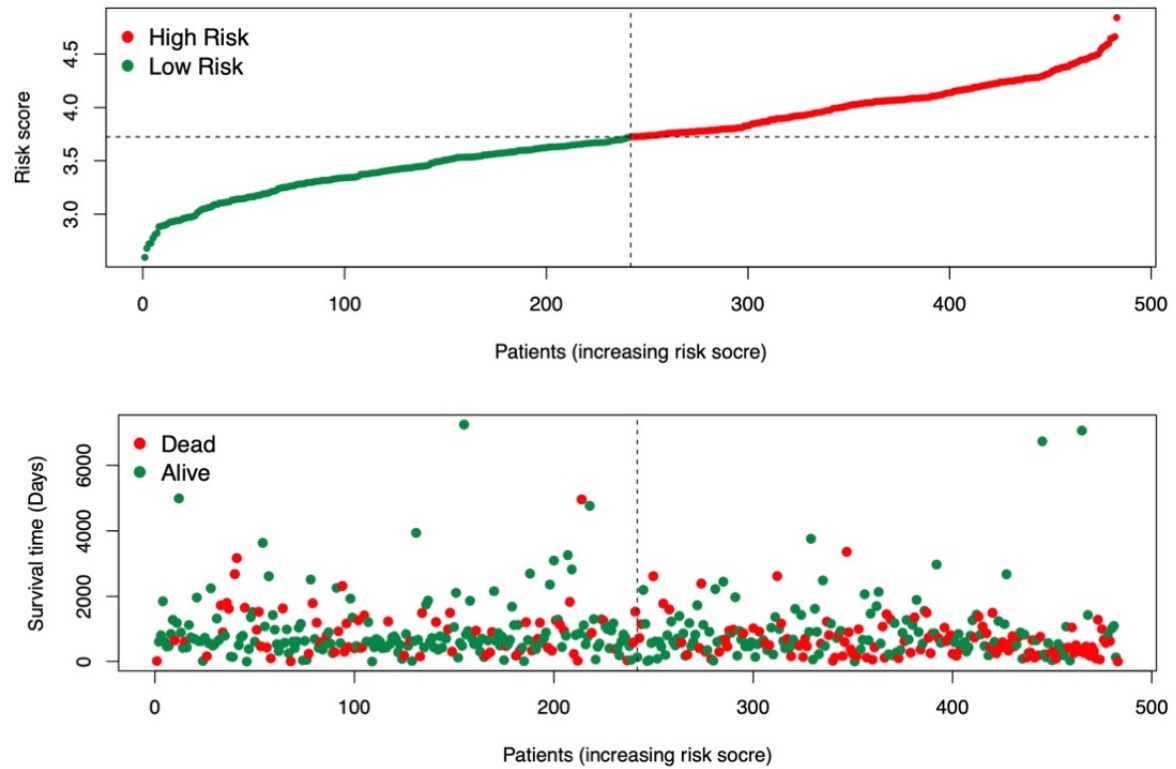
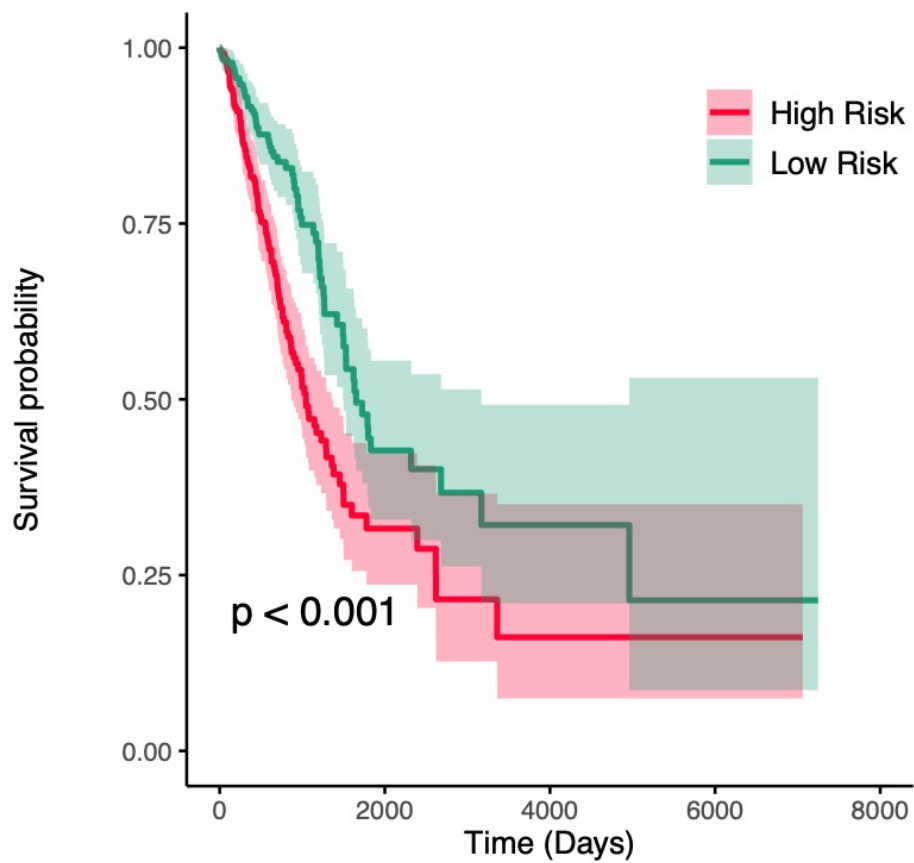


Figure 4.8: The plots showed the risk score distribution of TCGA-LUAD patients (above) and the survival status and duration of patients.

The risk score distribution of TCGA-LUAD patients (top), which was plotted in ascending order and marked as low-risk (green) or high-risk (red), as divided by the threshold (vertical black line). Survival status and duration of patients (bottom) with more deaths correspond to the higher risk score.



Number at risk					
High Risk	241	15	2	2	0
Low Risk	242	20	4	1	0

Figure 4.9: Survival curves showed the overall for the low-risk and high-risk groups in LUAD patients.

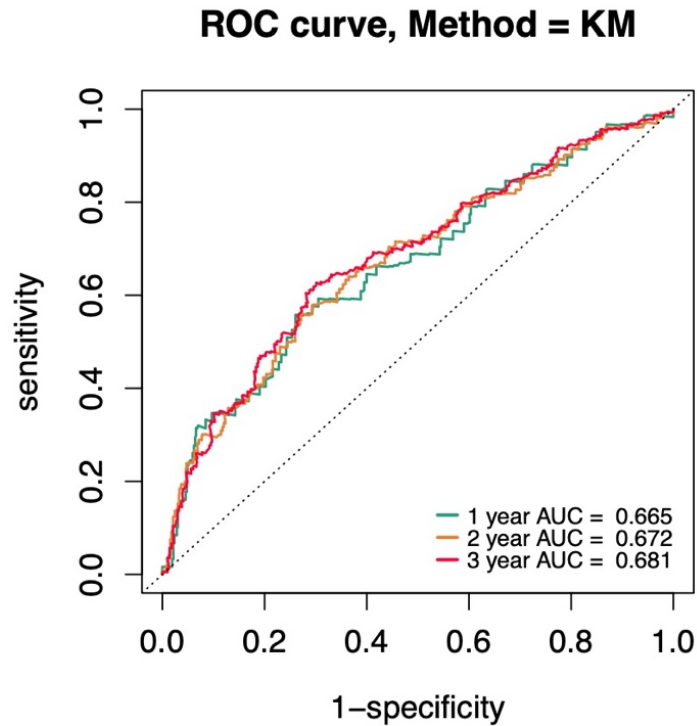


Figure 4.10: ROC curve showed the 1 - , 2 - and 3 - year overall survival of LUAD patients.

Using the Kaplan – Meier (KM) method to derive survival probabilities as the predictive metric. The curves represent the performance of the model of risk score in distinguishing 1-year (AUC = 0.665), 2 – year (AUC = 0.672), and 3 – year (AUC = 0.681) overall survival. The diagonal dashed line represents the reference for random prediction (AUC = 0.5).

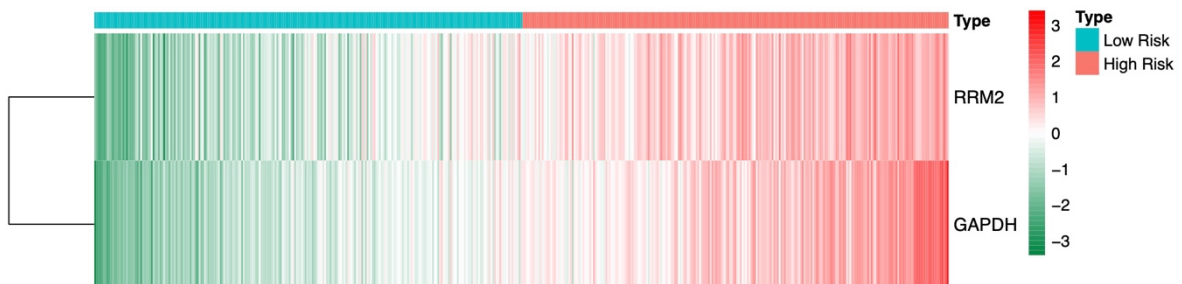


Figure 4.11: Heatmap of the two methylated DE-DDRGs expression in LUAD patients, with red indicating higher expression and green indicates lower expression.

4.4 RRM2 and GAPDH more accurately predict survival in LUAD patients

The expression profiles of prognostic genes in GSE31210 dataset were also extracted, and risk scores were calculated for each LUAD sample according using the same formula. Based on the median value of risk core (4138.758, 226), LUAD samples were divided into high- and low-risk groups containing 113 samples each. Information on survival time, survival status, risk score, and grouping of LUAD patients in the independent external validation set was available in **Appendix C12**. Similarly, risk curves and scatter plots were applied to illustrate the correlation between risk scores and survival status in LUAD patients. The results suggested that the occurrence of LUAD mortality depended on the risk score in an independent external validation set (**Figure 4.12**). K-M survival curves demonstrated that patients in the low-risk group had significantly better OS than the high-risk group ($P < 0.001$; **Figure 4.13**), indicating the prognostic value of the 2-gene based risk score. Subsequently, the ROC curve demonstrated the strong reliability of the risk score in predicting OS in patients with LUAD, with an AUC of 0.814 for predicting 1-year OS, 0.810 for 2-year OS, and 0.730 for 3-year OS in patients (**Figure 4.14**). The expression heat map of 2 methylated DE-DDRGs in LUAD showed that both RRM2 and GAPDH were highly expressed in the high-risk group (**Figure 4.15**).

Additionally, the GSE68465 validation set was used to further validate the prognostic model (**Figure 4.16**). The survival rate of the high-risk group was significantly lower than that of the low-risk group. The ROC curve AUCs for the 1-, 2-, and 3-year time points were all greater than 0.6. A heatmap of the expression of the two methylated DE-DDRGs in LUAD revealed that both RRM2 and GAPDH were highly expressed in the high-risk group. Independent external validation demonstrated that these two genetic markers were effective in predicting the OS of patients with LUAD.

Independent external validation demonstrated that the two genetic markers were effective in predicting the overall survival of LUAD patients. RRM2 gene encodes the catalytic subunit of the ribonucleotide reductase complex and is up-regulated in response to DNA damage for ensuring adequate deoxynucleoside triphosphate levels required for DNA repair (G. Chen et al., 2019; Zhang et al., 2009). The overexpression of RRM2 has been shown to enhance cell transformation, cancer cell proliferation, and progression (Fan et al., 1998; Fan et al., 1996; Morikawa, Hino, et al., 2010). The high expression of RRM2 may enhance immunotherapy sensitivity (Zijian Zhou et al., 2022). Numerous studies have reported RRM2 overexpression corrected with poor survival and identified it as a potential prognostic biomarker in various tumor types, including bladder cancer (Morikawa, Maeda, et al., 2010; Zijian Zhou et al., 2022), colorectal cancer (Liu et al., 2013), cervical cancer (Wang et al., 2020), NSCLC (Hsu et al., 2011; Chao Ma et al., 2020; Souglakos et al., 2008), breast cancer (Abdel-Rahman et al., 2022; Shi et al., 2022) and hepatocellular cancer (Qin et al., 2023). Elevated RRM2 may directly foster an immunosuppressive microenvironment by increasing tumor mutational burden, promoting recruitment of immunosuppressive cells and correcting correlation with PD-L1 upregulation LUAD (Abuduhailili et al., 2025).

GAPDH encodes a glycolytic enzyme and interacts with various proteins involved in DNA repair to regulate cell death and carcinogenesis (Colell et al., 2009; Kosova et al., 2017; Pacchiana et al., 2022; Zhang et al., 2015). GAPDH overexpression has been associated with poorer prognosis in various solid tumors, including colorectal cancer (CRC) (Tarrado-Castellarnau et al., 2017) and NSCLC (Puzone et al., 2013; Wang et al., 2013). Based on the critical roles of RRM2 and GAPDH in regulating DNA repair and cell survival, their transcription and translation must be tightly regulated through epigenetic, transcriptional, post-transcriptional modifications. It was identified in the findings that

RRM2 and GAPDH as one of the many hypomethylated and up-regulated genes in LUAD. It was speculated that the hypomethylation of RRM2 and GAPDH results in the upregulation of gene expression in LUAD, which leads to an increased aggressiveness and drug resistance of the RRM2-overexpressed or GAPDH-overexpressed tumor and poor prognosis of these patients.

The consistent overexpression of these two genes in high-risk patients is biologically significant. The combination of these two genes in the signature effectively captures key hallmarks of cancer: dysregulated proliferation (RRM2) and altered cellular metabolism with non-canonical oncogenic functions (GAPDH).

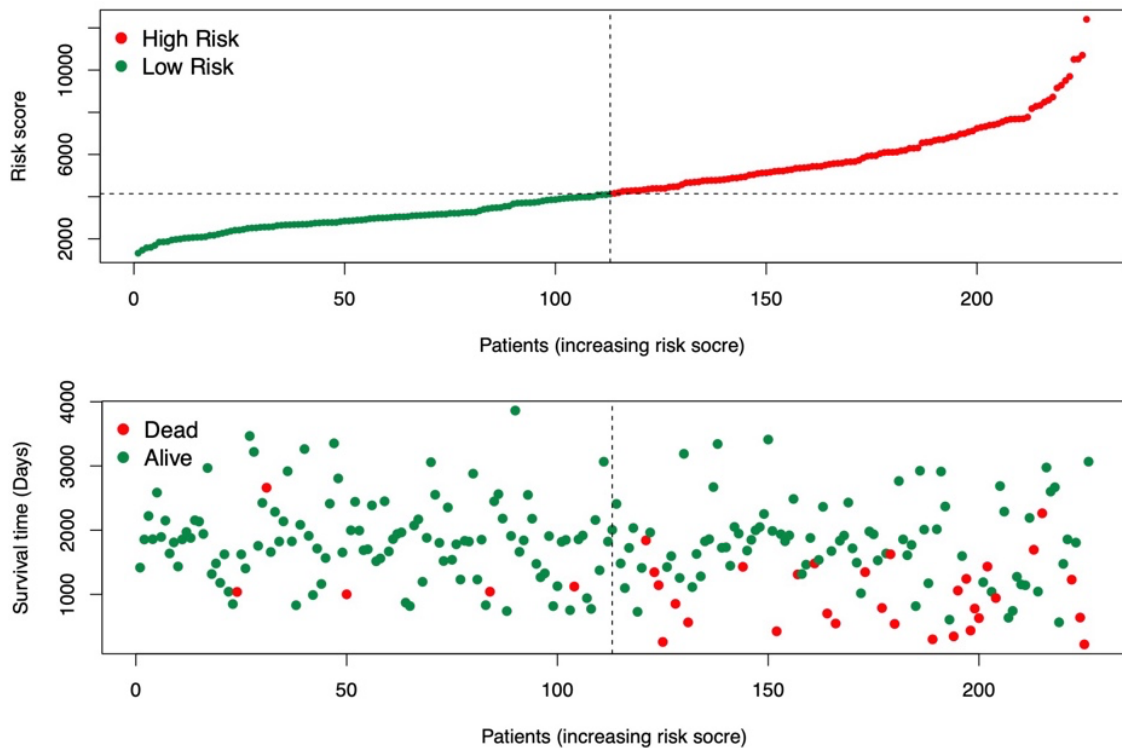


Figure 4.12: The risk curve was plotted based on the risk score of LUAD patients (above) and their survival distribution (bottom).

The risk curve depicted the risk score of LUAD patients. Green and red represent patients with low- and high-risk, respectively. The scatter plot was based on the survival status of each sample. The green and red dots represent survival and death, respectively.

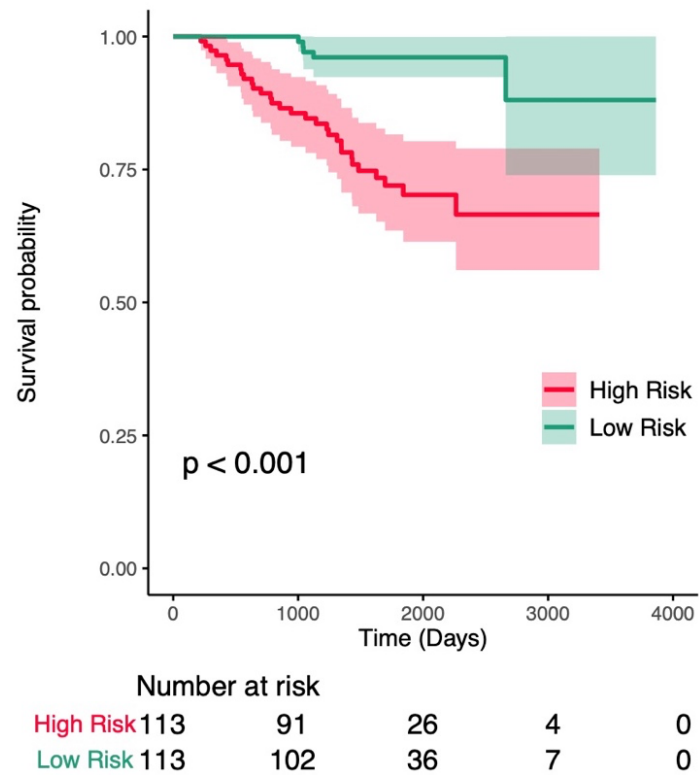


Figure 4.13: Survival curves showed the overall survival (OS) of low- and high-risk patients in the GSE31210 cohort.

Kaplan-Meier (KM) plot for overall survival (OS) based on risk score of the two gene-based signature of patients with LUAD in the GSE31210 cohort.

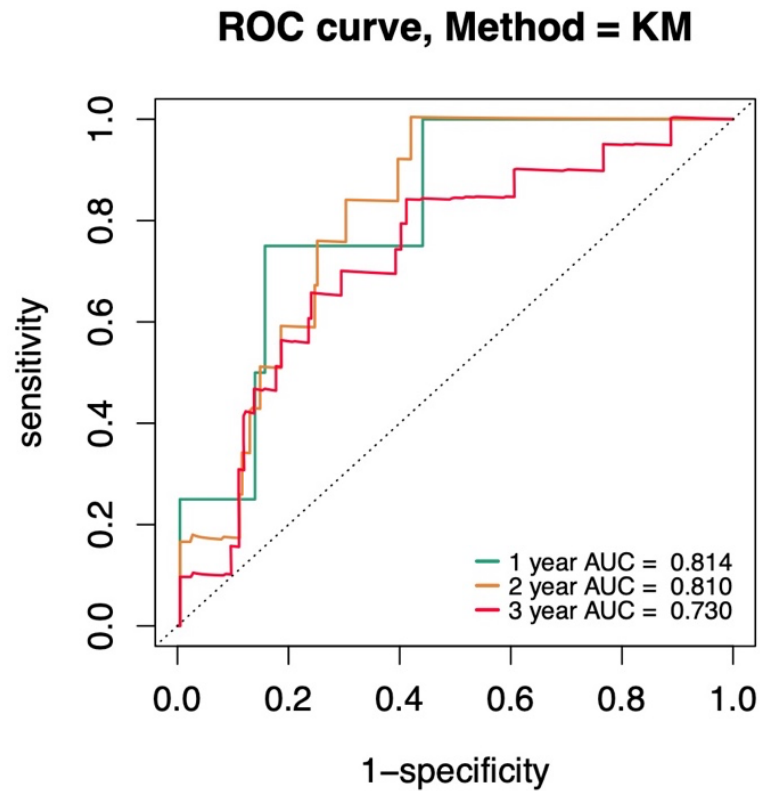


Figure 4.14: ROC curve showed the 1-, 2- and 3-year overall survival of LUAD patients in the GSE31210 cohort.

Using the Kaplan – Meier (KM) method to derive survival probabilities as the predictive metric. The curves represent the performance of the model of risk score in distinguishing 1-year (AUC = 0.814), 2 – year (AUC = 0.810), and 3 – year (AUC = 0.730) overall survival. The diagonal dashed line represents the reference for random prediction (AUC = 0.5).

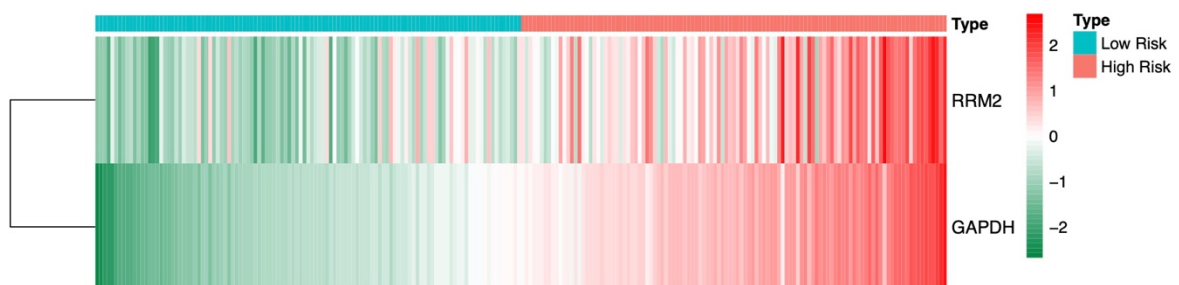


Figure 4.15: Heatmap displayed the expression levels of methylated DE-DDRGs in the high—and low- risk groups.

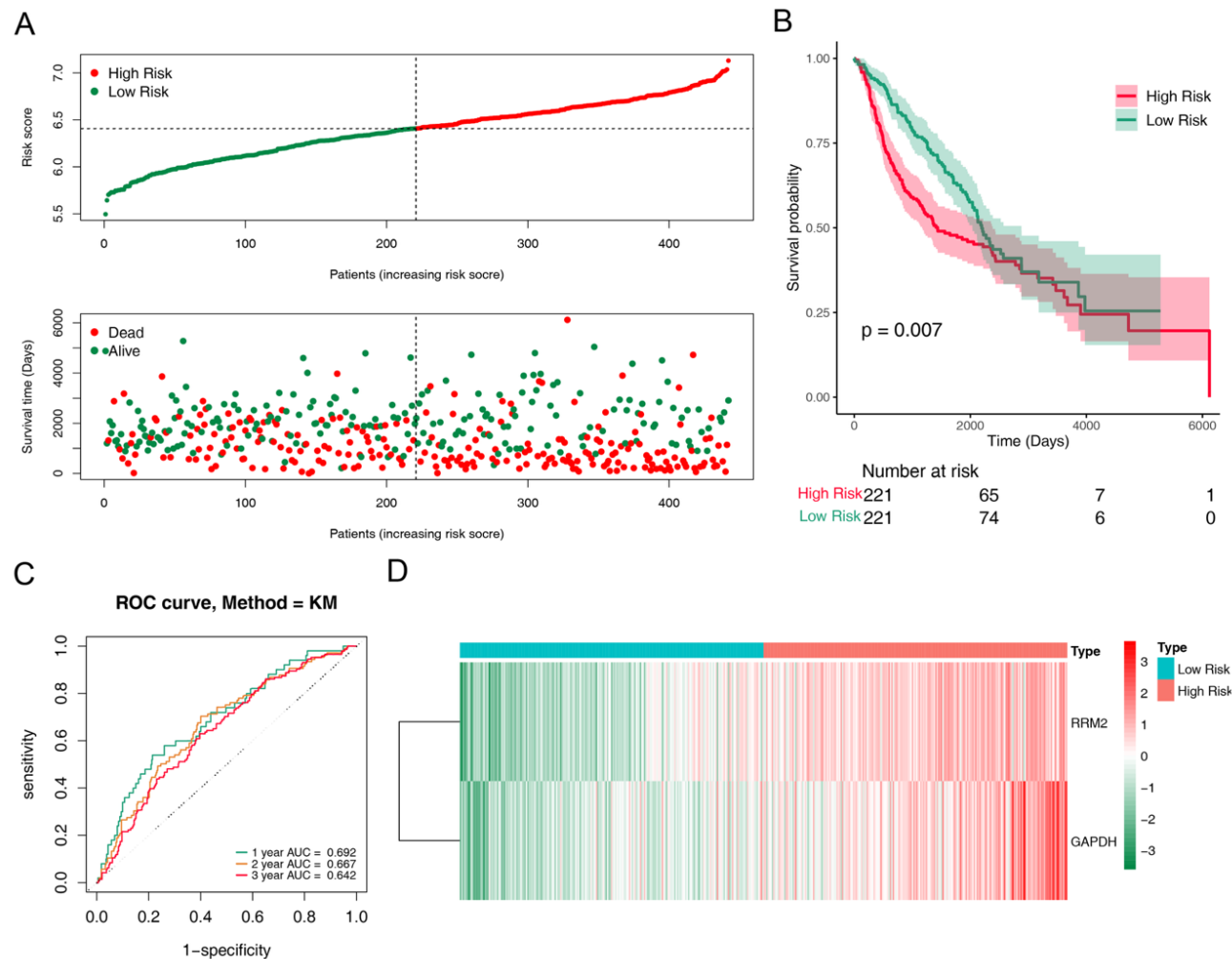


Figure 4.16: A compilation of plots using validation of prognostic prediction model based on two methylated DE-DDRGs's expression in the independent external validation cohort GSE68465 (n=442).

A) The risk curve was based on the risk score of each sample. Green and red represent patients with low- and high-risk, respectively. The scatter plot was based on the survival status of each sample. The green and red dots represent survival and death, respectively. B) Kaplan-Meier (KM) plot for overall survival (OS) based on risk score of the two gene-based signature of patients with LUAD in the GSE68465 cohort. C) ROC curve for 1-, 2- and 3-year overall survival. D) The heatmap displayed the expression levels of methylated DE-DDRGs in the high-risk and low-risk groups.

4.5 Nomograms constructed based on pathologic stage and risk score accurately predict LUAD survival

The independent prognostic value of the risk score was evaluated, revealing significant associations with clinical factors. As shown in **Figure 4.17**, clinical factors including pathologic stage (HR = 1.630, 95% CI = 1.418-1.873, $P < 0.001$), pathologic T (HR = 1.522, 95% CI = 1.287 -1.801, $P < 0.001$), and pathologic N (HR = 1.393, 95% CI = 1.221-1.588, $P < 0.001$) were significantly associated with survival in LUAD patients. Notably, the risk scores demonstrated the strongest univariate association with outcome (HR = 2.718, 95% CI = 1.875 -3.941, $P < 0.001$), suggesting its potent prognostic power. In multivariate Cox of clinical parameters analysis, forest plots showed that risk score (HR = 2.162, 95% CI = 1.486-3.145, $P < 0.001$) and pathologic stage (HR = 1.411, 95% CI = 1.170-1.702, $P < 0.001$) were the independent factors associated with OS in patients (**Figure 4.18**). Next, a nomogram model predicting 1-, 2-, and 3-year overall survival was developed using the TCGA-LUAD dataset based on the identified independent prognostic factors (**Figure 4.19**). The model had a C-index of 0.698. Also, the calibration curve showed the accurate predictive efficacy of the nomogram. (**Figure 4.20**).

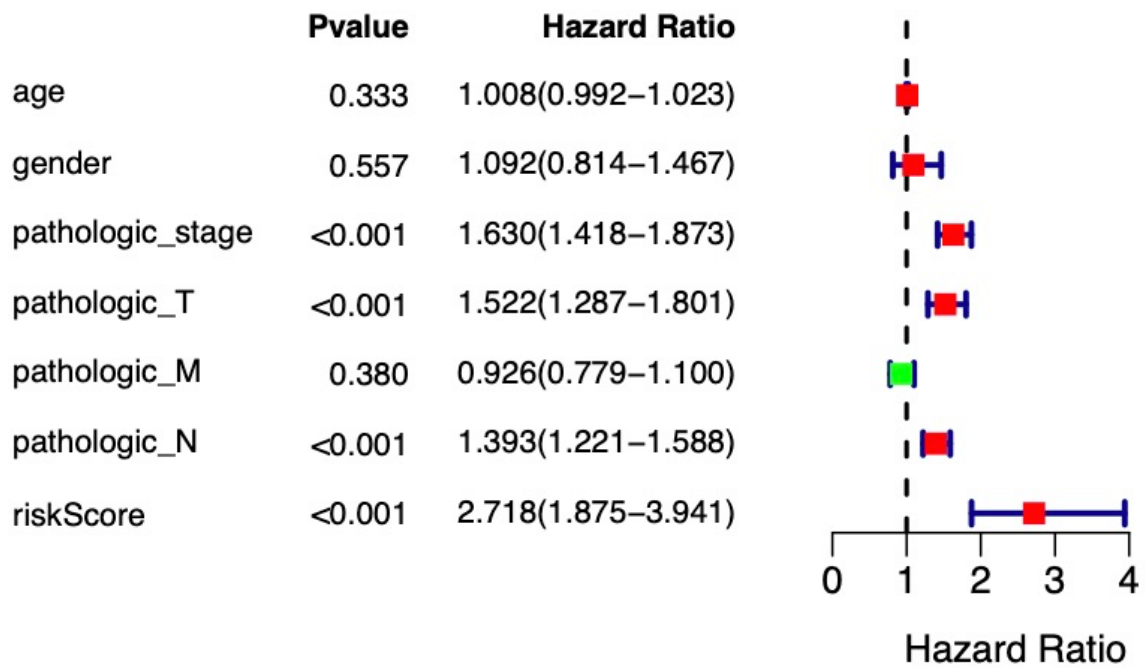


Figure 4.17: Forest plot of risk scores and other clinical factors based on a univariable Cox regression analysis.

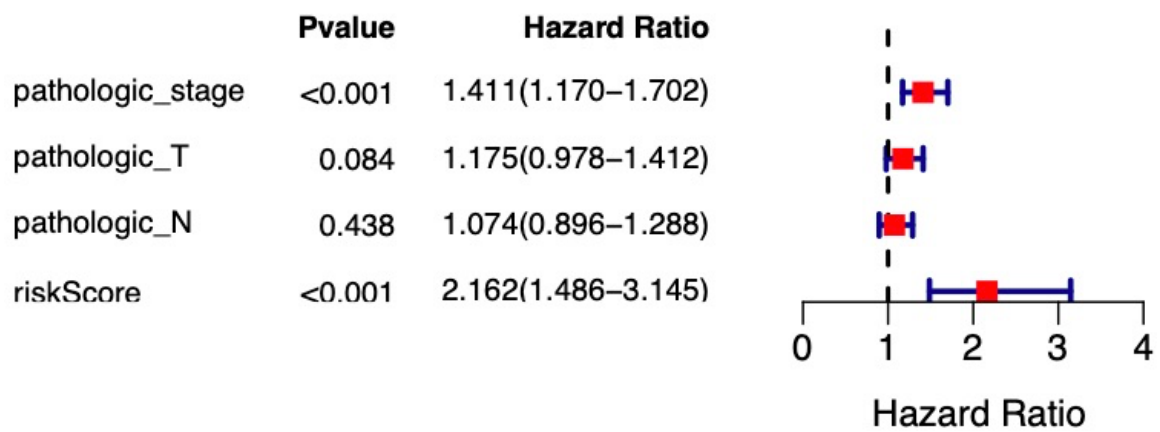


Figure 4.18: Forest plot of risk scores and other clinical factors based on multivariate Cox regression analysis

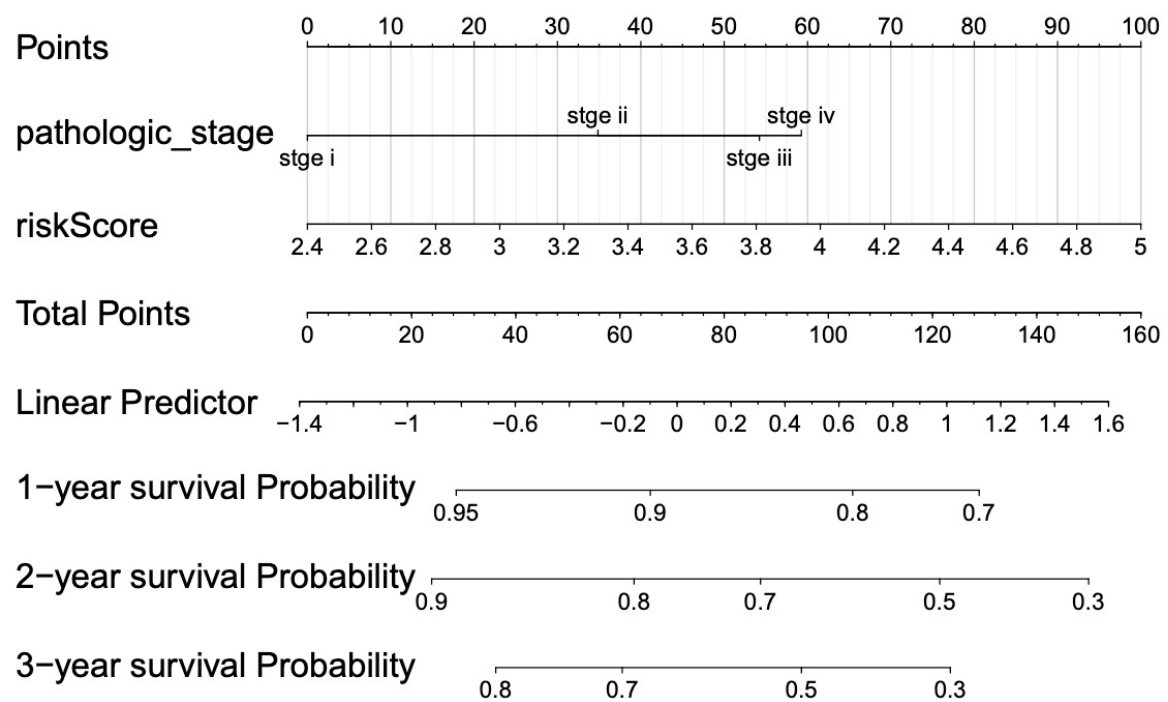


Figure 4.19: A nomogram consisting of risk score and other clinical indicators for predicting 1-, 2-, and 3-year OS of LUAD.

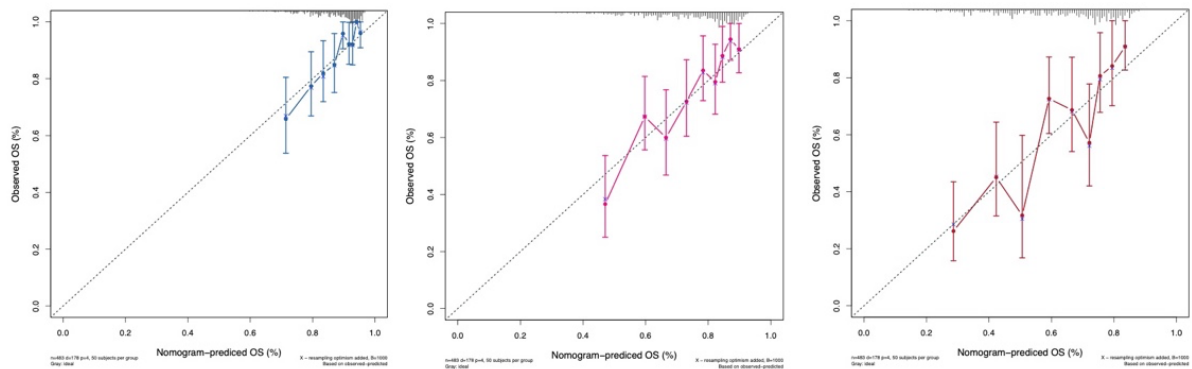


Figure 4.20: Calibration maps showed the prediction and actual survival rates for 1-, 2-, and 3-year in TCGA-LUAD cohorts.

Calibration maps were used to predict the 1-, 2-, 3-year in TCGA-LUAD cohort. The x-axis and y-axis represent the predicted and actual survival rates of the nomogram, respectively. The solid line represents the predicted nomogram, and the vertical line represents the 95% confidence interval.

The nomogram, which considers both the risk prediction model and pathological stage, was also established to predict the survival of patients. To the best of current knowledge, the prognostic model is the first prognostic model constructed in LUAD based on methylated DE-DDRGs. The core finding that underscores the nomogram's value is the demonstration that the two-gene risk score is not only prognostic but is also an independent predictor of survival. With the hazard ratio of 2.162, the risk score signifies that patients classified as high-risk face a greater than twofold increased risk of mortality compared to low-risk patients, even after adjusting for the significant influence of pathologic stage. This effect size is both statistically robust and clinically substantial, suggesting that is not fully accounted for traditional staging alone.

4.6 Lower immune cell abundance and immune scores were associated with poorer OS in LUAD patients

Tumor progression and prognosis have been confirmed to receive the influence of the tumor microenvironment (Liu et al., 2018; Miranda et al., 2019). In this study, significant differences were observed in immune scores, stromal scores, and ESTIMATE scores between high- and low-risk groups ($P < 0.05$), meaning that all these scores were higher in the low-risk group (**Figure 4.21**), suggesting both greater immune infiltration and more active stromal involvement. These findings indicate that the favourable active tumor microenvironment capable of mounting an effective anti-tumor response. The high-risk group suggests an exhausted immune phenotype.

To further investigate whether the 2-methylated DE-DDRGs prognostic signature could reflect the level of immune cells, the abundance of various immune cells in the tumor microenvironment was clarified by ssGSEA (**Figure 4.22**). A comparison of immune cell abundance between the low- and high-risk groups was then performed, as shown in **Figure**

4.23, with a total of 16 differentially distributed immune cells between the two groups. Specifically, in the low-risk group, only NK CD56^{dim} cells and Th2 cells were significantly reduced, whereas B cells, CD8 T cells, DCs, Eosinophils, iDCs, Macrophages, Mast cells, NK CD56^{bright} cells, NK cells, T cells, Tcm, Tem, TFH, and Th17 cells were increased ($P < 0.05$). The above evidence indicated that risk scores appeared to be negatively correlated with immune cells, implying that lower immune cell abundance and immune scores (and also stromal scores and ESTIMATE scores) were associated with poor OS in LUAD patients. This immune profile suggests a coordinated antitumor response in the low-risk group, characterized by robust antigen presentation, cytotoxic activity, and immune memory formation.

Elevated RRM2 may directly foster an immunosuppressive microenvironment by increasing tumor mutational burden, promoting recruitment of immunosuppressive cells (Z. Zhou et al., 2022) and correlating with PD-L1 upregulation LUAD (Abuduhailili et al., 2025; Li et al., 2018). GAPDH-mediated glycolytic metabolism in tumor cells depletes glucose and acidifies the tumor microenvironment through lactate production, thereby starving and functionally impairing cytotoxic T-cells and other immune effectors (Chang et al., 2015). The negative correlation between the risk score and immune activation provides mechanistic insight into the poorer outcomes observed in the high-risk group, suggesting an immunologically suppressed state in these patients. This observation demonstrates the potential clinical utility of the signature not only for prognostic stratification but also for predicting response to immunotherapeutic interventions.

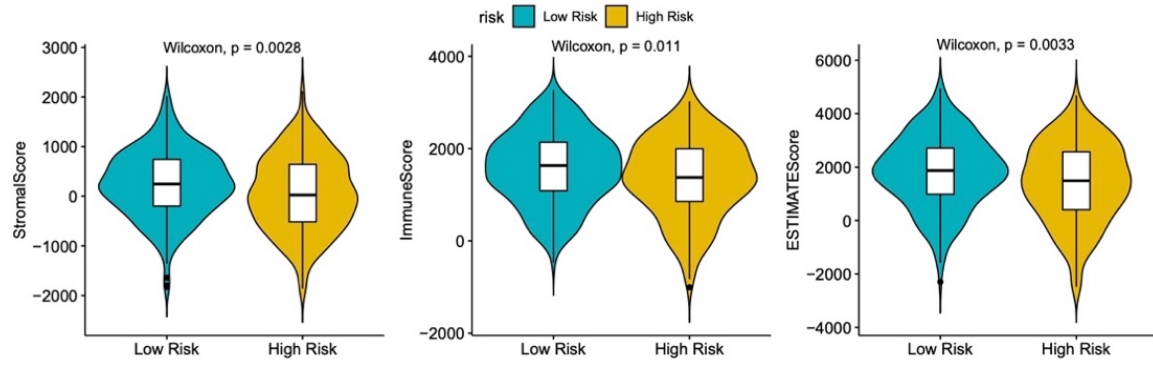


Figure 4.21: Box diagram demonstrating the stromal scores (left), immune scores (middle), and ESTIMATE scores (right) in the high- and low-risk groups.

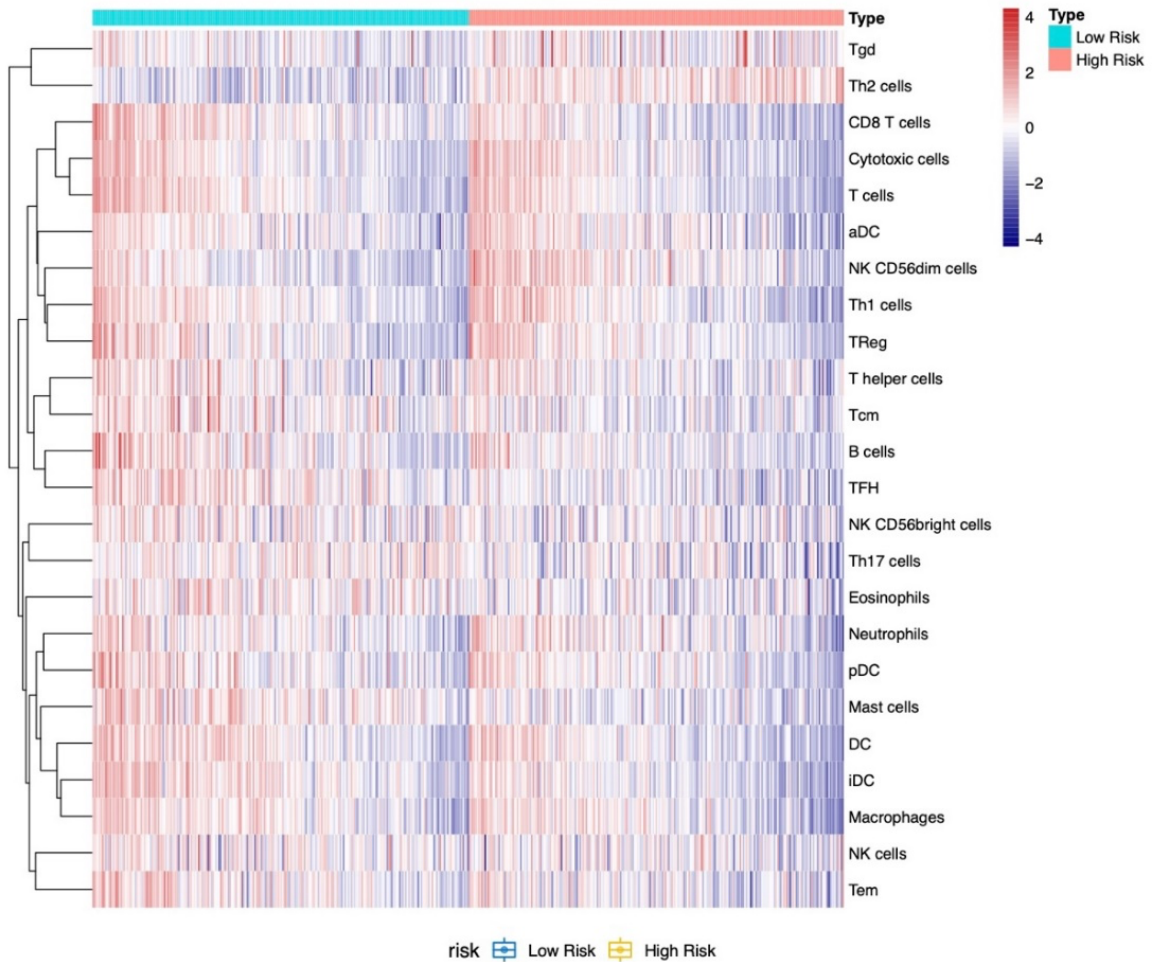


Figure 4.22: Heatmap showing the infiltration of immune cells between the high- and low-risk groups calculated by ssGSEA.

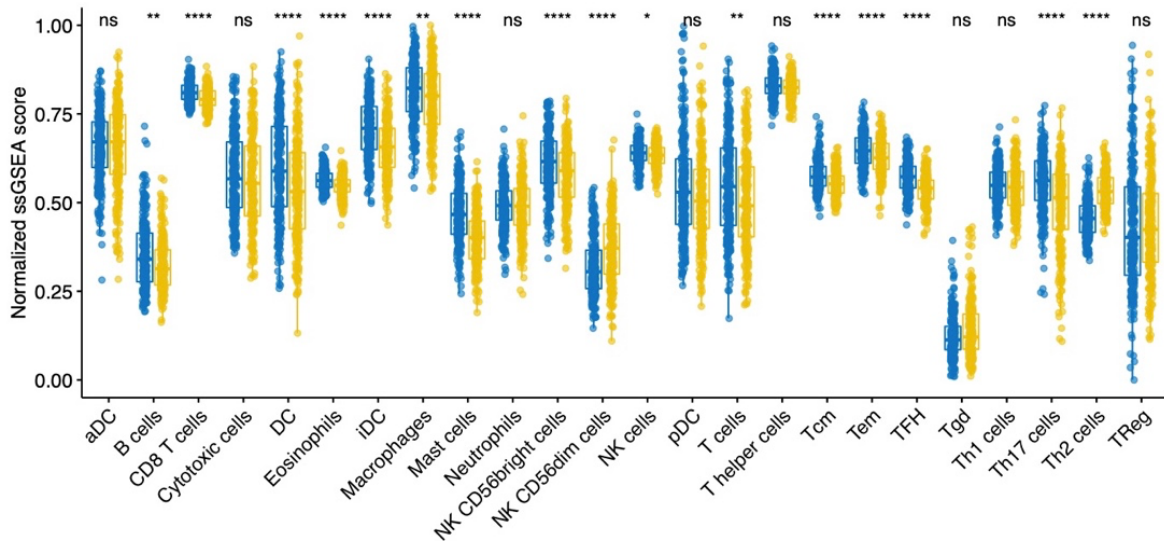


Figure 4.23: Comparisons of normalized ssGSEA score (NES) of immune cells between the low-risk and high-risk group, 14 immune cells showed higher NES in the low-risk group ($P < 0.05$).

4.7 Patients in the low-risk group may benefit from immunotherapy

Based on previous results, a correlation between the risk score and immune markers, especially the well-known immune checkpoints, was hypothesized. To test this, the expression levels of immune checkpoint molecules were compared between high- and low-risk groups. CD27 was highly expressed in the low-risk group, while PDCD1LG2, PDCD1 (PD1), LAG3, and CD274 (PD-L1) were all highly expressed in the high-risk group ($P < 0.05$; **Figure 4.24**). Besides, the prediction scores of immunotherapy markers (anti-PD1 and anti-CTLA4) were calculated by the TIDE algorithm for the high- and low-risk groups. As shown in **Figure 4.25**, the high-risk group showed higher TIDE scores. Consistently, subclass mapping analysis revealed that the high-risk group did not respond to anti-CTLA4 treatment (**Figure 4.26**). Furthermore, the low-risk group showed more patients who responded to immune checkpoint inhibitor therapy (**Figure 4.27**). Consequently, it was

assumed that LUAD patients in the low-risk group were probably more sensitive to immune checkpoint inhibitor therapy.

Immune checkpoint inhibitors (ICIs) have become the standard of care for NSCLC. However, not all patients can benefit from these agents as a result of complex and constantly evolving interactions between cancer cells and immune system. There have been many previous studies that incorporated biomarkers (Li et al., 2022; Shiravand et al., 2022; Wang et al., 2022). A recent review state the function and molecular mechanism of DDR in immunity and cancer immunotherapy, which showed the mRNA levels of many DDR factors were negatively associated with cytotoxic CD8⁺ T cells infiltration levels across various cancer types (Ye et al., 2021).

Several studies have shown the alteration of DDR pathway genes implicate the response of immune checkpoint inhibitors across various cancer types, including MMR status (Le et al., 2017; Le et al., 2015), deleterious DDR mutations in NSCLC (Lau et al., 2022; B. Ricciuti et al., 2020; Rizvi et al., 2015), 4 DDR genes (MRE11A, MSH2, ATM, and POLE) in CRC and bladder cancer (Zhang et al., 2021) , ERCC1-SNP status in NSCLC (Aiello et al., 2020). The findings also demonstrated that the high-risk patients with LUAD exhibit a distinct immune checkpoint profile, and potential altered responses of ICI therapy. Conversely, the low-risk group shows great sensitivity to ICIs.

Consequently, integrating biomarkers into immunotherapy can improve treatment outcome. Specifically, the expression levels of RRMA2 and GAPDH may predict patient response to ICIs, enabling the identification of candidates for immunotherapy. Moreover, monitoring the dynamic changes in these biomarkers could help assess potential risks and adverse reactions, allowing for tailored treatment strategies and personalized care plan.

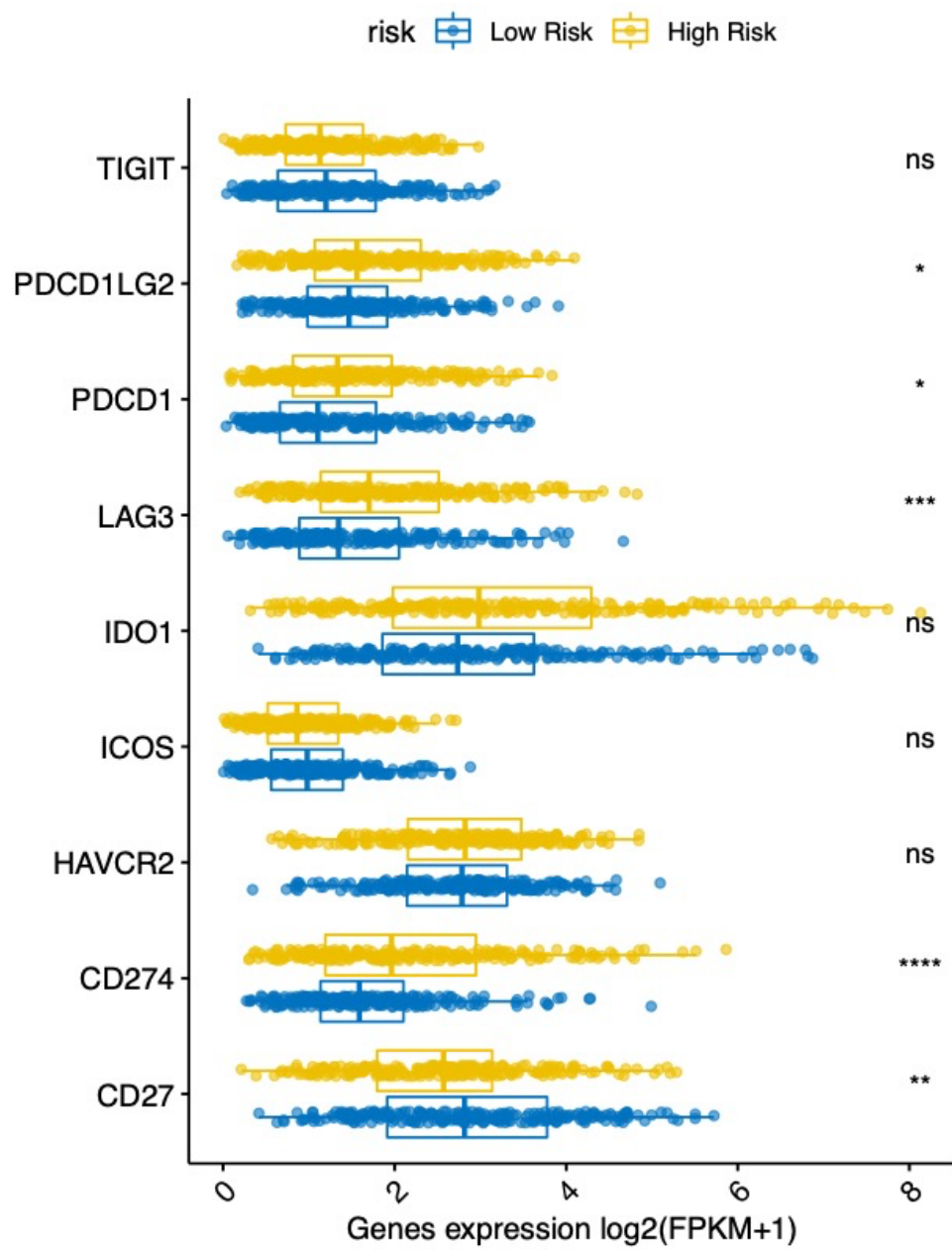


Figure 4.24: Gene expression of immune checkpoint molecules of between high- and low-risk groups in TCGA-LUAD cohort

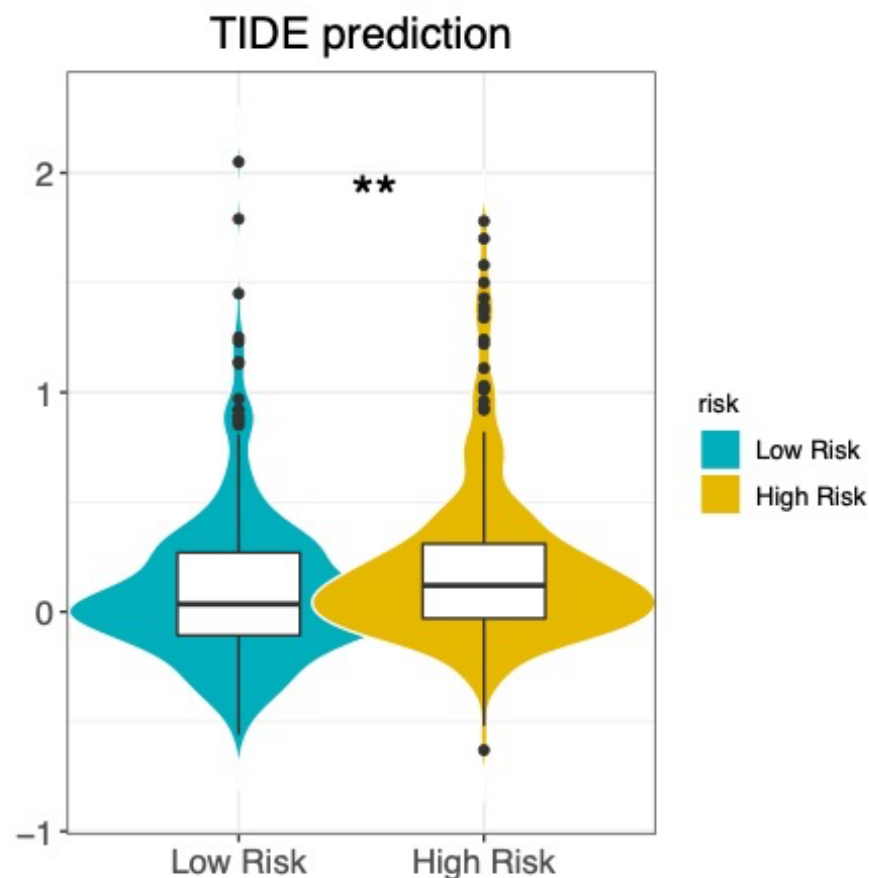


Figure 4.25: TIDE scores of the high- and low-risk groups using samples from the TCGA dataset.

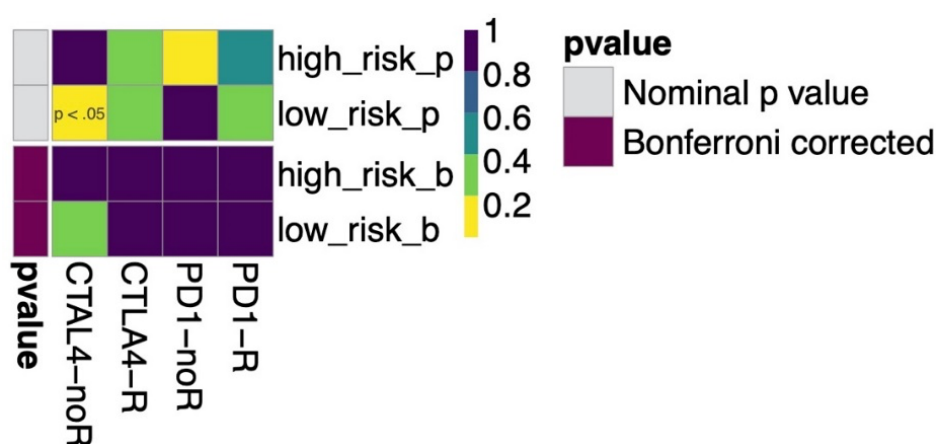


Figure 4.26: Immunotherapy responses between the high- and low-risk groups in the TCGA dataset.

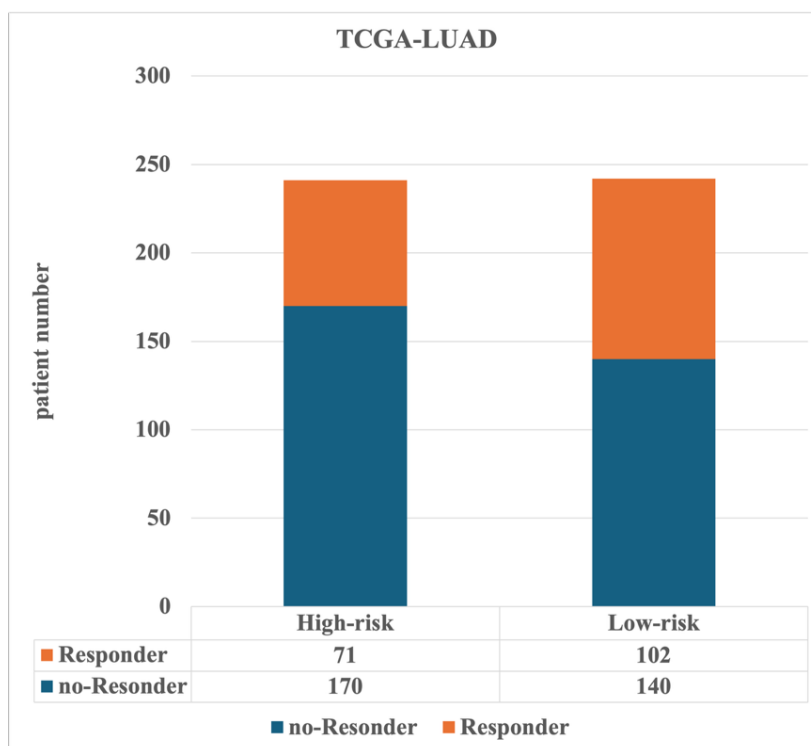


Figure 4.27: The proportion of patients who responded to immunotherapy in the high- and low-risk groups in the TCGA.

4.8 RRM2 and GAPDH were dramatically overexpressed in lung cancer cell lines

Gene expression analysis across the training and validation sets confirmed a significant upregulation of RRM2 and GAPDH in the disease group, following the same expression trend (**Figure 28**).

Furthermore, mRNA expression of RRM2 and GAPDH was assessed in three lung cancer cell lines (A549, NCI-H1395, and NCI-H1975) and the corresponding normal lung epithelial cells (BEAS-2B) by RT-PCR to confirm the role of prognostic genes in LUAD. The inclusion of these distinct molecular subtypes allows for the assessment of whether the role of RRM2 and GAPDH is generalizable across different LUAD oncogenic drivers or is specific to certain genetic backgrounds. As shown in **Figure 4.29**, the expression of RRM2 and GAPDH were significantly upregulated in lung cancer cell lines compared with the control (BEAS-2B) (both $P < 0.05$). This result was also concordant with the TCGA database,

which indicated higher RRM2 and GAPDH expression in LUAD samples than in normal tissues (**Appendix C5**). The consistent overexpression pattern observed across both experimental models and clinical datasets provides compelling evidence supporting the potential oncogenic roles of RRM2 and GAPDH in LUAD pathogenesis.

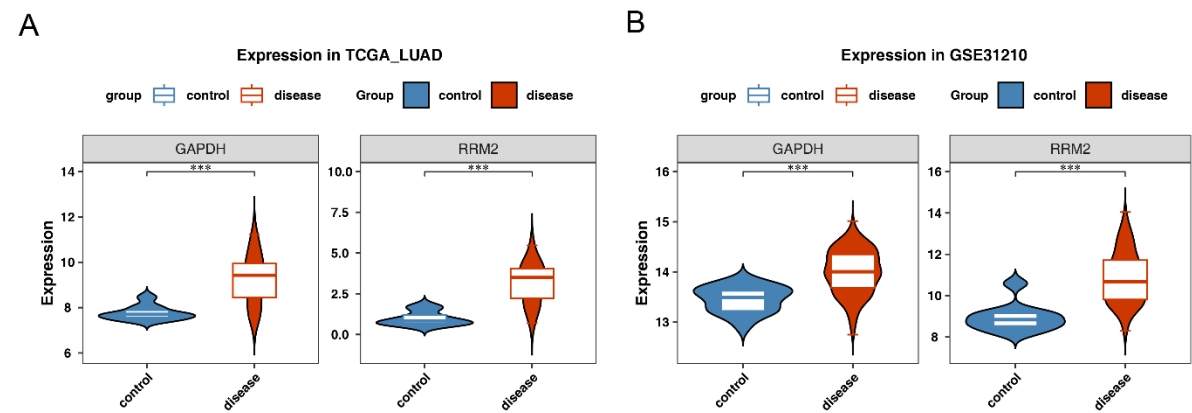


Figure 4.28: Validation of expression levels of RRM2 and GAPDH in different datasets. A. TCGA_LUAD dataset. B. GSE31210 dataset.

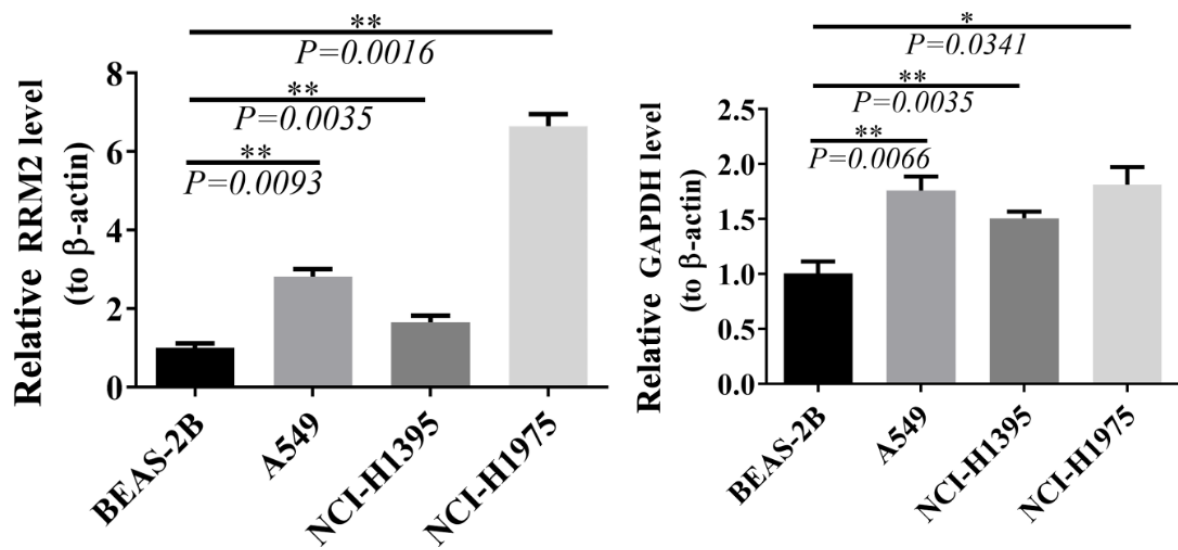


Figure 4.29: Histogram depicted the mRNA expression of RRM2 and GAPDH in 3 lung cancer cell lines in comparison with normal lung cell line.

The mRNA expression of RRM2 and GAPDH in three lung cancer cell lines (A549, NCI-H1395, and NCI-H1975) and the corresponding normal lung epithelial cells (BEAS-2B) by RT-PCR.; *, $P<0.05$; **, $P<0.01$; ***, $P<0.001$; ****, $P<0.0001$.

4.9 Discussion

This study provides a comprehensive analysis of the epigenetic regulation of DDR pathways in LUAD. Through integrated bioinformatics, nine methylated DE-DDRGs were discovered. The key finding is establishment of a novel, robust two-gene prognostic signature comprising RRM2 and GAPDH. Derived from the signature, the risk score proved to be powerful and independent predictor of overall survival in the training cohort (TCGA-LUAD) and two independent datasets (GSE31210 and GSE68465). Furthermore, the analysis revealed that the high-risk group was characterized by a significantly immunosuppressive tumor microenvironment (TME), which associated with a poorer predicted response to immunotherapy.

The study successfully establishes a critical link between the epigenetic regulation of DDR genes and the pathogenesis of LUAD. The promoter hypomethylation of specific

DDR genes, notably RRM2 and GAPDH, drives their overexpression, fostering a more aggressive tumor phenotype characterized by rapid proliferation, genomic instability, and the creation of an TME. This mechanism provides a unifying explanation for the poor prognosis observed in high-risk patients, connecting epigenetic dysregulation directly to immune evasion. The robust validation across the independent cohorts underscores that this is not a mere statistical association but a fundamental biological pathway with major clinical implications.

The oncogenic roles of RRM2 and GAPDH have been individually documented in various cancers. For instance, prior studies have consistently showed that RRM2 overexpression promotes tumor progression and chemoresistance across cancer types (Li et al., 2018; Morikawa, Hino, et al., 2010; Morikawa, Maeda, et al., 2010), while GAPDH's role beyond glycolysis in inhibiting apoptosis is also known (Colell et al., 2009). This research consolidates these findings specifically in LUAD.

While previous studies focused on genetic alterations or transcriptional upregulation of DDR genes, this study demonstrate that their expression is strongly associated with promoter hypomethylation, introducing a reversible epigenetic mechanism as a key regulator. Most importantly, the study discovers that high expression of RRM2 and GAPDH correlates with a “cold” TME offers a mechanistic explanation for immunotherapy resistance in this subset of patients, a area less explored in previous studies focused solely on proliferation.

Despite the compelling evidence, this study had several limitations that must be acknowledged, including a small initial discovery cohort (n=18 paired samples), a reliance on in silico analysis, a lack of data on smoking status, and the absence of web-lab experimental validation. These limitations also serve as directions for future investigation.

CHAPTER 5

CONCLUSION AND RECOMMENDATION

5.1 Conclusion

Bioinformatics methods have made significant strides in the study of lung cancer and related diseases. Whole-genome sequencing of patients with lung cancer has unveiled multiple driver mutations and novel biomarkers, providing a foundation for early diagnosis and targeted therapies (Dang et al., 2021). Transcriptomic analyses, exploring gene expression changes in lung cancer cells, have proven valuable in offering important prognostic information for clinical applications (Tran et al., 2023). With an increasingly sophisticated understanding of the tumor microenvironment, bioinformatics enables the analysis of immune cell infiltration characteristics and its correlation with patient prognosis.

This study leveraged bioinformatics techniques, utilizing transcriptomic and methylomic data with the paired normal and tumor tissue samples from the TCGA-LUAD cohort. The study systematically identified a panel of genes aberrantly methylated and differentially expressed in LUAD, culminating in the discovery of nine methylated DE-DDRGs. The central finding is the establishment of a novel, robust two-gene prognostic signature comprising RRM2 and GAPDH.

Subsequently, the study focused on the two DNA damage repair-related genes, RRM2 and GAPDH, were found to be hypomethylated and overexpressed, correlating with poor prognosis. Univariate and multivariate analyses confirmed the prognostic significance of these genes in TCGA-LUAD dataset. Furthermore, a risk prediction model based on the two methylated DE-DDRGs was developed and validated using two independent LUAD cohorts, demonstrating that high-risk patients consistently exhibited poorer prognoses. The

result confirm its generalizability across diverse patient populations and aligning with the critical need for reproducible biomarkers in oncology (Sams-Dodd, 2013) . Both univariate and multivariate analyses identified pathological stage and risk score from the prediction model as independent prognostic factors. A nomogram, incorporating both the risk prediction model and pathological stage, was constructed to predict patient survival. Notably, this prognostic model represents the first of its kind for LUAD based on methylated DE-DDRGs.

Beyond predicting survival, the analysis reveals the mechanistic underpinnings of the signature. A model whereby RRM2 and GAPDH overexpression drives tumor progression through dual pathways: RRM1 by fuelling DNA synthesis and repair to promote proliferation and genomic instability, and GAPDH by enhancing glycolytic flux to support biomass production and inhibit apoptosis. The study revealed that the high risk group, characterized by high RRM2 and GAPDH expression, is associated with a suppressed immune landscape; lower immune scores, reduced cytotoxic immune cell infiltration, and elevated expression of immune checkpoint inhibitors like PD-L1 and PD-1. This suggests a state of immune evasion, rendering the tumor “cold” and likely resistant to innate immune surveillance (Binnewies et al., 2018). This mechanistic insight is further supported by TIDE analysis prediction that the low-risk group may be more responsive to ICI therapy provides a crucial potential clinical application, suggesting that RRM2 and GAPDH signature could serve as a biomarker for predicting immunotherapy response.

The translational relevance of these findings is underscored by experimental validation. The consistent upregulation of RRM2 and GAPDH in these three distinct LUAD cell lines, representing key oncogenic drivers, confirms that their overexpression is a fundamental and generalizable feature of LUAD biology. This is consistent with the known

role of RRM2 in promoting proliferation and chemoresistance in KRAS-mutant cancers (Morikawa, Hino, et al., 2010) and the role of GAPDH in inhibiting apoptosis and supporting tumor metabolism (Colell et al., 2009).

5.2 Recommendation

This study identified RRM2 and GAPDH as potential biomarkers for LUAD. However, despite offering significant insights, several limitations should be noted.

- i. First, The initial discovery of aberrantly methylated DE-DDRGs relied on only 18 paired LUAD-normal samples, which may reduce the statistical robustness and generalizability of the epigenetic findings. While validated in larger cohorts, future studies should expand the paired epigenomic analysis to enhance reliability.
- ii. Second, some confounding factors - such as patient age, gender, comorbidities, lifestyle factors, and smoking status - were not fully accounted for in the analysis. To address these limitations, future studies should include larger datasets to enhance the generalizability of the findings and better control for confounding variables.
- iii. Additionally, the model was built and validated with publicly available datasets (TCGA and GSE). RT-PCR was employed to validate the expression of RRM2 and GAPDH at the cellular level, with results consistent with bioinformatics analysis, reinforcing their potential as prognostic biomarkers. However, it lacks external experimental validation weaken the mechanistic claims about methylation's role in gene regulation.

- iv. Furthermore, the clinical relevance of the identified biomarker (RRM2 and GAPDH) such as prognostic survival, predictive immunotherapy relied solely on in silico algorithms (TIDE, SubMap). While these tools are widely used, they remain hypothesis-generating and require validation in prospective clinical trials.

To address these limitations and build upon these findings, the following future directions are critically recommended to confirm its biological and translational significance:

- i. Future studies should prioritize prospective validation of RRM2/GAPDH signature in independent cohorts of ICT treated LUAD patients to definitively establish its predictive utility for immunotherapy response.
- ii. Although the analysis revealed a significant negative correlation between the methylation and expression of RRM2 and GAPDH, this observational evidence does not establish a direct causal relationship. A key experiment would involve treating LUAD cell lines with DNA methyltransferase inhibitors (DNMTis) to assess consequent changes in gene expression. The results of such experiments would powerfully demonstrate a mechanistic link between DNA methylation and transcriptional activation of these critical DDR genes, moving beyond correlation to establish causality and future solidifying their role in LUAD pathogenesis.
- iii. Furthermore, to move from association to definitive mechanistic insight, targeted functional assays- such as CRISPR-based methylation editing in LUAD cell lines and murine models - are essential. This approach would allow us to precisely test how hypomethylation of specific promoter regions of RRM2 and GAPDH directly orchestrates immune evasion via metabolic reprogramming (GAPDH) and genomic instability (RRM2).

- iv. Additionally, integrating this signature with established biomarkers (e.g., PD-L1 expression, TMB, and immune cell profiling) could refine risk stratification algorithms and identify patient subsets most likely to benefit from combination therapies, such as ICIs coupled with DDR inhibitors. Ultimately, these efforts aim to transform the computational insights into clinically actionable tools for treatment in LUAD.

In conclusion, despite these limitations, this study provides a foundational framework for leveraging epigenetic DDR biomarkers in LUAD. This study highlights two methylated DE-DDRGs and their association with poor prognosis and immunotherapy response in LUAD. It demonstrates that the promoter hypomethylation drives their upregulation, which is associated with aggressive tumor behaviour, a suppressed immune microenvironment, and poor patient survival. A powerful prognostic model based on this signature that serves as an independent predictor of outcomes in LUAD. Beyond prognosis, the finding delineates a potential mechanism of immune evasion, positioning RRM2 and GAPDH not only as prognostic biomarkers but also as promising predictive biomarkers for immunotherapy response. This work provides a compelling rationale for future functional studies to confirm causality and ultimately paves the way for more personalized therapeutic strategies, where modulating these epigenetic pathways could overcome treatment resistance and improve survival for patients with LUAD. However, future work should focus on mechanistic validation and prospective clinical translation to fully realize the potential these findings.

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APPENDICES

Appendix A: Journal Publications

1. Mao X, Lee NK, Saad SE, Fong IL. Clinical translation for targeting DNA damage repair in non-small cell lung cancer: a review. *Transl Lung Cancer Res.* 2024 Feb 29;13(2):375-397.
2. Mao X, Saad SE, Lee NK, Fong IL. DNA damage repair-related methylated genes RRM2 and GAPDH are prognostic biomarkers associated with immunotherapy for lung adenocarcinoma. *Genet Mol Biol.* 2025 May 9;48(2):e20240138.

Appendix B: Software List

Software	Version	Purpose
ggplot2	3.3.2	Drawing of volcano Jmap etc
limma	3.44.3	Differential gene detection
pheatmap	0.7.7	Heat map drawing
survival	3.2-3	Survival analysis
survivalROC	1.0.3	ROC curve drawing
GSVA	1.36.3	ssGSEA enrichment analysis
ggpubr	0.4.0	Whisker plot drawing
TIDE	website	TIDE immunotherapy analysis

Appendix C: Table Set

Appendix C 1: 243 DNA damage-related genes from the CancerSEA dataset

No.	Ensemble ID	Symbol	No. dataset	Direction
1	ENSG00000132646	PCNA	11	positive
2	ENSG00000117632	STMN1	10	positive
3	ENSG00000165304	MELK	10	positive
4	ENSG00000170312	CDK1	10	positive
5	ENSG00000176890	TYMS	10	positive
6	ENSG00000228716	DHFR	10	positive
7	ENSG00000077152	UBE2T	9	positive
8	ENSG00000120802	TMPO	9	positive
9	ENSG00000123416	TUBA1B	9	positive
10	ENSG00000135486	HNRNPA1	9	positive
11	ENSG00000164032	H2AFZ	9	positive
12	ENSG00000167088	SNRPD1	9	positive
13	ENSG00000175063	UBE2C	9	positive
14	ENSG00000189403	HMGB1	9	positive
15	ENSG00000196230	TUBB	9	positive
16	ENSG00000198830	HMG2	9	positive
17	ENSG00000088325	TPX2	8	positive
18	ENSG00000117724	CENPF	8	positive
19	ENSG00000123975	CKS2	8	positive
20	ENSG00000131747	TOP2A	8	positive
21	ENSG00000137804	NUSAP1	8	positive
22	ENSG00000167325	RRM1	8	positive
23	ENSG00000171848	RRM2	8	positive
24	ENSG00000181163	NPM1	8	positive
25	ENSG00000198901	PRC1	8	positive
26	ENSG00000011426	ANLN	7	positive
27	ENSG00000066279	ASPM	7	positive
28	ENSG00000124207	CSE1L	7	positive

Appendix C1: continued

29	ENSG00000126787	DLGAP5	7	positive
30	ENSG00000132341	RAN	7	positive
31	ENSG00000136824	SMC2	7	positive
32	ENSG00000138160	KIF11	7	positive
33	ENSG00000143228	NUF2	7	positive
34	ENSG00000143621	ILF2	7	positive
35	ENSG00000149554	CHEK1	7	positive
36	ENSG00000151725	CENPU	7	positive
37	ENSG00000164104	HMGB2	7	positive
38	ENSG00000164109	MAD2L1	7	positive
39	ENSG00000167900	TK1	7	positive
40	ENSG00000168496	FEN1	7	positive
41	ENSG00000177889	UBE2N	7	positive
42	ENSG00000187514	PTMA	7	positive
43	ENSG00000203760	CENPW	7	positive
44	ENSG00000005022	SLC25A5	6	positive
45	ENSG00000010292	NCAPD2	6	positive
46	ENSG00000075218	GTSE1	6	positive
47	ENSG00000089157	RPLP0	6	positive
48	ENSG00000089685	BIRC5	6	positive
49	ENSG00000093009	CDC45	6	positive
50	ENSG00000094916	CBX5	6	positive
51	ENSG00000104738	MCM4	6	positive
52	ENSG00000105011	ASF1B	6	positive
53	ENSG00000105640	RPL18A	6	positive
54	ENSG00000109971	HSPA8	6	positive
55	ENSG00000111206	FOXMI	6	positive
56	ENSG00000112312	GMNN	6	positive
57	ENSG00000112742	TTK	6	positive
58	ENSG00000113810	SMC4	6	positive
59	ENSG00000115053	NCL	6	positive
60	ENSG00000122566	HNRNPA2B1	6	positive

Appendix C1: continued

61	ENSG00000122952	ZWINT	6	positive
62	ENSG00000124795	DEK	6	positive
63	ENSG00000125835	SNRPB	6	positive
64	ENSG00000128708	HAT1	6	positive
65	ENSG00000131153	GINS2	6	positive
66	ENSG00000134690	CDCA8	6	positive
67	ENSG00000139618	BRCA2	6	positive
68	ENSG00000140525	FANCI	6	positive
69	ENSG00000142945	KIF2C	6	positive
70	ENSG00000145386	CCNA2	6	positive
71	ENSG00000148773	MKI67	6	positive
72	ENSG00000149273	RPS3	6	positive
73	ENSG00000162607	USP1	6	positive
74	ENSG00000163918	RFC4	6	positive
75	ENSG00000166451	CENPN	6	positive
76	ENSG00000166508	MCM7	6	positive
77	ENSG00000168393	DTYMK	6	positive
78	ENSG00000169679	BUB1	6	positive
79	ENSG00000171241	SHCBP1	6	positive
80	ENSG00000171858	RPS21	6	positive
81	ENSG00000173207	CKS1B	6	positive
82	ENSG00000183856	IQGAP3	6	positive
83	ENSG00000008988	RPS20	5	positive
84	ENSG00000012048	BRCA1	5	positive
85	ENSG00000065328	MCM10	5	positive
86	ENSG00000069275	NUCKS1	5	positive
87	ENSG00000076382	SPAG5	5	positive
88	ENSG00000079616	KIF22	5	positive
89	ENSG00000080986	NDC80	5	positive
90	ENSG00000083845	RPS5	5	positive
91	ENSG00000085840	ORC1	5	positive
92	ENSG00000087586	AURKA	5	positive

Appendix C1: continued

93	ENSG00000094804	CDC6	5	positive
94	ENSG00000099901	RANBP1	5	positive
95	ENSG00000100316	RPL3	5	positive
96	ENSG00000103121	CMC2	5	positive
97	ENSG00000104889	RNASEH2A	5	positive
98	ENSG00000105193	RPS16	5	positive
99	ENSG00000105968	H2AFV	5	positive
100	ENSG00000106355	LSM5	5	positive
101	ENSG00000106399	RPA3	5	positive
102	ENSG00000109805	NCAPG	5	positive
103	ENSG00000110958	PTGES3	5	positive
104	ENSG00000111602	TIMELESS	5	positive
105	ENSG00000112081	SRSF3	5	positive
106	ENSG00000112118	MCM3	5	positive
107	ENSG00000113648	H2AFY	5	positive
108	ENSG00000114346	ECT2	5	positive
109	ENSG00000115875	SRSF7	5	positive
110	ENSG00000116161	CACYBP	5	positive
111	ENSG00000120699	EXOSC8	5	positive
112	ENSG00000121152	NCAPH	5	positive
113	ENSG00000123219	CENPK	5	positive
114	ENSG00000125944	HNRNPR	5	positive
115	ENSG00000131462	TUBG1	5	positive
116	ENSG00000131469	RPL27	5	positive
117	ENSG00000132780	NASP	5	positive
118	ENSG00000134057	CCNB1	5	positive
119	ENSG00000137154	RPS6	5	positive
120	ENSG00000137807	KIF23	5	positive
121	ENSG00000139734	DIAPH3	5	positive
122	ENSG00000142937	RPS8	5	positive
123	ENSG00000143401	ANP32E	5	positive
124	ENSG00000143476	DTL	5	positive

Appendix C1: continued

125	ENSG00000143933	CALM2	5	positive
126	ENSG00000143977	SNRPG	5	positive
127	ENSG00000144034	TPRKB	5	positive
128	ENSG00000144381	HSPD1	5	positive
129	ENSG00000145425	RPS3A	5	positive
130	ENSG00000147274	RBMX	5	positive
131	ENSG00000147403	RPL10	5	positive
132	ENSG00000147604	RPL7	5	positive
133	ENSG00000149100	EIF3M	5	positive
134	ENSG00000150753	CCT5	5	positive
135	ENSG00000152234	ATP5F1A	5	positive
136	ENSG00000154473	BUB3	5	positive
137	ENSG00000156802	ATAD2	5	positive
138	ENSG00000157456	CCNB2	5	positive
139	ENSG00000161016	RPL8	5	positive
140	ENSG00000163808	KIF15	5	positive
141	ENSG00000164611	PTTG1	5	positive
142	ENSG00000164754	RAD21	5	positive
143	ENSG00000165480	SKA3	5	positive
144	ENSG00000165916	PSMC3	5	positive
145	ENSG00000167747	C19orf48	5	positive
146	ENSG00000168078	PBK	5	positive
147	ENSG00000171863	RPS7	5	positive
148	ENSG00000172115	CYCS	5	positive
149	ENSG00000174444	RPL4	5	positive
150	ENSG00000175305	CCNE2	5	positive
151	ENSG00000179750	APOBEC3B	5	positive
152	ENSG00000182481	KPNA2	5	positive
153	ENSG00000182628	SKA2	5	positive
154	ENSG00000197061	HIST1H4C	5	positive
155	ENSG00000237649	KIFC1	5	positive
156	ENSG00000276043	UHRF1	5	positive

Appendix C1: continued

157	ENSG00000006634	DBF4	4	positive
158	ENSG00000014641	MDH1	4	positive
159	ENSG00000024526	DEPDC1	4	positive
160	ENSG00000049541	RFC2	4	positive
161	ENSG00000071539	TRIP13	4	positive
162	ENSG00000079246	XRCC5	4	positive
163	ENSG00000089009	RPL6	4	positive
164	ENSG00000090889	KIF4A	4	positive
165	ENSG00000091651	ORC6	4	positive
166	ENSG00000092853	CLSPN	4	positive
167	ENSG00000100526	CDKN3	4	positive
168	ENSG00000100749	VRK1	4	positive
169	ENSG00000105372	RPS19	4	positive
170	ENSG00000106144	CASP2	4	positive
171	ENSG00000108055	SMC3	4	positive
172	ENSG00000108064	TFAM	4	positive
173	ENSG00000108298	RPL19	4	positive
174	ENSG00000109685	NSD2	4	positive
175	ENSG00000110700	RPS13	4	positive
176	ENSG00000111237	VPS29	4	positive
177	ENSG00000118193	KIF14	4	positive
178	ENSG00000119335	SET	4	positive
179	ENSG00000119403	PHF19	4	positive
180	ENSG00000119969	HELLS	4	positive
181	ENSG00000121211	MND1	4	positive
182	ENSG00000121621	KIF18A	4	positive
183	ENSG00000123485	HJURP	4	positive
184	ENSG00000124767	GLO1	4	positive
185	ENSG00000125743	SNRPD2	4	positive
186	ENSG00000126457	PRMT1	4	positive
187	ENSG00000129173	E2F8	4	positive
188	ENSG00000129195	PIMREG	4	positive

Appendix C1: continued

189	ENSG00000130816	DNMT1	4	positive
190	ENSG00000134419	RPS15A	4	positive
191	ENSG00000137563	GGH	4	positive
192	ENSG00000138182	KIF20B	4	positive
193	ENSG00000139343	SNRPF	4	positive
194	ENSG00000139921	TMX1	4	positive
195	ENSG00000142230	SAE1	4	positive
196	ENSG00000142534	RPS11	4	positive
197	ENSG00000142676	RPL11	4	positive
198	ENSG00000142731	PLK4	4	positive
199	ENSG00000143947	RPS27A	4	positive
200	ENSG00000144554	FANCD2	4	positive
201	ENSG00000144713	RPL32	4	positive
202	ENSG00000146670	CDCA5	4	positive
203	ENSG00000149136	SSRP1	4	positive
204	ENSG00000152253	SPC25	4	positive
205	ENSG00000154518	ATP5MC3	4	positive
206	ENSG00000156136	DCK	4	positive
207	ENSG00000156970	BUB1B	4	positive
208	ENSG00000161888	SPC24	4	positive
209	ENSG00000161970	RPL26	4	positive
210	ENSG00000162063	CCNF	4	positive
211	ENSG00000162521	RBBP4	4	positive
212	ENSG00000163923	RPL39L	4	positive
213	ENSG00000164985	PSIP1	4	positive
214	ENSG00000166441	RPL27A	4	positive
215	ENSG00000166801	FAM111A	4	positive
216	ENSG00000166803	PCLAF	4	positive
217	ENSG00000166851	PLK1	4	positive
218	ENSG00000168028	RPSA	4	positive
219	ENSG00000169607	CKAP2L	4	positive
220	ENSG00000170144	HNRNPA3	4	positive

Appendix C1: continued

221	ENSG00000170515	PA2G4	4	positive
222	ENSG00000170540	ARL6IP1	4	positive
223	ENSG00000170860	LSM3	4	positive
224	ENSG00000171320	ESCO2	4	positive
225	ENSG00000175216	CKAP5	4	positive
226	ENSG00000176208	ATAD5	4	positive
227	ENSG00000178999	AURKB	4	positive
228	ENSG00000182774	RPS17	4	positive
229	ENSG00000186468	RPS23	4	positive
230	ENSG00000188612	SUMO2	4	positive
231	ENSG00000188846	RPL14	4	positive
232	ENSG00000196262	PPIA	4	positive
233	ENSG00000197299	BLM	4	positive
234	ENSG00000197451	HNRNPAB	4	positive
235	ENSG00000198056	PRIM1	4	positive
236	ENSG00000198755	RPL10A	4	positive
237	ENSG00000198826	ARHGAP11A	4	positive
238	ENSG00000221983	UBA52	4	positive
239	ENSG00000231500	RPS18	4	positive
240	ENSG00000239672	NME1	4	positive
241	ENSG00000265241	RBM8A	4	positive
242	ENSG00000101439	CST3	4	negative
243	ENSG00000120885	CLU	4	negative

Appendix C2 : 387 DNA repair-related genes from the CancerSEA dataset

No.	Ensemble ID	Symbol	No. dataset	Direction
1	ENSG00000189403	HMGB1	17	positive
2	ENSG00000123416	TUBA1B	15	positive
3	ENSG00000176890	TYMS	15	positive
4	ENSG00000132646	PCNA	14	positive
5	ENSG00000164032	H2AFZ	14	positive
6	ENSG00000198830	HMG2	14	positive
7	ENSG00000077152	UBE2T	13	positive
8	ENSG00000117632	STMN1	13	positive
9	ENSG00000132341	RAN	13	positive
10	ENSG00000167088	SNRPD1	13	positive
11	ENSG00000005022	SLC25A5	12	positive
12	ENSG00000168496	FEN1	12	positive
13	ENSG00000094804	CDC6	11	positive
14	ENSG00000104738	MCM4	11	positive
15	ENSG00000166508	MCM7	11	positive
16	ENSG00000167900	TK1	11	positive
17	ENSG00000173207	CKS1B	11	positive
18	ENSG00000196230	TUBB	11	positive
19	ENSG00000196262	PPIA	11	positive
20	ENSG00000228716	DHFR	11	positive
21	ENSG00000120802	TMPO	10	positive
22	ENSG00000128050	PAICS	10	positive
23	ENSG00000131153	GINS2	10	positive
24	ENSG00000143977	SNRPG	10	positive
25	ENSG00000144554	FANCD2	10	positive
26	ENSG00000164104	HMGB2	10	positive
27	ENSG00000164109	MAD2L1	10	positive
28	ENSG00000167325	RRM1	10	positive
29	ENSG00000239672	NME1	10	positive
30	ENSG00000006625	GGCT	9	positive

Appendix C2: continued

31	ENSG00000106355	LSM5	9	positive
32	ENSG00000112118	MCM3	9	positive
33	ENSG00000128708	HAT1	9	positive
34	ENSG00000128951	DUT	9	positive
35	ENSG00000140525	FANCI	9	positive
36	ENSG00000144381	HSPD1	9	positive
37	ENSG00000165304	MELK	9	positive
38	ENSG00000171241	SHCBP1	9	positive
39	ENSG00000171848	RRM2	9	positive
40	ENSG00000012048	BRCA1	8	positive
41	ENSG00000065328	MCM10	8	positive
42	ENSG00000079246	XRCC5	8	positive
43	ENSG00000083845	RPS5	8	positive
44	ENSG00000089685	BIRC5	8	positive
45	ENSG00000099901	RANBP1	8	positive
46	ENSG00000100297	MCM5	8	positive
47	ENSG00000105968	H2AFV	8	positive
48	ENSG00000106399	RPA3	8	positive
49	ENSG00000111247	RAD51AP1	8	positive
50	ENSG00000112312	GMNN	8	positive
51	ENSG00000113810	SMC4	8	positive
52	ENSG00000122566	HNRNPA2B1	8	positive
53	ENSG00000122952	ZWINT	8	positive
54	ENSG00000125835	SNRPB	8	positive
55	ENSG00000131462	TUBG1	8	positive
56	ENSG00000134291	TMEM106C	8	positive
57	ENSG00000139343	SNRPF	8	positive
58	ENSG00000143476	DTL	8	positive
59	ENSG00000146731	CCT6A	8	positive
60	ENSG00000150753	CCT5	8	positive
61	ENSG00000163918	RFC4	8	positive
62	ENSG00000166803	PCLAF	8	positive

Appendix C2: continued

63	ENSG00000167747	C19orf48	8	positive
64	ENSG00000170312	CDK1	8	positive
65	ENSG00000177889	UBE2N	8	positive
66	ENSG00000181163	NPM1	8	positive
67	ENSG00000182628	SKA2	8	positive
68	ENSG00000011426	ANLN	7	positive
69	ENSG00000049541	RFC2	7	positive
70	ENSG00000073111	MCM2	7	positive
71	ENSG00000092470	WDR76	7	positive
72	ENSG00000092853	CLSPN	7	positive
73	ENSG00000093009	CDC45	7	positive
74	ENSG00000094916	CBX5	7	positive
75	ENSG00000109971	HSPA8	7	positive
76	ENSG00000111602	TIMELESS	7	positive
77	ENSG00000111716	LDHB	7	positive
78	ENSG00000116161	CACYBP	7	positive
79	ENSG00000116288	PARK7	7	positive
80	ENSG00000119335	SET	7	positive
81	ENSG00000119969	HELLS	7	positive
82	ENSG00000120699	EXOSC8	7	positive
83	ENSG00000123485	HJURP	7	positive
84	ENSG00000124207	CSE1L	7	positive
85	ENSG00000124795	DEK	7	positive
86	ENSG00000125743	SNRPD2	7	positive
87	ENSG00000131747	TOP2A	7	positive
88	ENSG00000136824	SMC2	7	positive
89	ENSG00000137563	GGH	7	positive
90	ENSG00000143947	RPS27A	7	positive
91	ENSG00000149100	EIF3M	7	positive
92	ENSG00000156802	ATAD2	7	positive
93	ENSG00000163468	CCT3	7	positive
94	ENSG00000170515	PA2G4	7	positive

Appendix C2: continued

95	ENSG00000170860	LSM3	7	positive
96	ENSG00000172115	CYCS	7	positive
97	ENSG00000182004	SNRPE	7	positive
98	ENSG00000182481	KPNA2	7	positive
99	ENSG00000197061	HIST1H4C	7	positive
100	ENSG00000007968	E2F2	6	positive
101	ENSG00000069275	NUCKS1	6	positive
102	ENSG00000072501	SMC1A	6	positive
103	ENSG00000076003	MCM6	6	positive
104	ENSG00000085840	ORC1	6	positive
105	ENSG00000088325	TPX2	6	positive
106	ENSG00000089157	RPLP0	6	positive
107	ENSG00000089220	PEBP1	6	positive
108	ENSG00000100162	CENPM	6	positive
109	ENSG00000100804	PSMB5	6	positive
110	ENSG00000104889	RNASEH2A	6	positive
111	ENSG00000105011	ASF1B	6	positive
112	ENSG00000105185	PDCD5	6	positive
113	ENSG00000106028	SSBP1	6	positive
114	ENSG00000109084	TMEM97	6	positive
115	ENSG00000111237	VPS29	6	positive
116	ENSG00000111445	RFC5	6	positive
117	ENSG00000111669	TPI1	6	positive
118	ENSG00000114346	ECT2	6	positive
119	ENSG00000115268	RPS15	6	positive
120	ENSG00000115541	HSPE1	6	positive
121	ENSG00000117748	RPA2	6	positive
122	ENSG00000122406	RPL5	6	positive
123	ENSG00000122565	CBX3	6	positive
124	ENSG00000124562	SNRPC	6	positive
125	ENSG00000126787	DLGAP5	6	positive
126	ENSG00000130816	DNMT1	6	positive

Appendix C2: continued

127	ENSG00000134001	EIF2S1	6	positive
128	ENSG00000136942	RPL35	6	positive
129	ENSG00000138182	KIF20B	6	positive
130	ENSG00000139618	BRCA2	6	positive
131	ENSG00000143106	PSMA5	6	positive
132	ENSG00000143401	ANP32E	6	positive
133	ENSG00000143621	ILF2	6	positive
134	ENSG00000146918	NCAPG2	6	positive
135	ENSG00000149273	RPS3	6	positive
136	ENSG00000149636	DSN1	6	positive
137	ENSG00000153044	CENPH	6	positive
138	ENSG00000157456	CCNB2	6	positive
139	ENSG00000160752	FDPS	6	positive
140	ENSG00000165672	PRDX3	6	positive
141	ENSG00000166226	CCT2	6	positive
142	ENSG00000166451	CENPN	6	positive
143	ENSG00000168393	DTYMK	6	positive
144	ENSG00000169679	BUB1	6	positive
145	ENSG00000175063	UBE2C	6	positive
146	ENSG00000175334	BANF1	6	positive
147	ENSG00000188612	SUMO2	6	positive
148	ENSG00000198034	RPS4X	6	positive
149	ENSG00000203760	CENPW	6	positive
150	ENSG00000276043	UHRF1	6	positive
151	ENSG00000010292	NCAPD2	5	positive
152	ENSG00000075142	SRI	5	positive
153	ENSG00000080986	NDC80	5	positive
154	ENSG00000091651	ORC6	5	positive
155	ENSG00000092199	HNRNPC	5	positive
156	ENSG00000100749	VRK1	5	positive
157	ENSG00000100911	PSME2	5	positive
158	ENSG00000101003	GIN51	5	positive

Appendix C2: continued

159	ENSG00000103018	CYB5B	5	positive
160	ENSG00000103121	CMC2	5	positive
161	ENSG00000105372	RPS19	5	positive
162	ENSG00000105640	RPL18A	5	positive
163	ENSG00000106144	CASP2	5	positive
164	ENSG00000106153	CHCHD2	5	positive
165	ENSG00000106462	EZH2	5	positive
166	ENSG00000106588	PSMA2	5	positive
167	ENSG00000108055	SMC3	5	positive
168	ENSG00000109805	NCAPG	5	positive
169	ENSG00000109919	MTCH2	5	positive
170	ENSG00000110700	RPS13	5	positive
171	ENSG00000111640	GAPDH	5	positive
172	ENSG00000112081	SRSF3	5	positive
173	ENSG00000112742	TTK	5	positive
174	ENSG00000113460	BRIX1	5	positive
175	ENSG00000114942	EEF1B2	5	positive
176	ENSG00000115053	NCL	5	positive
177	ENSG00000115875	SRSF7	5	positive
178	ENSG00000116120	FARSB	5	positive
179	ENSG00000117724	CENPF	5	positive
180	ENSG00000118193	KIF14	5	positive
181	ENSG00000122026	RPL21	5	positive
182	ENSG00000123219	CENPK	5	positive
183	ENSG00000123975	CKS2	5	positive
184	ENSG00000124614	RPS10	5	positive
185	ENSG00000124767	GLO1	5	positive
186	ENSG00000125691	RPL23	5	positive
187	ENSG00000125944	HNRNPR	5	positive
188	ENSG00000131469	RPL27	5	positive
189	ENSG00000132780	NASP	5	positive
190	ENSG00000135446	CDK4	5	positive

Appendix C2: continued

191	ENSG00000135486	HNRNPA1	5	positive
192	ENSG00000136518	ACTL6A	5	positive
193	ENSG00000137154	RPS6	5	positive
194	ENSG00000137310	TCF19	5	positive
195	ENSG00000137804	NUSAP1	5	positive
196	ENSG00000138160	KIF11	5	positive
197	ENSG00000138326	RPS24	5	positive
198	ENSG00000138376	BARD1	5	positive
199	ENSG00000142230	SAE1	5	positive
200	ENSG00000142534	RPS11	5	positive
201	ENSG00000142937	RPS8	5	positive
202	ENSG00000143742	SRP9	5	positive
203	ENSG00000144354	CDCA7	5	positive
204	ENSG00000145425	RPS3A	5	positive
205	ENSG00000145912	NHP2	5	positive
206	ENSG00000146263	MMS22L	5	positive
207	ENSG00000147274	RBMX	5	positive
208	ENSG00000147604	RPL7	5	positive
209	ENSG00000148773	MKI67	5	positive
210	ENSG00000151725	CENPU	5	positive
211	ENSG00000154473	BUB3	5	positive
212	ENSG00000154518	ATP5MC3	5	positive
213	ENSG00000161016	RPL8	5	positive
214	ENSG00000164611	PTTG1	5	positive
215	ENSG00000165264	NDUFB6	5	positive
216	ENSG00000168028	RPSA	5	positive
217	ENSG00000169813	HNRNPF	5	positive
218	ENSG00000171863	RPS7	5	positive
219	ENSG00000173436	MINOS1	5	positive
220	ENSG00000174371	EXO1	5	positive
221	ENSG00000174444	RPL4	5	positive
222	ENSG00000174748	RPL15	5	positive

Appendix C2: continued

223	ENSG00000175768	TOMM5	5	positive
224	ENSG00000182774	RPS17	5	positive
225	ENSG00000183684	ALYREF	5	positive
226	ENSG00000183856	IQGAP3	5	positive
227	ENSG00000187514	PTMA	5	positive
228	ENSG00000189057	FAM111B	5	positive
229	ENSG00000196531	NACA	5	positive
230	ENSG00000198015	MRPL42	5	positive
231	ENSG00000198056	PRIM1	5	positive
232	ENSG00000198901	PRC1	5	positive
233	ENSG00000231500	RPS18	5	positive
234	ENSG00000237649	KIFC1	5	positive
235	ENSG00000241468	ATP5MF	5	positive
236	ENSG00000206503	HLA-A	5	negative
237	ENSG00000001630	CYP51A1	4	positive
238	ENSG00000008988	RPS20	4	positive
239	ENSG00000013275	PSMC4	4	positive
240	ENSG00000024526	DEPDC1	4	positive
241	ENSG00000041357	PSMA4	4	positive
242	ENSG00000071539	TRIP13	4	positive
243	ENSG00000074800	ENO1	4	positive
244	ENSG00000076382	SPAG5	4	positive
245	ENSG00000079616	KIF22	4	positive
246	ENSG00000080824	HSP90AA1	4	positive
247	ENSG00000084623	EIF3I	4	positive
248	ENSG00000087191	PSMC5	4	positive
249	ENSG00000087586	AURKA	4	positive
250	ENSG00000089006	SNX5	4	positive
251	ENSG00000089009	RPL6	4	positive
252	ENSG00000090263	MRPS33	4	positive
253	ENSG00000091483	FH	4	positive
254	ENSG00000092201	SUPT16H	4	positive

Appendix C2: continued

255	ENSG00000099797	TECR	4	positive
256	ENSG00000100028	SNRPD3	4	positive
257	ENSG00000100353	EIF3D	4	positive
258	ENSG00000100526	CDKN3	4	positive
259	ENSG00000100567	PSMA3	4	positive
260	ENSG00000100632	ERH	4	positive
261	ENSG00000100714	MTHFD1	4	positive
262	ENSG00000101182	PSMA7	4	positive
263	ENSG00000101911	PRPS2	4	positive
264	ENSG00000102054	RBBP7	4	positive
265	ENSG00000106554	CHCHD3	4	positive
266	ENSG00000106628	POLD2	4	positive
267	ENSG00000107949	BCCIP	4	positive
268	ENSG00000108298	RPL19	4	positive
269	ENSG00000108384	RAD51C	4	positive
270	ENSG00000108953	YWHAE	4	positive
271	ENSG00000110955	ATP5F1B	4	positive
272	ENSG00000110958	PTGES3	4	positive
273	ENSG00000111206	FOXMI	4	positive
274	ENSG00000111678	C12orf57	4	positive
275	ENSG00000111775	COX6A1	4	positive
276	ENSG00000112306	RPS12	4	positive
277	ENSG00000113569	NUP155	4	positive
278	ENSG00000113648	H2AFY	4	positive
279	ENSG00000115484	CCT4	4	positive
280	ENSG00000116459	ATP5PB	4	positive
281	ENSG00000118181	RPS25	4	positive
282	ENSG00000120437	ACAT2	4	positive
283	ENSG00000120539	MASTL	4	positive
284	ENSG00000121152	NCAPH	4	positive
285	ENSG00000122545	7-Sep	4	positive
286	ENSG00000123473	STIL	4	positive

Appendix C2: continued

287	ENSG00000126067	PSMB2	4	positive
288	ENSG00000129084	PSMA1	4	positive
289	ENSG00000129173	E2F8	4	positive
290	ENSG00000130520	LSM4	4	positive
291	ENSG00000130741	EIF2S3	4	positive
292	ENSG00000131470	PSMC3IP	4	positive
293	ENSG00000132507	EIF5A	4	positive
294	ENSG00000133119	RFC3	4	positive
295	ENSG00000134057	CCNB1	4	positive
296	ENSG00000134333	LDHA	4	positive
297	ENSG00000134375	TIMM17A	4	positive
298	ENSG00000135624	CCT7	4	positive
299	ENSG00000138668	HNRNPD	4	positive
300	ENSG00000139180	NDUFA9	4	positive
301	ENSG00000139734	DIAPH3	4	positive
302	ENSG00000139921	TMX1	4	positive
303	ENSG00000140988	RPS2	4	positive
304	ENSG00000142945	KIF2C	4	positive
305	ENSG00000143933	CALM2	4	positive
306	ENSG00000144580	CNOT9	4	positive
307	ENSG00000144713	RPL32	4	positive
308	ENSG00000145386	CCNA2	4	positive
309	ENSG00000145592	RPL37	4	positive
310	ENSG00000145741	BTF3	4	positive
311	ENSG00000145907	G3BP1	4	positive
312	ENSG00000146670	CDCA5	4	positive
313	ENSG00000147155	EBP	4	positive
314	ENSG00000147669	POLR2K	4	positive
315	ENSG00000149136	SSRP1	4	positive
316	ENSG00000149554	CHEK1	4	positive
317	ENSG00000152253	SPC25	4	positive
318	ENSG00000152795	HNRNPDL	4	positive

Appendix C2: continued

319	ENSG00000156261	CCT8	4	positive
320	ENSG00000156482	RPL30	4	positive
321	ENSG00000156970	BUB1B	4	positive
322	ENSG00000161057	PSMC2	4	positive
323	ENSG00000161888	SPC24	4	positive
324	ENSG00000162607	USP1	4	positive
325	ENSG00000163002	NUP35	4	positive
326	ENSG00000163808	KIF15	4	positive
327	ENSG00000163882	POLR2H	4	positive
328	ENSG00000163923	RPL39L	4	positive
329	ENSG00000164587	RPS14	4	positive
330	ENSG00000164902	PHAX	4	positive
331	ENSG00000165480	SKA3	4	positive
332	ENSG00000165501	LRR1	4	positive
333	ENSG00000165609	NUDT5	4	positive
334	ENSG00000165678	GHITM	4	positive
335	ENSG00000165916	PSMC3	4	positive
336	ENSG00000166801	FAM111A	4	positive
337	ENSG00000167283	ATP5MG	4	positive
338	ENSG00000167815	PRDX2	4	positive
339	ENSG00000168078	PBK	4	positive
340	ENSG00000168090	COPS6	4	positive
341	ENSG00000169139	UBE2V2	4	positive
342	ENSG00000169567	HINT1	4	positive
343	ENSG00000169607	CKAP2L	4	positive
344	ENSG00000169714	CNBP	4	positive
345	ENSG00000170144	HNRNPA3	4	positive
346	ENSG00000171320	ESCO2	4	positive
347	ENSG00000171858	RPS21	4	positive
348	ENSG00000172757	CFL1	4	positive
349	ENSG00000172809	RPL38	4	positive
350	ENSG00000173418	NAA20	4	positive

Appendix C2: continued

351	ENSG00000175305	CCNE2	4	positive
352	ENSG00000176208	ATAD5	4	positive
353	ENSG00000176340	COX8A	4	positive
354	ENSG00000178035	IMPDH2	4	positive
355	ENSG00000178999	AURKB	4	positive
356	ENSG00000179750	APOBEC3B	4	positive
357	ENSG00000184445	KNTC1	4	positive
358	ENSG00000184983	NDUFA6	4	positive
359	ENSG00000186468	RPS23	4	positive
360	ENSG00000186871	ERCC6L	4	positive
361	ENSG00000188313	PLSCR1	4	positive
362	ENSG00000188846	RPL14	4	positive
363	ENSG00000189043	NDUFA4	4	positive
364	ENSG00000196419	XRCC6	4	positive
365	ENSG00000197299	BLM	4	positive
366	ENSG00000197451	HNRNPAB	4	positive
367	ENSG00000198554	WDHD1	4	positive
368	ENSG00000198826	ARHGAP11A	4	positive
369	ENSG00000198918	RPL39	4	positive
370	ENSG00000204392	LSM2	4	positive
371	ENSG00000204628	RACK1	4	positive
372	ENSG00000213551	DNAJC9	4	positive
373	ENSG00000213585	VDAC1	4	positive
374	ENSG00000221983	UBA52	4	positive
375	ENSG00000241343	RPL36A	4	positive
376	ENSG00000265241	RBM8A	4	positive
377	ENSG00000277791	PSMB3	4	positive
378	ENSG00000100345	MYH9	4	negative
379	ENSG00000105664	COMP	4	negative
380	ENSG00000109046	WSB1	4	negative
381	ENSG00000130066	SAT1	4	negative
382	ENSG00000130522	JUND	4	negative

Appendix C2: continued

383	ENSG00000166340	TPP1	4	negative
384	ENSG00000172146	OR1A1	4	negative
385	ENSG00000180573	HIST1H2AC	4	negative
386	ENSG00000187871	GFRAL	4	negative
387	ENSG00000269028	MTRNR2L12	4	negative

Appendix C3: 295 DNA damage & repair-related genes from MSigDB

GENE	GENE	GENE	GENE	GENE	GENE	GENE	GENE
53BP1	DCLRE1C	FANCG	MAD2L2	NUDT18	POLN	RIF1	TOP3A
ABH2	DDB1	FANCI	MBD4	OGG1	POLQ	RMI1	TOPBP1
ABRAXAS1	DDB2	FANCI	MDC1	p53R2	POLZ	RNF168	TP53
ADPRT	DEPC1	FANCL	METNASE	PALB2	PRIMPOL	RNF4	TP53BP1
ADPRTL2	DINB1	FANCM	MGMT	PARG	PRKDC	RNF8	TREX1
ADPRTL3	DJ-1	FANCN	MLH1	PARK7	PRPF19	RPA1	TREX2
ALKBH2	DMC1	FANCO	MLH3	PARP1	PSO4	RPA2	TTDA
ALKBH3	DNA2	FANCP	MMS19	PARP2	PTIP	RPA3	TTDN1
APE1	DNase	FANCT	MMS2	PARP3	RAD1	RPA4	TTRAP
APEX1	DNPH1	FEN1	MMS4L	PARPBP	RAD17	RRM2B	UBC13
APEX2	DNTT	GEN1	MNAT1	PAXIP1	RAD18	SEM1	UBE2A
APLF	DSS1	GIYD1	MPG	PCNA	RAD23A	SETMAR	UBE2B
APTX	DUT	GIYD2	MPLKIP	PDS5B	RAD23B	SHFM1	UBE2N
ATM	EME1	GTF2E2	MRE11A	PER1	RAD24	SHLD1	UBE2T
ATR	EME2	GTF2H1	MSH2	PMS1	RAD30B	SHLD2	UBE2V2
ATRIP	ENDOV	GTF2H2	MSH3	PMS2	RAD50	SHLD3	UNG
ATRX	ERCC1	GTF2H3	MSH4	PMS2L3	RAD51	SHPRH	USP1
BARD1	ERCC2	GTF2H4	MSH5	PMS2P3	RAD51B	SLX1A	UVSSA
BLM	ERCC3	GTF2H5	MSH6	PNKP	RAD51C	SLX1B	WDR48
BRCA1	ERCC4	H2AFX	MTH1	POL4P	RAD51D	SLX4	WRN
BRCA2	ERCC5	H2AX	MTH2	POLA1	RAD52	SMARCA3	XAB2
BRIP1	ERCC6	HCNP	MTH3	POLB	RAD52B	SMC5	XPA
C19orf40	ERCC8	HEL308	MTMR15	POLD1	RAD54B	SMC6	XPB
C1orf86	EXO1	HELQ	MUS81	POLD2	RAD54L	SMUG1	XPC
CAF1	EXO5	HERC2	MUTYH	POLD3	RAD6A	SNM1A	XPB
CCNH	FAAP100	HEX1	MYH	POLD4	RAD6B	SNM1B	XPD
CDK7	FAAP20	HFM1	NABP2	POLE	RAD9A	SPIRDR	XPF
CETN2	FAAP24	HLTF	NBN	POLE1	RBBP8	SPO11	XPG
CHAF1A	FAM35A	HMCES	NBS1	POLE2	RDM1	SPRTN	XRCC1
CHEK1	FAN1	HUS1	NEIL1	POLE3	RECQ1	SSB1	XRCC2
CHEK2	FANCA	KIAA1530	NEIL2	POLE4	RECQL	SWI5	XRCC3
CLK2	FANCB	KIAA1794	NEIL3	POLG	RECQL4	SWS1	XRCC4

Appendix C3: continued

CSA	FANCC	Ku70	NHEJ1	POLH	RECQL5	SWSAP1	XRCC5
CSB	FANCD1	Ku80	NTH1	POLI	REV1	TDG	XRCC6
CtIP	FANCD2	LIG1	NTHL1	POLK	REV1L	TDP1	XRCC9
DCLRE1A	FANCE	LIG3	NUDT1	POLL	REV3L	TDP2	ZSWIM7
DCLRE1B	FANCF	LIG4	NUDT15	POLM	REV7	TFIIH	

Appendix C4: 696 DDR-related genes (DDRGs; de-duplicated genes;) from the CancerSEA database and MSigDB database

GENE	GENE	GENE	GENE	GENE	GENE	GENE
ASPM	DTYMK	RPL32	RPS24	DNAJC9	GTF2E2	PRPF19
NUF2	BUB1	CDCA5	SRP9	VDAC1	GTF2H1	PSO4
GTSE1	SHCBP1	SSRP1	CDCA7	RPL36A	GTF2H2	PTIP
CDCA8	RPS21	SPC25	NHP2	PSMB3	GTF2H3	RAD1
RPL3	CKS1B	ATP5MC3	MMS22L	MYH9	GTF2H4	RAD17
RPS16	IQGAP3	BUB1B	NDUFB6	COMP	GTF2H5	RAD18
KIF23	RPS20	SPC24	HNRNPF	WSB1	H2AFX	RAD23A
TPRKB	MCM10	RPL39L	MINOS1	SAT1	H2AX	RAD23B
RPL10	NUCKS1	FAM111A	RPL15	JUND	HCNP	RAD24
ATP5F1A	SPAG5	PCLAF	TOMM5	TPP1	HEL308	RAD30B
RAD21	KIF22	RPSA	ALYREF	OR1A1	HELQ	RAD50
DBF4	NDC80	CKAP2L	FAM111B	HIST1H2AC	HERC2	RAD51
MDH1	RPS5	HNRNPA3	NACA	GFRAL	HEX1	RAD51B
KIF4A	ORC1	PA2G4	MRPL42	MTRNR2L12	HFM1	RAD51D
TFAM	AURKA	LSM3	ATP5MF	DUT	HLTF	RAD52
NSD2	CDC6	ESCO2	HLA-A	PARK7	HMCES	RAD52B
PHF19	RANBP1	ATAD5	CYP51A1	RPA2	HUS1	RAD54B
MND1	CMC2	AURKB	PSMC4	BARD1	KIAA1530	RAD54L
KIF18A	RNASEH2A	RPS17	PSMA4	EXO1	KIAA1794	RAD6A
PRMT1	H2AFV	RPS23	ENO1	POLD2	Ku70	RAD6B
PIMREG	LSM5	SUMO2	HSP90AA1	RAD51C	Ku80	RAD9A
RPS15A	NCAPG	RPL14	EIF3I	UBE2V2	LIG1	RBBP8
RPL11	PTGES3	PPIA	PSMC5	XRCC6	LIG3	RDM1
PLK4	TIMELESS	HNRNPAB	SNX5	53BP1	LIG4	RECQ1
DCK	SRSF3	PRIM1	MRPS33	ABH2	MAD2L2	RECQL
RPL26	MCM3	ARHGAP11A	FH	ABRAXAS1	MBD4	RECQL4
CCNF	H2AFY	UBA52	SUPT16H	ADPRT	MDC1	RECQL5
RBBP4	ECT2	RPS18	TECR	ADPRTL2	METNASE	REV1
PSIP1	SRSF7	NME1	SNRPD3	ADPRTL3	MGMT	REV1L
RPL27A	CACYBP	RBM8A	EIF3D	ALKBH2	MLH1	REV3L
PLK1	EXOSC8	PCNA	PSMA3	ALKBH3	MLH3	REV7
ARL6IP1	NCAPH	UBE2T	ERH	APE1	MMS19	RIF1

Appendix C4: continued

CKAP5	CENPK	CHEK1	MTHFD1	APEX1	MMS2	RMI1
RPL10A	HNRNPR	FEN1	PSMA7	APEX2	MMS4L	RNF168
CST3	TUBG1	UBE2N	PRPS2	APLF	MNAT1	RNF4
CLU	RPL27	BRCA2	RBBP7	APTX	MPG	RNF8
STMN1	NASP	FANCI	CHCHD3	ATM	MPLKIP	RPA1
MELK	CCNB1	USP1	BCCIP	ATR	MRE11A	RPA4
CDK1	RPS6	BRCA1	YWHAE	ATRIP	MSH2	RRM2B
TYMS	DIAPH3	RPA3	ATP5F1B	ATRX	MSH3	SEM1
DHFR	RPS8	XRCC5	C12orf57	BRIP1	MSH4	SETMAR
TMPO	ANP32E	FANCD2	COX6A1	C19orf40	MSH5	SHFM1
TUBA1B	DTL	BLM	RPS12	C1orf86	MSH6	SHLD1
HNRNPA1	CALM2	PAICS	NUP155	CAF1	MTH1	SHLD2
H2AFZ	SNRPG	GGCT	CCT4	CCNH	MTH2	SHLD3
SNRPD1	HSPD1	MCM5	ATP5PB	CDK7	MTH3	SHPRH
UBE2C	RPS3A	RAD51AP1	RPS25	CETN2	MTMR15	SLX1A
HMGB1	RBMX	TMEM106C	ACAT2	CHAF1A	MUS81	SLX1B
TUBB	RPL7	CCT6A	MASTL	CHEK2	MUTYH	SLX4
HMGN2	EIF3M	MCM2	7-Sep	CLK2	MYH	SMARCA3
TPX2	CCT5	WDR76	STIL	CSA	NABP2	SMC5
CENPF	BUB3	LDHB	PSMB2	CSB	NBN	SMC6
CKS2	ATAD2	CCT3	PSMA1	CtIP	NBS1	SMUG1
TOP2A	CCNB2	SNRPE	LSM4	DCLRE1A	NEIL1	SNM1A
NUSAP1	RPL8	E2F2	EIF2S3	DCLRE1B	NEIL2	SNM1B
RRM1	KIF15	SMC1A	PSMC3IP	DCLRE1C	NEIL3	SPIDR
RRM2	PTTG1	MCM6	EIF5A	DDB1	NHEJ1	SPO11
NPM1	SKA3	PEBP1	RFC3	DDB2	NTH1	SPRTN
PRC1	PSMC3	CENPM	LDHA	DEPC1	NTHL1	SSB1
ANLN	C19orf48	PSMB5	TIMM17A	DINB1	NUDT1	SWI5
CSE1L	PBK	PDCD5	CCT7	DJ-1	NUDT15	SWS1
DLGAP5	RPS7	SSBP1	HNRNPD	DMC1	NUDT18	SWSAP1
RAN	CYCS	TMEM97	NDUFA9	DNA2	OGG1	TDG
SMC2	RPL4	RFC5	RPS2	DNase	p53R2	TDP1
KIF11	CCNE2	TPI1	CNOT9	DNPH1	PALB2	TDP2
ILF2	APOBEC3B	RPS15	RPL37	DNTT	PARG	TFIIH

Appendix C4: continued

CENPU	KPNA2	HSPE1	BTF3	DSS1	PARP1	TOP3A
HMGB2	SKA2	RPL5	G3BP1	EME1	PARP2	TOPBP1
MAD2L1	HIST1H4C	CBX3	EBP	EME2	PARP3	TP53
TK1	KIFC1	SNRPC	POLR2K	ENDOV	PARPBP	TP53BP1
PTMA	UHRF1	EIF2S1	HNRNPDL	ERCC1	PAXIP1	TREX1
CENPW	DEPDC1	RPL35	CCT8	ERCC2	PDS5B	TREX2
SLC25A5	RFC2	PSMA5	RPL30	ERCC3	PER1	TTDA
NCAPD2	TRIP13	NCAPG2	PSMC2	ERCC4	PMS1	TTDN1
RPLP0	RPL6	DSN1	NUP35	ERCC5	PMS2	TTRAP
BIRC5	ORC6	CENPH	POLR2H	ERCC6	PMS2L3	UBC13
CDC45	CLSPN	FDPS	RPS14	ERCC8	PMS2P3	UBE2A
CBX5	CDKN3	PRDX3	PHAX	EXO5	PNKP	UBE2B
MCM4	VRK1	CCT2	LRR1	FAAP100	POL4P	UNG
ASF1B	RPS19	BANF1	NUDT5	FAAP20	POLA1	UVSSA
RPL18A	CASP2	RPS4X	GHITM	FAAP24	POLB	WDR48
HSPA8	SMC3	SRI	ATP5MG	FAM35A	POLD1	WRN
FOXMI	RPL19	HNRNPC	PRDX2	FAN1	POLD3	XAB2
GMNN	RPS13	PSME2	COPS6	FANCA	POLD4	XPA
TTK	VPS29	GIN51	HINT1	FANCB	POLE	XPB
SMC4	KIF14	CYB5B	CNBP	FANCC	POLE1	XPC
NCL	SET	CHCHD2	CFL1	FANCD1	POLE2	XPB
HNRNPA2B1	HELLS	EZH2	RPL38	FANCE	POLE3	XPE
ZWINT	HJURP	PSMA2	NAA20	FANCF	POLE4	XPF
DEK	GLO1	MTCH2	COX8A	FANCG	POLG	XPG
SNRPB	SNRPD2	GAPDH	IMPDH2	FANCI	POLH	XRCC1
HAT1	E2F8	BRIX1	KNTC1	FANCL	POLI	XRCC2
GIN52	DNMT1	EEF1B2	NDUFA6	FANCM	POLK	XRCC3
KIF2C	GGH	FARSB	ERCC6L	FANCN	POLL	XRCC4
CCNA2	KIF20B	RPL21	PLSCR1	FANCO	POLM	XRCC9
MKI67	SNRPF	RPS10	NDUFA4	FANCP	POLN	ZSWIM7
RPS3	TMX1	RPL23	WDHD1	FANCT	POLQ	
RFC4	SAE1	CDK4	RPL39	GEN1	POLZ	
CENPN	RPS11	ACTL6A	LSM2	GIYD1	PRIMPOL	
MCM7	RPS27A	TCF19	RACK1	GIYD2	PRKDC	

Appendix C5: Differentially expressed genes (DEGs) in lung adenocarcinoma (LUAD) including up-regulated and down-regulated genes

Gene	logFC	AveExpr	t	P.Value	adj.P.Val	B
LGI3	-3.72111	2.525461	-19.1213	5.00E-21	6.42E-17	37.50719
EMP2	-2.68958	6.08264	-17.1001	2.22E-19	1.43E-15	33.89347
TNNC1	-3.97098	3.884339	-15.9866	2.10E-18	8.96E-15	31.73639
FABP4	-4.68219	3.804835	-15.3895	7.33E-18	2.09E-14	30.52681
CLEC3B	-4.20182	4.644114	-15.3408	8.13E-18	2.09E-14	30.42646
ACADL	-2.27905	1.751335	-14.9711	1.80E-17	3.85E-14	29.65615
ALDH18A1	1.946362	4.229169	14.58366	4.20E-17	7.70E-14	28.83228
RGCC	-2.88848	6.843124	-14.444	5.73E-17	8.87E-14	28.53119
SFXN1	1.501722	2.293601	14.40702	6.22E-17	8.87E-14	28.45098
CAV1	-3.43014	6.679305	-14.2997	7.91E-17	9.36E-14	28.21745
CLIC5	-3.71263	3.654256	-14.2529	8.78E-17	9.36E-14	28.11527
RAMP2	-3.00178	4.736683	-14.2388	9.07E-17	9.36E-14	28.08448
GPIHBP1	-3.3627	2.79287	-14.2189	9.48E-17	9.36E-14	28.04099
UPK3B	-4.67989	3.617371	-14.1766	1.04E-16	9.56E-14	27.94807
ITLN2	-3.82961	2.358108	-14.1098	1.21E-16	1.04E-13	27.80108
ACVRL1	-2.25028	4.082189	-14.0457	1.40E-16	1.12E-13	27.65961
RALGPS2	1.635123	1.783968	13.73763	2.84E-16	2.06E-13	26.97274
STX11	-2.759	3.567355	-13.7294	2.89E-16	2.06E-13	26.95428
CA4	-3.50725	2.399541	-13.5568	4.31E-16	2.91E-13	26.56423
LIMS2	-2.4438	2.454016	-13.4225	5.89E-16	3.78E-13	26.25828
GPT2	2.255107	2.041829	13.37304	6.62E-16	3.92E-13	26.14492
KANK3	-2.16866	2.090539	-13.3665	6.72E-16	3.92E-13	26.12994
AGER	-6.24511	6.842546	-13.1456	1.13E-15	6.31E-13	25.62017
PYCR1	3.313118	3.481443	13.02666	1.50E-15	8.03E-13	25.34321
PECAM1	-2.10703	5.820197	-12.9726	1.71E-15	8.77E-13	25.21679
ADRB2	-2.54095	2.481984	-12.9495	1.81E-15	8.91E-13	25.16263
CDH5	-2.38065	4.340904	-12.919	1.94E-15	9.08E-13	25.09097
PDLIM2	-1.59263	2.133347	-12.9107	1.98E-15	9.08E-13	25.07154
S1PR1	-2.47391	4.670069	-12.8415	2.34E-15	1.03E-12	24.90839
WNT3A	-2.25356	1.347418	-12.8279	2.42E-15	1.03E-12	24.87643

Appendix C5: continued

ROBO4	-2.58663	3.157643	-12.8073	2.54E-15	1.05E-12	24.82759
FHL1	-3.23586	4.207137	-12.6415	3.80E-15	1.52E-12	24.43398
CD36	-2.7052	3.06958	-12.58	4.41E-15	1.70E-12	24.2871
SH2D3C	-2.02493	3.100349	-12.5714	4.50E-15	1.70E-12	24.26654
PLA2G1B	-3.38655	3.159921	-12.476	5.69E-15	2.08E-12	24.03739
BTNL9	-2.67898	2.095267	-12.41	6.69E-15	2.38E-12	23.87846
LIN7A	-1.49122	1.434333	-12.3749	7.29E-15	2.53E-12	23.79347
CRTAC1	-3.10678	3.946636	-12.3537	7.68E-15	2.53E-12	23.74221
SPOCK2	-3.30103	4.909279	-12.3527	7.70E-15	2.53E-12	23.73973
EDNRB	-2.94848	3.680396	-12.3049	8.67E-15	2.78E-12	23.62388
PRX	-2.89759	2.94415	-12.1894	1.15E-14	3.56E-12	23.34247
ECSCR	-1.71959	2.046569	-12.1859	1.16E-14	3.56E-12	23.33384
CAV2	-2.11669	4.885526	-11.9744	1.98E-14	5.90E-12	22.81388
HIGD1B	-2.44533	2.836377	-11.9461	2.12E-14	6.19E-12	22.744
FAM107A	-4.15927	3.682574	-11.8437	2.75E-14	7.83E-12	22.48978
COX4I2	-2.2798	3.480904	-11.7559	3.43E-14	9.57E-12	22.27063
GRK5	-2.17145	2.995259	-11.7393	3.58E-14	9.77E-12	22.22916
EPAS1	-2.74048	6.981237	-11.7307	3.66E-14	9.78E-12	22.20756
SGCA	-1.63643	2.024247	-11.7082	3.88E-14	1.01E-11	22.15114
CLIC3	-2.62056	4.356076	-11.6704	4.27E-14	1.10E-11	22.05625
RTKN2	-3.39006	2.773813	-11.6172	4.89E-14	1.23E-11	21.92258
IARS	1.161652	3.914504	11.59353	5.20E-14	1.28E-11	21.86279
ZC3HAV1L	1.163487	1.516534	11.54048	5.95E-14	1.44E-11	21.72878
STK39	1.414744	3.211604	11.52657	6.17E-14	1.45E-11	21.69357
PHKA1	1.344709	1.822375	11.52276	6.23E-14	1.45E-11	21.68395
RCC1	1.516826	3.212086	11.5076	6.48E-14	1.48E-11	21.64554
TEK	-2.56204	3.178784	-11.4717	7.10E-14	1.60E-11	21.55455
ADAMTS8	-2.72339	2.337499	-11.4542	7.43E-14	1.64E-11	21.50991
PLA2G4F	-2.75497	2.684087	-11.4347	7.82E-14	1.70E-11	21.46048
NCKAP5	-2.25228	1.766182	-11.409	8.35E-14	1.75E-11	21.39508
EMCN	-2.25475	2.858088	-11.4077	8.38E-14	1.75E-11	21.39175
PPAP2C	2.167747	2.243453	11.40369	8.47E-14	1.75E-11	21.38148

Appendix C5: continued

CRYAB	-2.01884	2.766362	-11.3842	8.91E-14	1.81E-11	21.33187
RAMP3	-3.17803	4.564289	-11.3739	9.15E-14	1.83E-11	21.30555
ESAM	-2.32264	4.746037	-11.3506	9.72E-14	1.92E-11	21.24594
DPEP2	-1.73716	2.014636	-11.3257	1.04E-13	2.02E-11	21.18226
DARS2	1.397117	2.979856	11.30572	1.09E-13	2.09E-11	21.1312
FAM189A2	-2.72959	2.966862	-11.2521	1.26E-13	2.37E-11	20.99371
JAM2	-1.86104	2.540828	-11.1646	1.58E-13	2.91E-11	20.76851
SGCG	-1.7697	1.204274	-11.162	1.59E-13	2.91E-11	20.7616
AOC3	-2.45311	4.923394	-11.1566	1.61E-13	2.91E-11	20.74784
TAL1	-1.40525	1.241992	-11.1467	1.65E-13	2.95E-11	20.72222
SLC39A8	-2.56398	5.328591	-11.129	1.73E-13	3.04E-11	20.6765
TRAP1	1.152681	3.110798	11.10392	1.85E-13	3.21E-11	20.61157
PDIA4	1.959561	6.281949	11.09406	1.90E-13	3.25E-11	20.58605
MYCT1	-1.7964	2.792177	-10.9905	2.49E-13	4.19E-11	20.31706
CSTF2	1.141509	3.024767	10.98635	2.52E-13	4.19E-11	20.3063
TMEM88	-2.32687	2.353084	-10.9822	2.55E-13	4.19E-11	20.29552
PHACTR1	-1.79138	2.006231	-10.9735	2.61E-13	4.23E-11	20.2727
SCUBE1	-1.79878	1.179643	-10.962	2.69E-13	4.31E-11	20.24283
CLDN5	-2.77082	4.030344	-10.8259	3.86E-13	6.11E-11	19.88673
STXBP6	-2.13592	1.777541	-10.8207	3.91E-13	6.12E-11	19.87305
PPAT	1.404445	1.667859	10.81188	4.00E-13	6.19E-11	19.84984
RASIP1	-2.00422	2.727605	-10.8052	4.07E-13	6.22E-11	19.8322
SRPK1	1.619622	3.228009	10.79068	4.24E-13	6.39E-11	19.79411
SLC6A4	-3.90047	2.315907	-10.7474	4.75E-13	7.06E-11	19.67999
EPRS	1.31533	4.744731	10.74459	4.79E-13	7.06E-11	19.6727
PLA2G3	-1.10393	0.93433	-10.6882	5.57E-13	8.11E-11	19.52371
HN1L	1.385002	4.582013	10.68313	5.65E-13	8.11E-11	19.51037
SBSPON	-1.72632	1.447984	-10.6788	5.71E-13	8.11E-11	19.49879
FAM46B	-2.21692	3.032094	-10.6732	5.80E-13	8.11E-11	19.48414
GPM6B	-1.52933	1.939422	-10.6719	5.82E-13	8.11E-11	19.48067
ACE	-1.69144	3.155522	-10.6644	5.94E-13	8.19E-11	19.4607
LGR4	2.622801	2.584573	10.64345	6.28E-13	8.57E-11	19.40527

Appendix C5: continued

GPD1	-2.93474	2.377653	-10.6372	6.39E-13	8.62E-11	19.3887
GLIPR2	-2.12206	4.472942	-10.6191	6.70E-13	8.96E-11	19.34076
PEBP4	-3.83789	4.54194	-10.6023	7.01E-13	9.18E-11	19.29607
LPL	-2.72255	4.422168	-10.6023	7.01E-13	9.18E-11	19.296
DES	-3.19186	3.397381	-10.5452	8.18E-13	1.06E-10	19.14404
LAMP3	-3.25812	5.921421	-10.5129	8.93E-13	1.15E-10	19.05799
PLAC9	-2.3685	3.158942	-10.4843	9.64E-13	1.22E-10	18.9818
TIE1	-1.61503	3.166882	-10.4818	9.71E-13	1.22E-10	18.97488
LMAN1	1.111781	4.859324	10.4696	1.00E-12	1.25E-10	18.94236
KCNN4	2.789215	2.620022	10.45896	1.03E-12	1.27E-10	18.9139
SLC35F2	1.921276	2.889043	10.45082	1.06E-12	1.29E-10	18.89211
NPR1	-2.42383	2.959879	-10.4235	1.14E-12	1.38E-10	18.81884
PTRF	-1.90413	6.740726	-10.41	1.18E-12	1.41E-10	18.78261
P3H2	-2.15515	3.478519	-10.4037	1.20E-12	1.42E-10	18.7659
SLC46A2	-2.09412	2.156451	-10.3965	1.22E-12	1.44E-10	18.74655
PAK1	1.333654	3.373112	10.39302	1.23E-12	1.44E-10	18.73717
GYPC	-1.4948	3.535162	-10.3703	1.31E-12	1.52E-10	18.67608
TMEM177	1.055061	1.715101	10.33973	1.43E-12	1.63E-10	18.5939
SLC2A1	3.616154	3.641874	10.33689	1.44E-12	1.63E-10	18.58625
C11orf80	1.074235	2.062632	10.32518	1.49E-12	1.67E-10	18.55469
HSPA12B	-2.1189	2.559481	-10.2984	1.60E-12	1.78E-10	18.48261
CLEC1A	-1.42835	1.633718	-10.2744	1.71E-12	1.89E-10	18.41763
SPAG4	1.64163	1.628954	10.26582	1.75E-12	1.92E-10	18.39455
ADPRH	-1.27108	2.762657	-10.258	1.78E-12	1.94E-10	18.37341
FGFR4	-2.31393	2.871608	-10.2414	1.87E-12	2.00E-10	18.32862
NECAB1	-1.62141	1.462283	-10.2406	1.87E-12	2.00E-10	18.32627
FIGF	-3.22767	3.025408	-10.2386	1.88E-12	2.00E-10	18.32094
AFF3	-1.44617	1.244918	-10.2309	1.92E-12	2.02E-10	18.30023
DAPK2	-1.63081	1.791416	-10.2267	1.94E-12	2.03E-10	18.2886
CACNA2D2	-3.40759	3.974928	-10.2195	1.98E-12	2.05E-10	18.26933
LRRC36	-2.10528	1.695134	-10.2029	2.08E-12	2.13E-10	18.22425
INMT	-3.40581	4.528404	-10.1896	2.15E-12	2.19E-10	18.18818

Appendix C5: continued

CFP	-1.2817	1.486608	-10.1673	2.29E-12	2.31E-10	18.12766
FMO2	-2.68948	4.009353	-10.1534	2.38E-12	2.38E-10	18.09004
GOLM1	2.707609	4.762247	10.13778	2.48E-12	2.47E-10	18.04745
RFWD3	1.195187	2.561827	10.11654	2.63E-12	2.60E-10	17.98967
HIST1H2BD	3.07023	3.537229	10.09574	2.79E-12	2.73E-10	17.93302
UBFD1	1.158122	2.870898	10.06111	3.06E-12	2.98E-10	17.83857
RADIL	-1.14717	0.964132	-10.012	3.51E-12	3.39E-10	17.70443
CAT	-1.76815	5.773947	-9.97751	3.86E-12	3.68E-10	17.60989
MFNG	-1.50995	3.16197	-9.97615	3.88E-12	3.68E-10	17.60616
GAS6	-1.83083	4.805803	-9.96969	3.95E-12	3.72E-10	17.58843
CCT3	1.464235	5.713631	9.949694	4.17E-12	3.91E-10	17.53359
DIEXF	1.079089	1.850829	9.913978	4.61E-12	4.28E-10	17.43547
SDPR	-2.95383	5.522717	-9.91068	4.65E-12	4.28E-10	17.42641
TOP2A	3.081702	2.598512	9.909241	4.67E-12	4.28E-10	17.42245
SGPL1	1.136078	3.591056	9.906489	4.70E-12	4.28E-10	17.41488
CLNS1A	1.023557	3.745385	9.897217	4.83E-12	4.36E-10	17.38937
FCN3	-4.39411	3.831929	-9.86362	5.30E-12	4.75E-10	17.29684
KL	-1.58493	1.472184	-9.85672	5.40E-12	4.81E-10	17.27782
HSPD1	1.270585	5.608728	9.845392	5.58E-12	4.93E-10	17.24658
FERMT1	2.125173	1.616667	9.823957	5.92E-12	5.17E-10	17.18741
GDF10	-2.4895	2.249596	-9.81264	6.11E-12	5.30E-10	17.15615
TFB2M	1.263	3.319643	9.794639	6.43E-12	5.53E-10	17.10639
IARS2	1.198197	4.94484	9.789496	6.52E-12	5.55E-10	17.09217
LDB2	-2.04439	3.126221	-9.78883	6.53E-12	5.55E-10	17.09034
STARD8	-1.47752	2.578581	-9.77312	6.82E-12	5.76E-10	17.04686
TMEM204	-1.62758	4.073938	-9.771	6.86E-12	5.76E-10	17.04097
RMI2	1.481705	1.701147	9.767056	6.94E-12	5.78E-10	17.03006
KCNK3	-2.43026	2.242987	-9.73793	7.53E-12	6.23E-10	16.94935
PC	1.303041	2.087074	9.73233	7.65E-12	6.29E-10	16.93382
ANKRD22	2.629218	2.463858	9.718972	7.94E-12	6.48E-10	16.89675
PTCRA	-1.15121	0.885531	-9.69649	8.46E-12	6.82E-10	16.83431
SLC39A11	1.501207	3.198723	9.688195	8.66E-12	6.92E-10	16.81127

Appendix C5: continued

GYPE	-1.15838	0.870004	-9.68734	8.68E-12	6.92E-10	16.8089
PRPS2	1.022694	4.049595	9.669061	9.14E-12	7.23E-10	16.75805
WNT7A	-1.56266	1.219596	-9.66043	9.36E-12	7.37E-10	16.73402
ARHGAP6	-1.19071	1.288021	-9.65272	9.57E-12	7.48E-10	16.71256
CASKIN2	-1.64548	3.503175	-9.6424	9.85E-12	7.66E-10	16.68382
E2F8	1.253568	0.836145	9.638014	9.97E-12	7.70E-10	16.67161
ARHGEF15	-1.9614	2.3294	-9.62456	1.04E-11	7.95E-10	16.63411
KLK10	-2.04354	1.741372	-9.62059	1.05E-11	7.97E-10	16.62303
PGM2L1	1.57659	1.946237	9.619444	1.05E-11	7.97E-10	16.61984
STT3A	1.038322	4.439096	9.615737	1.06E-11	8.01E-10	16.60951
ZBTB41	1.198198	2.341773	9.612761	1.07E-11	8.03E-10	16.6012
HSPB8	-2.16201	4.144685	-9.60897	1.08E-11	8.07E-10	16.59064
HBA2	-4.31219	5.168203	-9.59315	1.13E-11	8.37E-10	16.54647
NUP155	1.383363	2.405714	9.591813	1.14E-11	8.37E-10	16.54274
CLDN18	-5.42904	5.376964	-9.5822	1.17E-11	8.55E-10	16.51588
SLC25A13	1.146085	3.035498	9.572052	1.20E-11	8.75E-10	16.48753
HYOU1	1.47677	4.743395	9.551323	1.27E-11	9.18E-10	16.42956
LHFP	-1.60163	4.499789	-9.54758	1.29E-11	9.18E-10	16.41909
WWC2	-1.74057	3.16559	-9.54713	1.29E-11	9.18E-10	16.41783
PTPN21	-1.8256	2.849534	-9.537	1.33E-11	9.40E-10	16.38947
SLFN13	1.407121	1.762907	9.533653	1.34E-11	9.41E-10	16.3801
UBE2T	2.631959	2.561614	9.529265	1.36E-11	9.41E-10	16.36781
ERG	-1.6384	2.543113	-9.49849	1.48E-11	1.02E-09	16.28157
MYO19	1.01966	1.547587	9.485649	1.53E-11	1.05E-09	16.24553
CNTN6	-1.61522	1.169073	-9.4603	1.65E-11	1.11E-09	16.17434
ST8SIA6	-1.73046	1.339761	-9.45754	1.66E-11	1.12E-09	16.16658
TMOD1	-1.26583	1.454987	-9.43948	1.75E-11	1.17E-09	16.11583
DUOX1	-2.58479	3.451498	-9.43092	1.79E-11	1.19E-09	16.09174
FEZ1	-1.29212	1.837799	-9.42962	1.80E-11	1.19E-09	16.08808
GKN2	-3.56458	3.176417	-9.42068	1.84E-11	1.21E-09	16.06292
SIRPB1	-1.71244	1.741813	-9.41832	1.86E-11	1.21E-09	16.05629
HSPB7	-1.11765	1.409472	-9.41551	1.87E-11	1.22E-09	16.04837

Appendix C5: continued

NES	-1.90713	3.790116	-9.3993	1.96E-11	1.26E-09	16.00269
H1F0	1.248872	6.436931	9.396758	1.97E-11	1.26E-09	15.99554
FBLN5	-2.13229	4.01403	-9.39434	1.99E-11	1.26E-09	15.98873
LYVE1	-2.50471	2.997022	-9.36575	2.16E-11	1.36E-09	15.9081
HYAL2	-1.29733	4.618751	-9.34754	2.27E-11	1.43E-09	15.85669
PPP1R14B	1.826165	4.602424	9.343567	2.30E-11	1.44E-09	15.84546
CPB2	-3.38399	2.774419	-9.34124	2.31E-11	1.44E-09	15.83888
TMEM100	-3.60285	3.476582	-9.33439	2.36E-11	1.46E-09	15.81952
DUOXA1	-1.98726	2.928829	-9.33093	2.38E-11	1.47E-09	15.80975
TRPV2	-1.54295	3.862937	-9.3252	2.42E-11	1.48E-09	15.79355
PROM2	2.463104	2.705355	9.323194	2.43E-11	1.48E-09	15.78788
GRASP	-1.97465	2.972807	-9.32254	2.44E-11	1.48E-09	15.78602
COPA	1.095084	5.681316	9.289459	2.68E-11	1.61E-09	15.69241
SEMA3G	-2.29527	2.488047	-9.27303	2.81E-11	1.68E-09	15.64586
MCEMP1	-3.72158	4.029211	-9.21872	3.28E-11	1.96E-09	15.49176
RASAL1	1.430386	0.845099	9.213551	3.33E-11	1.98E-09	15.47706
VIPR1	-2.65164	2.7013	-9.20547	3.41E-11	2.01E-09	15.4541
LRRC32	-2.20513	4.142418	-9.20448	3.42E-11	2.01E-09	15.45126
ITIH5	-1.53268	1.913855	-9.17812	3.69E-11	2.16E-09	15.37629
FANCG	1.009091	2.010055	9.16848	3.79E-11	2.21E-09	15.34884
KIF11	1.960539	1.756025	9.165848	3.82E-11	2.22E-09	15.34134
MYL9	-1.82772	6.504131	-9.16381	3.84E-11	2.22E-09	15.33553
DHTKD1	1.226983	2.991641	9.158633	3.90E-11	2.24E-09	15.32079
PNPLA6	-1.37193	3.944427	-9.15167	3.98E-11	2.27E-09	15.30095
COX7A1	-1.59367	3.295384	-9.14385	4.07E-11	2.30E-09	15.27866
FGR	-2.01825	3.617062	-9.13597	4.16E-11	2.33E-09	15.25618
KAL1	-2.10441	3.598165	-9.1222	4.33E-11	2.42E-09	15.2169
F10	-1.28921	1.718171	-9.10495	4.55E-11	2.53E-09	15.16767
GPM6A	-2.5175	1.959624	-9.10324	4.58E-11	2.53E-09	15.16279
EFNA4	1.782037	2.808416	9.081244	4.88E-11	2.68E-09	15.09993
ARHGEF26	-2.19346	2.955353	-9.06947	5.04E-11	2.75E-09	15.06626
SERTM1	-2.15976	1.217343	-9.05905	5.20E-11	2.81E-09	15.03645

Appendix C5: continued

SOX7	-2.40466	2.339932	-9.05755	5.22E-11	2.81E-09	15.03216
NOTCH4	-1.45259	2.425318	-9.04407	5.43E-11	2.91E-09	14.99355
NOVA2	-1.21543	1.072299	-9.04017	5.49E-11	2.93E-09	14.9824
STARD13	-1.27858	2.300994	-9.03972	5.50E-11	2.93E-09	14.9811
PDIA6	1.166751	5.698917	9.035766	5.56E-11	2.94E-09	14.96978
HSP90B1	1.033241	7.335402	9.035544	5.56E-11	2.94E-09	14.96915
FBXO32	2.015173	2.477028	9.014631	5.91E-11	3.11E-09	14.90921
DENND3	-1.46381	2.653772	-8.98902	6.37E-11	3.33E-09	14.83573
ZWINT	2.000054	2.555272	8.985008	6.44E-11	3.35E-09	14.82421
MPZL1	1.00499	4.582718	8.984722	6.44E-11	3.35E-09	14.82339
ADRB1	-2.59596	2.276976	-8.95658	6.99E-11	3.62E-09	14.74255
CNOT11	1.003407	4.142026	8.936612	7.41E-11	3.80E-09	14.68512
FXYD1	-1.29426	1.068959	-8.91318	7.93E-11	4.04E-09	14.61767
MFAP4	-2.8927	6.507258	-8.9089	8.03E-11	4.04E-09	14.60535
FEN1	1.452834	3.04526	8.907958	8.05E-11	4.04E-09	14.60263
RASGRP4	-1.09332	1.297262	-8.90724	8.07E-11	4.04E-09	14.60057
EFCC1	-1.94088	2.109053	-8.90589	8.10E-11	4.04E-09	14.59667
FAM150B	-1.8037	1.397962	-8.90384	8.15E-11	4.05E-09	14.59077
SEC14L6	-1.99141	1.973265	-8.89365	8.40E-11	4.16E-09	14.5614
GIMAP6	-1.78718	3.696747	-8.89079	8.47E-11	4.18E-09	14.55314
FGD5	-1.68715	2.797932	-8.88573	8.59E-11	4.22E-09	14.53855
CCNB1	2.420322	2.669806	8.882707	8.67E-11	4.24E-09	14.52985
ST14	1.497999	5.291319	8.878223	8.78E-11	4.27E-09	14.51691
CYYR1	-1.80867	3.209397	-8.8781	8.78E-11	4.27E-09	14.51657
DACH1	-1.48708	1.496549	-8.87262	8.93E-11	4.32E-09	14.50076
EPT1	1.083857	2.431591	8.869105	9.02E-11	4.35E-09	14.49061
CAMP	-1.72503	1.331276	-8.84227	9.75E-11	4.65E-09	14.41313
SFTPC	-6.98715	9.525409	-8.84203	9.76E-11	4.65E-09	14.41243
PLK1	1.909292	1.503628	8.833619	1.00E-10	4.73E-09	14.38813
ST6GALNAC6	-1.1817	4.07677	-8.81977	1.04E-10	4.91E-09	14.34809
TMEM184A	1.431074	1.2825	8.811751	1.07E-10	4.99E-09	14.3249
PUS7	1.106885	2.198806	8.808272	1.08E-10	5.02E-09	14.31484

Appendix C5: continued

S1PR4	-1.49693	2.698753	-8.80105	1.10E-10	5.11E-09	14.29394
OSCAR	-2.16152	3.48441	-8.7906	1.13E-10	5.23E-09	14.2637
MCM4	1.996887	2.874955	8.786833	1.15E-10	5.27E-09	14.25278
CD300LG	-2.03116	1.14258	-8.78548	1.15E-10	5.27E-09	14.24886
BUB1B	1.72252	1.196571	8.783821	1.16E-10	5.28E-09	14.24406
XPR1	1.647398	3.395539	8.77513	1.19E-10	5.40E-09	14.21889
DLC1	-2.20348	3.885784	-8.75595	1.25E-10	5.65E-09	14.16329
SFXN4	1.271467	3.09079	8.746136	1.29E-10	5.79E-09	14.13484
DENND2A	-1.23894	2.127574	-8.73902	1.32E-10	5.89E-09	14.1142
SOX17	-1.72609	1.931483	-8.73706	1.33E-10	5.91E-09	14.10849
SPAG5	1.737372	1.53821	8.728456	1.36E-10	6.02E-09	14.08353
FXYD6	-1.63146	2.854219	-8.72217	1.39E-10	6.11E-09	14.06529
ANKRD1	-3.95376	2.861335	-8.70982	1.44E-10	6.31E-09	14.0294
SLC1A1	-2.22789	3.211817	-8.70676	1.45E-10	6.35E-09	14.02051
PAICS	1.638569	3.265007	8.697854	1.49E-10	6.48E-09	13.99464
MYZAP	-1.98915	1.887747	-8.69702	1.49E-10	6.48E-09	13.9922
GRIA1	-1.56895	1.148609	-8.69524	1.50E-10	6.50E-09	13.98703
CENPF	2.085222	1.473092	8.694078	1.50E-10	6.50E-09	13.98366
EZH2	1.449077	1.465835	8.691835	1.51E-10	6.52E-09	13.97714
C5orf38	-1.97859	2.263879	-8.69063	1.52E-10	6.52E-09	13.97362
DLGAP5	1.878798	1.322379	8.665767	1.63E-10	6.99E-09	13.90131
MMRN2	-1.63126	3.375155	-8.66299	1.65E-10	7.02E-09	13.89322
PKNOX2	-1.25336	1.235376	-8.65559	1.68E-10	7.11E-09	13.87169
GPX3	-2.57546	6.937518	-8.65552	1.68E-10	7.11E-09	13.87148
EIF2S3	1.138021	5.679239	8.652489	1.70E-10	7.15E-09	13.86265
EPCAM	1.446869	6.55476	8.650468	1.71E-10	7.16E-09	13.85677
LPGAT1	1.501659	3.487157	8.649632	1.71E-10	7.16E-09	13.85433
TARS2	1.125154	2.969748	8.642145	1.75E-10	7.30E-09	13.83252
JRKL	1.058146	2.493466	8.634226	1.79E-10	7.40E-09	13.80945
CD52	-2.48347	6.059753	-8.63124	1.81E-10	7.44E-09	13.80076
ECT2	1.883857	2.580814	8.625069	1.84E-10	7.52E-09	13.78276
NEK2	2.160476	1.451102	8.62436	1.85E-10	7.52E-09	13.78069

Appendix C5: continued

FHL5	-1.71659	2.005292	-8.62369	1.85E-10	7.52E-09	13.77874
FANCI	1.440046	1.641041	8.610796	1.92E-10	7.75E-09	13.74113
SCN4B	-1.82188	2.005766	-8.60992	1.93E-10	7.75E-09	13.73857
MGAT3	-2.49725	2.371211	-8.59496	2.01E-10	8.07E-09	13.69491
OCIAD2	1.977005	4.248222	8.570787	2.16E-10	8.64E-09	13.62432
SPTBN2	1.750893	1.701476	8.563585	2.21E-10	8.77E-09	13.60327
FAM114A1	1.236911	3.934346	8.563448	2.21E-10	8.77E-09	13.60287
HELLS	1.07771	0.861602	8.561938	2.22E-10	8.78E-09	13.59846
TCF21	-2.27334	2.417242	-8.56025	2.23E-10	8.78E-09	13.59352
GMNN	1.306415	2.440464	8.559935	2.23E-10	8.78E-09	13.59261
ARHGAP31	-1.66131	3.43578	-8.55697	2.25E-10	8.83E-09	13.58392
IL3RA	-1.48024	2.716953	-8.55503	2.26E-10	8.86E-09	13.57827
TAF1D	1.089785	2.692923	8.548647	2.31E-10	9.00E-09	13.5596
RHOJ	-1.49351	2.77776	-8.53189	2.42E-10	9.42E-09	13.51057
CALCOCO1	-1.13787	3.656336	-8.52692	2.46E-10	9.53E-09	13.49604
PRAM1	-1.55405	1.791007	-8.52232	2.49E-10	9.64E-09	13.48255
PLEK2	2.366604	2.58723	8.513227	2.56E-10	9.87E-09	13.45594
TONSL	1.076134	1.226416	8.501623	2.65E-10	1.02E-08	13.42194
ARHGAP44	-1.4884	2.313348	-8.50151	2.65E-10	1.02E-08	13.42162
CD300C	-1.50671	2.496017	-8.49583	2.70E-10	1.03E-08	13.40497
SYNPO	-1.69519	4.36764	-8.49398	2.71E-10	1.03E-08	13.39955
RRAS	-1.57265	5.780366	-8.49283	2.72E-10	1.03E-08	13.39617
SUSD2	-3.62223	5.253552	-8.4771	2.85E-10	1.07E-08	13.35005
MS4A7	-1.85685	3.988895	-8.47647	2.86E-10	1.07E-08	13.34822
C10orf54	-1.49174	4.130943	-8.46206	2.98E-10	1.12E-08	13.30592
SLC19A3	-1.70342	1.542272	-8.45962	3.00E-10	1.12E-08	13.29875
NHSL1	-1.50982	2.477521	-8.45164	3.07E-10	1.14E-08	13.27533
CSRNP1	-2.29256	5.12113	-8.45083	3.08E-10	1.14E-08	13.27295
NUSAP1	2.047811	2.405581	8.449142	3.10E-10	1.14E-08	13.268
PTPRB	-2.12876	3.046611	-8.44848	3.10E-10	1.14E-08	13.26605
KIAA1324L	-1.55614	2.605571	-8.44527	3.13E-10	1.15E-08	13.25662
KIF20A	1.802095	1.463212	8.441938	3.16E-10	1.16E-08	13.24685

Appendix C5: continued

FAM136A	1.0727	3.350111	8.436986	3.21E-10	1.17E-08	13.2323
CALCRL	-2.06271	3.88073	-8.43501	3.23E-10	1.17E-08	13.2265
BCHE	-1.54433	1.564192	-8.43156	3.26E-10	1.18E-08	13.21637
IGSF9	1.95871	1.30792	8.42392	3.34E-10	1.20E-08	13.1939
CHEK1	1.347802	1.247893	8.423513	3.34E-10	1.20E-08	13.19271
B3GNT3	3.071349	2.123564	8.42098	3.37E-10	1.21E-08	13.18526
CD93	-1.84752	5.106433	-8.40577	3.52E-10	1.25E-08	13.14054
UHRF1	1.661141	1.142506	8.403278	3.55E-10	1.26E-08	13.13321
ENTPD7	1.448012	2.264583	8.397648	3.61E-10	1.28E-08	13.11664
WIF1	-4.25361	4.192882	-8.39206	3.67E-10	1.29E-08	13.10019
WASF3	-1.61819	2.122185	-8.38831	3.71E-10	1.30E-08	13.08915
ITM2C	1.131386	5.096086	8.387479	3.72E-10	1.30E-08	13.08672
TNS1	-2.17975	5.000454	-8.37913	3.81E-10	1.33E-08	13.06214
DAAM2	-1.31031	2.292634	-8.37607	3.85E-10	1.33E-08	13.05312
MAMDC2	-2.33185	2.947087	-8.37552	3.85E-10	1.33E-08	13.05152
FAM111B	1.448182	1.206757	8.373061	3.88E-10	1.33E-08	13.04427
SEMA6A	-1.55075	1.567683	-8.36891	3.93E-10	1.34E-08	13.03203
CLDN12	1.272085	3.059144	8.368747	3.93E-10	1.34E-08	13.03156
VEPH1	-2.15814	2.625719	-8.36793	3.94E-10	1.34E-08	13.02914
C12orf49	-1.20319	4.023273	-8.36509	3.97E-10	1.35E-08	13.02078
CRABP2	4.501835	3.93073	8.352347	4.13E-10	1.40E-08	12.98323
KRT4	-2.56579	2.079881	-8.34937	4.16E-10	1.41E-08	12.97446
SLC9A7	1.356732	1.781755	8.340734	4.27E-10	1.44E-08	12.949
ODAM	-1.28804	0.951695	-8.3367	4.32E-10	1.45E-08	12.93709
ABI3BP	-2.14368	2.850761	-8.33177	4.39E-10	1.47E-08	12.92256
HEATR1	1.287381	2.425652	8.323689	4.49E-10	1.50E-08	12.89872
KIF4A	1.931512	1.305425	8.323262	4.50E-10	1.50E-08	12.89746
MKI67	2.056028	1.675972	8.321293	4.53E-10	1.50E-08	12.89165
SFTPD	-3.52338	7.66762	-8.31977	4.55E-10	1.50E-08	12.88715
MCM6	1.417131	3.186064	8.308181	4.71E-10	1.55E-08	12.85294
PTH1R	-1.15652	1.412923	-8.30716	4.72E-10	1.55E-08	12.84992
SHMT2	1.244945	3.66	8.300939	4.81E-10	1.57E-08	12.83156

Appendix C5: continued

LHFPL3	-1.26854	0.963437	-8.29396	4.91E-10	1.60E-08	12.81094
PFKP	2.088526	4.16782	8.272312	5.24E-10	1.70E-08	12.74696
GNPNAT1	1.275074	2.930787	8.264034	5.37E-10	1.74E-08	12.72248
CCM2L	-1.58633	1.87079	-8.26326	5.38E-10	1.74E-08	12.7202
PODXL2	2.408957	2.87737	8.252869	5.55E-10	1.78E-08	12.68945
CCNB2	2.020839	1.78346	8.250665	5.59E-10	1.79E-08	12.68293
SPN	-1.74914	2.953845	-8.24418	5.70E-10	1.82E-08	12.66375
MFSD2A	-2.0683	4.100386	-8.24337	5.71E-10	1.82E-08	12.66133
CD300LF	-1.5751	2.928654	-8.23918	5.78E-10	1.84E-08	12.64893
CDCA7	1.760845	1.529266	8.239128	5.78E-10	1.84E-08	12.64879
MRPL3	1.139444	4.646496	8.236209	5.83E-10	1.85E-08	12.64014
PARP1	1.273926	4.462247	8.232158	5.91E-10	1.86E-08	12.62815
GIMAP8	-1.9394	3.354798	-8.23064	5.93E-10	1.86E-08	12.62365
ZNF146	1.057829	4.273779	8.223778	6.05E-10	1.89E-08	12.60333
MME	-1.937	2.513953	-8.22303	6.07E-10	1.89E-08	12.6011
CDC20	2.653686	2.304033	8.219723	6.13E-10	1.90E-08	12.59132
PPP1R14A	-1.95635	3.209354	-8.21765	6.17E-10	1.91E-08	12.58517
NCAPG2	1.348813	1.833269	8.217162	6.18E-10	1.91E-08	12.58373
FHL2	2.21613	2.611358	8.211158	6.29E-10	1.94E-08	12.56594
GIN52	1.609364	1.318184	8.206465	6.38E-10	1.96E-08	12.55203
RSPO1	-1.23631	0.950667	-8.20038	6.49E-10	1.99E-08	12.53401
RXFP1	-1.11804	0.886115	-8.19948	6.51E-10	1.99E-08	12.53134
THBD	-2.29554	4.636185	-8.19931	6.51E-10	1.99E-08	12.53081
TCEAL2	-1.68238	1.500167	-8.19806	6.54E-10	1.99E-08	12.52713
USHBP1	-1.10013	1.037492	-8.1953	6.59E-10	2.00E-08	12.51895
ABCG1	-1.24411	3.531512	-8.193	6.64E-10	2.01E-08	12.5121
RAI2	-1.803	3.217671	-8.18531	6.79E-10	2.06E-08	12.4893
FOLR3	-1.35057	0.977722	-8.18294	6.84E-10	2.06E-08	12.48227
AK1	-1.40896	3.221082	-8.1766	6.97E-10	2.09E-08	12.46345
KDEL3	2.158694	3.54611	8.176339	6.98E-10	2.09E-08	12.46269
SEMA5A	-1.73382	2.660331	-8.1748	7.01E-10	2.09E-08	12.45811
HMGB3	2.536937	3.912037	8.174085	7.03E-10	2.09E-08	12.456

Appendix C5: continued

FLAD1	1.291861	3.136304	8.171229	7.09E-10	2.10E-08	12.44752
PID1	-1.62714	3.212477	-8.17098	7.09E-10	2.10E-08	12.44679
OTUD1	-1.60864	3.667906	-8.16938	7.12E-10	2.10E-08	12.44203
PEAR1	-1.34471	1.853974	-8.1647	7.23E-10	2.12E-08	12.42815
IQGAP3	1.86113	1.358356	8.163301	7.26E-10	2.13E-08	12.42399
HSPB6	-2.88548	3.129144	-8.16167	7.29E-10	2.13E-08	12.41916
TPX2	2.638088	2.371493	8.153395	7.47E-10	2.18E-08	12.39457
CCT5	1.288844	4.762567	8.152445	7.50E-10	2.18E-08	12.39175
KIF2C	2.035905	1.53635	8.151523	7.52E-10	2.18E-08	12.38901
AGRP	-1.60243	1.400525	-8.14986	7.55E-10	2.19E-08	12.38408
STIL	1.137905	0.919625	8.142938	7.71E-10	2.23E-08	12.36351
PXDC1	-1.27886	4.390161	-8.13322	7.94E-10	2.29E-08	12.33462
TGFBR2	-1.46424	6.225877	-8.12696	8.09E-10	2.33E-08	12.31603
ARRB2	-1.04078	4.015289	-8.11675	8.34E-10	2.39E-08	12.28568
DOK2	-1.76243	3.663947	-8.10351	8.68E-10	2.48E-08	12.24629
ANLN	2.40627	1.8052	8.101555	8.73E-10	2.48E-08	12.24047
CDC6	1.759521	1.298752	8.087978	9.10E-10	2.58E-08	12.20006
NUP62CL	1.222807	1.217818	8.084383	9.19E-10	2.60E-08	12.18935
CCNA2	2.008529	1.837185	8.081567	9.27E-10	2.61E-08	12.18097
COL10A1	3.206509	2.162094	8.080992	9.29E-10	2.61E-08	12.17926
B4GALT2	1.114684	3.491238	8.079281	9.34E-10	2.62E-08	12.17416
AURKA	1.729112	1.981135	8.072472	9.53E-10	2.67E-08	12.15388
CLEC14A	-1.96745	4.543499	-8.07068	9.58E-10	2.68E-08	12.14853
CBX4	1.018039	3.349713	8.061991	9.83E-10	2.74E-08	12.12266
WFS1	-1.63346	4.518643	-8.03135	1.08E-09	2.96E-08	12.03129
UHMK1	1.121593	4.229617	8.029123	1.09E-09	2.98E-08	12.02466
F11	-1.27537	1.096132	-8.02738	1.09E-09	2.99E-08	12.01946
KIF26B	1.679881	1.22611	8.025489	1.10E-09	3.00E-08	12.01381
BCL6B	-1.48857	2.633081	-8.01309	1.14E-09	3.10E-08	11.97682
GPA33	-2.00927	1.431296	-8.00716	1.16E-09	3.15E-08	11.95909
TTK	1.340702	0.937004	8.005099	1.17E-09	3.17E-08	11.95295
TTC39C	1.249028	1.861431	8.000433	1.18E-09	3.20E-08	11.93902

Appendix C5: continued

CEP55	2.223039	1.829332	7.998004	1.19E-09	3.22E-08	11.93176
C1orf106	2.041913	2.322379	7.990991	1.22E-09	3.28E-08	11.91082
FOXF1	-2.00374	2.79113	-7.98999	1.22E-09	3.28E-08	11.90783
CYBRD1	-1.73246	5.535518	-7.97355	1.28E-09	3.44E-08	11.8587
TIMELESS	1.304252	2.335046	7.970785	1.29E-09	3.46E-08	11.85043
SAPCD2	1.734971	1.19841	7.967185	1.31E-09	3.49E-08	11.83967
ORC5	1.049538	2.299522	7.961461	1.33E-09	3.53E-08	11.82255
SEZ6L2	1.553728	3.748906	7.961277	1.33E-09	3.53E-08	11.822
FAM162B	-1.59487	2.38796	-7.96103	1.33E-09	3.53E-08	11.82127
HLA-E	-1.36255	8.830638	-7.95868	1.34E-09	3.53E-08	11.81424
SELP	-1.83658	2.575448	-7.95702	1.35E-09	3.53E-08	11.80927
SFTPA2	-4.24623	10.70812	-7.95674	1.35E-09	3.53E-08	11.80844
SFTPA1	-4.35548	10.55854	-7.95661	1.35E-09	3.53E-08	11.80804
CCNF	1.022532	1.289087	7.948429	1.38E-09	3.60E-08	11.78357
GIMAP1	-1.43162	1.980141	-7.94748	1.39E-09	3.61E-08	11.78073
LTBP4	-2.08202	4.752657	-7.94303	1.41E-09	3.63E-08	11.76742
SPRYD7	-1.03668	2.878568	-7.93543	1.44E-09	3.71E-08	11.74468
GFPT1	1.358273	4.032903	7.931956	1.46E-09	3.74E-08	11.73427
GLDN	-1.59497	1.604379	-7.92967	1.47E-09	3.76E-08	11.72742
SULT1A2	-1.19551	1.497524	-7.92651	1.48E-09	3.79E-08	11.71797
NDRG2	-1.54779	3.170727	-7.91953	1.51E-09	3.84E-08	11.69707
BHLHA15	1.203769	1.147539	7.904372	1.58E-09	4.00E-08	11.65166
KAT2A	1.203228	2.989894	7.895673	1.62E-09	4.09E-08	11.62559
DNAJC10	1.023383	2.751486	7.888951	1.66E-09	4.15E-08	11.60544
CDT1	1.610536	1.512876	7.888106	1.66E-09	4.15E-08	11.60291
PRDX4	1.573132	5.275587	7.88541	1.67E-09	4.18E-08	11.59482
MAGED1	1.03814	4.949928	7.875572	1.73E-09	4.29E-08	11.56532
PDK1	1.06	1.233127	7.871346	1.75E-09	4.33E-08	11.55264
AQP4	-3.36089	4.958499	-7.87021	1.75E-09	4.33E-08	11.54924
LRRK2	-2.18566	3.750018	-7.8613	1.80E-09	4.42E-08	11.52249
CARD11	1.735398	2.198092	7.85945	1.81E-09	4.44E-08	11.51695
FAM60A	1.124563	3.503982	7.852402	1.85E-09	4.52E-08	11.4958

Appendix C5: continued

HHIP	-2.13258	2.245282	-7.84729	1.88E-09	4.57E-08	11.48044
STX1A	1.410029	1.295834	7.846966	1.88E-09	4.57E-08	11.47948
ANGPTL1	-1.45762	1.63019	-7.84573	1.89E-09	4.58E-08	11.47575
APOBR	-1.77961	2.784339	-7.83739	1.94E-09	4.69E-08	11.45072
GINS1	1.455205	1.238024	7.831929	1.97E-09	4.76E-08	11.43432
CD34	-1.49341	3.265631	-7.82987	1.98E-09	4.78E-08	11.42814
KNTC1	1.221598	1.220379	7.82533	2.01E-09	4.84E-08	11.4145
PDGFB	-1.53663	3.483937	-7.81769	2.06E-09	4.93E-08	11.39155
CCDC34	1.118122	1.514778	7.812256	2.09E-09	4.99E-08	11.37521
TRAF4	1.043729	3.82593	7.81077	2.10E-09	5.01E-08	11.37074
CDO1	-1.59252	1.703265	-7.8103	2.10E-09	5.01E-08	11.36932
INCENP	1.123408	2.184229	7.807848	2.12E-09	5.03E-08	11.36196
RGS9	-1.07192	0.970263	-7.80494	2.14E-09	5.07E-08	11.35321
COPB2	1.01656	4.49025	7.802335	2.15E-09	5.10E-08	11.34538
TGM1	-1.23464	1.040397	-7.8013	2.16E-09	5.10E-08	11.34226
ANKRD29	-1.91249	2.585139	-7.79834	2.18E-09	5.13E-08	11.33338
TDRKH	1.154968	2.244671	7.792128	2.22E-09	5.21E-08	11.31469
FIGNL1	1.16167	1.592227	7.790609	2.23E-09	5.23E-08	11.31012
TOX2	-1.4313	2.185578	-7.78481	2.27E-09	5.29E-08	11.29267
ZNF217	1.328771	3.357801	7.778245	2.32E-09	5.39E-08	11.27292
PODXL	-1.25955	4.072552	-7.7756	2.34E-09	5.42E-08	11.26495
P4HB	1.156062	7.32057	7.773842	2.35E-09	5.44E-08	11.25967
C1orf162	-1.70895	3.615211	-7.77219	2.36E-09	5.45E-08	11.2547
MDK	2.080669	4.96017	7.771919	2.36E-09	5.45E-08	11.25388
ELMO3	1.268266	3.588738	7.770878	2.37E-09	5.46E-08	11.25075
PRC1	1.779116	1.873489	7.754896	2.49E-09	5.72E-08	11.20263
BMPER	-1.24276	1.042229	-7.75445	2.49E-09	5.72E-08	11.20129
FAM83A	3.980175	2.152565	7.746443	2.55E-09	5.84E-08	11.17717
SLC16A11	-1.29589	1.453005	-7.7416	2.59E-09	5.90E-08	11.16259
SNX22	-1.27333	1.485605	-7.73981	2.60E-09	5.92E-08	11.1572
ACTL6A	1.061633	3.642796	7.73565	2.64E-09	5.98E-08	11.14466
AGTR1	-1.10605	1.181753	-7.73555	2.64E-09	5.98E-08	11.14435

Appendix C5: continued

TMPRSS4	2.765557	1.664275	7.730265	2.68E-09	6.06E-08	11.12843
RBP2	-1.739	1.227096	-7.72458	2.73E-09	6.15E-08	11.11129
GPR146	-1.02217	1.01263	-7.72351	2.74E-09	6.16E-08	11.10807
DKC1	1.011889	3.679452	7.723084	2.74E-09	6.16E-08	11.10679
SHCBP1	1.378632	1.236055	7.716435	2.80E-09	6.27E-08	11.08674
BRI3BP	1.147202	2.103154	7.715282	2.81E-09	6.28E-08	11.08326
ODF3L1	-1.19442	1.100178	-7.69825	2.96E-09	6.56E-08	11.03189
CCDC85A	-1.14665	1.05494	-7.69816	2.96E-09	6.56E-08	11.03163
ZNF385B	-1.94967	2.336794	-7.69575	2.98E-09	6.60E-08	11.02436
2-Mar	-1.34804	3.432075	-7.69478	2.99E-09	6.61E-08	11.02141
CDH3	2.879077	2.90811	7.68676	3.06E-09	6.76E-08	10.99722
MTFR1	1.196222	2.679466	7.685142	3.08E-09	6.77E-08	10.99234
ITM2A	-1.89179	4.147852	-7.68397	3.09E-09	6.78E-08	10.98879
NME1	1.845172	3.069765	7.683054	3.10E-09	6.79E-08	10.98604
ALPL	-2.5469	5.260142	-7.68226	3.10E-09	6.79E-08	10.98363
NXPH3	-1.10683	1.11391	-7.68071	3.12E-09	6.81E-08	10.97895
FANCF	1.105386	2.119066	7.659957	3.32E-09	7.21E-08	10.9163
TWF1	1.106474	3.83529	7.655816	3.36E-09	7.29E-08	10.90379
HBB	-4.17421	7.11504	-7.65286	3.39E-09	7.34E-08	10.89486
SORD	1.085661	1.772276	7.650439	3.42E-09	7.38E-08	10.88754
SLIT2	-1.86397	2.859992	-7.64938	3.43E-09	7.40E-08	10.88433
TOM1L2	-1.23516	3.242177	-7.64831	3.44E-09	7.41E-08	10.88111
HMMR	1.756052	1.359595	7.646797	3.46E-09	7.43E-08	10.87654
EXO1	1.404202	0.944596	7.644751	3.48E-09	7.45E-08	10.87035
RETN	-2.81968	3.054459	-7.64216	3.51E-09	7.50E-08	10.86253
XDH	1.808237	1.168274	7.638612	3.54E-09	7.55E-08	10.8518
FAM110D	-1.43237	1.624713	-7.63715	3.56E-09	7.58E-08	10.84739
HPS3	1.017016	2.677632	7.635083	3.58E-09	7.61E-08	10.84113
MSRB3	-1.40848	3.241146	-7.62729	3.67E-09	7.78E-08	10.81756
MCM2	1.847506	2.736737	7.622747	3.72E-09	7.88E-08	10.80383
ASPM	1.438992	0.896009	7.614491	3.82E-09	8.05E-08	10.77886
UBE2C	2.919251	2.69206	7.614006	3.82E-09	8.05E-08	10.7774

Appendix C5: continued

PCNA	1.119738	5.224469	7.611722	3.85E-09	8.09E-08	10.77049
FRMD3	-1.16959	1.385394	-7.6097	3.87E-09	8.13E-08	10.76438
CTHRC1	3.183361	3.058328	7.609077	3.88E-09	8.13E-08	10.76248
SKA3	1.203249	0.900907	7.601276	3.97E-09	8.31E-08	10.73888
C15orf48	3.265375	3.81484	7.600457	3.98E-09	8.32E-08	10.7364
NMUR1	-1.14933	0.931518	-7.59775	4.02E-09	8.38E-08	10.72822
CGNL1	-1.87394	3.309337	-7.59478	4.05E-09	8.43E-08	10.71922
NCAPH	1.628822	1.341571	7.587968	4.14E-09	8.56E-08	10.6986
CPAMD8	-1.76171	2.238668	-7.58121	4.22E-09	8.73E-08	10.67814
CKS1B	1.607905	2.921225	7.576855	4.28E-09	8.80E-08	10.66496
GPR87	2.921031	1.67634	7.569733	4.37E-09	8.95E-08	10.64338
MS4A15	-3.53232	3.257803	-7.56444	4.45E-09	9.07E-08	10.62734
MND1	1.05694	0.876119	7.562393	4.47E-09	9.10E-08	10.62115
TACC1	-1.53428	4.212119	-7.5429	4.75E-09	9.58E-08	10.56208
TMEM150B	-1.35351	1.955387	-7.53701	4.84E-09	9.74E-08	10.54422
KIF23	1.351858	1.209294	7.527218	4.98E-09	1.00E-07	10.51452
FUT2	1.82662	1.405084	7.522975	5.05E-09	1.01E-07	10.50166
PVRL4	2.027854	2.984124	7.512997	5.20E-09	1.03E-07	10.47139
GIMAP7	-1.77026	4.165096	-7.51031	5.25E-09	1.04E-07	10.46325
EPN3	1.614978	1.162521	7.50812	5.28E-09	1.05E-07	10.45659
TMED2	1.02024	6.328507	7.506026	5.32E-09	1.05E-07	10.45023
TSPAN7	-2.43535	3.561062	-7.49699	5.47E-09	1.07E-07	10.4228
ADAMTSL4	-1.70695	2.94211	-7.49635	5.48E-09	1.07E-07	10.42088
CBLC	2.404409	2.231583	7.493358	5.53E-09	1.08E-07	10.41178
NPNT	-2.27956	4.279816	-7.48949	5.59E-09	1.09E-07	10.40005
HOOK1	1.042138	2.418255	7.487207	5.63E-09	1.09E-07	10.39311
SLC11A1	-1.65475	2.706414	-7.48633	5.65E-09	1.10E-07	10.39045
CHAF1B	1.029323	1.188528	7.48363	5.69E-09	1.10E-07	10.38225
NLN	1.102333	1.744224	7.479096	5.77E-09	1.12E-07	10.36848
TMEM178A	-1.20628	1.179545	-7.47229	5.90E-09	1.14E-07	10.34781
SASH1	-1.4222	3.043391	-7.46733	5.99E-09	1.15E-07	10.33274
SLCO2A1	-2.2313	4.284818	-7.4651	6.03E-09	1.16E-07	10.32596

Appendix C5: continued

SPARCL1	-1.75981	6.622646	-7.45832	6.15E-09	1.18E-07	10.30537
ABCA3	-2.68637	5.708274	-7.45011	6.31E-09	1.20E-07	10.2804
FAT1	1.694176	3.342514	7.44697	6.37E-09	1.21E-07	10.27086
FHDC1	-1.07049	2.548643	-7.43735	6.56E-09	1.24E-07	10.24162
VPS72	1.006476	3.37012	7.436307	6.58E-09	1.24E-07	10.23844
KIF1C	-1.19057	4.719897	-7.43186	6.67E-09	1.26E-07	10.22493
AMICA1	-1.30058	2.489794	-7.43168	6.68E-09	1.26E-07	10.22438
BUB1	1.552602	1.377758	7.429513	6.72E-09	1.26E-07	10.21778
CANT1	1.054822	4.437388	7.427503	6.76E-09	1.27E-07	10.21167
LMCD1	-1.21317	3.022213	-7.42068	6.91E-09	1.29E-07	10.19091
ALG1L	1.949699	1.685162	7.402808	7.30E-09	1.35E-07	10.13653
DHCR24	-1.1906	7.560178	-7.3992	7.38E-09	1.36E-07	10.12555
TMTC4	1.029528	1.962584	7.396809	7.43E-09	1.37E-07	10.11827
CBX3	1.066938	4.894129	7.395515	7.46E-09	1.37E-07	10.11433
ACKR1	-2.43745	3.618803	-7.39259	7.53E-09	1.38E-07	10.10542
SYNJ2	1.154639	1.637152	7.391898	7.55E-09	1.38E-07	10.10332
FLI1	-1.2642	2.559111	-7.3893	7.61E-09	1.39E-07	10.09541
CHD1L	1.04168	3.912226	7.386945	7.66E-09	1.40E-07	10.08824
COL3A1	3.102972	6.733751	7.386203	7.68E-09	1.40E-07	10.08598
MELK	1.910698	1.416357	7.382339	7.77E-09	1.41E-07	10.07421
LAMC3	-1.4558	2.163373	-7.38184	7.78E-09	1.41E-07	10.07268
SRD5A1	1.293391	1.758097	7.374676	7.96E-09	1.43E-07	10.05087
MYBL2	2.678022	2.213238	7.372476	8.01E-09	1.44E-07	10.04417
EMR1	-1.53056	1.545027	-7.36718	8.14E-09	1.46E-07	10.02805
OLR1	-2.56084	4.482871	-7.36492	8.20E-09	1.47E-07	10.02115
GJA4	-1.2929	2.975537	-7.36358	8.23E-09	1.47E-07	10.01707
PPP1R15A	-1.80152	5.539999	-7.35978	8.33E-09	1.49E-07	10.00548
GALNT7	1.704778	2.904698	7.347468	8.65E-09	1.54E-07	9.967964
DTL	1.4862	1.524457	7.346567	8.67E-09	1.54E-07	9.965219
MARCO	-3.15141	5.885823	-7.3382	8.90E-09	1.58E-07	9.939719
AURKB	1.723366	1.421157	7.338158	8.90E-09	1.58E-07	9.939582
IRAK1	1.134812	4.804344	7.332568	9.06E-09	1.60E-07	9.922537

Appendix C5: continued

THBS2	2.817297	3.579161	7.332013	9.07E-09	1.60E-07	9.920843
TMCO1	1.015691	4.325135	7.32536	9.26E-09	1.63E-07	9.900555
PCOLCE2	-1.78844	2.389916	-7.3246	9.28E-09	1.63E-07	9.89823
CDCA8	1.933115	1.80971	7.314479	9.57E-09	1.68E-07	9.867361
NDC80	1.386452	1.121446	7.305282	9.85E-09	1.72E-07	9.839298
CYP4B1	-3.89921	5.039926	-7.29111	1.03E-08	1.79E-07	9.796048
MSH2	1.128262	2.871516	7.289589	1.03E-08	1.80E-07	9.791397
KHDRBS2	-1.36997	1.305615	-7.28879	1.04E-08	1.80E-07	9.788949
ADCY4	-1.17473	1.434846	-7.28632	1.04E-08	1.81E-07	9.781427
CTTN	1.01058	5.113095	7.277196	1.07E-08	1.85E-07	9.753557
CKAP2L	1.239867	0.896086	7.276373	1.08E-08	1.85E-07	9.751041
ATAD2	1.496552	2.219536	7.273247	1.09E-08	1.87E-07	9.741496
PTGDS	-2.12356	5.28276	-7.2718	1.09E-08	1.87E-07	9.73706
KIF20B	1.011314	1.362938	7.27014	1.10E-08	1.88E-07	9.732004
VAR5	1.13719	3.86334	7.263928	1.12E-08	1.90E-07	9.713029
TBC1D2	-1.12481	4.279411	-7.25824	1.14E-08	1.93E-07	9.695661
ENG	-1.82873	5.783655	-7.25806	1.14E-08	1.93E-07	9.695091
PITX1	2.051563	1.186484	7.255923	1.15E-08	1.94E-07	9.68857
RAB19	1.119338	1.068253	7.254573	1.15E-08	1.94E-07	9.684445
LAD1	1.874234	4.498617	7.252673	1.16E-08	1.95E-07	9.67864
ACOXL	-1.27156	1.365323	-7.25244	1.16E-08	1.95E-07	9.677923
WDHD1	1.055496	1.279274	7.240413	1.20E-08	2.01E-07	9.641168
ADH1B	-3.27314	4.239614	-7.23852	1.21E-08	2.02E-07	9.635374
CPD	1.40095	4.229405	7.237362	1.21E-08	2.02E-07	9.631841
NUF2	1.766543	1.222778	7.237191	1.22E-08	2.02E-07	9.631319
P4HA1	1.147739	4.840626	7.233343	1.23E-08	2.05E-07	9.619554
TNS2	-1.53703	3.930166	-7.23158	1.24E-08	2.05E-07	9.614172
ADM2	1.264834	0.917219	7.231303	1.24E-08	2.05E-07	9.613317
SLC27A3	-1.4736	3.250455	-7.22896	1.25E-08	2.06E-07	9.606153
ICAM2	-1.10297	2.765306	-7.22415	1.26E-08	2.09E-07	9.591437
GMFG	-1.44532	4.494588	-7.22384	1.27E-08	2.09E-07	9.590486
SPC24	1.348066	1.196416	7.22091	1.28E-08	2.10E-07	9.581536

Appendix C5: continued

GPR4	-1.59375	2.210368	-7.21812	1.29E-08	2.11E-07	9.57299
C11orf96	-2.04481	4.481142	-7.21776	1.29E-08	2.11E-07	9.571904
WISP2	-1.69482	2.3463	-7.21746	1.29E-08	2.11E-07	9.570999
AATK	-1.64556	1.949055	-7.21693	1.29E-08	2.11E-07	9.569366
TSPAN18	-1.59521	2.781525	-7.21623	1.30E-08	2.11E-07	9.567219
PTGES	2.273426	3.003643	7.209822	1.32E-08	2.15E-07	9.547623
BIRC5	2.375026	1.981471	7.2087	1.33E-08	2.15E-07	9.54419
IDH2	1.004117	4.932153	7.201355	1.36E-08	2.20E-07	9.521717
KIFC1	1.674358	1.844364	7.192023	1.40E-08	2.25E-07	9.493158
ERO1L	1.930786	3.99074	7.1882	1.41E-08	2.28E-07	9.481458
KDM5B	1.220067	3.079093	7.186576	1.42E-08	2.28E-07	9.476486
PLK4	1.006276	1.032358	7.181437	1.44E-08	2.31E-07	9.460757
RASGRF1	-1.93737	2.019697	-7.1778	1.46E-08	2.34E-07	9.449624
IRX2	-2.18985	2.939085	-7.17693	1.46E-08	2.34E-07	9.446965
MSI2	1.160893	1.839282	7.1693	1.50E-08	2.39E-07	9.423595
AVL9	1.144432	2.354809	7.165262	1.52E-08	2.42E-07	9.41123
RECQL4	1.576741	1.467754	7.159499	1.54E-08	2.46E-07	9.393578
ADAMTSL3	-1.20156	1.502893	-7.15879	1.55E-08	2.46E-07	9.391413
KIF2A	1.044166	2.695931	7.155205	1.57E-08	2.48E-07	9.380425
MCM10	1.178599	0.772751	7.147196	1.60E-08	2.54E-07	9.35589
NQO1	2.675985	4.666586	7.145044	1.62E-08	2.55E-07	9.349296
TNNI2	-1.35312	1.643192	-7.1407	1.64E-08	2.58E-07	9.335993
NGEF	1.767274	1.096623	7.139311	1.64E-08	2.59E-07	9.331729
CD101	-1.58794	1.885186	-7.13177	1.68E-08	2.64E-07	9.308633
SOCS2	-2.00402	2.920612	-7.13079	1.69E-08	2.65E-07	9.305613
CENPU	1.504292	1.74181	7.13022	1.69E-08	2.65E-07	9.303868
HJURP	1.696412	1.162173	7.126293	1.71E-08	2.68E-07	9.291832
SHROOM4	-1.36507	2.491703	-7.12532	1.72E-08	2.68E-07	9.288834
MAN2A1	1.009631	2.775431	7.124311	1.72E-08	2.68E-07	9.285757
VWF	-1.98496	5.548549	-7.1222	1.73E-08	2.70E-07	9.279294
P3H4	1.520976	2.468405	7.116017	1.77E-08	2.74E-07	9.260327
ORC1	1.350503	1.088537	7.114419	1.78E-08	2.76E-07	9.255429

Appendix C5: continued

MAD2L1	1.367233	1.26919	7.108534	1.81E-08	2.79E-07	9.237381
HDGF	1.132237	6.290585	7.10491	1.83E-08	2.81E-07	9.226269
RAD51	1.110947	1.091646	7.104337	1.83E-08	2.82E-07	9.224511
LGALSL	-1.56455	3.306104	-7.10097	1.85E-08	2.84E-07	9.214187
NDC1	1.059944	2.622185	7.092944	1.90E-08	2.90E-07	9.189567
GJB2	2.706833	1.952064	7.089499	1.92E-08	2.92E-07	9.178997
RFC4	1.391514	2.067454	7.088142	1.93E-08	2.93E-07	9.174832
COL6A6	-1.639	1.86919	-7.08746	1.93E-08	2.93E-07	9.172732
NLRC4	-1.12886	1.835562	-7.0863	1.94E-08	2.94E-07	9.169171
SPI1	-1.81418	4.845139	-7.08287	1.96E-08	2.97E-07	9.158673
EMR3	-1.09213	1.065607	-7.07797	1.99E-08	3.00E-07	9.143629
ABCA8	-1.64521	1.810118	-7.07414	2.01E-08	3.03E-07	9.131872
ASF1B	1.660244	2.112589	7.052863	2.15E-08	3.21E-07	9.066554
PIP5K1B	-1.77398	2.354457	-7.05206	2.15E-08	3.21E-07	9.064101
MOCS1	-1.1076	2.192605	-7.04813	2.18E-08	3.24E-07	9.052023
CHMP4C	1.113656	3.508199	7.046333	2.19E-08	3.25E-07	9.046502
ETV4	1.952569	1.851083	7.044366	2.21E-08	3.27E-07	9.040461
NSUN2	1.054591	3.842654	7.040135	2.24E-08	3.30E-07	9.027466
CFD	-2.38617	5.465383	-7.03774	2.25E-08	3.33E-07	9.020105
PLA1A	-1.54443	2.305506	-7.03652	2.26E-08	3.33E-07	9.016351
GPRIN1	1.37698	1.133226	7.035307	2.27E-08	3.34E-07	9.012636
HBA1	-2.02919	1.388105	-7.03172	2.29E-08	3.38E-07	9.001626
UGGT1	1.092727	3.400448	7.031379	2.30E-08	3.38E-07	9.000571
CDCA5	1.679613	1.573479	7.027704	2.32E-08	3.40E-07	8.98928
RRM2	2.142556	2.060657	7.020421	2.38E-08	3.46E-07	8.966903
GALNT18	-1.36227	3.664565	-7.01977	2.38E-08	3.46E-07	8.964888
PTTG1	1.799413	2.508892	7.013774	2.43E-08	3.51E-07	8.946477
SLC15A3	-1.32971	3.524081	-7.01071	2.45E-08	3.53E-07	8.937048
EEF1A2	3.233223	2.000741	7.009548	2.46E-08	3.54E-07	8.933492
PPIL1	1.046395	3.873137	7.006394	2.48E-08	3.56E-07	8.923798
CXCL13	3.515315	2.361788	7.003735	2.50E-08	3.58E-07	8.915624
GATA2	-1.63394	2.411005	-7.00273	2.51E-08	3.59E-07	8.912533

Appendix C5: continued

MANF	1.168965	4.488094	6.999147	2.54E-08	3.62E-07	8.901521
ABCC3	2.089953	3.192898	6.995523	2.57E-08	3.66E-07	8.89038
NPM3	1.452919	3.68227	6.98153	2.68E-08	3.78E-07	8.847354
TMEM74B	-1.1007	1.374839	-6.9776	2.71E-08	3.82E-07	8.835283
RHBDL2	1.561784	1.340186	6.976769	2.72E-08	3.82E-07	8.832712
ITGB4	2.056332	4.376779	6.976754	2.72E-08	3.82E-07	8.832667
A2M	-1.89635	8.352002	-6.97662	2.72E-08	3.82E-07	8.832254
NINJ2	-1.26621	3.249032	-6.96022	2.87E-08	4.00E-07	8.781815
EPHB2	1.356383	1.33456	6.953583	2.93E-08	4.07E-07	8.761387
NDST1	-1.3048	4.272778	-6.94464	3.01E-08	4.16E-07	8.733858
CD97	-1.41213	5.056863	-6.94325	3.02E-08	4.17E-07	8.729596
DSP	2.417409	4.100932	6.93815	3.07E-08	4.22E-07	8.713893
TPPP	-1.92817	2.540812	-6.93567	3.09E-08	4.25E-07	8.706261
ADTRP	-1.26634	1.754066	-6.93544	3.09E-08	4.25E-07	8.705538
PRKDC	1.515333	3.644304	6.930414	3.14E-08	4.31E-07	8.690079
JUND	-1.71592	6.586188	-6.93029	3.14E-08	4.31E-07	8.6897
TOM1L1	1.062408	2.555793	6.928175	3.17E-08	4.33E-07	8.683187
IKBKE	1.0832	2.067961	6.926146	3.19E-08	4.35E-07	8.676941
CHPF2	1.139202	4.222728	6.925776	3.19E-08	4.35E-07	8.6758
TGFB3	-1.8844	2.6384	-6.91704	3.28E-08	4.46E-07	8.648912
SLC25A10	1.049469	1.23228	6.913503	3.31E-08	4.50E-07	8.63801
INSIG1	-1.18839	4.161244	-6.90925	3.36E-08	4.56E-07	8.624899
PLEKHA6	1.479044	2.277564	6.897613	3.48E-08	4.70E-07	8.589069
MYO1E	1.310425	3.078922	6.893266	3.53E-08	4.75E-07	8.575678
NRN1	-1.62525	2.605324	-6.89318	3.53E-08	4.75E-07	8.575415
SYNM	-1.10684	1.972598	-6.89209	3.54E-08	4.76E-07	8.572052
NDNF	-2.40284	4.781754	-6.89065	3.56E-08	4.77E-07	8.567634
TK1	2.3027	3.629655	6.886338	3.61E-08	4.83E-07	8.554336
ARHGEF16	1.265922	2.140374	6.879902	3.68E-08	4.92E-07	8.534504
SOX4	1.654141	4.336345	6.878407	3.70E-08	4.93E-07	8.529896
DLG5	1.35087	2.216144	6.875622	3.73E-08	4.97E-07	8.521315
HS6ST2	2.561404	1.764155	6.87354	3.75E-08	4.99E-07	8.514898

Appendix C5: continued

LPHN2	-1.43229	3.543813	-6.86854	3.81E-08	5.07E-07	8.499473
AQP1	-2.39974	7.335744	-6.86781	3.82E-08	5.07E-07	8.497252
TSPAN6	1.291089	3.348183	6.851853	4.01E-08	5.32E-07	8.448048
DCAF13	1.01652	2.259269	6.849523	4.04E-08	5.35E-07	8.440863
CKAP5	1.001004	3.448997	6.847888	4.06E-08	5.36E-07	8.435823
PRKCE	-1.20818	2.242711	-6.84058	4.16E-08	5.47E-07	8.413274
PAFAH1B3	1.529012	3.274385	6.839474	4.17E-08	5.48E-07	8.409878
LMNB1	1.652482	2.931143	6.839026	4.18E-08	5.48E-07	8.408496
ILF2	1.139641	6.173679	6.835973	4.22E-08	5.52E-07	8.399081
TNFRSF21	1.588916	4.73615	6.832432	4.27E-08	5.57E-07	8.38816
CES1	-2.39679	5.182582	-6.83094	4.28E-08	5.59E-07	8.383554
SULT1A1	-1.1254	2.011152	-6.82974	4.30E-08	5.60E-07	8.379847
ENAH	1.075852	3.394538	6.827574	4.33E-08	5.62E-07	8.373178
BAALC	-1.27724	1.337808	-6.82731	4.33E-08	5.62E-07	8.37235
GPR133	-1.54486	2.065274	-6.82425	4.38E-08	5.67E-07	8.362936
RSPO4	-1.51525	1.34663	-6.8221	4.40E-08	5.70E-07	8.356304
RACGAP1	1.244239	2.532013	6.816924	4.48E-08	5.79E-07	8.340325
NCAPG	1.509348	1.129176	6.812975	4.53E-08	5.85E-07	8.328139
DPYSL2	-1.34476	5.27161	-6.81055	4.57E-08	5.89E-07	8.320658
XAGE2B	-1.76536	1.322931	-6.80981	4.58E-08	5.90E-07	8.318365
LILRA5	-1.68283	2.39661	-6.80723	4.61E-08	5.92E-07	8.310411
CCBE1	-1.69201	1.827144	-6.7967	4.77E-08	6.10E-07	8.277913
PDLIM1	-1.34491	6.411164	-6.79411	4.81E-08	6.12E-07	8.269916
KANK2	-1.31216	4.337038	-6.79037	4.86E-08	6.17E-07	8.258385
GORAB	1.022814	2.102021	6.790361	4.86E-08	6.17E-07	8.258356
TYMS	1.476494	2.43644	6.789269	4.88E-08	6.19E-07	8.254985
RHPN1	1.165224	1.947986	6.788508	4.89E-08	6.19E-07	8.252636
LIMCH1	-1.54306	4.615361	-6.78799	4.90E-08	6.20E-07	8.25105
MCM7	1.129592	4.139398	6.786391	4.92E-08	6.22E-07	8.246102
C2	-1.44433	4.04685	-6.78498	4.95E-08	6.24E-07	8.241736
HEG1	-1.64471	4.227071	-6.78197	4.99E-08	6.29E-07	8.232463
LMO2	-1.40602	2.949423	-6.78124	5.00E-08	6.30E-07	8.230193

Appendix C5: continued

PSAT1	2.184647	1.980909	6.77992	5.02E-08	6.32E-07	8.226128
SLC15A2	-1.5725	2.866682	-6.77787	5.06E-08	6.34E-07	8.219801
SELPLG	-1.45887	4.65082	-6.77781	5.06E-08	6.34E-07	8.219598
DKK2	-1.35133	1.597613	-6.77599	5.09E-08	6.37E-07	8.214004
DTX2	1.091966	2.519987	6.775372	5.10E-08	6.38E-07	8.212088
JDP2	-1.23259	3.100941	-6.77318	5.13E-08	6.42E-07	8.205312
PRKCZ	-1.05791	2.809073	-6.75557	5.42E-08	6.76E-07	8.150937
SLIT3	-1.89767	2.666925	-6.7494	5.53E-08	6.88E-07	8.131873
PLEKHN1	1.089169	0.874304	6.745284	5.60E-08	6.96E-07	8.119174
CDK1	1.660917	2.148554	6.743246	5.63E-08	7.00E-07	8.112876
FFAR4	-1.15265	1.110265	-6.74069	5.68E-08	7.05E-07	8.104973
ESRP1	1.071634	4.016639	6.734973	5.78E-08	7.15E-07	8.087322
FERMT2	-1.06489	3.466526	-6.73188	5.84E-08	7.21E-07	8.077769
SLC5A3	1.222213	2.111605	6.729676	5.88E-08	7.26E-07	8.070956
PDZD2	-1.56995	2.176049	-6.72879	5.89E-08	7.27E-07	8.068221
NET1	1.438151	4.67728	6.723025	6.00E-08	7.37E-07	8.050404
HMGA1	2.078997	5.565698	6.720489	6.05E-08	7.42E-07	8.042568
DEPDC1B	1.297104	0.865205	6.718914	6.08E-08	7.42E-07	8.037701
AGTR2	-2.44247	2.289692	-6.71524	6.15E-08	7.50E-07	8.026351
HK3	-1.5758	3.035219	-6.7108	6.23E-08	7.59E-07	8.012641
SNRPE	1.1859	4.521443	6.705587	6.34E-08	7.69E-07	7.996516
PKDCC	-1.42537	2.442	-6.70429	6.36E-08	7.71E-07	7.992499
SULT1C4	-1.30257	1.47232	-6.70199	6.41E-08	7.76E-07	7.985399
STEAP1	2.324726	2.568832	6.687368	6.71E-08	8.10E-07	7.940196
PTGFRN	1.46959	3.442582	6.686318	6.73E-08	8.11E-07	7.93695
ALDH2	-1.33412	4.970598	-6.68548	6.75E-08	8.12E-07	7.934348
MMP11	3.019795	1.759107	6.683181	6.80E-08	8.16E-07	7.927251
C5AR1	-1.93166	4.141017	-6.67863	6.89E-08	8.26E-07	7.913189
KIAA0040	-1.01622	4.176147	-6.67727	6.92E-08	8.29E-07	7.908966
ACKR4	-1.17792	1.191054	-6.6751	6.97E-08	8.33E-07	7.902266
SLC9A3R2	-1.32243	5.170501	-6.66664	7.16E-08	8.47E-07	7.876111
CORO2B	-1.24546	1.463721	-6.66656	7.16E-08	8.47E-07	7.875859

Appendix C5: continued

PALD1	-1.10409	2.725228	-6.6647	7.20E-08	8.50E-07	7.870095
KIAA1462	-1.37814	3.516092	-6.66181	7.27E-08	8.57E-07	7.861147
FOXM1	1.868834	1.647099	6.660096	7.30E-08	8.61E-07	7.855861
CCNE1	1.471267	1.12588	6.659219	7.32E-08	8.62E-07	7.853149
NKD2	-1.24581	2.520944	-6.64819	7.58E-08	8.89E-07	7.819047
MANEAL	1.193652	1.967298	6.646455	7.62E-08	8.93E-07	7.813667
PTPRH	1.858051	1.022305	6.641735	7.74E-08	9.04E-07	7.799063
PDXDC1	1.01243	3.91649	6.636423	7.87E-08	9.17E-07	7.782629
ACP5	-1.75614	5.90631	-6.62771	8.08E-08	9.38E-07	7.755681
NDRG4	-1.46656	1.448316	-6.62557	8.14E-08	9.43E-07	7.749041
GATA6	-1.84138	2.865681	-6.62482	8.16E-08	9.44E-07	7.746738
RILPL2	-1.01844	2.880307	-6.62364	8.19E-08	9.47E-07	7.743086
SORBS3	-1.38753	3.977165	-6.6139	8.44E-08	9.74E-07	7.712936
GGCT	1.157354	3.943852	6.612769	8.47E-08	9.76E-07	7.70943
SLC50A1	1.439396	4.470093	6.609133	8.57E-08	9.87E-07	7.698179
ADARB1	-1.32936	2.316014	-6.60126	8.78E-08	1.01E-06	7.673805
STEAP3	1.077392	3.69481	6.598931	8.85E-08	1.01E-06	7.6666
ABCA12	1.295134	0.671447	6.595129	8.95E-08	1.02E-06	7.654829
HLTF	1.161165	2.829973	6.581182	9.35E-08	1.06E-06	7.611646
SLC7A7	-1.32356	3.532222	-6.58108	9.35E-08	1.06E-06	7.611317
LDLR	-2.07583	4.740574	-6.57389	9.57E-08	1.09E-06	7.589063
C8B	-2.04923	1.57299	-6.57351	9.58E-08	1.09E-06	7.587897
PRKG2	-1.05136	1.179522	-6.57023	9.68E-08	1.09E-06	7.577727
TMEM139	-1.66346	2.250866	-6.56683	9.78E-08	1.10E-06	7.567208
UBASH3B	-1.1361	2.000312	-6.56554	9.82E-08	1.11E-06	7.563207
CALU	1.315097	5.669014	6.562313	9.92E-08	1.12E-06	7.553217
METTL7A	-1.75644	4.96493	-6.55972	1.00E-07	1.12E-06	7.545184
PDK4	-2.2016	4.636174	-6.55849	1.00E-07	1.13E-06	7.54137
ASCC3	1.01895	2.448655	6.552565	1.02E-07	1.15E-06	7.523022
BCL2L15	1.612146	1.096467	6.548126	1.04E-07	1.16E-06	7.509273
KIAA0101	1.559725	1.440707	6.542718	1.05E-07	1.18E-06	7.492521
ARHGAP11A	1.283863	1.340436	6.541861	1.06E-07	1.18E-06	7.489866

Appendix C5: continued

COL5A2	2.212602	3.888738	6.53855	1.07E-07	1.19E-06	7.479608
C17orf53	1.163026	0.947908	6.53468	1.08E-07	1.20E-06	7.467619
ANGPT1	-1.49637	2.22995	-6.53184	1.09E-07	1.21E-06	7.458823
HYAL1	-2.12014	3.340889	-6.52505	1.11E-07	1.23E-06	7.437795
SLC1A4	1.067913	2.458289	6.5224	1.12E-07	1.24E-06	7.429572
PILRA	-1.41304	3.359708	-6.51991	1.13E-07	1.24E-06	7.421866
AP1S1	1.179643	4.625115	6.513066	1.16E-07	1.27E-06	7.400648
SORBS1	-1.12823	2.367022	-6.5103	1.17E-07	1.28E-06	7.39208
NEDD9	-1.47571	4.695716	-6.50507	1.19E-07	1.29E-06	7.375878
CENPA	1.410361	1.017461	6.503993	1.19E-07	1.30E-06	7.372532
CLDN11	-1.02723	1.064602	-6.49724	1.22E-07	1.32E-06	7.351586
KRT80	2.056247	2.69902	6.496891	1.22E-07	1.32E-06	7.350519
MAOB	-1.63044	3.398369	-6.49596	1.22E-07	1.32E-06	7.347626
SEPP1	-1.46475	4.986727	-6.4947	1.23E-07	1.33E-06	7.343741
FAM105A	-1.54908	3.657437	-6.49458	1.23E-07	1.33E-06	7.343346
TMED3	1.033805	2.460633	6.494302	1.23E-07	1.33E-06	7.342494
HIST1H2AC	1.583713	4.593671	6.490148	1.24E-07	1.34E-06	7.329618
HSPA5	1.018377	7.433783	6.489313	1.25E-07	1.35E-06	7.32703
CBX7	-1.28293	2.728468	-6.48323	1.27E-07	1.37E-06	7.308161
ESYT3	-1.1081	1.708836	-6.48161	1.28E-07	1.37E-06	7.303165
BARX2	1.730205	1.08351	6.476209	1.30E-07	1.39E-06	7.286409
CADM1	-1.56399	3.801659	-6.46423	1.35E-07	1.44E-06	7.249276
HSD17B6	-2.38179	4.207944	-6.46378	1.35E-07	1.44E-06	7.247871
MSR1	-1.90861	4.080041	-6.46331	1.35E-07	1.44E-06	7.246401
SLC52A2	1.148054	4.056837	6.463175	1.35E-07	1.44E-06	7.245997
SPP1	4.033901	4.690224	6.460286	1.37E-07	1.45E-06	7.237038
ARAP3	-1.10909	2.466306	-6.45957	1.37E-07	1.46E-06	7.234809
CDKN3	1.490119	1.470006	6.457869	1.38E-07	1.46E-06	7.229544
MYADM	-2.18307	6.060235	-6.45633	1.38E-07	1.46E-06	7.224782
TBX4	-1.64322	2.535563	-6.45596	1.38E-07	1.46E-06	7.223616
UGDH	1.415501	4.329762	6.452286	1.40E-07	1.48E-06	7.212232
EGLN3	1.706424	1.853957	6.444643	1.43E-07	1.51E-06	7.188532

Appendix C5: continued

FAM83D	1.579709	1.805016	6.444573	1.43E-07	1.51E-06	7.188316
SMIM22	1.7584	3.364001	6.441165	1.45E-07	1.52E-06	7.177746
CREB3L4	1.374856	2.645604	6.440093	1.46E-07	1.53E-06	7.174419
SMAD9	-1.1902	1.68802	-6.43944	1.46E-07	1.53E-06	7.172391
PRG4	-2.03021	1.868767	-6.4256	1.52E-07	1.58E-06	7.129462
HNF4G	1.26453	0.782566	6.42109	1.54E-07	1.60E-06	7.115481
PCSK9	-1.76908	2.104657	-6.41312	1.58E-07	1.64E-06	7.090746
CLSPN	1.112422	0.790946	6.411116	1.59E-07	1.65E-06	7.08454
FAM65A	-1.38807	3.636077	-6.41025	1.60E-07	1.65E-06	7.081867
HN1	1.496824	4.549405	6.40765	1.61E-07	1.66E-06	7.073787
DEPDC1	1.311632	0.822321	6.405102	1.62E-07	1.67E-06	7.065884
RHBDL1	1.17571	0.889684	6.396346	1.67E-07	1.71E-06	7.038719
PMP22	-1.111	5.352607	-6.3954	1.67E-07	1.71E-06	7.035773
BAIAP2L1	1.027402	3.671666	6.388698	1.71E-07	1.74E-06	7.014991
GRAMD3	1.010212	2.508582	6.387939	1.71E-07	1.74E-06	7.012633
WWTR1	-1.05764	3.999348	-6.38502	1.73E-07	1.76E-06	7.003564
PYCR1	1.095678	2.343017	6.384688	1.73E-07	1.76E-06	7.002547
PROS1	-1.31505	4.208853	-6.38307	1.74E-07	1.76E-06	6.997532
S100A3	-1.75902	2.239363	-6.36601	1.84E-07	1.86E-06	6.944597
CD302	-1.13547	2.882639	-6.36341	1.85E-07	1.87E-06	6.936507
CCDC69	-1.43223	4.033874	-6.36192	1.86E-07	1.88E-06	6.931902
CHRD1	-2.13691	3.553383	-6.361	1.87E-07	1.88E-06	6.92903
SULF1	2.246738	2.990972	6.359886	1.87E-07	1.89E-06	6.92558
PHYHD1	-1.56914	2.513887	-6.35715	1.89E-07	1.90E-06	6.917095
CYP27A1	-1.76629	5.090881	-6.35503	1.90E-07	1.91E-06	6.910523
TSTA3	1.161817	4.144295	6.353173	1.91E-07	1.92E-06	6.904746
CSF3R	-1.72284	3.00625	-6.34845	1.94E-07	1.95E-06	6.890085
TIMP3	-1.4192	2.754326	-6.34803	1.94E-07	1.95E-06	6.888796
GOLPH3L	1.028886	3.839002	6.345844	1.96E-07	1.96E-06	6.881998
SCD5	-1.48585	2.827767	-6.34363	1.97E-07	1.97E-06	6.875118
CCL23	-1.53438	2.121619	-6.34314	1.97E-07	1.97E-06	6.873607
CACYBP	1.001084	3.721622	6.333329	2.03E-07	2.03E-06	6.843153

Appendix C5: continued

ALDH1A2	-1.05038	1.074471	-6.33047	2.05E-07	2.04E-06	6.834264
BZW2	1.161754	4.083922	6.328726	2.06E-07	2.05E-06	6.828864
SLC14A1	-1.17983	0.914077	-6.32581	2.08E-07	2.07E-06	6.819805
KIF18B	1.287475	0.875834	6.32538	2.09E-07	2.07E-06	6.818476
RBP4	-2.19571	2.778225	-6.32344	2.10E-07	2.08E-06	6.81246
SLC5A9	-1.36745	1.063118	-6.31802	2.14E-07	2.11E-06	6.795641
LEPR	-1.27786	2.318442	-6.31758	2.14E-07	2.11E-06	6.79427
KCNAB2	-1.09071	2.463174	-6.31561	2.15E-07	2.12E-06	6.788148
VMP1	1.221833	4.480484	6.313832	2.16E-07	2.13E-06	6.782626
CDCA2	1.150803	0.807364	6.308428	2.20E-07	2.16E-06	6.765848
SIX4	1.22886	1.138487	6.307972	2.20E-07	2.16E-06	6.764432
FKBP11	1.282764	2.475289	6.30643	2.21E-07	2.17E-06	6.759645
PKMYT1	1.038451	0.861826	6.306352	2.21E-07	2.17E-06	6.759403
SH3BP5	-1.08931	2.626479	-6.30578	2.22E-07	2.17E-06	6.757637
LSR	1.074367	5.538913	6.303649	2.23E-07	2.18E-06	6.751012
CPXM1	1.816983	1.899351	6.302474	2.24E-07	2.19E-06	6.747362
FAM64A	1.244251	0.970299	6.294404	2.30E-07	2.24E-06	6.722305
KIAA0907	1.088376	2.498926	6.289113	2.34E-07	2.27E-06	6.705879
GPC3	-2.52852	4.369495	-6.27999	2.41E-07	2.33E-06	6.677534
SPDEF	2.543075	2.544266	6.274154	2.45E-07	2.37E-06	6.659426
FBP1	-1.67406	6.362608	-6.26741	2.50E-07	2.42E-06	6.638499
EFNA3	1.193337	1.052869	6.262968	2.54E-07	2.44E-06	6.624688
MAPK4	-1.04897	0.973066	-6.2599	2.56E-07	2.47E-06	6.615151
PSMG3	1.112245	3.397414	6.257678	2.58E-07	2.48E-06	6.60826
CCRL2	-1.26914	2.346852	-6.2511	2.64E-07	2.53E-06	6.587824
TROAP	1.455152	0.989215	6.250211	2.64E-07	2.53E-06	6.585072
CFL2	-1.22868	2.896098	-6.24951	2.65E-07	2.53E-06	6.582879
MEX3A	1.523719	1.05422	6.245661	2.68E-07	2.56E-06	6.570939
CYB5R3	-1.10821	5.448124	-6.24292	2.70E-07	2.58E-06	6.56241
TOPBP1	1.007725	2.717578	6.240352	2.73E-07	2.59E-06	6.554449
LYSMD1	1.077169	2.10609	6.240259	2.73E-07	2.59E-06	6.554162
BOP1	1.215911	3.115091	6.235488	2.77E-07	2.63E-06	6.539342

Appendix C5: continued

DBNDD1	1.198795	2.002005	6.230682	2.81E-07	2.66E-06	6.524415
LMOD1	-1.35336	3.224213	-6.21671	2.94E-07	2.77E-06	6.481025
ATIC	1.160948	3.967752	6.211565	2.98E-07	2.81E-06	6.465035
GTSE1	1.249983	0.94307	6.210513	2.99E-07	2.82E-06	6.461767
DAB2IP	-1.00199	3.554686	-6.21007	3.00E-07	2.82E-06	6.460375
SLC44A2	-1.03206	5.637271	-6.20811	3.02E-07	2.83E-06	6.4543
TPBG	1.286724	2.075991	6.20365	3.06E-07	2.87E-06	6.440447
CAMK2N1	-1.49354	4.108392	-6.19008	3.19E-07	2.97E-06	6.398289
FAM167B	-1.43203	2.663457	-6.18939	3.20E-07	2.98E-06	6.39616
NCAPD2	1.109112	3.311888	6.188878	3.20E-07	2.98E-06	6.394556
ALOX5	-1.4739	4.661695	-6.1888	3.21E-07	2.98E-06	6.394318
ITPRIP	-1.33064	3.368209	-6.18683	3.23E-07	3.00E-06	6.38818
PKM	1.068763	6.827109	6.17727	3.32E-07	3.07E-06	6.358497
TACC3	1.141933	2.273448	6.161904	3.49E-07	3.22E-06	6.310755
ITGA8	-1.55156	2.633743	-6.15384	3.58E-07	3.29E-06	6.285698
FAM134B	-1.20594	2.505022	-6.14825	3.64E-07	3.33E-06	6.268324
TPSAB1	-1.8804	3.930859	-6.14621	3.67E-07	3.34E-06	6.261987
KCNJ8	-1.19504	3.030463	-6.14512	3.68E-07	3.35E-06	6.258618
NRGN	-2.40704	4.401889	-6.13534	3.79E-07	3.45E-06	6.228224
CITED2	-1.17938	5.877382	-6.12243	3.95E-07	3.57E-06	6.188095
DSG2	1.752575	4.555888	6.122001	3.96E-07	3.57E-06	6.186776
CXorf36	-1.23239	2.183268	-6.12063	3.97E-07	3.59E-06	6.182519
PKP3	1.232614	3.610811	6.119598	3.99E-07	3.60E-06	6.17931
ID4	-2.04314	3.495492	-6.11757	4.01E-07	3.62E-06	6.172994
PAPSS2	-1.28117	5.189558	-6.11712	4.02E-07	3.62E-06	6.171619
C1orf198	-1.16729	4.95915	-6.11235	4.08E-07	3.66E-06	6.156784
SKA1	1.173263	0.878774	6.111217	4.09E-07	3.67E-06	6.153268
FAM3C	1.208818	3.858657	6.108441	4.13E-07	3.69E-06	6.144644
UNC5CL	1.488241	1.343984	6.104995	4.17E-07	3.73E-06	6.133934
CCDC167	1.308051	3.890173	6.091199	4.36E-07	3.87E-06	6.091068
RHOV	2.587878	2.15607	6.091178	4.36E-07	3.87E-06	6.091003
PALMD	-1.32705	2.067699	-6.08843	4.40E-07	3.90E-06	6.082475

Appendix C5: continued

ARC	-1.71898	1.24547	-6.08439	4.45E-07	3.94E-06	6.0699
SRD5A3	1.267459	3.260504	6.084212	4.46E-07	3.94E-06	6.069357
TBL1XR1	1.02642	3.739868	6.082773	4.48E-07	3.96E-06	6.064887
CDC45	1.373926	1.130549	6.082039	4.49E-07	3.96E-06	6.062604
THSD1	-1.30585	1.87575	-6.07849	4.54E-07	4.00E-06	6.051567
SDC2	-1.06409	4.024507	-6.07578	4.58E-07	4.03E-06	6.043168
ANXA3	-1.56101	4.452087	-6.06936	4.67E-07	4.10E-06	6.023199
CYS1	-1.47922	2.033794	-6.06779	4.69E-07	4.12E-06	6.018318
PRR11	1.487681	1.588917	6.066206	4.72E-07	4.13E-06	6.013405
KLF9	-1.2761	4.584683	-6.05784	4.84E-07	4.24E-06	5.987408
TNFSF13	-1.00286	3.900337	-6.05738	4.85E-07	4.24E-06	5.985972
MYOZ1	-1.38791	1.611409	-6.05502	4.88E-07	4.26E-06	5.978634
FUT8	1.086169	2.603452	6.033901	5.22E-07	4.52E-06	5.913024
STYK1	1.405104	1.1747	6.030054	5.28E-07	4.56E-06	5.901071
SCNN1B	-1.78985	3.793948	-6.02633	5.35E-07	4.61E-06	5.889503
NOSTRIN	-1.30414	2.259511	-6.02531	5.36E-07	4.62E-06	5.886327
RECK	-1.01167	2.102193	-6.01673	5.51E-07	4.73E-06	5.859674
GPI	1.013786	4.707561	6.012593	5.58E-07	4.77E-06	5.846815
BNIP3	1.224859	3.634895	6.012082	5.59E-07	4.78E-06	5.845227
SMAD7	-1.01465	3.568884	-6.00825	5.66E-07	4.82E-06	5.833317
BTK	-1.05996	2.439224	-6.00662	5.69E-07	4.84E-06	5.828253
ENC1	1.132896	3.409536	6.002827	5.76E-07	4.89E-06	5.816468
TPSB2	-1.90504	4.040718	-5.9994	5.82E-07	4.94E-06	5.805829
DSCC1	1.049294	1.350176	5.998139	5.84E-07	4.96E-06	5.801903
CHPF	1.055402	4.798638	5.99357	5.93E-07	5.02E-06	5.787706
SCNN1G	-1.68576	2.581923	-5.98819	6.03E-07	5.10E-06	5.77099
SOSTDC1	-2.55612	2.272447	-5.98181	6.15E-07	5.19E-06	5.751179
ARRB1	-1.25289	3.90319	-5.98005	6.19E-07	5.21E-06	5.745693
TNS4	2.479235	1.610129	5.9798	6.19E-07	5.21E-06	5.74492
DUSP8	-1.27921	2.233483	-5.97814	6.22E-07	5.23E-06	5.739773
MMP12	2.935296	1.98845	5.977824	6.23E-07	5.23E-06	5.738781
TSPAN12	-1.47514	4.070296	-5.97507	6.28E-07	5.27E-06	5.730216

Appendix C5: continued

SELENBP1	-2.02895	5.909258	-5.97463	6.29E-07	5.27E-06	5.728866
CXCL14	2.949341	3.216177	5.973439	6.32E-07	5.28E-06	5.725157
FKBP1B	-1.124	1.77004	-5.97055	6.37E-07	5.32E-06	5.716185
CARD16	-1.02182	2.93582	-5.96637	6.46E-07	5.38E-06	5.703186
P2RY6	1.563147	1.367984	5.963678	6.51E-07	5.42E-06	5.694829
PGK1	1.037864	6.571496	5.962893	6.53E-07	5.42E-06	5.692392
SNX25	-1.27105	3.625007	-5.96153	6.56E-07	5.44E-06	5.688167
KLF2	-1.67732	4.347369	-5.9575	6.64E-07	5.49E-06	5.675636
ASNS	1.067977	2.346967	5.956741	6.66E-07	5.50E-06	5.673278
CEMP	1.854294	2.360692	5.950979	6.78E-07	5.60E-06	5.655376
HBEGF	-2.12831	4.268473	-5.94679	6.87E-07	5.65E-06	5.642345
GIMAP4	-1.31104	4.469649	-5.94366	6.94E-07	5.70E-06	5.632648
SMAD6	-1.55418	2.023235	-5.93142	7.21E-07	5.90E-06	5.594613
HKDC1	1.502023	2.038166	5.931384	7.21E-07	5.90E-06	5.594499
GYG2	1.226822	1.217388	5.926656	7.32E-07	5.97E-06	5.579811
TCF7L1	-1.45056	2.552329	-5.92199	7.43E-07	6.04E-06	5.565328
PXMP4	-1.07767	3.118314	-5.9186	7.51E-07	6.09E-06	5.554793
SEMA3B	-1.91958	3.310622	-5.91776	7.53E-07	6.10E-06	5.552168
DNASE2B	-1.25148	1.037884	-5.91617	7.56E-07	6.13E-06	5.547247
SSR4	1.067538	5.127558	5.911931	7.67E-07	6.20E-06	5.534068
C1QA	-1.77291	7.70653	-5.90933	7.73E-07	6.25E-06	5.525981
ADAM28	1.624586	1.494581	5.904385	7.85E-07	6.33E-06	5.510626
SPRY4	-1.28696	3.819958	-5.9007	7.94E-07	6.39E-06	5.49917
SPINT2	1.024667	6.164697	5.899497	7.97E-07	6.41E-06	5.495443
HIST1H2BK	1.495162	5.670763	5.898391	8.00E-07	6.42E-06	5.492009
GRAMD2	-1.62098	2.454591	-5.89834	8.00E-07	6.42E-06	5.491839
GPR115	1.328606	0.740196	5.890608	8.20E-07	6.57E-06	5.467834
ABCG2	-1.04269	1.665915	-5.88858	8.25E-07	6.61E-06	5.461519
ARNTL2	1.868985	1.826898	5.888433	8.26E-07	6.61E-06	5.461077
C10orf128	-1.08956	2.531698	-5.88787	8.27E-07	6.61E-06	5.45932
MYOC	-1.54408	1.012893	-5.88274	8.41E-07	6.72E-06	5.443384
CKAP2	1.045886	2.27323	5.879016	8.50E-07	6.78E-06	5.431829

Appendix C5: continued

EHD2	-1.56912	5.688589	-5.87527	8.61E-07	6.86E-06	5.420188
GREM1	2.071044	1.154771	5.872631	8.68E-07	6.91E-06	5.411998
RNF122	-1.24367	3.137858	-5.86903	8.78E-07	6.97E-06	5.400802
CABYR	1.204786	0.745675	5.868881	8.78E-07	6.97E-06	5.400351
DTYMK	1.056328	2.99608	5.866899	8.84E-07	7.01E-06	5.394196
PBK	1.668109	1.315601	5.864445	8.90E-07	7.06E-06	5.386572
COL5A1	1.983205	3.823646	5.863164	8.94E-07	7.08E-06	5.382594
EPHX3	1.549025	2.194757	5.860288	9.02E-07	7.14E-06	5.373663
EGFL7	-1.31971	4.300986	-5.84956	9.33E-07	7.36E-06	5.340363
HIST1H4I	1.159974	2.787942	5.848868	9.35E-07	7.37E-06	5.3382
FAM184A	-1.07459	1.617884	-5.84771	9.39E-07	7.39E-06	5.334613
TNFSF12	-1.31617	4.227012	-5.84414	9.49E-07	7.46E-06	5.323527
PTN	-1.3779	2.688991	-5.84178	9.56E-07	7.50E-06	5.316185
AFAP1L1	-1.08713	2.646256	-5.8391	9.64E-07	7.53E-06	5.307856
FABP5	-1.65484	3.722836	-5.83878	9.65E-07	7.54E-06	5.306878
GMDS	1.19033	2.333812	5.835227	9.76E-07	7.61E-06	5.295841
RPL39L	2.084047	2.830116	5.829412	9.94E-07	7.73E-06	5.277783
GNG11	-1.74049	4.202542	-5.81862	1.03E-06	7.95E-06	5.244282
CENPH	1.011093	1.71925	5.816712	1.03E-06	7.99E-06	5.238352
TPI1	1.145858	7.041868	5.812626	1.05E-06	8.08E-06	5.225666
OSTC	1.041221	5.488505	5.811232	1.05E-06	8.10E-06	5.22134
AK4	1.600219	1.377142	5.798065	1.10E-06	8.43E-06	5.180465
TIMP1	1.570995	7.394429	5.791738	1.12E-06	8.59E-06	5.160821
RAMP1	1.532981	3.31663	5.790671	1.12E-06	8.61E-06	5.157512
LRRN3	-1.37257	1.400385	-5.78542	1.14E-06	8.75E-06	5.141198
PPAP2B	-1.03484	4.65478	-5.77879	1.17E-06	8.92E-06	5.120629
ADAMTS1	-1.92533	3.799995	-5.77785	1.17E-06	8.94E-06	5.117729
SPC25	1.117487	1.084117	5.777579	1.17E-06	8.94E-06	5.116873
KCNQ3	1.132451	1.197367	5.774973	1.18E-06	9.00E-06	5.108785
TRIP13	1.69855	1.687786	5.771348	1.19E-06	9.10E-06	5.097534
STAC	-1.34253	2.083887	-5.76998	1.20E-06	9.12E-06	5.093299
PCDH12	-1.14873	2.56331	-5.76778	1.21E-06	9.18E-06	5.086466

Appendix C5: continued

SLC25A39	1.012538	4.891107	5.762829	1.23E-06	9.31E-06	5.071095
RNASEH2A	1.034039	2.818708	5.758703	1.24E-06	9.40E-06	5.058293
GADD45B	-1.80204	5.73014	-5.75585	1.25E-06	9.47E-06	5.049436
PLEKHO2	-1.05424	4.31002	-5.75488	1.26E-06	9.49E-06	5.046419
KIAA1524	1.12789	1.148632	5.751987	1.27E-06	9.55E-06	5.037452
C1QTNF6	1.427411	1.496831	5.749128	1.28E-06	9.62E-06	5.02858
PRF1	-1.51374	3.132053	-5.7307	1.36E-06	1.01E-05	4.9714
COL17A1	2.635529	1.612096	5.725678	1.38E-06	1.02E-05	4.955823
MRPL24	1.107537	4.597723	5.722464	1.39E-06	1.03E-05	4.945853
TMEM106C	1.023797	3.953325	5.721297	1.40E-06	1.04E-05	4.942231
CDH1	1.22742	5.814495	5.720327	1.40E-06	1.04E-05	4.939223
POC1A	1.005454	1.685558	5.715676	1.42E-06	1.05E-05	4.924793
DNAJC22	1.149816	0.710724	5.711751	1.44E-06	1.06E-05	4.912619
NFAM1	-1.10033	2.316852	-5.71013	1.45E-06	1.07E-05	4.907583
SKP2	1.232535	2.098601	5.708326	1.46E-06	1.07E-05	4.901995
KLF6	-1.29652	5.897728	-5.70503	1.47E-06	1.08E-05	4.891784
TMEM156	1.302959	1.060947	5.698899	1.50E-06	1.10E-05	4.872758
GAPDH	1.49801	8.513642	5.698733	1.50E-06	1.10E-05	4.872242
CKAP4	1.006592	4.901927	5.697169	1.51E-06	1.11E-05	4.867392
TBX3	-1.33164	2.33999	-5.69317	1.53E-06	1.12E-05	4.855002
BMP5	-1.53245	2.239327	-5.69298	1.53E-06	1.12E-05	4.854414
DNAJC12	1.652306	1.390655	5.684418	1.57E-06	1.14E-05	4.827848
NEXN	-1.09301	2.559835	-5.68178	1.58E-06	1.15E-05	4.819664
VSIG4	-2.0884	5.425213	-5.68002	1.59E-06	1.16E-05	4.814202
SHE	-1.45035	2.199497	-5.67717	1.61E-06	1.17E-05	4.80539
OIP5	1.063537	0.958681	5.676071	1.61E-06	1.17E-05	4.801969
KLF13	-1.14053	4.168261	-5.66341	1.68E-06	1.21E-05	4.762704
TYROBP	-1.88462	6.750632	-5.65291	1.73E-06	1.25E-05	4.730165
C1QTNF7	-1.19754	1.463635	-5.652	1.74E-06	1.25E-05	4.727335
MARCKSL1	1.586175	5.586068	5.651752	1.74E-06	1.25E-05	4.726575
GPRIN2	-1.64878	2.823967	-5.64425	1.78E-06	1.27E-05	4.70333
LY86	-1.32866	3.679815	-5.63971	1.81E-06	1.29E-05	4.689245

Appendix C5: continued

FUT3	1.510774	2.250975	5.63939	1.81E-06	1.29E-05	4.68826
ADAM12	1.558237	1.130825	5.636273	1.83E-06	1.30E-05	4.6786
APBB1	-1.16811	2.770444	-5.63564	1.83E-06	1.30E-05	4.676634
SMPDL3B	1.384236	3.280129	5.631983	1.85E-06	1.31E-05	4.665304
TMEM125	-1.30001	5.352113	-5.63026	1.86E-06	1.32E-05	4.659962
SCIMP	-1.03325	1.997362	-5.62839	1.87E-06	1.33E-05	4.654157
NT5E	1.801972	3.170101	5.618746	1.93E-06	1.36E-05	4.624289
EDN1	-1.67306	4.762707	-5.61433	1.96E-06	1.38E-05	4.610619
GPRC5A	-1.8643	6.524847	-5.60902	1.99E-06	1.40E-05	4.594141
GPX8	1.483811	2.546127	5.599668	2.05E-06	1.44E-05	4.565185
COL11A1	2.636398	1.464378	5.5965	2.07E-06	1.45E-05	4.555372
MATN3	-1.51511	2.535166	-5.59629	2.07E-06	1.45E-05	4.554734
FGF2	-1.07838	1.437126	-5.592	2.10E-06	1.46E-05	4.541449
ALDOA	1.08578	7.088378	5.591492	2.10E-06	1.46E-05	4.539862
MGP	-1.40348	6.543539	-5.58623	2.14E-06	1.48E-05	4.523571
KCNJ5	-1.26777	1.694401	-5.58487	2.15E-06	1.49E-05	4.519343
FAM101B	-1.10676	3.172961	-5.58424	2.15E-06	1.49E-05	4.517389
NCF2	-1.44371	4.666649	-5.58237	2.17E-06	1.50E-05	4.511599
DNASE1L3	-1.91974	1.722794	-5.58148	2.17E-06	1.50E-05	4.508841
FLRT3	-1.82812	3.942723	-5.57417	2.22E-06	1.53E-05	4.486224
TPPP3	-2.53885	4.518425	-5.57216	2.24E-06	1.54E-05	4.479987
ADAM8	1.913851	2.896981	5.571589	2.24E-06	1.54E-05	4.478229
FAM167A	-1.60442	2.502667	-5.56774	2.27E-06	1.55E-05	4.466301
AIM2	2.119208	1.711775	5.567264	2.27E-06	1.56E-05	4.464837
F8	-1.07914	2.240738	-5.56604	2.28E-06	1.56E-05	4.461036
SLC12A7	1.135758	4.210693	5.563946	2.29E-06	1.57E-05	4.454564
RASL12	-1.15149	2.983595	-5.56343	2.30E-06	1.57E-05	4.452979
GSTM5	-1.08538	1.277388	-5.55744	2.34E-06	1.60E-05	4.434429
LYPLA1	1.197447	4.174381	5.556772	2.35E-06	1.60E-05	4.432357
CXCL16	-1.19641	6.015039	-5.55479	2.36E-06	1.61E-05	4.42622
CCL14	-1.04261	0.987319	-5.55355	2.37E-06	1.61E-05	4.422394
BMP2	-1.63888	3.739281	-5.55111	2.39E-06	1.62E-05	4.414841

Appendix C5: continued

AHNAK2	1.628192	1.819149	5.549714	2.40E-06	1.63E-05	4.410509
URB1	1.022824	2.174447	5.544312	2.44E-06	1.65E-05	4.393789
GNL3L	1.029765	2.443078	5.543988	2.44E-06	1.65E-05	4.392789
TBX2	-1.43564	2.986481	-5.5372	2.50E-06	1.69E-05	4.371773
CDCA4	1.047002	2.443056	5.52603	2.59E-06	1.74E-05	4.337219
SERPINB5	1.811523	1.025817	5.517562	2.66E-06	1.78E-05	4.311021
CPED1	-1.11286	2.101231	-5.51666	2.66E-06	1.79E-05	4.308224
CCNO	1.257583	1.250585	5.515489	2.67E-06	1.79E-05	4.304608
MRC1	-1.90372	5.407521	-5.51309	2.69E-06	1.80E-05	4.297199
RNF43	1.27512	2.168704	5.51097	2.71E-06	1.81E-05	4.290629
MXRA5	1.787454	3.146142	5.502074	2.79E-06	1.86E-05	4.263116
ADAMTS12	1.315723	1.517058	5.500782	2.80E-06	1.86E-05	4.25912
ITGAV	1.234884	4.466458	5.50007	2.81E-06	1.87E-05	4.256918
MYEOV	1.961356	1.062221	5.497019	2.83E-06	1.88E-05	4.247482
MVB12B	-1.14516	2.516647	-5.4942	2.86E-06	1.90E-05	4.238769
CYP24A1	2.947331	1.637789	5.493428	2.86E-06	1.90E-05	4.236377
LIMD1	-1.05568	2.83812	-5.47896	3.00E-06	1.98E-05	4.191636
PLLP	-1.35741	2.669628	-5.47779	3.01E-06	1.99E-05	4.188043
FA2H	1.596673	1.908727	5.475414	3.03E-06	2.00E-05	4.180684
PKIG	-1.10544	4.469542	-5.47461	3.04E-06	2.00E-05	4.178199
HIST1H2BG	2.305574	1.458202	5.473898	3.05E-06	2.00E-05	4.175998
MB	1.565518	1.138744	5.465764	3.12E-06	2.05E-05	4.150858
LIMK1	1.038671	3.215955	5.465572	3.13E-06	2.05E-05	4.150264
SLCO4C1	-1.53764	2.225398	-5.45899	3.19E-06	2.08E-05	4.129936
PSD3	1.127898	1.760786	5.451374	3.27E-06	2.13E-05	4.106391
ALOX5AP	-1.81509	5.346607	-5.44809	3.30E-06	2.15E-05	4.096243
ACY3	1.073819	0.884947	5.444866	3.34E-06	2.17E-05	4.086283
LCOR	1.016417	1.747468	5.440376	3.38E-06	2.19E-05	4.072414
CD37	-1.32429	3.371942	-5.43981	3.39E-06	2.20E-05	4.070673
RPS6KA2	-1.01839	4.209705	-5.43718	3.42E-06	2.21E-05	4.062551
C2orf40	-1.71722	1.817667	-5.43576	3.43E-06	2.22E-05	4.058153
STEAP2	1.372054	1.920453	5.43085	3.49E-06	2.25E-05	4.04299

Appendix C5: continued

MT-ND6	-3.1243	9.620147	-5.4298	3.50E-06	2.25E-05	4.039753
SVEP1	-1.21365	2.256052	-5.4291	3.51E-06	2.26E-05	4.037579
EVI2B	-1.26603	4.135779	-5.4231	3.57E-06	2.30E-05	4.019054
FAM43A	-1.20645	2.499699	-5.42215	3.58E-06	2.30E-05	4.016115
MT-ND5	-2.35512	9.393213	-5.4211	3.60E-06	2.30E-05	4.012883
NFE2L3	1.120878	2.793289	5.420865	3.60E-06	2.30E-05	4.012155
CHML	1.33209	2.421919	5.418451	3.63E-06	2.32E-05	4.004702
NETO2	1.158247	1.815491	5.415451	3.66E-06	2.33E-05	3.995439
LAPTM4B	1.257399	5.830649	5.414914	3.67E-06	2.34E-05	3.99378
RAD51AP1	1.177953	1.498112	5.409779	3.73E-06	2.37E-05	3.977927
MYOF	1.038213	4.990622	5.406526	3.76E-06	2.39E-05	3.967887
ARHGAP39	1.030088	1.632264	5.404277	3.79E-06	2.41E-05	3.960943
SSTR1	-1.45894	1.429961	-5.40252	3.81E-06	2.42E-05	3.955531
TGFA	1.268715	2.672699	5.397099	3.88E-06	2.45E-05	3.938789
CYGB	-1.0094	3.077173	-5.39578	3.89E-06	2.46E-05	3.93472
CDK5R1	1.094293	1.071704	5.3913	3.95E-06	2.49E-05	3.920894
DERL3	1.4972	2.113122	5.390323	3.96E-06	2.50E-05	3.917877
DRAM1	-1.45554	5.245043	-5.39003	3.96E-06	2.50E-05	3.916975
ALDH1B1	1.091856	3.363954	5.388615	3.98E-06	2.51E-05	3.912609
IGSF10	-1.56939	1.481809	-5.38485	4.03E-06	2.53E-05	3.900984
TLR4	-1.18757	3.114619	-5.38348	4.05E-06	2.54E-05	3.896767
ITPKA	2.102876	1.26279	5.383377	4.05E-06	2.54E-05	3.896446
LDHA	1.181774	6.372671	5.383224	4.05E-06	2.54E-05	3.895974
LGSN	1.748542	1.00161	5.378855	4.11E-06	2.57E-05	3.882494
SERINC2	1.501106	4.374257	5.37843	4.11E-06	2.57E-05	3.881183
LST1	-1.35814	3.488289	-5.37577	4.15E-06	2.59E-05	3.87298
NFIX	-1.57466	4.224589	-5.36876	4.24E-06	2.64E-05	3.851342
MSMO1	-1.11373	5.180005	-5.36796	4.25E-06	2.64E-05	3.848901
SECISBP2L	-1.01025	3.87829	-5.36675	4.27E-06	2.65E-05	3.845148
C1QB	-1.78118	7.616469	-5.36666	4.27E-06	2.65E-05	3.844884
OLFML1	-1.07287	2.610931	-5.3605	4.35E-06	2.70E-05	3.825882
MAP3K8	-1.2412	3.128183	-5.36	4.36E-06	2.70E-05	3.824327

Appendix C5: continued

KPNA2	1.494482	4.064772	5.359858	4.36E-06	2.70E-05	3.823903
MRPL15	1.134714	4.831625	5.359598	4.36E-06	2.70E-05	3.823099
VSIG2	-2.37136	4.292702	-5.35881	4.37E-06	2.71E-05	3.820657
EFNA5	1.236211	2.353978	5.352966	4.45E-06	2.75E-05	3.802653
OASL	-1.12585	2.501499	-5.35288	4.46E-06	2.75E-05	3.802374
NTN4	-1.25197	4.579555	-5.35286	4.46E-06	2.75E-05	3.802312
PLAU	2.485354	4.65223	5.346937	4.54E-06	2.79E-05	3.784065
GJA1	-1.44156	5.820514	-5.34645	4.55E-06	2.80E-05	3.782568
RHOBTB2	-1.3493	4.241809	-5.34395	4.58E-06	2.82E-05	3.774848
MDFI	1.066277	2.569005	5.330813	4.77E-06	2.92E-05	3.734367
SOWAHB	1.165252	1.932283	5.330313	4.78E-06	2.92E-05	3.732829
HEYL	-1.06538	3.066668	-5.32974	4.79E-06	2.93E-05	3.731061
SIGLEC1	-1.29448	2.620563	-5.32935	4.80E-06	2.93E-05	3.729873
FPR2	-1.84229	2.05022	-5.32662	4.84E-06	2.95E-05	3.721442
EMB	1.34444	3.551168	5.323039	4.89E-06	2.98E-05	3.710413
HPCAL1	-1.12278	4.22016	-5.31769	4.98E-06	3.02E-05	3.693941
HIST1H2AE	2.345721	1.558417	5.315384	5.01E-06	3.04E-05	3.686834
APOA1BP	1.029179	5.302701	5.313215	5.05E-06	3.06E-05	3.68015
CD2AP	1.035557	4.002495	5.312754	5.05E-06	3.06E-05	3.678733
TFAP2A	1.195537	0.721539	5.304632	5.18E-06	3.13E-05	3.653719
TUBB6	-1.26469	4.41592	-5.29572	5.33E-06	3.20E-05	3.626263
MMP1	2.930836	2.364115	5.294697	5.35E-06	3.21E-05	3.623127
RHOD	1.195257	3.613683	5.294495	5.35E-06	3.21E-05	3.622504
EFEMP1	-1.40305	5.664108	-5.29409	5.36E-06	3.22E-05	3.621245
POLB	1.068098	2.471794	5.285478	5.50E-06	3.30E-05	3.594747
EPB41L2	-1.00582	3.10525	-5.28531	5.51E-06	3.30E-05	3.594224
NMU	2.058854	1.222493	5.284704	5.52E-06	3.30E-05	3.592366
ID2	-1.06421	4.637253	-5.28299	5.55E-06	3.31E-05	3.587079
CILP2	1.310837	0.911029	5.276572	5.66E-06	3.37E-05	3.567337
ST6GALNAC5	-1.29796	2.398302	-5.27306	5.72E-06	3.40E-05	3.55654
CTSW	-1.35824	2.890929	-5.26931	5.79E-06	3.44E-05	3.544985
SMKR1	1.134936	1.018713	5.263687	5.89E-06	3.50E-05	3.527694

Appendix C5: continued

TNXB	-1.86902	2.452787	-5.26107	5.94E-06	3.52E-05	3.519647
VPREB3	1.153933	0.868009	5.260686	5.95E-06	3.53E-05	3.518463
CASQ2	-1.11899	1.024602	-5.26033	5.96E-06	3.53E-05	3.517363
SRPX2	1.79334	2.643944	5.25995	5.96E-06	3.53E-05	3.516198
PPM1H	1.231081	2.028793	5.259183	5.98E-06	3.53E-05	3.51384
COL4A3	-1.48644	1.991749	-5.25766	6.01E-06	3.55E-05	3.509164
PGM5	-1.19419	1.907364	-5.25386	6.08E-06	3.58E-05	3.497469
CNN1	-1.17071	3.061123	-5.24671	6.22E-06	3.66E-05	3.475491
CD83	-1.63149	4.094654	-5.24423	6.27E-06	3.68E-05	3.467843
FAM83H	1.029266	3.950004	5.240719	6.33E-06	3.72E-05	3.457061
STOM	-1.03435	7.083223	-5.23912	6.37E-06	3.74E-05	3.452141
HCST	-1.25947	3.53304	-5.23813	6.39E-06	3.74E-05	3.449094
PPAPDC1B	1.043771	3.227613	5.223648	6.68E-06	3.90E-05	3.404594
DOCK4	-1.02354	2.543908	-5.21962	6.77E-06	3.94E-05	3.392213
VIM	-1.16323	7.777221	-5.21863	6.79E-06	3.95E-05	3.389175
ARHGAP40	1.297578	0.823955	5.208886	7.00E-06	4.07E-05	3.359244
CRIP2	-1.15662	4.642012	-5.20634	7.05E-06	4.09E-05	3.351431
RXRG	-1.14984	1.124005	-5.2053	7.08E-06	4.10E-05	3.348221
GLB1L2	1.192856	1.865721	5.199969	7.20E-06	4.17E-05	3.331862
CHST15	1.104561	3.377799	5.197873	7.24E-06	4.19E-05	3.325426
MBOAT1	1.069106	2.893375	5.196829	7.27E-06	4.20E-05	3.322218
VASH1	-1.00554	2.535009	-5.19605	7.29E-06	4.21E-05	3.319818
HIST1H1C	1.921011	5.676702	5.195405	7.30E-06	4.22E-05	3.317848
BCL9	1.141337	2.472679	5.194103	7.33E-06	4.23E-05	3.313851
PTGER4	-1.02374	2.940386	-5.19219	7.37E-06	4.25E-05	3.307978
ITGA11	1.596564	1.3946	5.184927	7.54E-06	4.34E-05	3.285682
PRELP	-1.82285	4.406042	-5.18435	7.56E-06	4.35E-05	3.283922
COL1A1	2.761991	6.123165	5.18062	7.65E-06	4.39E-05	3.272463
CST5	-1.03667	0.915104	-5.17935	7.68E-06	4.40E-05	3.268567
CPNE7	1.264603	0.850005	5.177221	7.73E-06	4.42E-05	3.262033
SERPING1	-1.78091	6.805261	-5.17182	7.86E-06	4.48E-05	3.245476
COLEC12	-1.22593	3.682897	-5.16629	8.00E-06	4.55E-05	3.228487

Appendix C5: continued

PLEKHH2	-1.26276	1.883329	-5.16231	8.10E-06	4.61E-05	3.216279
TNFRSF18	1.520878	1.572759	5.161916	8.11E-06	4.61E-05	3.215081
RCAN1	-1.28019	3.445825	-5.16151	8.12E-06	4.61E-05	3.213843
COCH	1.11541	0.695547	5.157954	8.21E-06	4.65E-05	3.202931
CNR1	-1.01148	1.231821	-5.15636	8.25E-06	4.67E-05	3.19803
ZFP36	-2.07206	7.493237	-5.14106	8.65E-06	4.87E-05	3.15113
PERP	1.268618	5.463891	5.140311	8.67E-06	4.87E-05	3.148841
PLXNB3	1.008692	0.846302	5.122564	9.17E-06	5.11E-05	3.094462
MYH11	-1.56277	3.642744	-5.12019	9.24E-06	5.14E-05	3.087187
LYPD3	1.933397	1.696675	5.113001	9.45E-06	5.24E-05	3.065176
CCDC64	1.153334	1.353237	5.112548	9.46E-06	5.25E-05	3.063788
B3GNT8	-1.31816	3.166509	-5.11098	9.51E-06	5.27E-05	3.05898
CLEC4E	-1.30305	1.936408	-5.10826	9.59E-06	5.31E-05	3.050667
CTSH	-1.58646	6.424907	-5.10826	9.59E-06	5.31E-05	3.050652
H2AFX	1.053367	4.062372	5.104469	9.70E-06	5.36E-05	3.039051
FAP	1.42646	1.391983	5.10332	9.74E-06	5.38E-05	3.035536
FGD6	1.014984	2.297493	5.102864	9.75E-06	5.38E-05	3.034138
ADAM9	1.019042	5.099815	5.101898	9.78E-06	5.39E-05	3.031182
ANP32E	1.036291	4.510383	5.101566	9.79E-06	5.40E-05	3.030165
DDIT4	1.571636	5.5043	5.092636	1.01E-05	5.53E-05	3.002836
MAL	-1.36489	2.506408	-5.09021	1.01E-05	5.56E-05	2.995396
WISP1	1.414744	1.533062	5.087887	1.02E-05	5.60E-05	2.988303
FLVCR2	-1.03199	2.583215	-5.0878	1.02E-05	5.60E-05	2.988049
HIST1H2BC	2.026285	2.639905	5.086033	1.03E-05	5.62E-05	2.982633
ETV5	-1.01385	3.856061	-5.08138	1.04E-05	5.70E-05	2.968386
MICALCL	-1.05221	1.878956	-5.08009	1.05E-05	5.72E-05	2.964461
EXOSC5	1.014559	3.109803	5.078221	1.05E-05	5.74E-05	2.958736
TXNDC17	1.235044	3.35877	5.067825	1.09E-05	5.92E-05	2.926944
ITGAL	-1.24267	3.066936	-5.06168	1.11E-05	6.02E-05	2.908154
FOSB	-3.53274	4.358482	-5.05887	1.12E-05	6.06E-05	2.899582
ADAM15	1.066451	4.719549	5.044397	1.17E-05	6.31E-05	2.855347
FAM83B	1.227862	0.698702	5.040463	1.18E-05	6.38E-05	2.843329

Appendix C5: continued

TMEM159	1.055622	4.073681	5.03915	1.19E-05	6.40E-05	2.839319
RSPO2	-1.04647	0.98277	-5.03466	1.21E-05	6.47E-05	2.825592
AMOTL1	-1.09897	3.269017	-5.03463	1.21E-05	6.47E-05	2.825507
SNX30	-1.01591	3.230404	-5.02927	1.23E-05	6.56E-05	2.809145
SCN7A	-1.56431	2.660239	-5.02269	1.25E-05	6.67E-05	2.789049
C2orf54	-1.42852	2.866845	-5.01859	1.27E-05	6.74E-05	2.776538
ENO1	1.040701	8.158642	5.011648	1.30E-05	6.87E-05	2.755365
MFAP2	1.100936	2.51881	5.009929	1.30E-05	6.90E-05	2.75012
VCAN	1.644748	3.539343	5.007975	1.31E-05	6.94E-05	2.744159
TBX15	1.052221	0.808969	5.006332	1.32E-05	6.97E-05	2.739146
CITED4	-1.05451	2.39606	-5.00041	1.34E-05	7.08E-05	2.721094
COMP	2.182622	2.054369	4.993478	1.37E-05	7.21E-05	2.699948
ITGA2	1.581725	3.328726	4.991077	1.38E-05	7.25E-05	2.692627
DEPTOR	1.326013	2.800038	4.990669	1.38E-05	7.26E-05	2.691382
CR2	1.09718	0.695534	4.98971	1.39E-05	7.28E-05	2.688458
CP	2.955849	3.27957	4.975634	1.45E-05	7.57E-05	2.645562
CA9	2.427553	1.343497	4.973926	1.46E-05	7.60E-05	2.640358
OPLAH	1.00899	2.245771	4.97367	1.46E-05	7.61E-05	2.639576
C1orf115	-1.39524	3.624377	-4.9723	1.47E-05	7.63E-05	2.635394
AARD	-1.05929	1.190144	-4.96654	1.49E-05	7.75E-05	2.617862
CYB5A	-1.23843	4.411265	-4.96008	1.52E-05	7.88E-05	2.598178
HEY1	-1.07691	2.580211	-4.95706	1.54E-05	7.94E-05	2.589003
PVRL1	1.253906	2.320504	4.950967	1.57E-05	8.08E-05	2.570442
CST1	2.384742	1.249316	4.948335	1.58E-05	8.14E-05	2.562433
NR4A3	-1.83519	2.316808	-4.93743	1.63E-05	8.38E-05	2.529264
PPIF	1.006068	4.049677	4.935465	1.64E-05	8.42E-05	2.523273
ABLIM3	-1.01633	2.445071	-4.93319	1.66E-05	8.47E-05	2.516351
TMEM47	-1.15303	3.413603	-4.91885	1.73E-05	8.80E-05	2.472763
THEM5	1.06098	1.899152	4.912541	1.76E-05	8.96E-05	2.453576
ARID5A	-1.17408	3.33338	-4.91156	1.77E-05	8.98E-05	2.450588
MAP7D2	1.416599	0.933287	4.908553	1.79E-05	9.04E-05	2.44146
GSTA4	-1.13912	3.668327	-4.90562	1.80E-05	9.11E-05	2.432553

Appendix C5: continued

HORMAD1	1.439899	0.811447	4.902613	1.82E-05	9.18E-05	2.423414
ARHGAP30	-1.004	3.485298	-4.8989	1.84E-05	9.28E-05	2.41214
TLCD1	1.223427	2.959175	4.898135	1.85E-05	9.29E-05	2.409813
CYP27B1	1.114046	0.985945	4.890787	1.89E-05	9.49E-05	2.387503
KRT16	2.025398	1.0702	4.883439	1.93E-05	9.69E-05	2.365198
IL4I1	1.356035	1.844295	4.879965	1.95E-05	9.78E-05	2.354655
POSTN	2.066937	4.597033	4.871071	2.01E-05	0.0001	2.327671
CSF3	-3.16637	2.31092	-4.86869	2.02E-05	0.000101	2.320447
BTG2	-1.55118	6.083441	-4.868	2.03E-05	0.000101	2.318352
CXCL2	-2.55196	5.163486	-4.86565	2.04E-05	0.000101	2.311224
SLC51B	-1.28106	1.90387	-4.86471	2.05E-05	0.000102	2.308392
LIFR	-1.36211	3.467396	-4.86303	2.06E-05	0.000102	2.303287
SLPI	-2.06431	9.077481	-4.86297	2.06E-05	0.000102	2.303107
SLC16A5	-1.09953	3.420754	-4.86284	2.06E-05	0.000102	2.302723
GALNT3	1.127634	3.639279	4.860862	2.07E-05	0.000103	2.29671
STRIP2	1.191075	0.950432	4.858888	2.08E-05	0.000103	2.290728
PI16	-1.60646	1.400328	-4.85652	2.10E-05	0.000104	2.283558
CELF2	-1.02261	3.688992	-4.85651	2.10E-05	0.000104	2.28353
FSTL3	-1.27848	4.25836	-4.85538	2.11E-05	0.000104	2.280106
GPER1	-1.15006	1.633718	-4.84953	2.15E-05	0.000106	2.262365
GOLGA7B	1.088745	1.176164	4.846219	2.17E-05	0.000107	2.25233
GALNT14	1.563183	1.231315	4.845081	2.18E-05	0.000107	2.248883
TMEM45B	1.292108	3.16982	4.845038	2.18E-05	0.000107	2.248753
SCG5	1.286522	1.218006	4.843331	2.19E-05	0.000107	2.24358
ERICH2	-1.25341	2.4043	-4.83767	2.23E-05	0.000109	2.226427
WNT9A	-1.01562	2.065404	-4.8355	2.24E-05	0.00011	2.219852
SYT7	1.587299	1.800521	4.83407	2.25E-05	0.00011	2.21553
CFB	1.365613	1.80896	4.832953	2.26E-05	0.00011	2.212148
MMRN1	-1.44836	2.331766	-4.82221	2.34E-05	0.000114	2.179629
APOLD1	-1.36665	2.843029	-4.8175	2.37E-05	0.000115	2.165362
HLF	-1.40493	2.378562	-4.81137	2.42E-05	0.000117	2.146827
PPP1R14D	2.07092	1.31526	4.80979	2.43E-05	0.000117	2.14205

Appendix C5: continued

SRPX	-1.40184	3.280845	-4.80895	2.43E-05	0.000118	2.139496
MFI2	1.72481	1.288279	4.808262	2.44E-05	0.000118	2.137428
KLK11	-2.00664	2.351791	-4.80772	2.44E-05	0.000118	2.135783
SPTBN1	-1.25198	5.509105	-4.8031	2.48E-05	0.00012	2.121815
F2RL3	-1.31572	2.133981	-4.80038	2.50E-05	0.00012	2.113595
EPHB3	1.182248	2.307891	4.79975	2.50E-05	0.000121	2.111687
BAIAP2L2	1.022948	0.7661	4.798257	2.52E-05	0.000121	2.107174
NR4A1	-2.07354	4.212718	-4.79617	2.53E-05	0.000122	2.100864
FOXA1	1.054048	3.4268	4.788474	2.59E-05	0.000124	2.077608
ATOH8	-1.73484	2.919925	-4.78792	2.60E-05	0.000124	2.075921
PTMS	-1.35976	6.720039	-4.78209	2.65E-05	0.000126	2.058317
KPNA7	1.037005	1.024839	4.778765	2.67E-05	0.000128	2.048279
RGS16	-1.39121	4.167251	-4.77727	2.68E-05	0.000128	2.043768
KLF15	-1.3106	2.3628	-4.77646	2.69E-05	0.000128	2.04133
OLFML2A	-1.00706	2.716605	-4.77439	2.71E-05	0.000129	2.03508
MMP14	1.29249	5.614276	4.765397	2.79E-05	0.000132	2.007921
BMP6	-1.41149	2.303572	-4.76463	2.79E-05	0.000132	2.005607
RNF144B	-1.14302	3.822469	-4.76358	2.80E-05	0.000133	2.002438
CDCP1	1.180638	3.274211	4.763056	2.81E-05	0.000133	2.000854
AC105009.1	1.615403	0.884556	4.761908	2.82E-05	0.000133	1.997389
TMPRSS11E	2.239996	1.195429	4.757712	2.85E-05	0.000135	1.984729
GGTLC1	-2.44495	3.236019	-4.75367	2.89E-05	0.000136	1.972551
CDKN2A	1.317251	1.114964	4.751965	2.90E-05	0.000137	1.967396
CXCR2	-1.17573	1.463053	-4.74821	2.94E-05	0.000138	1.956059
GINS4	1.093736	0.853538	4.736756	3.04E-05	0.000143	1.921543
FOXF2	-1.07908	2.417287	-4.73293	3.08E-05	0.000144	1.91001
ID3	-1.17638	4.880141	-4.73178	3.09E-05	0.000144	1.906555
GJB3	1.997205	1.59093	4.73016	3.11E-05	0.000145	1.901668
NKG7	-1.635	3.65944	-4.72734	3.13E-05	0.000146	1.893162
MTURN	-1.23714	3.285921	-4.72147	3.19E-05	0.000148	1.875501
TDRD10	-1.03748	1.168054	-4.71933	3.21E-05	0.000149	1.869059
KLF4	-1.61848	4.565693	-4.71882	3.22E-05	0.000149	1.867521

Appendix C5: continued

CTF1	-1.10452	2.629168	-4.71657	3.24E-05	0.00015	1.860732
SLC2A3	-1.24381	3.912408	-4.71492	3.26E-05	0.000151	1.855764
SFTP8	-2.5887	10.53411	-4.71114	3.29E-05	0.000152	1.844402
RNASE1	-1.58117	8.353891	-4.69745	3.44E-05	0.000158	1.803204
SOD3	-1.52748	4.423007	-4.69506	3.46E-05	0.000159	1.796036
GJA5	-1.28971	3.682447	-4.69398	3.47E-05	0.000159	1.79278
RFX2	-1.29332	1.827385	-4.69377	3.48E-05	0.000159	1.792149
FERMT3	-1.00578	4.062605	-4.68747	3.54E-05	0.000162	1.773196
METTL7B	1.294765	2.083941	4.67821	3.65E-05	0.000166	1.745379
HIST1H4H	2.235726	2.453015	4.677363	3.66E-05	0.000166	1.742834
SLCO2B1	-1.14555	3.957913	-4.67073	3.73E-05	0.000169	1.722901
FCER1G	-1.53045	6.131	-4.66909	3.75E-05	0.00017	1.717999
KLF10	-1.10502	4.818643	-4.66482	3.80E-05	0.000172	1.705177
EPHX4	1.17373	0.923603	4.655835	3.91E-05	0.000176	1.6782
MYRF	-1.66489	2.727713	-4.64861	3.99E-05	0.000179	1.656522
IL20RB	1.896358	1.27513	4.638998	4.11E-05	0.000184	1.627706
HPGDS	-1.07103	2.03197	-4.63717	4.14E-05	0.000185	1.622217
APLN	-1.47014	2.610598	-4.63401	4.18E-05	0.000187	1.612755
SEC14L4	-1.06169	1.704852	-4.63225	4.20E-05	0.000187	1.607479
GCNT3	2.00915	1.213699	4.630412	4.22E-05	0.000188	1.601974
SEMA6D	-1.01096	1.196767	-4.62867	4.25E-05	0.000189	1.596742
KRT6A	2.684677	1.536084	4.610955	4.48E-05	0.000198	1.543712
C7	-1.96668	4.834735	-4.60644	4.55E-05	0.000201	1.530191
CD24	1.316627	5.20935	4.605077	4.57E-05	0.000202	1.526124
SLC7A8	-1.09797	3.044399	-4.60014	4.64E-05	0.000204	1.511348
SESN1	-1.00774	2.89916	-4.59856	4.66E-05	0.000205	1.506638
UBE2S	1.153588	2.218203	4.596385	4.69E-05	0.000206	1.500124
MMP19	-1.67884	2.917031	-4.59308	4.74E-05	0.000208	1.490238
MNDA	-1.26929	3.962312	-4.58873	4.80E-05	0.000211	1.477247
BIK	1.200911	2.003112	4.587941	4.81E-05	0.000211	1.474884
NPR3	-1.21432	2.156878	-4.58774	4.82E-05	0.000211	1.47427
CXCR1	-1.32515	1.217947	-4.57399	5.02E-05	0.000219	1.433196

Appendix C5: continued

CPA3	-1.44361	4.449224	-4.5718	5.06E-05	0.00022	1.426657
PPARG	-1.16951	2.992001	-4.57175	5.06E-05	0.00022	1.426527
SFTA3	-1.60801	4.646408	-4.57054	5.08E-05	0.000221	1.422899
SEMA4B	1.286156	4.053543	4.562874	5.20E-05	0.000226	1.400024
SPINK1	3.492613	2.419364	4.562518	5.20E-05	0.000226	1.398962
MT1M	-2.15806	3.503228	-4.56027	5.24E-05	0.000227	1.392247
PGC	-3.42972	6.317071	-4.55753	5.28E-05	0.000229	1.384078
COL1A2	1.679173	6.519397	4.556803	5.30E-05	0.000229	1.38191
FGFR2	-1.43614	2.807166	-4.55607	5.31E-05	0.00023	1.379724
TSKU	1.202204	3.31081	4.555685	5.31E-05	0.00023	1.378575
SAMHD1	-1.04458	5.231763	-4.55235	5.37E-05	0.000232	1.368631
SPOCK1	1.370755	1.062744	4.545472	5.48E-05	0.000236	1.348121
SYNDIG1L	-1.12743	0.978602	-4.54474	5.49E-05	0.000237	1.345947
KIAA1683	-1.27568	1.132154	-4.54397	5.51E-05	0.000237	1.343658
IFITM2	-1.0167	6.249034	-4.53996	5.58E-05	0.00024	1.331683
APOL3	-1.09233	3.198807	-4.53247	5.71E-05	0.000244	1.30938
FIBIN	-1.34463	3.438392	-4.53128	5.73E-05	0.000245	1.305827
SLC6A8	1.177161	2.142554	4.521286	5.90E-05	0.000252	1.27608
HIST2H2BE	1.153402	3.344612	4.521181	5.91E-05	0.000252	1.275768
SERTAD1	-1.03617	4.187521	-4.51934	5.94E-05	0.000253	1.270296
MMP13	2.651615	1.441074	4.513612	6.04E-05	0.000257	1.253246
CDKN1C	-1.01937	3.123206	-4.51277	6.06E-05	0.000257	1.250736
XKRX	1.235347	1.282069	4.509882	6.11E-05	0.000259	1.242153
LAPTM5	-1.17455	6.992192	-4.50947	6.12E-05	0.000259	1.240939
LEMD1	1.145198	0.902781	4.507553	6.16E-05	0.000261	1.235227
SCGB1A1	-4.26937	7.151252	-4.50313	6.24E-05	0.000264	1.222065
UGT8	1.282774	1.297315	4.498935	6.32E-05	0.000267	1.209606
HIST1H3H	1.573993	1.460366	4.498087	6.34E-05	0.000267	1.207085
VAMP2	-1.29745	4.498006	-4.49716	6.36E-05	0.000268	1.204321
HIST1H3D	1.958673	1.190906	4.482839	6.64E-05	0.000278	1.161793
SYTL2	1.095213	1.957892	4.477967	6.74E-05	0.000282	1.147331
RPL22L1	1.044877	3.039911	4.47036	6.90E-05	0.000286	1.12476

Appendix C5: continued

FDCSP	1.540023	1.08709	4.462569	7.06E-05	0.000293	1.101656
CEBPA	-1.03653	3.311958	-4.45458	7.24E-05	0.000299	1.077982
BEAN1	1.011557	0.728318	4.453609	7.26E-05	0.000299	1.075098
TMEM132A	1.189247	2.097414	4.453503	7.26E-05	0.000299	1.074785
APOC1	-1.99419	6.335365	-4.45054	7.33E-05	0.000302	1.066007
CDKN2B	-1.24488	3.24468	-4.45034	7.33E-05	0.000302	1.065407
PKIB	1.413399	1.61412	4.44437	7.47E-05	0.000306	1.047732
CASS4	-1.00911	1.997412	-4.44182	7.53E-05	0.000308	1.040174
ITLN1	-2.22832	1.621409	-4.43527	7.68E-05	0.000314	1.020808
F2RL1	1.090116	2.896574	4.435063	7.68E-05	0.000314	1.020183
ALAS2	-1.00124	0.728428	-4.43194	7.76E-05	0.000317	1.010952
OGN	-1.62213	2.295067	-4.42486	7.93E-05	0.000322	0.990002
GABARAPL1	-1.00308	4.690961	-4.42157	8.01E-05	0.000325	0.980261
CLIC2	-1.06114	4.082804	-4.42065	8.03E-05	0.000325	0.977547
IL20RA	-1.22292	2.0562	-4.41509	8.16E-05	0.00033	0.961116
FKBP10	1.280934	3.922821	4.413203	8.21E-05	0.000331	0.955543
CENPM	1.149751	1.584101	4.40963	8.30E-05	0.000334	0.944985
CA3	-1.18313	1.648947	-4.40761	8.35E-05	0.000336	0.939034
MTHFD2	1.266348	3.498827	4.405884	8.40E-05	0.000337	0.933921
TOX3	1.394298	1.317503	4.395835	8.66E-05	0.000347	0.904255
MMP28	-1.498	3.636119	-4.39447	8.69E-05	0.000348	0.90022
NPC2	-1.0924	7.457291	-4.39149	8.77E-05	0.00035	0.891448
S100A2	1.928949	2.39541	4.391145	8.78E-05	0.00035	0.890417
GPR110	1.378347	1.627794	4.390317	8.80E-05	0.000351	0.887975
GCLC	1.687879	2.662157	4.389986	8.81E-05	0.000351	0.886998
MUC13	2.162181	1.254374	4.388841	8.84E-05	0.000353	0.883622
HOXB7	1.168227	1.866924	4.386594	8.90E-05	0.000355	0.876993
C4BPA	-2.35269	6.154331	-4.38058	9.07E-05	0.000361	0.859252
B3GNT7	-1.03103	4.04156	-4.37791	9.14E-05	0.000363	0.851401
COL6A3	1.417068	4.700118	4.360498	9.64E-05	0.00038	0.800108
SLC17A9	1.102472	1.309596	4.356774	9.75E-05	0.000384	0.789149
HIF3A	-1.15993	1.520818	-4.35508	9.80E-05	0.000386	0.784166

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SCTR	-1.29201	2.028417	-4.34786	0.0001	0.000392	0.762939
LMO7	-1.16226	4.827344	-4.34649	0.000101	0.000394	0.758904
TUBA1A	-1.07074	5.816912	-4.34644	0.000101	0.000394	0.758759
CILP	1.343703	1.272103	4.344668	0.000101	0.000396	0.75354
IGFBP3	1.610259	4.573452	4.334952	0.000104	0.000406	0.724986
NME4	1.023555	3.835991	4.334847	0.000104	0.000406	0.724678
ELOVL6	1.000315	1.504447	4.334755	0.000104	0.000406	0.724407
SYT12	1.184288	0.636581	4.33397	0.000104	0.000406	0.722101
KRT15	1.536587	1.558841	4.332206	0.000105	0.000408	0.716919
SIX1	1.300717	1.271925	4.32675	0.000107	0.000414	0.700898
ALOX15B	-1.82071	4.289657	-4.32673	0.000107	0.000414	0.70084
GYLTL1B	1.145103	1.985349	4.326113	0.000107	0.000414	0.699027
IL6	-2.39357	3.30403	-4.31945	0.000109	0.000422	0.679475
CERCAM	1.112458	2.592922	4.319339	0.000109	0.000422	0.679143
LYPD1	1.071519	0.709725	4.313551	0.000111	0.000428	0.662165
IL7R	-1.4363	4.375183	-4.31338	0.000111	0.000429	0.661656
FPR1	-1.4889	3.70216	-4.30645	0.000114	0.000436	0.641337
NFKBIA	-1.25986	7.088008	-4.30294	0.000115	0.00044	0.631054
FCN1	-1.15031	2.535731	-4.30213	0.000115	0.000441	0.628677
GNLY	-1.27921	2.089322	-4.29726	0.000117	0.000446	0.614423
SOX18	-1.26824	2.43091	-4.29686	0.000117	0.000447	0.613241
EMP1	-1.464	5.176371	-4.29342	0.000118	0.00045	0.603155
CEBPD	-1.05902	5.917583	-4.27846	0.000124	0.000469	0.559368
RAC3	1.249868	2.097716	4.275736	0.000125	0.000472	0.551415
KLK7	-1.16435	0.860864	-4.27163	0.000126	0.000477	0.53942
PCDH17	-1.06171	2.527483	-4.26482	0.000129	0.000486	0.519504
DUSP4	1.525537	2.620037	4.263965	0.000129	0.000487	0.517007
RGS5	-1.03443	4.181747	-4.25748	0.000132	0.000495	0.498067
DCN	-1.04618	5.84227	-4.24751	0.000136	0.000509	0.468952
C2CD4A	1.00127	0.910842	4.235016	0.000141	0.000527	0.432528
KCNJ15	-1.25196	3.089246	-4.22401	0.000146	0.000542	0.400473
HIST3H2A	1.668916	2.038658	4.22398	0.000146	0.000542	0.400375

Appendix C5: continued

CX3CL1	-1.67072	4.245198	-4.21963	0.000148	0.000548	0.387713
C10orf10	-1.52664	6.042195	-4.21391	0.00015	0.000557	0.371061
PDGFRL	1.156246	2.287129	4.213553	0.00015	0.000557	0.370025
EMP3	-1.07658	4.956291	-4.21259	0.000151	0.000559	0.367237
FZD4	-1.16161	3.062818	-4.2088	0.000152	0.000564	0.356209
MMP9	2.128526	3.791052	4.204723	0.000154	0.00057	0.344342
SLC25A25	-1.20935	3.177773	-4.20257	0.000155	0.000573	0.338076
PLOD2	1.613716	3.065681	4.19662	0.000158	0.000582	0.320795
C1QC	-1.33874	7.426649	-4.18925	0.000162	0.000593	0.29939
POMK	1.398623	1.41983	4.188469	0.000162	0.000594	0.297119
PER1	-1.03366	4.422457	-4.18227	0.000165	0.000603	0.27914
SLC34A2	-1.55201	8.548822	-4.181	0.000166	0.000605	0.275433
COL4A4	-1.07729	2.378329	-4.1791	0.000167	0.000608	0.269923
PFN2	1.485798	3.847731	4.177648	0.000167	0.00061	0.265718
AOC1	1.420873	1.021267	4.167181	0.000173	0.000626	0.23537
SLC7A5	1.578178	3.293179	4.163676	0.000175	0.000632	0.225213
RASL11A	-1.087	2.769391	-4.16296	0.000175	0.000633	0.223146
LAMB3	1.355744	6.145943	4.151261	0.000181	0.000652	0.189266
CDC42EP2	-1.0921	3.155924	-4.15056	0.000182	0.000654	0.187223
SIGLEC14	-1.03255	1.989264	-4.13988	0.000187	0.000673	0.156332
MET	1.307542	4.652182	4.136731	0.000189	0.000678	0.147244
TRIM2	1.283946	3.03712	4.133151	0.000191	0.000684	0.136898
PTK6	1.182774	2.397083	4.126624	0.000195	0.000696	0.118045
FGFBP2	-1.69558	1.58243	-4.12358	0.000197	0.000702	0.109252
C16orf89	-1.89936	5.906272	-4.11697	0.000201	0.000713	0.090182
HLA-DRB1	-1.21302	9.614726	-4.11657	0.000201	0.000714	0.089015
PTPN13	-1.07542	3.276034	-4.11583	0.000201	0.000715	0.086891
S100A12	-1.48399	1.928448	-4.11064	0.000205	0.000725	0.071917
ZBTB16	-1.25324	1.79653	-4.09626	0.000214	0.000753	0.030481
SPTB	1.175744	0.860978	4.095234	0.000214	0.000755	0.027532
MAFF	-1.27224	3.333081	-4.09154	0.000217	0.000761	0.016904
UNC13B	-1.08393	4.385751	-4.07889	0.000225	0.000785	-0.01948

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ASPH	1.236048	4.009333	4.067704	0.000232	0.000808	-0.05164
JUNB	-1.08677	7.102188	-4.06727	0.000233	0.000809	-0.05289
IRX1	-1.11542	1.336178	-4.06437	0.000235	0.000816	-0.06121
ATP13A4	-1.61422	3.053616	-4.06285	0.000236	0.000819	-0.06557
DUSP1	-1.26019	8.080833	-4.06279	0.000236	0.000819	-0.06576
COL7A1	1.151215	0.830516	4.049045	0.000246	0.00085	-0.10518
ALDH3B2	1.00282	0.984141	4.045061	0.000249	0.000858	-0.1166
DNTTIP1	1.180156	4.27517	4.030559	0.00026	0.000892	-0.15813
FCGR3A	-1.27495	5.650071	-4.02188	0.000266	0.000912	-0.18295
EIF4EBP1	1.226265	4.29639	4.020895	0.000267	0.000915	-0.18577
SCEL	-1.59086	4.358847	-4.0199	0.000268	0.000917	-0.1886
ZBED2	-1.4164	2.209481	-4.01889	0.000269	0.000919	-0.19151
MUC20	1.33035	2.08225	4.016095	0.000271	0.000926	-0.19949
HHIPL2	1.636337	0.860401	4.015441	0.000272	0.000927	-0.20136
MROH6	1.159693	1.965387	4.005185	0.00028	0.000951	-0.23065
IL23A	1.373856	1.164685	4.001493	0.000283	0.00096	-0.24119
B4GALNT4	1.123034	0.685909	4.001241	0.000283	0.000961	-0.24191
GPX2	2.627002	2.104365	4.000635	0.000284	0.000962	-0.24364
EGR1	-1.87146	6.467145	-3.99439	0.000289	0.000976	-0.26144
HIST1H2AD	1.894108	1.108238	3.989668	0.000293	0.000988	-0.27491
CXCL17	-1.95126	6.497815	-3.98912	0.000294	0.00099	-0.27648
SCARA3	-1.03534	2.641622	-3.98583	0.000296	0.000999	-0.28584
SRGN	-1.19056	7.4489	-3.98005	0.000302	0.001013	-0.3023
CEACAM1	1.153416	2.290903	3.973102	0.000308	0.001031	-0.32209
HIST1H4K	1.038507	0.741121	3.972908	0.000308	0.001032	-0.32264
ADAMDEC1	1.447193	1.30803	3.970954	0.00031	0.001037	-0.3282
NAPSA	-1.71589	8.228573	-3.96538	0.000315	0.001052	-0.34406
HCAR2	-1.22231	2.312118	-3.96523	0.000315	0.001053	-0.34447
GPR116	-1.46762	5.535346	-3.9588	0.000321	0.00107	-0.36276
ATF3	-1.47615	4.091099	-3.95628	0.000323	0.001077	-0.36991
FOXA2	-1.30709	3.347307	-3.9456	0.000334	0.001108	-0.40025
CD27	1.083431	2.042695	3.944426	0.000335	0.001111	-0.40356

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RAB27B	1.007118	2.652396	3.942898	0.000337	0.001115	-0.4079
PRRX2	1.160718	1.478267	3.941831	0.000338	0.001117	-0.41093
TP53INP2	-1.10748	3.689977	-3.94025	0.000339	0.001121	-0.41542
LCN2	1.782294	4.433582	3.936639	0.000343	0.00113	-0.42565
GALNT6	1.281508	2.454805	3.935177	0.000344	0.001134	-0.42979
FNDC1	1.421935	1.77383	3.933801	0.000346	0.001138	-0.43369
HTR3A	1.288186	0.678835	3.932181	0.000347	0.001142	-0.43828
CLEC12A	-1.00727	1.840576	-3.92876	0.000351	0.001152	-0.44796
COL15A1	1.29472	3.052143	3.92568	0.000354	0.001161	-0.4567
VAMP5	-1.02852	5.609815	-3.92085	0.000359	0.001176	-0.47037
HLA-DPB1	-1.08667	7.512863	-3.91187	0.000369	0.001205	-0.49578
HIST1H2AI	1.867134	1.043273	3.911428	0.000369	0.001206	-0.49702
SFRP5	-1.38308	1.503978	-3.91081	0.00037	0.001207	-0.49875
LRRC15	1.383782	1.648806	3.897593	0.000385	0.001252	-0.53611
BEX5	-1.10869	2.331865	-3.89502	0.000387	0.001261	-0.54338
SLC16A14	1.234818	1.491857	3.892902	0.00039	0.001267	-0.54934
ICAM1	-1.49258	6.700664	-3.87244	0.000414	0.001332	-0.60701
CHI3L2	-1.36515	3.276194	-3.86828	0.000419	0.001347	-0.61872
KRTCAP3	1.151616	4.129446	3.860624	0.000429	0.001373	-0.64026
SERPINE2	1.104717	1.700947	3.860436	0.000429	0.001374	-0.64079
CD74	-1.11713	10.30389	-3.85806	0.000432	0.001382	-0.64747
ELN	-1.03199	4.081313	-3.85183	0.00044	0.001405	-0.66496
MUC4	1.35357	1.378149	3.848106	0.000445	0.001419	-0.67543
FAM101A	1.22131	1.076508	3.844581	0.000449	0.001433	-0.68533
ALDH1A1	-1.5281	5.492809	-3.84164	0.000453	0.001441	-0.69357
SLC7A11	1.444997	1.280746	3.830395	0.000468	0.001485	-0.72511
SCD	-1.11312	6.458344	-3.82677	0.000473	0.001498	-0.73525
KCNK1	1.058967	3.012486	3.807139	0.000501	0.001572	-0.79019
REEP6	1.070945	1.835665	3.807031	0.000501	0.001572	-0.79049
IER2	-1.015	4.875271	-3.80558	0.000503	0.001578	-0.79455
GJB5	1.070513	0.846924	3.793598	0.000521	0.001624	-0.828
HIST1H2AG	1.358052	0.851576	3.792592	0.000523	0.001628	-0.83081

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SORL1	1.034973	2.781845	3.785903	0.000533	0.001657	-0.84946
CLDN10	1.56374	1.114627	3.770942	0.000557	0.00172	-0.89113
IL2RA	1.109493	1.671242	3.769763	0.000559	0.001725	-0.89441
HGD	1.288851	1.198506	3.759048	0.000576	0.001773	-0.92421
POU2AF1	1.079599	1.225948	3.756975	0.00058	0.001782	-0.92997
ARSE	1.326393	2.327468	3.746072	0.000598	0.001829	-0.96024
PHLDA2	1.520999	3.410724	3.74473	0.000601	0.001834	-0.96396
ERV3-1	1.067514	2.429022	3.736409	0.000615	0.001876	-0.98703
PLA2G4A	1.266777	2.76959	3.73468	0.000618	0.001883	-0.99182
GBP4	-1.18857	3.80153	-3.72991	0.000627	0.001907	-1.00504
CNFN	1.018345	1.055251	3.729092	0.000629	0.001911	-1.0073
SLC16A3	1.06685	3.671197	3.721985	0.000642	0.001944	-1.02697
CPM	-1.14723	4.669068	-3.72191	0.000642	0.001944	-1.02719
VSTM2L	1.548132	3.650701	3.71755	0.00065	0.001964	-1.03924
SBK1	1.059804	1.424469	3.713423	0.000658	0.001982	-1.05064
DCBLD2	1.19797	3.236025	3.706964	0.00067	0.002011	-1.06849
HIST1H2BH	1.775197	1.025214	3.705337	0.000673	0.002019	-1.07298
CECR1	-1.10403	4.362274	-3.70524	0.000673	0.002019	-1.07324
TMPRSS2	-1.48086	4.171817	-3.70305	0.000678	0.002029	-1.0793
HLA-DPA1	-1.01568	6.933027	-3.70201	0.00068	0.002035	-1.08215
LOXL2	1.249757	2.724464	3.701428	0.000681	0.002037	-1.08377
HRCT1	-1.06242	1.797955	-3.70051	0.000683	0.002041	-1.08631
SCARA5	-1.55048	1.953849	-3.69939	0.000685	0.002047	-1.08939
SELE	-1.45581	1.336162	-3.69516	0.000693	0.00207	-1.10107
B3GNT6	1.661607	0.969335	3.693874	0.000696	0.002076	-1.1046
MS4A4A	-1.01287	3.748507	-3.69197	0.0007	0.002084	-1.10985
WFDC3	1.038736	0.828694	3.686482	0.000711	0.002111	-1.12497
BASP1	1.390971	4.253768	3.673635	0.000738	0.002183	-1.16033
IL1RL1	-1.71832	2.099377	-3.67337	0.000738	0.002185	-1.16106
CYR61	-1.26138	6.837396	-3.65775	0.000772	0.002275	-1.20397
DIO2	1.057286	0.889194	3.654392	0.00078	0.002295	-1.21317
PRRX1	1.073027	2.469763	3.646068	0.000798	0.002346	-1.23599

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SOCS3	-1.52597	6.422764	-3.64237	0.000807	0.002367	-1.24611
PDPN	-1.01155	3.854075	-3.64014	0.000812	0.00238	-1.25223
HAS1	-1.2304	1.096447	-3.62923	0.000838	0.002445	-1.28207
SPRR1B	1.598588	0.886035	3.624494	0.000849	0.002474	-1.29502
AADAC	-1.49479	2.2147	-3.62407	0.00085	0.002476	-1.29617
CD79A	1.579756	2.659804	3.617841	0.000866	0.002517	-1.31319
MAOA	-1.11684	4.944924	-3.61642	0.000869	0.002525	-1.31707
RCN3	1.298316	3.292523	3.614555	0.000874	0.002538	-1.32216
LY6D	1.289771	0.70091	3.610011	0.000885	0.002565	-1.33455
CTGF	-1.15056	7.06349	-3.60317	0.000903	0.00261	-1.3532
QPCT	1.350742	2.517687	3.600238	0.00091	0.002627	-1.36119
HOPX	-1.33924	4.942194	-3.56945	0.000994	0.002832	-1.44486
ID1	-1.18067	5.801369	-3.55924	0.001023	0.002898	-1.47253
CA2	-1.55811	4.376395	-3.5494	0.001052	0.002968	-1.49916
HLA-DRA	-1.11305	10.54703	-3.54916	0.001053	0.002969	-1.49981
FCGR3B	-1.20154	1.551378	-3.54811	0.001056	0.002976	-1.50266
CCL24	-1.48147	2.328714	-3.54595	0.001063	0.00299	-1.50848
DMBT1	-1.85096	4.513419	-3.54431	0.001068	0.003001	-1.51292
SGK1	-1.00677	4.159129	-3.54394	0.001069	0.003003	-1.51392
C11orf86	1.123802	0.579405	3.539033	0.001084	0.003041	-1.52718
NR0B2	-1.16768	1.614283	-3.53783	0.001087	0.00305	-1.53043
SPNS2	-1.06751	3.247782	-3.52781	0.001119	0.003122	-1.55745
IL33	-1.46605	4.257871	-3.52162	0.001139	0.003168	-1.57416
PANX2	1.097508	1.437362	3.520845	0.001141	0.003173	-1.57624
UBD	1.430429	2.360454	3.518905	0.001147	0.003187	-1.58146
RRAD	-1.46206	4.221715	-3.50866	0.001181	0.003267	-1.60904
THY1	1.267166	3.082686	3.507758	0.001184	0.003274	-1.61146
TNNT1	1.49772	1.723206	3.507386	0.001185	0.003277	-1.61246
HIST1H4E	2.280064	1.273833	3.501035	0.001207	0.003325	-1.62952
HIST1H2BJ	1.528527	1.413281	3.4991	0.001213	0.00334	-1.63472
FND4	1.070393	1.996347	3.495383	0.001226	0.003369	-1.6447
LRRN4	-1.51347	3.133258	-3.48694	0.001256	0.003438	-1.66736

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C2CD4B	-1.0151	1.580389	-3.4863	0.001258	0.003443	-1.66905
HILPDA	1.102787	2.824886	3.484716	0.001264	0.003456	-1.6733
HIST1H3E	1.102712	1.133495	3.484451	0.001265	0.003457	-1.67401
SLAMF7	1.203736	2.549638	3.468288	0.001324	0.003595	-1.71727
SGPP2	1.196497	3.948788	3.468096	0.001324	0.003596	-1.71779
TCN1	1.941916	1.13246	3.465656	0.001333	0.003619	-1.72431
EGR2	-1.15939	2.56377	-3.46484	0.001336	0.003626	-1.72648
RAB11FIP1	-1.04166	4.539459	-3.45842	0.001361	0.003683	-1.74364
KDM6B	-1.0735	3.347651	-3.45238	0.001384	0.00374	-1.75975
TXNRD1	1.203828	5.096569	3.451088	0.001389	0.003752	-1.76319
CCL19	1.542136	3.379242	3.447672	0.001403	0.003783	-1.7723
PAEP	2.191995	1.415197	3.442387	0.001424	0.003834	-1.78638
NCCRP1	1.225093	0.878685	3.441711	0.001426	0.00384	-1.78818
FOLR1	-1.58965	6.394936	-3.43552	0.001451	0.003896	-1.80465
TRIM31	1.019475	0.691088	3.431761	0.001467	0.003934	-1.81465
FOS	-1.43522	6.935768	-3.43136	0.001468	0.003937	-1.81571
CFTR	-1.06404	1.877036	-3.41071	0.001556	0.004135	-1.87052
HIST1H2AM	1.515985	0.817534	3.408032	0.001567	0.004161	-1.87763
S100P	2.561878	3.502064	3.40787	0.001568	0.004162	-1.87806
NDUFA4L2	-1.04156	2.904155	-3.40544	0.001579	0.004181	-1.88448
HIST2H2BF	1.038026	0.687867	3.396503	0.001619	0.004273	-1.90814
CT83	1.693999	0.940994	3.389458	0.001651	0.004349	-1.92676
NTM	-1.32926	2.157978	-3.38692	0.001663	0.004374	-1.93346
AKR1B10	2.528161	1.390027	3.383788	0.001677	0.004405	-1.94173
BCL2A1	-1.07142	3.762458	-3.37872	0.001701	0.004458	-1.9551
SYT13	1.007991	0.734457	3.376899	0.00171	0.004478	-1.9599
MMP7	1.807019	3.725233	3.369721	0.001744	0.004559	-1.97881
TFF1	2.524399	1.363348	3.355102	0.001816	0.00472	-2.01726
RTN4RL2	1.162321	1.352067	3.343916	0.001874	0.00485	-2.04662
HIST1H2BF	1.459823	0.766865	3.34373	0.001875	0.004851	-2.04711
SMOC1	1.298601	1.085646	3.321875	0.001992	0.005105	-2.10432
AHNAK	-1.12865	6.350703	-3.31022	0.002057	0.005253	-2.13474

Appendix C5: continued

CCL2	-1.62253	4.926027	-3.29547	0.002142	0.005447	-2.17317
KRT17	2.176162	3.252888	3.293114	0.002156	0.005477	-2.1793
MT-ND1	-1.91462	10.3436	-3.28868	0.002183	0.005534	-2.19082
PCP4	1.141733	0.855242	3.282171	0.002222	0.005626	-2.20773
MZB1	1.3792	2.643939	3.276262	0.002259	0.005705	-2.22306
GZMH	-1.00876	2.406784	-3.2719	0.002286	0.005765	-2.23438
TREM1	-1.09259	4.01572	-3.2684	0.002308	0.005816	-2.24344
SLC16A9	1.079907	1.265385	3.243423	0.002472	0.006164	-2.30798
SLC22A3	-1.15499	3.245559	-3.24046	0.002492	0.006209	-2.31563
CEACAM5	2.374121	3.071193	3.240336	0.002493	0.006209	-2.31594
MT-CYB	-1.58607	10.60218	-3.21261	0.002689	0.006632	-2.38724
GAL	1.016966	0.618632	3.196664	0.002808	0.00689	-2.42807
POF1B	1.103319	1.527247	3.192977	0.002836	0.006947	-2.4375
NFKBIZ	-1.18957	3.45758	-3.17935	0.002943	0.00718	-2.4723
SERPINA1	-1.18404	7.459261	-3.17914	0.002945	0.007182	-2.47283
HIST1H1D	1.767006	0.92812	3.16979	0.003021	0.007354	-2.49665
PKP2	1.040669	1.632188	3.166031	0.003052	0.007419	-2.50621
IVL	1.481617	0.930866	3.158331	0.003116	0.007561	-2.52578
CACNG4	-1.1674	2.412927	-3.15248	0.003166	0.007663	-2.54063
IGLL5	1.542753	3.84303	3.138047	0.003292	0.007938	-2.57721
HIST1H2BO	1.547075	0.861402	3.135918	0.003311	0.007973	-2.5826
RND1	-1.54585	3.465437	-3.1272	0.003389	0.008124	-2.60463
PRAME	1.333223	0.693219	3.124355	0.003415	0.008179	-2.61181
ASPN	1.069189	3.350613	3.117997	0.003474	0.008302	-2.62785
HIST1H1E	2.249483	1.23652	3.115241	0.0035	0.008354	-2.6348
AGR2	1.630482	5.704757	3.111245	0.003538	0.008427	-2.64486
APOBEC3B	1.021189	1.494929	3.093501	0.003711	0.008786	-2.68947
LAMC2	1.122763	5.280236	3.082355	0.003823	0.009029	-2.71741
S100A7	1.274391	0.667254	3.075096	0.003898	0.009187	-2.73557
FOXA3	1.072854	0.998645	3.067686	0.003976	0.009345	-2.75409
FGL1	1.358703	0.771215	3.043248	0.004244	0.009898	-2.81496
KRT81	1.564807	0.909832	3.036496	0.00432	0.010056	-2.83173

Appendix C5: continued

CDA	1.669313	2.918442	2.99156	0.004867	0.011173	-2.94274
AQP9	-1.03676	2.778342	-2.97078	0.00514	0.011724	-2.99373
TMEM45A	1.126925	2.244714	2.966849	0.005194	0.011814	-3.00336
MT-ND2	-1.92875	10.2882	-2.96377	0.005236	0.011898	-3.01089
TESC	1.663665	2.947498	2.960829	0.005277	0.011977	-3.01808
CXCL3	-1.2883	2.211934	-2.95706	0.005329	0.012084	-3.02729
LTF	1.662752	3.348664	2.955605	0.00535	0.012121	-3.03084
FGB	2.495992	1.401522	2.953853	0.005374	0.012164	-3.03511
PMAIP1	1.174825	2.581296	2.928529	0.005743	0.012907	-3.09674
HIST1H2BE	1.484934	0.854271	2.924195	0.005808	0.013043	-3.10725
FBLN1	-1.05481	5.21343	-2.91359	0.005971	0.013355	-3.13294
TNC	1.259405	4.216809	2.888602	0.006372	0.014116	-3.19322
VSIG1	1.610113	1.464173	2.886803	0.006402	0.014168	-3.19755
BARX1	1.045376	0.562829	2.883434	0.006458	0.01427	-3.20565
MT-ND4	-1.66134	11.11885	-2.87991	0.006517	0.014384	-3.21411
UCHL1	1.565296	2.390284	2.872739	0.00664	0.014618	-3.23132
ERN2	1.137141	0.901984	2.866723	0.006744	0.01482	-3.24574
TMSB15A	-1.10295	1.501431	-2.8509	0.007025	0.015335	-3.28355
CLU	-1.03916	5.564252	-2.84449	0.007142	0.015567	-3.29885
CD163	-1.06153	4.723509	-2.84168	0.007194	0.015667	-3.30553
HIST2H2AC	1.739733	1.460164	2.837265	0.007276	0.015832	-3.31604
SAA1	1.357038	2.556698	2.836054	0.007299	0.015879	-3.31892
HIST1H4D	1.708717	0.932225	2.829704	0.007419	0.0161	-3.33401
MT-ND3	-1.09373	10.74038	-2.82467	0.007516	0.016273	-3.34595
MT-ND4L	-1.27126	9.667654	-2.81165	0.007771	0.016752	-3.37679
MUC5B	1.946364	2.025	2.800912	0.007988	0.017136	-3.40215
MUC21	1.700174	2.106606	2.793377	0.008143	0.017428	-3.41991
BCAS1	1.159187	1.218227	2.778058	0.008467	0.017999	-3.45591
HIST1H1B	1.773849	0.903892	2.773662	0.008563	0.018172	-3.46622
HIST1H3C	1.457249	0.733628	2.768004	0.008687	0.018399	-3.47947
HIST1H3B	1.681866	0.853195	2.759136	0.008885	0.018759	-3.50021
WFDC2	1.100208	6.362127	2.746938	0.009164	0.019241	-3.52865

Appendix C5: continued

SPRR2D	1.011068	0.62919	2.742256	0.009273	0.019435	-3.53955
FCER1A	-1.09634	2.691608	-2.74096	0.009303	0.019489	-3.54256
HLA-DRB5	-1.15354	8.08232	-2.73904	0.009349	0.019571	-3.54702
MT1A	-1.65434	2.963563	-2.72321	0.00973	0.020257	-3.58375
SFRP4	1.059524	3.470261	2.718649	0.009842	0.020478	-3.59431
HIST1H2AL	1.214601	0.624249	2.713432	0.009973	0.020722	-3.60636
AGT	1.218644	1.908901	2.706899	0.010138	0.021031	-3.62144
CST6	-1.0144	3.801892	-2.69796	0.010368	0.021464	-3.64202
MT-ATP8	-1.63411	9.73885	-2.68631	0.010675	0.022001	-3.6688
BHMT2	1.044906	1.302364	2.684493	0.010724	0.022083	-3.67296
PCSK1N	1.033478	1.721536	2.679585	0.010857	0.022327	-3.68421
SCGB3A2	-2.11732	6.909848	-2.66638	0.011221	0.022969	-3.7144
MT-ATP6	-1.51941	10.78112	-2.65839	0.011446	0.023367	-3.73261
PKP1	1.065746	1.637743	2.635325	0.012122	0.024538	-3.78501
CPS1	1.271616	0.920948	2.629648	0.012293	0.024817	-3.79785
CLDN3	1.09141	4.465358	2.615658	0.012726	0.02557	-3.82943
CRLF1	1.236854	1.868703	2.615195	0.012741	0.025592	-3.83047
STEAP4	-1.01575	4.472571	-2.61197	0.012843	0.02578	-3.83774
TGFBI	1.004776	5.061404	2.60889	0.012941	0.025944	-3.84466
SFTA2	-1.15324	7.197325	-2.58239	0.013813	0.027461	-3.90404
HIST1H2BL	1.168174	0.689876	2.574625	0.014078	0.027896	-3.92136
HIST1H4C	1.721168	0.916167	2.558113	0.014659	0.028922	-3.95807
HIST1H2AJ	1.263401	0.638248	2.556338	0.014722	0.029017	-3.962
HIST1H2BI	1.206441	0.610066	2.552837	0.014848	0.029212	-3.96976
HMOX1	-1.13294	4.991788	-2.54545	0.015118	0.029674	-3.9861
TSPAN8	1.222299	3.521109	2.542301	0.015235	0.029871	-3.99306
CLDN1	1.110033	3.705751	2.532566	0.0156	0.030493	-4.01453
CLDN6	1.303536	0.829026	2.530285	0.015686	0.030639	-4.01956
HIST1H2BM	1.074252	0.537126	2.5205	0.016063	0.031261	-4.04106
TRIM29	1.045903	1.560219	2.511251	0.016427	0.031878	-4.06134
AKAP12	-1.08139	3.591408	-2.50995	0.016478	0.031967	-4.06418
AGR3	-1.4652	5.021298	-2.50616	0.01663	0.032233	-4.07248

Appendix C5: continued

INHA	1.122835	0.661454	2.505509	0.016656	0.032279	-4.0739
SCGB3A1	-1.96748	6.366877	-2.50314	0.016752	0.032429	-4.07907
CHI3L1	1.184867	4.501617	2.493136	0.017161	0.033116	-4.1009
S100A4	-1.17117	7.759025	-2.47787	0.017803	0.034124	-4.13408
PPBP	-1.20852	2.006791	-2.47739	0.017823	0.034158	-4.13511
INSL4	1.02067	0.515876	2.474325	0.017955	0.03438	-4.14176
BPIFA1	1.92425	2.282872	2.47266	0.018027	0.034492	-4.14536
HIST1H2AB	1.115096	0.563888	2.465933	0.01832	0.034969	-4.15991
HIST1H4B	1.395743	0.731117	2.436964	0.019632	0.037044	-4.22225
HIST2H2AB	1.215213	0.666003	2.434758	0.019735	0.037222	-4.22697
HIST1H3F	1.175856	0.608226	2.434545	0.019745	0.037236	-4.22743
EDN2	1.105865	1.540703	2.431546	0.019887	0.037463	-4.23385
HIST1H3I	1.195813	0.630988	2.418521	0.020511	0.038465	-4.26165
HIST1H4A	1.099168	0.561148	2.410001	0.020929	0.039152	-4.27978
HIST1H2AH	1.217759	0.643445	2.383814	0.022263	0.041357	-4.33522
HIST1H4F	1.000719	0.50036	2.332022	0.02513	0.046006	-4.44353
HIST1H4L	1.115543	0.564569	2.320632	0.025803	0.047095	-4.46711
SLC26A9	-1.0219	2.804647	-2.31535	0.026121	0.047567	-4.47802
MUC5AC	1.47477	0.997043	2.309678	0.026466	0.047991	-4.48971
C20orf85	-1.60663	2.877341	-2.3009	0.027008	0.048824	-4.50776

Appendix C6: Hypermethylated genes in lung adenocarcinoma (LUAD)

GENE	GENE	GENE	GENE	GENE	GENE	GENE
SCT	C1orf94	DTNBP1	COMP	SMAD7	KLK13	MLNR
TBX4	IRX4	ZFHX3	CTXN2	BEND4	ADRB1	ST8SIA6
C12orf42	PROCR	KCNA6	ZFHX4	GRIA2	SCUBE3	ZNF804A
PCDH17	SEMA4A	NECAB1	HES3	EHMT1	MOGAT3	PUF60
ST18	HPCAL1	CCDC3	LYPD5	NID2	PRHOXNB	SCFD2
LRBA	CCDC101	PRRX1	GSX1	SGIP1	KCNJ10	MAP3K14
TAOK2	RBPMS2	COCH	TSPAN9	ZBTB16	AMOTL1	OPCML
ZIC4	AJAP1	ZNF366	MAP1A	CYTSA	SOBP	SYNGR3
PITX1	TBPL2	LAYN	GRIN3A	KIF26B	IGLON5	INSC
DOCK9	CNGA3	SLC37A1	MLL2	TRIM54	C12orf65	LOC100128239
ARRB1	NHLH1	ZNRF1	CDH4	LOC643719	C17orf72	GALR3
BAHCC1	PODN	LOC646999	KSR2	MYPN	RGS9BP	GALNTL2
CBLN4	CAPN2	ZNF697	MCOLN2	ACOT11	TP53INP1	GPER
ASAP2	ZNFX1	PHACTR2	FAM135B	PPP2R2C	GRIN2C	F2RL3
PCDHGA4	ALX4	TCF15	HOXA4	MOV10L1	PDE2A	PRKCE
PTPRN2	PKLR	IQSEC1	ST8SIA1	MUC4	MGAT5B	IGFBP2
HOXD12	MIR548F5	PTGER4	MSRB3	ADAP2	ANP32A	KANK4
ZIC1	LYRM4	PRDM16	ADAMTS18	SMO	ITPRIPL1	NDST1
RBMS1	NKX6-1	BCAN	MPO	MYBPC1	MAP3K8	MDGA1
N4BP1	C2orf65	SLC24A4	PTPRU	EPHA8	CORIN	POU3F1
CD36	SLITRK1	ACHE	ITGA8	RPH3A	C4orf38	CUGBP2
IFFO1	MRV11	HOXB7	SIPA1	CNNM1	MYO1G	LOC284798
FAM102A	SLC12A5	DLX4	F7	THY1	PCDHGA5	NRG2
C1orf198	CALCOCO2	DUSP16	GBX2	SYT6	P2RX1	CDH7
KDR	LHFP	F10	CHL1	FAM115A	SLC22A17	VGLL2
LRP2	PRDM6	C10orf46	AVIL	ZNF529	GRID2	TNRC4
SATB2	NEUROG1	WBSCR17	L1TD1	SOD3	KANK3	SEL1L3
DPP6	PAX2	C7orf41	ASCL2	EPHA5	ADAM22	KIAA0182
ERICH1	TMEFF2	BDNF	MIR129-2	MPPED2	RAI14	NKAIN4
RGS3	ADAM30	DIP2C	HERC3	ARID3A	ODZ3	TCP11
PEAR1	TMEM88	MMP9	PBX1	NTNG1	NAGK	HRNBP3
HOXD4	GAD1	JAKMIP3	MOBK12C	KCNMA1	OLFM3	C6orf27
GMDS	P2RY12	RIMS3	VENTX	RASSF2	DGCR10	MIR641
GLI2	PNPLA1	FOXF1	ISL2	GSC2	CLVS1	ZNF830
SKI	HOXA9	MAPK14	PRAC	LOC441177	C21orf88	MAPT
YPEL2	SEPN1	C20orf117	CLRN1	ALOX12P2	C19orf41	EFCAB2
EDNRB	C1QL3	ITIH5	GLRA1	MYLK	PROKR2	PPP1R16A
CLEC14A	COLEC11	HOXB6	ATXN2	UTS2R	MYO15B	EYA2
DCHS2	NFATC2	LVRN	AVPR1A	PDZRN4	CACNA1H	GEFT
TP73	B3GNTL1	MDF1	GPR78	PIF1	TMEM220	PPT2

Appendix C6: continued

ATP1A1	CNGB1	ZNF608	RSPH6A	ACSF2	KCNAB1	TMOD3
SIM1	MSC	NKX2-3	SLC6A2	DNAJC6	EYA4	ZNF215
FOKK1	GABRG3	CALCA	EPO	KIF1A	POFUT2	RNF150
NOD1	PHOX2A	DPYSL2	CDH8	ZEB2	INSM1	JAK3
TNS1	CPXM2	DLX5	RUSC1	CBX7	RBP4	LRMP
SKAP2	GRK5	GJA4	KCNG3	TOX2	RFX1	DPYSL5
HOXD10	ZIC5	MAPK4	CLDN18	ADCY9	BTN1A1	CXCR6
CRYL1	LHX3	ASCL4	KCNK9	SLC17A8	ZFR2	GALNTL6
MAP1D	ELL	GPC6	FAM49A	NPY5R	SLC17A9	SH3BP4
CASZ1	MNX1	EBF3	PDGFRA	DAB1	RIMS2	ETV6
AGER	HOXC12	ACTL6B	HERC1	LIN28	FAM19A4	OTOP1
MAP3K3	UVRAG	GDF7	PAX8	UCP1	TLR5	SLC9A1
TAL1	RNF39	TTBK1	CACNA2D4	H2AFY	CRIL	SRGAP3
TFAP2D	FMN2	CRAMP1L	CPXM1	LRIT1	RYR3	FRMD3
PAX9	PRIMA1	LRP5	ROBO3	LPPR3	FARP1	ZNF667
SDK1	HDAC7	MEGF10	GAS1	ARL5C	TCTE1	TSHZ3
PITX2	HOXD13	KLHDC7B	MYO10	CLDN5	KCNN2	ZNF300
DLX6AS	MAP3K11	SYN2	ATOH7	TCERG1L	C12orf66	ELMO1
PINX1	CSMD1	KCNIP4	CHD9	FIBIN	NGF	GABRB1
CDC42	GATA3	SLC32A1	FAM123C	CBX2	PDZRN3	FAM150B
FGF14	CRYBA2	NOL4	CCNY	IGF2AS	CYP26C1	RYR1
KCNJ8	LHX8	NPHS2	GRID1	WNT10A	TNXB	RNF219
C2orf55	MAML3	TBX20	AKAP13	NOTCH1	PARP15	PLK5P
ZSCAN18	SLC9A3R2	C1orf70	ECEL1	SHANK2	SNX29	ADAMTS2
HAS1	HLX	BARX1	SP8	LOC149134	RASGEF1C	CRYM
DCUN1D2	GRM1	CPT1B	KIAA1409	SETBP1	BARHL1	CRTC1
GP1BB	ADCYAP1	LOC494141	OCA2	AGAP11	CHRNA4	RINL
INO80	NKAIN3	FREM3	NR1I2	HTR5A	HEPACAM	ABCG5
NDUFA4L2	SLC7A14	POU2F2	ATP2A3	PACSIN1	GPC5	VCAN
GDNF	FAM38B	NR1H3	GIPC2	COX10	ABHD12B	ZBTB20
5-Sep	MYO1B	HAND1	BTBD3	LECT1	SLC10A5	C1orf190
HOXD9	C4orf31	TBX18	GPBAR1	SLC22A16	KLHDC4	RAB8B
MEGF11	TGFB3	SPEG	ASCL1	CDX1	NLRP6	ANKK1
TBCD	RERE	SH3PXD2A	FAM43B	GPATCH8	NOS1	PRICKLE1
DNAH17	TMEM14E	TRPC7	KLHL33	ITGAL	GUCY2D	ATP6V1B2
MEX3A	CPEB3	PLD5	KLHL29	CACNG2	EDARADD	KIAA1217
WNT3	GABRG2	ABCA3	POU3F3	FCHSD2	GMPPA	TNRC6C
ZNF232	ZFP42	C14orf39	SNCA	ULK4	ITM2B	DOCK6
C7orf49	DRD5	BARHL2	ADAM11	RTKN	SLC30A2	FAM71E2
TRAF7	ANKMY1	MESTIT1	TEK	PISD	ZNF385D	C19orf38
MIR124-2	FOXI2	SLC26A9	ITPKA	HAS3	DDK3	FAF1

Appendix C6: continued

SMARCA5	TBX1	CNTNAP5	PRKCB	GRM8	UNC13A	PPPDE1
CRCP	GPR26	NEUROD1	IGF2BP1	CHODL	ART4	NRG3
EFNA5	ZNF274	GDF2	ST6GAL2	HIST1H4F	ICAM5	MUPCDH
GRIK2	PCDHB17	SLC8A3	GABRA1	GFRA1	PLEKHB1	ASGR1
MEIS1	SHANK3	PRKCZ	LASP1	PHF17	PDS5B	ATG9B
ZFP106	PAX7	SHISA3	CDKN2A	HAPLN4	SLC24A2	ARPC5
IFT140	MAMDC2	VPS13D	CPLX2	ADARB2	DES	TMEM8B
LHX9	MRGPRF	NRG1	C11orf75	ISLR2	EDEM3	TRPA1
LRRK1	HOXB3	SNRPN	CLUAP1	SMTNL2	LOC285419	CREB3L1
NXN	UGT3A1	SASH1	CLVS2	MIR124-3	PTHLH	DUSP27
LOC158376	KCNA1	HOXC8	SRL	SLC27A1	LOC100101938	SPTY2D1
JARID2	FGF5	SHC1	RXRG	KCNC1	FAM5B	PCBP1
EMX2	11-Mar	TRPC3	MAP4K4	DUOX1	PSMA1	PPYR1
TIE1	ANKRD6	NTRK1	SLC4A4	TOM1L2	COL4A1	DOK5
LHX1	HCG9	TTC28	PPP3CA	CARTPT	HEMGN	TM6SF1
CTBP2	INF2	PRRT1	SYNPR	GDF10	SULT4A1	PLAGL2
TLX3	HOXB1	LRRC16A	PDPN	INCA1	C16orf72	MME
MIER2	SNX20	WIT1	WNK4	DOC2A	TNFSF11	ZNF280B
TULP1	FBRSL1	MIR145	VGLL4	HOXC11	LSM12	HGF
BHMT	ITGB5	CHST12	MIR10A	NPY	KCP	ARPC2
VPS53	CMIP	ROBO1	CCDC102A	PDIA3P	IGF2BP3	MAD1L1
PCDH8	ATP8A2	BSX	LOC80054	C6orf132	C19orf35	TMEM179
ST8SIA3	LMX1A	CPNE7	ZAR1	COL14A1	ITGA5	PDE10A
HOXD11	HOXA7	PARD3B	RARRES2	INA	KCNA2	LDB2
ARHGEF4	SPARCL1	C9orf5	NRSN1	TMPRSS2	JAKMIP1	STK24
SIPA1L1	ADAM5P	RXRA	NKX2-4	RUNDC2A	COL11A2	FZD7
PCDHA2	FGF8	S1PR5	TRIM62	POM121L2	UBE2QL1	C13orf15
SLC41A3	KIAA1161	SHISA9	NPBWR1	SLC5A8	PHACTR3	CLIC4
ABCG1	KLHL26	LOC200726	MEIS2	CASKIN2	SDK2	TSPYL5
MAP7D1	DBP	ODZ4	C1orf114	ATP5G2	ARPC1B	ASTN1
C6orf147	SGMS2	CCDC152	SHISA7	ITGA6	SYT10	C13orf33
TBC1D24	KLHDC8B	SHH	ALPL	LOC441601	HRH3	OTOP2
MCF2L	RBMS2	ASTN2	B4GALT5	PCDHA1	FSCN1	GRIN2B
HOXA2	SLC12A4	UTRN	AMH	OBSL1	KLHL21	MIR196B
FAM53B	KCNB1	HECW2	NCOR2	NPDC1	PLXND1	HIST1H2BH
NBLA00301	LBXCOR1	FGF12	NPAS4	PPP2R2B	ME3	FAT4
C10orf11	LOC440839	LOC100192378	ADAMTS5	SLC30A10	CD247	ZNF804B
RD3	CAMTA1	SOX7	NPTX2	PRKG1	ARHGAP18	HIF3A
EHBP1	CCDC140	PDLIM1	TMEM26	TUBB6	GABRA2	ARHGAP20
C17orf93	CHRM1	SOX2OT	ZMYND15	SNORD1A	PTH2	NRP2
SPTBN1	EPHA10	C10orf105	CNTNAP2	C2orf84	CCNJL	LEF1

Appendix C6: continued

ERN2	EMILIN1	DMRT3	RGS14	LMO2	SLC13A5	KIF1B
IGFBPL1	ZNF208	ONECUT3	GPRC5B	SLC25A33	4-Mar	MC4R
ELAVL4	TBC1D22A	PLEKHN1	ZIC2	SYT3	PTPRO	NDRG4
OTX1	SIX3	CDH22	RAX	PTPRF	KCNH4	SFRP4
OTUD7A	LHX5	RGS20	VIPR2	NEURL	C21orf7	CCNA1
HTR1A	DGKI	C1orf187	PRR18	PCDH21	SLC12A8	SOX5
ADAMTS20	DGKA	PEX14	LTBP2	ATOH1	LIMA1	ACACA
EOMES	NSD1	TRAF3	EHBP1L1	C1QL2	SCRT2	ARNTL
FERD3L	GLB1L2	LOC642597	ISL1	TRIM36	C22orf45	LIMS1
SRCIN1	KRT72	UFSP1	CAST	TDRD10	SLC19A3	SNAP91
MESDC1	ZNF98	ABI3	NEFH	PDE4B	PKHD1	LIFR
FES	C1QL1	BCL11B	GLRX	SLITRK5	DEXI	ITGBL1
GDF1	SLC18A3	ZNF536	LOXL2	PCDHB7	CADM3	GPR37
AMOTL2	CUEDC1	KIF13B	AKAP12	KCNB2	GTF2IRD1	MAFA
B4GALNT1	ANKS1A	BRUNOL4	CASKIN1	SLC17A7	CLEC4G	PRKAR1A
EN1	FLJ12825	ARHGAP26	ALDH1A2	ZSCAN23	PLXNA4	B3GALT2
C16orf80	POMC	EMX2OS	FEV	FNDC3B	RNASE7	FGD6
CPEB2	CTSK	CCK	HBM	HOXB13	TM6SF2	CTSA
HOXC4	PPP1R16B	KLC1	EPS8L1	FGF2	MAPK10	PSEN2
ATP11A	CHKA	ZNF560	SP9	SCARA5	ABCB1	HIST1H3E
NXPH1	SDCCAG8	CCDC36	VAC14	RICH2	FBXL18	C5orf49
DDX25	MAL	ZNF876P	LRRK2	PGLYRP2	BACH2	ITPRIP
KCNS2	MEI1	KCNA5	COL5A2	C20orf46	ZIK1	DKFZP434H168
SPG7	KLHL2	UBE2V1	COX7A1	UGT3A2	FEZ1	KIF13A
PAX3	ST8SIA5	GABRA5	LOC100188947	IGSF9B	GPR88	CSGALNACT1
LOC404266	CRISPLD2	SHANK1	KCNH5	PLEKHO1	FBXL7	RNF126P1
FLJ42709	LOC619207	HSPB2	WDFY2	SCUBE1	ZDHHC3	EXPH5
RGS16	RFX4	WDR20	PRDM12	FAM19A5	CCDC109A	FRMD4B
ZSCAN12L1	C9orf98	TMC2	C16orf45	CARD14	NEUROD2	ZNF879
PIK3CA	SLCO3A1	GRM3	AIFM3	ZNF660	LAMA2	ZNF703
ZMIZ1	SIPA1L2	LRIG1	DOCK3	CALN1	LOC285954	PLA2G7
PRDM8	ANKRD55	TMEM145	TRIM40	RMST	ALDH1A3	CYP11A1
FOXK2	TSSK6	ZNF577	CACHD1	LAMB1	LRRC3	FSCN2
CMTM2	CSMD3	MAP2K1	UBE2O	TTYH1	LPIN2	MMP16
MSX1	ZNF833	ERCC4	UNC5A	TNIK	ZNF471	ALS2CR12
GNA12	TMEM63C	SPAG6	GPRIN1	CAMKK2	TMEM130	RNF220
FEZF2	C7orf50	PITPNM2	TRABD	PPP1R13L	ZBPB	GRIN1
TFAP2A	IGFBP4	KCNG1	C8orf58	SSH2	EPHB2	KCTD2
LEP	GATA4	ADIPOR1	CALY	FTO	SLC26A5	APBB1IP
HAND2	ZBPB2	PCDHGA1	TMEM90B	POU4F3	GNAL	ASAM
YJEFN3	TNIP1	1-Mar	ACTN1	ANKS1B	WNT3A	SYT9

Appendix C6: continued

HS3ST3B1	SLC6A17	CADPS	BCL2L11	RLTPR	GPR120	GULP1
DLX1	RYBP	PTPRM	SHF	THSD7A	DNMT3B	FGD4
HOXD3	LOC285548	C7orf16	DLX2	CTTNBP2	C21orf84	CDH12
KLHL31	SHOX2	ABHD2	HOXA1	PDE4D	NHLH2	VAV3
SOX17	TLX1	MYOD1	LOC100128811	ITGA2B	SYDE1	TNK2
PRDM14	GSC	CMTM8	KCNA4	SLC35F1	SOSTDC1	CD96
EMID2	GPR83	IGSF21	IQCE	KLC2	P4HA3	NOTCH4
CTDSPL	RASAL1	EDN3	TTLL10	UHRF1BP1L	MPV17L	OSBPL5
PCDHB15	SOX1	LOC100189589	NODAL	DYNC11I	PCDHB5	PKIA
MIR10B	DUOXA2	CHST11	VAMP5	FAM65B	NFASC	NKD2
GAK	VILL	KCNQ1	C7orf52	ZNF238	CD300A	DPF3
A2BP1	GALR1	CDH23	KCNK12	AKT1	PTPN5	GJB2
TBR1	CAPZB	CACNG3	ARID3C	RASA3	SRGN	SRD5A2
VSTM2A	GCM2	RALA	CALB1	PAPPA	SEMA6D	GLI3
FLJ32063	JDP2	LOC100128731	CRABP1	C5orf62	MSI1	MERTK
ONECUT2	FOXP4	DPYSL3	RARG	UBE2Q1	KCNK10	JAM2
C11orf49	9-Sep	FZD2	ACVRL1	SYT2	GHR	LTBP4
SMPD3	APBA2	RASGRP2	PIK3R5	ZNF154	FAM123A	KCNIP1
GRK7	PCDHB3	FIGLA	DOCK2	MOS	TRIM8	SLC38A2
ALX3	FAM110A	CYTL1	SLC6A7	LRRC3B	RNF112	PREP
LHX2	VARS2	NOS3	TBC1D10C	COL11A1	EFCAB1	CNTD2
PLOD2	FOXG1	CYTH1	FER1L4	ITGB4	PSTPIP1	COL12A1
SCARF1	SLC2A14	DAGLA	MARCKS	ZNF521	THADA	ETS2
TBX15	COL2A1	KLHL1	GATAD2B	MLLT1	TMC1	CATSPER4
SND1	HMX2	RALYL	INPP5B	DPYSL4	MAD2L2	EFEMP1
CLDN19	FOXL2	C19orf51	PTPRG	FLRT2	NTRK3	TACC1
PCDHA6	NGEF	RUNX1	PDE1A	LOC399959	MMP2	STX1B
DUSP5P	CTNND2	CADM2	GAB4	GABBR1	PKD2L2	CDK15
TOLLIP	GRASP	GIT2	ADCY1	WNT6	NPTX1	PRSS27
PITX3	CNIH3	ZMYM4	WDR88	BCAS3	GGPS1	DYDC1
KRT81	C10orf47	SYCP1	NRN1L	ARHGAP10	CCDC108	CD1D
PXN	RREB1	HOPX	RGS13	C7orf58	P2RX2	NEDD4L
HOXA5	LOC145845	GPR149	CACNA1A	KCNA3	DNER	PHF21A
VAX1	CHAD	HCN1	SCHIP1	LRRC2	ZNF389	ZNF781
TSPAN14	RESP18	TMEM90A	FZD10	BCL3	CMAH	LOC151174
CACNA1B	C3orf27	NDUFS2	ARSG	C11orf9	GAL	EPS15L1
ELTD1	GPNMB	NOX4	AKNA	TRIM26	SAMD12	ATP2A1
MAGI2	GPR20	TIMP2	C1orf87	SYT14	SOX9	
CRYGD	LRRFIP1	DLL1	C1orf54	PTPRR	8-Mar	
COL23A1	KCNJ3	HK1	VMO1	MDGA2	C17orf104	
EVX2	CCDC146	GRP	CILP2	LOC401463	PLCG1	

Appendix C6: continued

EVX1	CUX1	SLC8A2	WNK2	FGF3	CCDC40	
GPR6	PIGV	APCDD1L	SRRM4	P2RX6	CD302	
NR4A3	HOXA10	FOXD3	SORCS3	ACVR1B	OPRD1	
CA3	SLC30A3	TMEM132D	C8orf73	DIXDC1	MIR184	
PLEKHO2	NRXN2	MAGI1	KCNT1	NTM	LAMC3	
PPFIA4	CABC1	TTC36	SMOC2	RBBP6	TCL1A	
GPR21	HYAL2	ATP2B4	ADAMTS16	SV2C	PAK7	
PDX1	HCK	GMIP	GFPT2	GDAP1	SHISA2	
CUL1	RNU5E	NETO1	P4HA1	VPS37B	ZNF323	
C1orf83	PTGDR	FMN1	FAM83F	CRHR2	SYCN	
PITPNM1	PXK	CORO1C	MMP23A	APC2	PSTPIP2	
TRAPPC9	KCNH7	LPCAT1	DUOXA1	GPR139	CLCF1	
XPO4	RIBC2	SOX11	PP14571	GFOD1	SCD5	
PCDHB16	ATXN7L1	DLC1	CHST2	SH3BP5	JSRP1	
LMX1B	DPYS	GDF3	MKRN1	CNR2	SLC13A3	
LOC134466	GPR25	PRKCG	CNTN6	MINPP1	LOC646405	
PCDHGA2	RARA	ITGA4	FEZF1	PAQR9	SNCB	
NAALADL1	PID1	PTH1R	SALL3	ZNF578	RBM38	
CPN1	ALOX5	LOC148824	LRAT	ILDR2	MADCAM1	
EEF1A2	ZNF648	ULBP1	CTNNA3	TET1	AKAP7	
SST	OVOL1	DBX1	MPPED1	ALK	MIR196A2	
C6orf201	CYP26A1	CHRD12	HECW1	NUB1	TBCEL	
ALX1	TXNIP	CTDSP2	PIK3R1	AGTR1	DTX1	
PTF1A	SFRP5	ARHGEF3	FLT1	IRF4	ELAVL3	
NKAPL	RASGRP3	PCGF3	KSR1	APBA1	BAT4	
CACNA1I	IRX1	ABCA4	SLC11A2	MATK	PAK1	
OTX2OS1	PKMYT1	ABCC8	RAPGEF5	RGMA	CECR6	
SBNO2	PCDHB18	CRCT1	SFRP1	IL17REL	C14orf159	
MBNL2	S1PR1	LOC100132215	ASPG	ZNF397OS	LSAMP	
RBM20	BOP1	TSSC1	HOXC13	FGF10	KIFC2	
EBPL	POU4F1	KIAA0564	PNMA2	LOC389458	LOC100130274	
CBLN1	OPLAH	TLX2	PIWIL1	ZNF677	IRF8	
PEX5L	LOC644145	LEPR	UNC5D	NFIX	CYP26B1	
NKX2-5	NYNRIN	MFAP4	C20orf26	KIAA0922	PPM1H	
SCN1B	DRD2	NRXN1	C10orf93	FAM19A3	CTNNAL1	
SIX2	FRZB	DLK1	BCAT1	UNC80	IFI44L	
CCDC105	PGLYRP1	CRMP1	SPHKAP	SLC6A1	DCBLD1	
PRLHR	LOC145474	GJA3	SERPING1	IGF1	IFIT1	
CSDAP1	EGFLAM	PAX5	DSTYK	COX6B2	ZNF473	
SLC45A4	GAL3ST3	GPR123	HOXC9	C5orf38	SLC5A7	
EPB41	TRH	MATN4	ECE2	ASB2	MAP4K1	

Appendix C6: continued

PCDHB19P	CDK17	PFN3	HOXB8	RASGRF2	PTGIS	
TCF21	GDF6	AOX1	GFI1	HHIP	KIRREL3	
C1QL4	GSTM5	TNK1	KIAA1239	JAKMIP2	SYT5	
CACNG8	AOC2	TRIM58	HRK	GLDC	ACAN	
FOXB1	VSX1	GRID2IP	RELN	PHLDB2	SOX8	
NKX2-6	TRIM59	GREM1	LOC146336	LRRRC8C	GPR137B	
KRCC1	MEOX2	GRIK1	NGB	GP5	LOC157627	
PHACTR1	TSPAN4	PAPOLB	MED24	TRIM71	OR2L13	
CNRIP1	C1QTNF4	SOX10	HSPG2	PPM1L	KY	
TWIST1	TIGD3	MT3	FLJ45983	CRHR1	FOXI3	
PHOX2B	HS3ST2	GFRA2	EGR2	SCN5A	IL21R	
CD248	C18orf1	VWA5B1	CA10	FAM198B	NID1	
ZDHHC14	HOXA3	SFMBT2	HSPA12A	PALM	TNFRSF11B	
KLF7	NMBR	HS3ST1	FOXR1	PLEKHG7	GAB1	
FOXEO3	CYYR1	HOXC10	PHF21B	FAM59B	ADAMTSL3	
ANKRD35	C5orf56	TMPRSS12	HIST1H1A	ARID4B	PCDHA12	
CHAT	SALL1	FAM124B	QRFPR	FGF19	SLC6A3	
LOC645323	C13orf26	TNFAIP8L3	HSH2D	PHF2	ATP1B2	
SLC17A6	KCNH2	DSC3	XPO7	UMOD	C1orf61	
SLC6A5	GNG4	ARHGEF10	NPY2R	ASB18	SARM1	
C3orf21	C8orf56	DIO3	CHRD	JAM3	KLF14	
ADRA2A	DACH1	ANKRD50	PREX1	SRRM3	GABRB2	
NEFM	KCNQ4	PAX1	PCMT1	MMEL1	VWCE	
CRY2	C6orf174	NR5A2	AMIGO3	MAST1	RASL10B	
SLC25A2	ZNF132	CSF3R	CASR	SLC18A2	SCN8A	
DOCK5	LOC650226	SEZ6L2	PRX	NEFL	CIT	
HOXA11AS	TCHH	LRRN2	ACTL9	TMEM59L	CCDC65	
T	SORCS1	AKR7L	STAC2	KCNA7	RFX2	
FLJ40504	SLC38A10	MTMR7	RASL11B	PITPNA	PPP1R14A	
DRD4	ZC3H3	LOC145814	CYB5R3	CELSR3	TMEM132E	
ZNF709	ESAM	SLC44A5	CHST8	BST1	HOXD1	
AMDHD1	GLT1D1	MTSS1	CIDEA	STK40	NBEAL2	
KCNC2	RXFP3	ABR	PIP4K2A	SLC6A15	SLC27A6	
FAM114A1	WDR8	EFNA2	ALOX15	OTOP3	PARM1	
MKX	TBKBPI	CCDC8	SUFU	C11orf87	SH2B2	
NHSL1	TMEM196	ITPKB	KCNK17	ANK2	GLIPR1L1	
LEPREL1	PBX2	FAM171A1	SPARC	PTPRD	KIAA1024	
HDAC4	MIR30B	OSBPL6	KCNN4	ARL10	CPLX1	
NR2F1	ACTA1	TBX3	FBXO39	HFM1	TEPP	
CALCRL	SLC10A4	NPR3	SLC8A1	GPR150	ROR1	
DMRTA2	LHFPL4	TRPM8	CHGA	PPP2R5A	LOC389493	

Appendix C6: continued

TACC2	ZNF710	ADCY8	YPEL4	PRR15	GBE1	
GJA5	ASAP1	ADRB3	TWIST2	ADAM12	DSE	
CLDN11	HLA-G	HTR1B	C10orf53	DSCAML1	LIPA	
CD8A	R3HDM2	KDM2B	ELANE	TTYH3	EMILIN2	
CNTNAP1	IL13	FLJ43390	SALL4	NR5A1	CLDN22	
TBX5	WT1	HOXB4	FKBP5	RIMS4	RING1	
CD34	CCDC81	LRCH1	C20orf56	SLCO5A1	C20orf103	
ADAM19	CHRNA1	NPHS1	GLIPR2	CA12	GATA5	
TSPAN10	LPAR5	DMRT1	TRIM61	C16orf11	C13orf36	
C15orf41	UNCX	SPOCK1	THBS4	OXR1	IQSEC3	
DENND3	ARHGAP22	C5orf4	SVOP1	SCGN	XRCC3	
SIX6	FOXD2	HMX3	AHRR	DTNA	GDA	
TFAP2B	DDAH2	VSX2	NXPH2	GPR44	SALL2	
HIPK2	HOXD8	CLDN14	AFF1	LOC283392	COL1A2	
OTP	ZFYVE28	FBXO34	NOX3	GRIK3	ZNF835	
CDO1	MEF2D	KCTD1	RGS10	KIAA1614	PKDCC	
MBP	SFRP2	TF	OLIG2	FER1L5	SYT11	
LBX1	MYH9	FOXF2	RSPO4	NKD1	HKR1	
GUCA1A	CDKN1A	NTN1	C15orf27	LIN7A	BHLHE22	
EN2	NECAB2	VWC2	ABAT	FERMT2	MKLN1	
OSR2	IRX2	MIR196A1	SCN4B	C3orf72	C1orf173	
FAM19A2	LOC401097	LOC389333	CDK2AP1	AGRN	VGFB	
KIF21B	HEATR2	HRH2	DDIT3	TNFRSF8	SEMA6A	
RPTOR	CWH43	PPH1N1	PRRT4	ANGPTL2	USP24	
OSR1	FLJ90757	EBF1	PLCXD3	B3GAT1	HIST1H3G	
VSTM2B	FLJ22536	SLIT2	ARVCF	CDC14A	FLNB	
RGS12	LOC150197	ANKRD13B	MACC1	PACS2	ZNF662	
ADAMTS10	C1orf14	ADRA2C	RAPGEF3	NFAM1	XKR7	
PAX6	PLEKHA6	RHOJ	POLR1A	SCARB2	C3orf26	
CDX2	NINJ1	BHLHA9	RPL22	LOC100190940	GPSM3	
CNPY1	CDK5R2	FLT4	AQP1	D4S234E	SPTBN4	
ADRA1A	NEK6	CXCL5	SPOP	NAT8L	TLE3	
FBN2	GRIN2A	C10orf82	ADPRH	PROK2	FOXD1	
OTX2	CECR2	GATA6	TACR3	USP12	ELMO2	
PSKH2	NKX3-2	LIN28B	CLEC2L	FOXA2	LOC283731	
CHST13	PDE4DIP	KCNK2	PPAPDC1A	WFIKKN2	IFFO2	
EPAS1	CCDC69	OPRK1	FLJ42875	NCAN	TRAK2	
TBC1D1	RSPO2	LOC730755	MAN1C1	DSCAM	C6orf145	
SNTG1	OPRM1	FAM181B	YWHAG	CBLN2	C9orf171	
ARHGEF2	PCDHB13	C10orf26	ANTXR2	GRIA1	CUX2	
EMX1	TMPRSS6	TRIM15	HFE2	MGC70857	CREBBP	

Appendix C6: continued

GAD2	KANK2	COL5A3	BHLHE23	MSX2P1	CCDC106	
PER2	NRN1	CTNNA2	GPR116	CHRNA1	ATRN1	
ESRRG	ZC3H12D	SORBS1	NAALAD2	PRDM1	TPM4	
PRDM13	GABRA4	NT5DC1	RAB11FIP4	TGFB11I	ENSA	
PUS3	C9orf129	TUBA8	LYST	CACNB2	HYAL1	
VAX2	FOXB2	CACNA2D3	KIRREL2	PIP5K1C	CLDN6	
GCNT2	GLB1L3	SVIL	GALR2	BTG2	PCDHB14	
POU4F2	ZBTB7B	ZNF541	CHRM2	AGAP1	CRH	
LIMCH1	GRM6	SPON1	KREMEN2	KLF16	SCNN1B	
SMG6	NDRG2	DAB2	ZSCAN1	SNAR-F	TMEM171	
C20orf27	FPR2	SPRED3	CLEC1A	ST8SIA2	C2orf80	
ZNF837	FAM163A	ACSL6	FAM166B	KCNK3	CREB5	
C14orf23	EXOSC7	KIAA0146	ACCN4	ARHGEF15	ANKRD45	
TMEM132C	PENK	SGCZ	CRTAC1	DST	EPC2	
FBXL21	STAG3	NTSR1	WNT2	SEZ6	ANKRD33B	
GHSR	SLC4A11	FYN	CLCC1	CFTR	CCDC37	
HOTAIR	TRIM72	DCC	HLA-DPB2	CLINT1	ADAMTS8	
SULT1C4	SLC25A25	SOX14	FLI1	FGF4	RFXP4	
GCK	ANKFY1	TNNC2	C1orf162	MTNR1B	MFAP3L	
MCM6	ZNF454	ITPR1	TSC22D4	KCNQ1DN	INPP5A	
SSBP3	DIDO1	C1orf200	PREX2	JAK1	ARNT	
PCDHB4	PDLIM2	MMD2	NMS	SLIT3	ATCAY	
PRKAR1B	RAB37	GALNT9	ADCY2	IL1R1	HOXA13	
SYCE1	GJD2	MAML2	FAM129C	KRT222	C2orf89	
GATA2	PRR14	ANKRD34C	TRIM9	KRBA1	CPAMD8	
MYF6	LHX4	SSTR1	GABRB3	CCDC48	SAMD14	
GRM7	TCTEX1D1	UTF1	FGR	CYTH2	SNORD123	
TTC22	C2orf40	AGAP3	CSPG5	ABLM2	C14orf138	
FZD4	MAPK8IP2	HOXB9	IGDCC3	RGS22	EPN2	
PCSK1	FGFR2	WNT16	NES	ANK1	LRP4	
SLC12A7	STMN2	CACNG7	MCAM	SH3YL1	BMP6	
NR2E1	ETS1	RNF122	SLC35F3	SCRT1	BICC1	
LIMD2	CCR7	PSD3	FOXL1	ZNF385A	SETD3	
FOXE1	ABCC1	HIST1H2BK	N4BP2L1	NTF3	MGA	
KIAA0247	IKZF1	FLJ41350	PSMA8	C2orf72	TDRD5	
HPSE2	KCNH3	EXT1	ALDH5A1	EFR3B	NT5C1A	
THRA	FOXC2	RBM24	ATG7	PWWP2B	KLF13	
FSTL4	ZNF598	EMILIN3	INS-IGF2	TRIM67	NEDD9	
ID3	MED13L	FAM54B	NFYC	SEPW1	MLLT11	
ZDHHC24	RAP1GAP	NBEA	SMAD6	TLX1NB	TMTC1	
ZNF438	PTCHD2	ZNF492	NCRNA00092	USP10	SYNPO2L	

Appendix C6: continued

LBX2	CCND3	BOLA3	PRMT8	CYP2A7	C22orf46	
FRMD4A	ARID1B	HBQ1	THSD1	KIAA1324	FAM110B	
ZNF718	SEC31B	MIR125B1	MOXD1	NPR2	BAI1	
RUNX3	GRIA4	IPCEF1	LPAR6	GAS7	RPGRIP1	
MGC14436	C19orf57	CD200	MYO3A	CLU	FGL2	
SPATA18	SUV420H1	FAM78B	BCL6B	PTPRZ1	PROCA1	
ONECUT1	SIM2	LINGO3	ST7	C21orf29	WWP2	
DBX2	LOC100129354	HOXA11	NRCAM	FAM26F	RUSC2	
OLIG3	ZBTB4	CDH13	PITPNC1	PCDH20	C7	
TRAF3IP2	MGC45800	CRHBP	HTR7	CD59	DIP2A	
LOC254559	CPEB1	PCDH10	BMP4	C1orf53	NXPH4	
KIAA1804	SLITRK3	ZAP70	STARD13	PHYHIP	MTMR3	
SPOCK3	TPM1	LHFPL3	LRFN5	LOC100287216	MT1G	
GPHN	HSPA2	PMEP A1	TERT	SLC38A11	WIF1	
ERC1	SNTG2	MRPL44	LASS3	STXBP5L	XKR6	
AKAP2	TAC1	KLHL5	RTP1	LPPR5	HMGCS1	
RBPM5	C1QTNF3	MPP5	FAM168A	SYNM	NCAM1	
KCNS1	DUOX2	MUC12	ALDH1L2	BAALC	CCBE1	
ANKRD43	FAM83A	FAM19A1	ACTN2	LTC4S	LYPD3	
ACVR1	PRCD	MCF2L2	GABRD	RUNDC3A	ENPP2	
ANKRD30B	BNC1	COL9A1	HTR6	FAM194B	MICAL3	
MAN1A1	ARHGEF17	KIF19	MIR548H4	HLF	FAM193B	
ACCN1	B3GNT9	MCHR2	RABGGTA	TRNT1	FOXP1	
DLEU7	FAIM2	CRYAB	ENG	RYR2	HS3ST3A1	
PTPRB	NHLRC1	FAM196A	PKNOX2	CACNA1E	COL5A1	
ZNF177	C12orf68	PIK3CG	MYO16	CPNE5	FAM5C	
SLC22A18	EBF2	MTUS1	STIM2	LMO7	RFTN1	
NKX2-8	SLFN12L	SLC6A11	ADCY4	HTR4	CYMP	
FBLL1	PRPF40B	GNA11	PCDHGB4	TANC2	IZUMO1	
NKX6-2	DNMT3A	HSPB6	HOXB2	PROX2	ADAM23	
EMCN	CDH2	PTPRN	NKX2-2	APBB1	SNED1	
STX11	LY6H	SSTR4	ZNF382	CTDSP1	GSG1L	

Appendix C7: Hypomethylated genes in lung adenocarcinoma (LUAD)

GENE	GENE	GENE	GENE	GENE	GENE	GENE
COASY	NUDT13	KIAA1026	OR8B8	FCN1	TMEM45A	MRPL15
MIR1204	ADAMTS14	SMURF1	ST14	HN1	FAM49A	SCGB1D1
P2RY13	FAM131B	EBF3	ACAP2	GFAP	SETBP1	RARRES1
MUC1	FBXL18	PRKCH	TTLL8	OR51E2	SLC6A3	LPGAT1
ITGA8	OCA2	SLC8A1	RBM12B	FAM155A	TRIM40	ITGB6
SNN	KCNN1	NLRP3	VOPP1	SEPX1	KATNB1	PREX2
TSPAN18	EHMT2	CCDC102B	ZCCHC14	NPPB	MIR592	WISP2
ATIC	LAMC2	DGKA	GLYCAM1	IL22RA2	TIGIT	ZNHIT6
MGAT5B	FOSL1	RAET1K	GSDMB	BCKDHB	PLXDC2	TNNI1
PHC3	SERPING1	KERA	SPRR2C	TRPV3	COL5A1	SPRR2G
44531	GKN1	SFRS8	FCRL6	FUCA1	C17orf102	RGS5
BCAR3	PLEKHA6	ADAP1	C7orf47	ITK	SLC2A13	FAM83H
TNN	SLC35F1	SNHG4	PIGT	TPRG1	MKLN1	DNM3
CAMK1G	ARFRP1	LOC84740	TMEM177	MFI2	PCYT2	A1CF
CDKAL1	RAB40C	SDK1	TIPIN	SLC33A1	LHFP	MGC23284
GFRA2	FPR1	EP400	SLC27A4	FIBCD1	NPR3	CRY2
PKM2	ZNF589	OR51B6	GNASAS	KLK2	KRTAP4-1	AGPAT3
DOCK4	SIK3	FAM180A	MEPE	RUVBL1	NHLRC1	RIMS1
FAM78B	TNFAIP8L2	REG3A	TNFRSF25	ITPK1	SMYD3	ABCA9
RRS1	MIR487A	LOC728276	ARMC2	TSPAN9	HK3	FAM71D
ANO2	AUTS2	SLC38A10	MMP13	LCE1B	HTRA1	CHRNA7
CAPSL	MAL2	FLJ46361	C1orf38	OXSRI	ADAMTS17	RBM22
NTM	LRRN2	PCYT1A	C14orf4	KIF26A	TRIM10	EBF1
APBB2	ANK1	SLC9A9	OR2T6	SYT11	FAM196B	NCOA1
SHROOM3	BPHL	GNA13	GTF2H3	ART1	SOX15	OR8K5
C20orf160	CHDH	MUC13	C1orf150	OR6N2	GPR81	PPFIA4
SH3BP4	TMTC1	SORCS3	FAM172A	ADCY8	MSGN1	C10orf82
REG1B	COL21A1	RGS10	PKD1L1	PUSL1	OR5L2	SH3RF1
SLC7A14	AMPD3	CGN	KY	FAM119B	CFB	OR5P2
MIR657	ADAM12	PCGF1	MIR1197	ABCD3	HNRNPU	TSPAN8
TMEM156	DCD	SH2D4A	HNF4A	XDH	C3orf77	PLCL2
OAS1	KRTAP6-2	DIP2C	KRTAP19-5	TMEM200A	TOX2	EXOC3
OR10S1	LNX1	TTC39B	CHMP4C	FAM83B	CD300C	WHSC1
KRTAP7-1	KRTAP24-1	SORBS1	C1QTNF7	POSTN	PROM2	C6orf170
ZNF385A	CCDC43	GTF2E2	TCHHL1	KCTD21	KEL	OS9
SAR1A	SCN10A	CHTF18	RPL3	KRTAP21-2	IQUB	ZNF404
OPCML	ALX4	MRPL38	TEKT5	ETS1	ZNF804B	LAMC3
CLTC	ASCC1	CACNA2D1	TRAF1	LMTK3	ERG	MZF1
GSR	MRPS36	OR14I1	DDK3	OR9K2	CNIH3	MDGA2
FO XK1	TSLP	KIAA0922	ESYT2	LHCGR	HLA-DQB2	ADAMTS7

Appendix C7: continued

CNTNAP5	SFN	C4orf26	APPL2	SDK2	HIVEP2	CYLC2
CD80	LPP	TMEM169	BMPER	TARBP1	RIOK3	FMO6P
SH3RF3	RAB11FIP1	MMP2	TGFBR3	C1orf210	GALNT6	PGK2
ABCC3	NRXN3	ZFP41	MET	SHANK1	OR51B4	LOC285830
VHL	ENPP6	XPO6	XYLT1	GPC6	GTF3C1	ABCC11
CASP9	KCNQ2	PPTC7	SNX18	SEC16B	LCE4A	GMD5
HDAC4	TRIP4	RNASE7	SF3B3	CD300LG	PDE10A	FLT1
TSTD1	ABTB2	NEK11	TULP1	SIRPG	TMCC2	HIBADH
LUC7L3	DLEU2	FGF18	FCRL3	SNRK	SPTA1	CCNYL1
RELN	GTF2I	MYH11	ZNF80	SLC45A4	PLEKHM3	WIPF3
AEBP1	DNAJC5B	MEST	KHDRBS2	PYGB	PPAPDC1A	RP1
ITGA2	ADCY3	NFE2L3	MOGAT2	WISP1	CXCL2	PPAP2C
SLC34A3	WSCD2	TULP4	TRIM6- TRIM34	OSMR	KCMF1	CTNND2
PBX1	ZNF469	ZNF536	FCN2	SFXN5	TPPP2	AMFR
SNHG3-RCC1	BTBD17	OR1J4	MIR411	LOC10013087 2-SPON2	GPR158	UBE2O
LDB2	RGS6	OR8G1	KCNK18	CPEB3	PTCD2	TDO2
NR2F2	TNNT2	C14orf37	SYN3	LOC285768	BRSK2	FAM129A
TNS4	FBXO5	WDR86	SDCCAG8	FAM190B	PZP	ODZ4
PLEKHG6	DAK	MYL5	C1orf106	C2orf78	PLEKHG4B	MLPH
SHISA9	SPRED2	OR6B2	ESPN	TXNDC3	C7orf53	DERL1
TNFRSF10A	C20orf196	CCL13	PMVK	TBX6	OR51M1	KRTAP10-8
RIMBP2	CCND1	BUB1B	APLNR	SGCD	TCHH	B3GALT5
PARP4	SLC39A11	LRFN2	VAR5	OGDHL	EPHB4	TNRC6A
GRAMD4	DEFB121	MIR921	ABCC12	GPLD1	SORCS1	KRT15
DPP6	RER1	COL9A3	PTGER3	PDE4D	TERT	DNER
GPR56	DNTT	XKR4	C7orf16	NALCN	SLC16A3	OR52A1
C1orf95	TMEM184A	HCRTR1	XIRP2	KCNA4	DCLK2	CASZ1
CALN1	KCND3	AFG3L1	MS4A4A	RIMS3	RGS17	C5orf39
C10orf110	SFT2D3	OR4D11	AFMID	PLEKHA7	ST6GAL2	PTCHD2
ELF1	TMOD3	HTR1E	LY6D	CBX2	OR6K3	TEX264
TRIM29	CPNE1	MASP1	MIR377	SLC38A8	IL1B	CNR2
S100A10	KCNQ1	SLC12A1	NOD2	OR51B5	CCL8	ISX
C7orf34	GP2	C10orf90	AGTPBP1	CRP	RGS7	KNDC1
FHIT	CLN6	HHLA2	BAI1	RNASE11	YOD1	C7
PMEPA1	KIAA1143	JPH3	SNORD114-31	SNORA63	PXMP3	COPS8
TTC15	IRF2	CLDN1	TTLL1	OR56A1	TLN1	NDUFA4
SHCBP1	DAPP1	MED1	RFFL	GAP43	PPM1L	ZNRD1
TCN1	LOXHD1	DDR1	OVCH1	GATA4	APOBEC3A	BTBD9
PRRX2	TMCC1	LSP1	SVIL	OR56A3	EPS8	CACNB2

Appendix C7: continued

MIR21	OR10W1	THSD7B	LIG3	ITLN2	ELAVL4	AQP11
CLCC1	HRNBP3	TCF7L2	WDR25	IQCK	OR8D1	USP24
KRT80	FILIP1	PILRB	SCN8A	LOC388965	VTI1A	CCR2
EZR	PRLR	SERTAD2	CPLX4	IFLTD1	LRP12	VIPR2
TPCN2	TRPM2	KIAA0513	DUSP13	PDGFRA	ADD2	ATP2A2
KIAA1609	SIRT6	SQSTM1	LELP1	MIR190B	C6orf176	SLC26A9
MOXD2	EFHD2	SPRR2D	GMCL1L	LOC100128542	MYO1D	WWOX
RAPGEF1	TBXAS1	KLHL29	LPPR4	CD1C	SAP30BP	MUC6
NKD2	CNTNAP2	KIR3DX1	EFCAB2	PRSS27	ALG1L	LRP5
YWHAZ	AOX2P	FGGY	SORBS2	PRIMA1	ZNF532	MYH8
SNORD93	OPN3	S100A8	NUAK1	RGS12	BAG3	SNORD113-5
C16orf78	GMPR	C16orf73	MFSD4	OR2AT4	CYP11B1	PAK6
COL18A1	PTPRH	TCL1B	NLRP4	HSF2BP	PDE11A	C15orf38
TBC1D16	HDAC5	TWF2	RBP3	ZNF783	ARHGAP26	FRS2
TNR	FAIM3	CCL14-CCL15	CDH22	BLCAP	IGFL3	LTBP3
DPYD	TMEM19	OR8A1	FCRL2	C7orf10	FAM18A	DNAH2
UNC5D	NCRNA00114	MYH1	STK31	SYT4	OR52B2	MFHAS1
ZDHHC14	PIGW	COL29A1	HABP2	PGCP	HS6ST3	SLC1A3
POMT2	LRRC8D	GRID1	NLRP7	EMP3	PPP2R2B	AGPAT4
TRAF7	IL16	C4BPB	TEX14	LOC202781	SLC4A1	LOC100216001
ZNF217	TRAF2	HIVEP3	PFN1	BRPF1	IL18	ESRRG
CST9	FNDC5	OPTC	ENGASE	ST6GALNAC3	TBC1D22B	C8orf34
FGF6	MIR19A	CHD2	LOC134466	PIP5K1A	ESPNL	SNORD47
SEMA5B	PALLD	UNC5A	OR2Y1	TLR4	GOLSYN	RBCK1
NRP2	PPARGC1B	OR4K5	ACTR3	YIPF7	LYPLA2	PDE4B
KRT8	IL7R	SBSN	SLC35F3	EHD4	HDAC11	ZNF250
CASP8	GPR115	C1orf226	MIR122	DOCK2	DLG5	LRRFIP1
CBFA2T3	VAV2	TMEM80	RPL30	WISP3	OR5AS1	MEGF11
MPPED2	NOTCH4	OLIG1	DSP	TG	GHR	ATP5C1
NAV2	OR1F2P	ZNF831	GRXCR1	ACTN2	ACSM1	STEAP3
KRTAP11-1	TSHZ2	UBE2V2	IGSF21	PARD6B	NOS1AP	HAS1
TPRXL	WEE1	LOC643406	OR5P3	GALP	CHD1L	FAT3
CMKLR1	D4S234E	SH3GL3	CTBP2	OR51B2	TAS2R40	LMLN
C11orf60	COL11A2	BRE	ZFPM2	ZBTB20	CPNE7	CD58
SLC2A1	ITGB2	ADAMTS16	DBH	HLA-DOA	RAI1	TNIP3
CCL22	PPAN-P2RY11	ATXN1	RPL13AP5	KIAA0146	GAS5	C6orf27
MYEOV	SCTR	SPTLC3	OR2G6	GPR26	SERPINB11	SIRPD
ARL16	BATF	GSTP1	SYT12	PTHLH	DRD3	C1orf125
SCN4A	KCNN4	OR2M3	C1QB	OBSL1	STRADA	MIR1283-2
TRIM15	KIR2DL4	RALA	PARK7	GNG7	FKBP2	CENPJ

Appendix C7: continued

CUX1	DNAH9	RPS8	AOAH	OR10C1	SNORD70	ADCY10
FHL2	FAM13A	VANGL1	STK39	C21orf34	ZNF517	NPAS2
GLIS1	MAML3	KRTAP15-1	MICALL2	C20orf85	IRF8	ZSCAN12
TAGLN3	KRTAP13-2	NPY1R	TRYX3	MYH7	FAM111A	OR2T4
CSMD1	LOC100128191	COL6A6	FMN2	TRIM41	NPVF	CSNK1G3
SPSB1	CASQ1	ANXA4	MIR299	PLCH2	MGAM	CLEC4E
MIRLET7C	SRCRB4D	CLSTN1	ENDOD1	THBS4	OSBPL3	LSAMP
FAT1	DPF3	LMTK2	ENTPD6	PAG1	SP1	NLRP13
ANKRD46	ZNRF2	DEFB118	TBX19	PRDX1	DLGAP2	MEG8
TMEM132C	MRGPRD	UNC93A	TNIP2	MEF2D	CLTB	TYR
PIP4K2A	LOC339568	RAMP1	CD1E	LCP2	UBE2QL1	TRIM42
LTBP1	UNC5B	RBM15B	FAR2	NFKBIB	TRAF3IP3	LCE1D
RICS	FARP1	RNU5E	MAN1C1	ANKRD33B	TMEM33	GRM3
ENO1	DSCAM	SERINC5	CPLX2	MMP1	TBC1D22A	FNDC1
CDH13	OR10A3	NOLC1	OSGIN2	CAPG	SLAIN2	AP1S1
HDAC9	LFNG	IL1F9	NMNAT3	CCL18	OR10K2	C16orf11
LRIG3	JUP	RGS20	SRPK2	DGKI	LILRA2	ABL2
USP2	HSPA14	SPOCK1	GJB3	LRRC55	CACNA2D3	FAAH
ABLIM1	CEP55	LOC730811	PHACTR1	KALRN	OR4D2	NEIL3
DUT	RAG1AP1	UNC93B1	SEPHS2	LMO7	SH3PXD2B	MIR549
FAM83A	FMNL2	ABI1	MIR487B	SPATS2L	PLD1	C19orf41
TLL2	KRTAP19-8	C16orf72	WDR35	ASTN1	ELMOD1	NECAB1
DLGAP1	ASPSCR1	TM4SF4	NLRP11	ST6GALNAC5	OR5T1	CEBPG
SMCHD1	MPPED1	HCK	DHX9	VGLL3	MAMDC2	COQ3
HCG27	SOBP	NKPD1	SDC4P	XBPI	PRKD1	NHEJ1
ARPM1	FAM105B	CD207	LHFPL3	TMEM44	LCE1F	ARHGAP10
GRIN2A	MS4A15	C21orf29	GRIK4	SHISA6	MRPS25	CRIM1
RPS15	ZNF662	KPRP	MIR206	C14orf49	44256	LPIN1
CHRNA9	FSCN2	IL12RB2	TLK1	MIR1185-2	COL28A1	ZFP2
TMC8	SLCO3A1	RTN1	WDFY3	IGFBP5	GIMAP4	DSC1
MFRP	GRM8	MYOCD	KPNA7	D2HGDH	KIAA1549	MERTK
MAGI2	CDH4	APRT	NMI	RABGAP1L	CLP1	LAMA4
FAM178B	SEMG1	TMEM51	CRYBB1	RPL23A	PON3	CHRNA1
IRS1	ADAP2	RRM2	CLIP2	MS4A2	ENAH	FGF23
SOLH	AGAP1	FAM19A4	ZNF511	NAPEPLD	AP3B2	OR6B3
PTK2B	SLAMF7	GRIN2B	CHST6	ELFN1	MBOAT2	LCE2D
C17orf48	PVT1	VPS37C	FNDC7	SPATA16	ZSCAN1	HIF1A
AGPAT9	LOC644649	SLC22A6	P2RY6	KRT2	VANGL2	FBXL16
ANTXR1	OR5A1	FEZ1	RCAN2	IL17RD	MMD	TUBB1
LY96	CSDE1	PREX1	CADM3	THAP11	GPR113	MYH15

Appendix C7: continued

AIP	OR9Q1	SLC17A1	MIR298	SELE	IL22	CAPRIN2
G6PC	GPR39	LAMA3	ACOT7	TECTA	FLG2	LARP1B
C14orf182	LOC340094	DEFB134	NPAS4	EIF4EBP1	LOC646627	LRRC32
CCL26	CD68	ACVR1B	CCDC150	ZFAND2A	NNMT	PERP
KRT5	YAP1	PRMT3	BAIAP2L2	RASAL1	LOC349114	OR2T10
HCCA2	OR6T1	KCNIP4	OR10G9	OAT	FAM154A	ZBTB46
GHITM	CSMD2	IGF1R	LOC285205	UGT3A1	C17orf58	ATP2B4
CACNA1C	GPR4	CPZ	ARHGDI A	CTSB	ELMO1	BAT3
SAMD14	FRMD6	LOC285780	EPCAM	NPEPPS	LOC732275	NPFFR1
SMAD2	STON1- GTF2A1L	PANK4	FAM53A	REPS1	ACTL6B	CHORDC1
KRTAP21-1	DIRC3	NEUROD4	RABGGTB	SLC19A2	KRT1	KIAA0802
FGD6	GPM6A	FAM135B	LOC642006	SEC63	KRT6B	FAM24A
KIAA1217	PTPRN2	TRAF5	RP1L1	TM2D3	SLC20A1	LRRC24
MST1R	SUGT1L1	ARL13B	SHANK2	HLA-DOB	FBRSL1	SLC7A13
SLC41A3	DLG4	CRMP1	DCAF4L2	ACOX3	ST3GAL3	PPP2R2D
CHRM2	FAM20C	ATF7	ATP1B1	KCNN2	S100A12	C10orf107
PEX6	ITPR2	REG1A	HECW2	SEMA3A	MTHFD1	COIL
SCHIP1	TUFT1	HCFC1R1	CPAMD8	OR6X1	OR4D6	OR4A16
MYCBPAP	RASAL2	PLXDC1	SNORD114-23	ATP8A2	LAMP3	CREM
VAT1L	ESR1	ACBD5	FOXP1	UPP1	GPR155	SFRS1
CCDC6	ARNTL2	PYCR1	SLC6A12	PLEKHA5	NPM1	ASCL4
TRPM8	ADAMTSL1	MSR1	STAU2	PIGB	RPL13	GCHFR
MGAT5	LRRC3B	RFX4	SNORD115-10	SCN1A	UFSP1	ARID5B
CUEDC1	TNRC6B	ZFH X4	ISG20L2	HBBP1	CLCN1	PIK3R1
MYT1L	OR51L1	LCP1	CCDC109B	MMP16	TINAGL1	ANKS1B
MYLK	AFF3	C6orf118	OR51D1	KCNA1	OR10G4	C11orf41
ATG9B	C20orf103	SNRPA	PACRG	CLIC6	WBSCR17	GRB2
UAP1L1	CENPM	OR10X1	TNFRSF9	CMTM8	SH3BP5	HS3ST4
HNRNPF	RNF145	C5orf37	AMTN	C2orf28	C8orf84	BDNFOS
SPI1	MREG	PITPNM2	SH2D2A	ABHD6	MTPN	EXT1
FAM92A3	NAGPA	SEMA6D	SPEF2	UGT3A2	CDC42SE2	PPP1R3D
WDR90	FGF1	TBCD	OR5B2	FLJ43860	IL1R2	NUP62
NUP43	EPHA10	TM9SF4	ENTPD7	TCP11L1	PLCL1	RSRC2
OR2B11	SLC8A3	TMEM225	FRMPD2	LCE1C	ROR2	NOS1
CAMK1D	HSPA2	HPVC1	CHCHD6	USH2A	HHLA1	TP63
RPTOR	GLT25D2	LOC399959	CAPN2	MIR1179	TTLL2	BSN
CTNNA2	GON4L	COPS7A	GLYAT	RAB25	CRYL1	DEPDC7
TMEM49	ACCN1	KIFC3	FAM189A1	CELSR1	LOC10013098 7	SNORD113-4
RIT1	DUS1L	USP29	TRERF1	KIAA1274	CACNG3	ATAD5
HEPACAM	BBC3	GRIN1	GRIK5	MIR380	GEM	INADL

Appendix C7: continued

MAP2K6	BAIAP2	TRIM58	TRAF3	GRIA4	TMEM39A	CCDC84
HMG2A	GPR139	DUSP14	IL21	AZGP1	GNS	GRHL2
NDRG4	RASA3	GIMAP1	PIK3CB	TTC7A	C2orf62	GPR183
C17orf73	SERPINA10	NID2	DRD2	C6orf106	MIR1207	ARHGAP5
GK2	FAM38B	COL8A1	EPHA4	SLC7A11	PARK2	IKZF1
TXNDC11	HPYR1	KIAA1199	SNORD114-6	SNX10	LUZP2	CTTNBP2
SYT7	C1orf107	MYOM2	OSBP2	CHST4	SV2B	SST
NR5A2	SPRR3	ARPP-21	MMEL1	HECW1	KRT71	INPP5B
PARD3	IVL	OR6P1	CYP11B2	44266	TRIT1	IL4R
BTNL2	AGA	ARNT2	PPM1G	ANKRD24	ZC3HAV1L	LEPR
C20orf114	RPS6KA2	OC90	CD164L2	PTPN22	DZIP1L	CNBD1
EMB	PRKG1	CCDC57	CD1D	KIF16B	TXN	HMGB4
NRP1	CXCR1	PROX1	COL13A1	C2orf90	PBRM1	DRGX
KSR1	RAB17	PDE1A	WDR36	ABCA2	HBP1	KC6
CPA4	COBL	C11orf93	SLC12A9	TMEM163	E2F6	MXI1
IQCE	ADAMTS12	COX6C	TCL1A	OR10V1	EYA4	KIF26B
ADAMTS8	NDRG1	NRAP	TTLL6	ROBO1	OR6K2	COL16A1
APCS	OVOL1	CDH8	GAS7	DOCK1	ALDH3B2	RBL1
TAF1B	SUB1	GNA15	MACF1	HTR3A	RASGRP3	MIR155HG
SCOC	KRTAP13-3	NTF3	NOTO	DEFB126	C12orf74	UBE2Z
PAX4	AHR	HLA-DPB2	EPB41L2	IQSEC3	C1orf204	SNIP1
CYYR1	CACNA2D4	FAM131C	GALNTL2	GDPD4	KCNN3	SIRPB1
ANKRD10	LOC100134259	DUXA	JAZF1	NXN	NOL10	OGDH
C10orf93	CUX2	AGBL1	RBM20	RIN3	PRICKLE2	SRD5A1
CC2D2A	TBPL2	TRIM31	RANBP3L	ROD1	CP	GPR125
PIP	TNNT3	OR2G2	SLC34A1	SULT2B1	RNLS	PLCB2
SYTL1	AGXT2	NTRK3	KRTAP19-1	KIAA0406	RARB	LRCH1
CEACAM19	MYH4	SH2D4B	SLC16A1	C10orf128	C3orf26	CLDN8
BNC2	CX3CR1	PAK7	LOC150568	CMA1	C1orf92	CYHR1
EIF4E	IL21R	MAP3K9	HHIPL2	SNORD113-6	ETV6	USP36
RIN1	TPK1	MIR543	MSRB3	CPA3	CNKSR3	DNAJB6
HELB	PLCD1	MIR495	LOC90246	ABCC2	UBASH3B	CTNS
TBL1XR1	GEMIN5	LRIT1	BGLAP	ETV3L	ATP6V0D1	ZSCAN18
TMEM63A	C7orf58	OR2G3	NCOR2	TRPV2	ITPR1	OR6K6
PFKFB2	ITIH2	GHRH	CYFIP1	PATE2	CNPY1	ATP10A
MIR520C	PRKAG2	RAPGEF4	VTCN1	SPRR1A	UBFD1	TNFRSF1A
SERPINB5	PET112L	OLFML2B	TMEM40	PDILT	TRAPPC9	PRKAR1B
GPR111	DEFB135	CCDC40	LRP11	TRHR	C21orf2	LHX6
MTRR	FAM19A5	EMR4P	LOC148696	COL22A1	FAM13C	AP3S2

Appendix C7: continued

RCSD1	ENTPD8	MMP26	RNASE13	EMX1	NSMCE2	SLC6A19
HMCN1	GYPC	OR51F2	RALYL	C11orf94	MAEA	RPL22L1
C1orf101	FBXL22	MIR154	RNASE3	STK38L	YTHDC1	HMGB1
KCNT1	FOXN2	OR8D4	PEG3	CNST	BMP1	GRAP2
RGNEF	PLEKHG5	KCNK12	MITF	FRMD1	SLC5A10	RYR1
HPCAL4	CES8	PAPPA2	LOC283867	MOBK2C	NCOA2	RSPH3
SCN11A	KRT26	TBC1D14	PLEC1	SPATA19	FAM107B	C6
T-SP1	LCE3E	KCNA5	ARID1A	FAM38A	MYH6	AKR1D1
PRKCB	OVCH2	OR51G2	PRR21	APOLD1	DKFZp566F0947	C8orf44
PLXNA4	IMMP2L	VDAC3	RPS18	CD109	NF1	PLEKHH2
NRG3	SPTBN1	PLA2G4C	TMCO7	MIR670	MIR412	IGFBP7
SLA	DGUOK	UBXN11	ZBTB7C	INPP4B	RASGRP2	STL
TMIE	ALLC	MIR515-2	SLC22A18AS	AGR2	BEND7	EFCAB9
ADAM28	TTF2	TAF1D	CACNA1E	RNF149	CDYL	TMEM131
SLC12A7	IL23A	C4orf34	CALD1	FSCN1	SPEG	DLGAP3
TGFB1I1	CACNA1H	TSPAN5	PLD6	ADPRH	OR51S1	INTS3
FAM55B	HRH1	NCRNA00162	ANO1	LCE1A	FLJ33360	SNORD16
MOCS1	CSNK1G1	GABBR1	OLFM4	OR10T2	AMPH	ATF3
ASAM	PNOC	GPX6	FCRLB	PROCA1	PANX1	RPL6
GAS2L1	NRG2	MRGPRX4	GCNT2	GEFT	FLJ39653	BRCA1
HNRNPA1L2	RUNDC3A	ACP6	C16orf45	GPSM2	HLX	COL6A1
TTC39A	MYO3A	SNORD114-29	OR10A6	ANO4	HS3ST3A1	BCLAF1
UPF2	BTBD16	LOC440335	JARID2	TBC1D21	UNC84A	PGAM1
TMIGD1	PEAR1	ELK3	LGALS2	ZCCHC4	HNMT	SFMBT2
NRXN1	FOXI1	AADACL3	SAMD12	KIR3DL2	DBNDD1	ADAM10
ZFHX3	SORL1	DKFZp434L192	RPH3A	LMF1	LEUTX	VWC2L
C3orf59	FAM113B	C1orf105	WHAMM	GJB2	SNCA	EDEM1
ACTA2	PSORS1C1	LPO	PITX3	C4orf19	ZBTB11	CAPN8
ROBO4	SORBS3	ZNF648	OR11L1	GPC5	BANF2	TATDN1
GALNT9	ELF3	BAALC	ABR	LOC100130017	GABRA6	ITLN1
SFRS13A	HMGA1	CDH23	MOG	DENND5A	ATP1A2	KMO
CLIC3	GDF15	KIRREL3	KRTAP2-4	NAAA	LOC339524	FUBP1
PTP4A2	ZC3H12A	TNP1	KIR3DP1	DCC	PKP4	ADCY1
GAL3ST4	OR8B2	WDR81	LGR4	ZNF341	CST7	RFESD
SLC39A12	EMR3	SV2C	NCKAP5	MIR654	PDZRN3	METTL9
ZC3H12D	TRIO	KCNMB1	C18orf1	OR8J3	LOC100128977	GARNL3
IL1A	LY6G6E	NAA25	DUSP27	ZSWIM1	TSKU	C11orf40
PKP3	SMYD5	SYNJ2	HLA-L	RASGRF2	FXYD3	FAM82A1
GALNT7	MIR329-2	RPLP0P2	PIK3CD	MCTP1	SPINK5L3	MDC1

Appendix C7: continued

CACNA1B	CHRNA6	ZBTB25	THSD4	MNDA	TFPI	TRIP13
PKNOX2	LRRC4C	SNHG11	OR9A4	C19orf6	EFTUD1	FRAS1
C1QTNF1	PPP2CB	KRT6A	FAM160B1	OR51A7	MIR134	SERPINB13
LOC285194	CD44	HSD17B8	SELENBP1	CST5	ZC3HAV1	CCL16
ARHGEF3	IFFO2	KCNJ2	BPIL1	ATF7IP	PLA2G10	RPL24
TCERG1L	SMAD3	C5orf49	DRAM1	PTPRE	NAALADL2	LOC100124692
PANX3	CPNE5	RYR2	KCNA6	NPAS3	C20orf118	MIR376B
FBXL7	AFAP1L2	B3GNT3	C3orf67	KCNQ3	TRPV6	PI4KA
BBOX1	POLR3A	OR1A2	HOOK2	ACPP	NKAIN2	OR2AK2
OR8D2	C20orf199	SLC39A2	CD164	SLC22A8	UMOD	LAIR1
UBTD1	TAS2R38	SPATA8	TMPRSS4	ZYG11A	NCRNA00157	THNSL2
PHLDA2	DLC1	KCNK9	C20orf54	AICDA	OPRM1	PTDSS2
PYCARD	NPS	LOC645323	UBE4B	PHACTR3	R3HCC1	TTC33
B3GNTL1	RNF207	OR10J3	GLYATL2	TRNT1	PEX14	LOH12CR1
SECTM1	CDK14	OR9Q2	RAC1	ARHGAP9	HBE1	CAMKK2
TRIM14	DNMT3B	DST	SEMG2	ZCCHC8	PABPC4L	ICK
KCNJ6	VAMP5	CPO	EFCAB1	TINAG	EPHB6	RUNX1T1
EEF1A1	TCF25	SLC35F2	SLC26A8	HMOX2	OR2D2	HRNR
SPSB4	ZNF827	ITGB7	LOH12CR2	U58	RUFY1	AKT3
RASGEF1B	KCNJ1	ALOX5AP	AKNAD1	GRB10	NTNG1	SLC30A8
OBSCN	OR6N1	ORAI2	NPW	CTNNBIP1	PSMD14	OR2T11
TNFAIP8	NUDT1	LMX1A	FAM167A	CDK5RAP1	EGFLAM	WWC1
DEGS1	FCRLA	LEKR1	KIAA1409	SLC35F4	NELL1	ZNF7
C1orf94	LRIT2	CNTNAP4	TTLL11	XKR6	C6orf150	ILDR2
SLC25A38	C10orf81	HTATIP2	AJAP1	RNF121	OR5AU1	LOC257358
NLRP10	ADCYAP1R1	SYT8	IL5RA	C1orf229	HUS1	C1orf9
GPR87	ASAP2	LOC253724	DPYSL3	RASGRF1	SH2B2	EVC2
AATK	ICMT	ANK2	ADCY9	PATE3	DCBLD1	LRRIQ4
MAP1LC3B2	GRIA1	BUD31	SELPLG	C8orf22	KRT73	VWC2
GRK5	IFFO1	HS3ST2	LGALS8	GPRC5B	SP6	SIK1
SNAPC5	C22orf25	OR1C1	TBC1D9	HN1L	MICALCL	HTR1D
MCC	MYT1	OAZ1	SLC45A3	GUCY1A2	KDELRL3	RAP2B
PDZD2	CLUAP1	C2orf60	ELOVL5	MAD1L1	TPSG1	
TMBIM4	NMS	GPX5	ARMC7	KRTDAP	RWDD2B	
SLC12A5	MIR488	KLHDC8A	IGF2BP3	LOC285692	C9orf173	
CXCR5	LOC154822	PRKCE	METTL11B	OR2L8	C13orf28	
LY9	SGK3	GLI2	SH3RF2	DCK	TSPYL6	
INTS6	PSMG3	TDRG1	OR4F6	UNC13C	SNORD87	
GIPC3	LOC100132111	TSPAN10	RHOJ	MGC27382	UBAC2	

Appendix C7: continued

NQO1	VAV3	TTYH3	LOC285954	DYNC1I1	PPARGC1A	
EIF2AK1	AMN1	CPA5	MYO3B	RECQL5	AACS	
PSMB2	IRF7	SRD5A3	OR4C16	ENOSF1	OR5D16	
MIR496	PC	SCGB1D2	AP3S1	MIR548I4	WIPF1	
ECHDC2	C5orf32	BTF3L1	POM121L12	OR5L1	SNORA64	
NECAB2	OR6Q1	ACOXL	CLRN3	KIAA0748	KCNA7	
HMGCL	CLEC16A	COL4A1	TMOD1	FTO	CLDN12	
EBI3	DAAM1	STK24	MAFK	LAPTM5	TRPV5	
KRT7	OR2C3	MDS2	ADAMTS10	RAB37	LRTM2	
KRTAP8-1	ADARB2	C8orf85	MIR758	PTPN21	C11orf85	
HSD17B2	DOCK10	IL31RA	SLC36A2	CACNA1G	RNF11	
TNXB	CAMTA1	ZNHIT1	SNX29	ZMYND8	PFDN2	
VTRNA1-2	WDR64	GALNT2	CTHRC1	SLC35B3	KRTAP20-3	
MORN1	MIR770	TPO	ADAM9	TCEA1	HKDC1	
MIR548G	FBXL13	ZBTB32	LCE6A	LOC284009	DCP2	
GREB1	CNTN2	SNORD113-2	ANKH	SPTB	FRMD4B	
BSND	FBN2	TTPAL	TMEM90A	LOC145820	STEAP2	
TCL6	HACE1	TTC38	RAI14	PHRF1	PTGDR	
CALHM3	DAB1	CCDC19	DPP10	OR52L1	CUBN	
ARHGAP15	PLAT	OR8B4	ACTN1	PFDN5	EVI2A	
CHD5	WBP2NL	ADA	SNORD18A	RNF214	CADPS	
MYH16	PPM1H	MS4A3	PADI1	SLC25A41	IL17A	
FLOT1	PCDH21	ERICH1	BSG	SULF1	OR8K3	
GRHL3	ACSBG1	NFE2L2	CES7	LAMA5	NID1	
TERC	MIR526A2	OR51F1	NCOA7	OSBPL6	CXCL12	
C3orf32	PTPN14	CDH20	MGC42105	IGDCC4	RPS6KC1	
ADCY2	TRPM5	DACH1	ITPKB	HEATR7B2	OR8H1	
EXOC4	CLEC2B	FLT4	TAS1R3	KCTD19	PLXNA1	
IRF2BP1	C6orf48	UNKL	MFSD7	COL9A1	FLG	
CLEC7A	MAPK15	GFRA1	VSTM2A	ATF6B	FCRL4	
SLIT3	FASTK	DEFB119	CLDN17	CBLB	FAM110B	
CABLES1	KCNH1	A2BP1	FYB	FRMD4A	ATP13A5	
AMHR2	IER5	OR52A4	RBMXL2	HAVCR1	B3GALT4	
CARS	CSF1R	C1orf111	SNAP47	GRAMD3	EFNA5	
EIF2C2	FN1	CYP3A43	SYNPO2	HSD17B12	CHTA	
OR4D1	TIAM2	OR6M1	CSNK1A1L	SMOC2	STX1A	
CMIP	SLC5A4	BAIAP2L1	STXBP1	PPP2R3A	MCM3	
SLC2A9	MCF2L	SNHG12	ACYP2	NUP153	RARRES3	
RUNX1	OR5B12	DUSP4	FGD5	GDPD5	TMEM108	
MYO1E	SYN2	ASB13	ACCSL	LOC388796	PRR5- ARHGAP8	

Appendix C7: continued

AHSP	OR2W5	OR8B12	FAM55D	PSCA	N4BP1	
ODZ2	FAM173B	ZP4	MS4A13	ECE1	GIF	
LCE2A	EFNA4	MIR493	LOC728606	PDGFC	TCEB1	
SLC22A18	EGFR	ATXN7L1	MAPK13	ADAMTS3	CAMTA2	
APOBEC1	GABRG3	GABRB3	ZNF365	CHRM3	GPR162	
OR2A5	KIAA0182	NDUFAF3	C3orf25	PTCH2	PTPRG	
SEL1	SIPA1L1	CLPTM1L	C1orf14	FSTL4	MIR889	
CCR7	PTN	DNAJB13	KIF2B	CREB3L2	GORASP2	
44259	FBXO32	OR2W1	C1orf68	PRDM16	CD38	
C1orf128	EIF2AK4	KIF13A	SH3PXD2A	TECR	NEFM	
DSC2	INPP5A	LRRC7	ASB1	PDYN	C20orf79	
BZW2	TMEM132D	FLJ22536	SORCS2	RND3	TMEM48	
GAPDH	OR6Y1	HNRNPA3P1	VPS52	FSHR	JAM3	
BCAT1	ZNF423	TRABD	CRTAC1	PSMB11	MAP4	
S100A11	KCNIP1	C1RL	CHGA	MARK4	BPIL3	
BCL9	TIMP2	LCE3D	LOC400794	FAM171A1	ARL14	
GRIP1	C18orf20	PXDN	C8orf73	RHOV	MIR200B	
NAV1	ATRNL1	RPL39L	PURG	APOL5	BNC1	
TRAM1	LILRA4	HCRT	HTR5A	ANKDD1A	PMP22	
KCNMA1	DNAH14	GLI3	CIB3	PFKP	IGFL2	
CPVL	BEND5	RORA	RNF19A	CAPN11	AIG1	
STAT4	ANKRD22	OPN5	CA10	EDN3	TCF15	
CLSTN2	CRCP	MYO7B	OR10J5	ACTR1B	BMP10	
CDH11	CLNK	CREB5	KCP	INS-IGF2	ANK3	
SLURP1	TCAP	CDCP2	CCL11	HCG22	TSGA14	
CACNG5	ELL3	COL17A1	FURIN	MFAP5	C1orf158	
COX10	OCIAD2	NMUR2	KCNU1	KLF12	CD1B	
KRTAP20-1	SLC4A11	DLG2	GTF2IRD1	PARP12	NCRUPAR	
F11R	LOC150622	SLC26A4	OR4D5	AIM1	TM4SF19	
MX2	PRNP	TRIM4	GPR123	CYTH1	RPSAP52	
TRIM27	FAM19A2	NFASC	LOC285733	LVRN	STK19	
PFKFB3	CRTAM	OR10J1	SNCAIP	SPRR4	IGF2R	
CCDC162	TLN2	LYPD1	EAPP	LYN	SRGAP1	
KRTAP13-1	SLC6A18	AIM2	KCNH5	KIF25	SNORD24	
ZBED2	NEDD9	LY86	GYG1	CCDC46	TFF1	
LOC100130331	OR10Z1	CACNA1A	C1orf183	ANXA2	LOC730755	
EPN3	OR51E1	S100A7L2	CD84	PRAMEF12	PPP1R13L	
PRKCA	C2orf3	POTEA	THADA	PDE9A	SLC17A2	
LOC731789	COL4A2	EIF3G	TRPC7	NEK10	LOC100133612	
REG1P	PATE1	APOB	LPA	SCGB1D4	MIR1295	

Appendix C7: continued

44448	SUFU	GBAP1	RPS3	RGS4	ALDH3B1	
TMEM132B	SNTG2	BHLHE40	TMEM151A	TGM5	SEC23B	
FAM40A	C22orf43	TMPRSS13	SPATS2	LOC286094	SLC4A4	
VAC14	FLJ43663	TUBA1C	MAP4K4	MAP3K4	DMRT3	

Appendix C8: The hypomethylated-high expression and hypermethylated-low expression genes in TCGA database.

Hypomethylated-high expression genes	Hypermethylated-low expression genes
PYCR1, ZC3HAV1L, STK39, PPAP2C, HN1L, LGR4, KCNN4, SLC35F2, TMEM177, SLC2A1, UBF1, PC, ANKRD22, SLC39A11, PROM2, RASAL1, EFNA4, FBXO32, ST14, TMEM184A, BUB1B, EPCAM, LPGAT1, OCIAD2, TAF1D, B3GNT3, ENTPD7, CLDN12, PFKP, FHL2, KDELR3, KIF26B, CEP55, C1orf106, STX1A, ZNF217, FAM83A, TMPRSS4, SHCBP1, XDH, CTHRC1, GPR87, EPN3, FAT1, ALG1L, SYNJ2, CHD1L, SRD5A1, GALNT7, VARS, NQO1, GJB2, CHMP4C, RRM2, ABCC3, DSP, PLEKHA6, MYO1E, DLG5, ENAH, HMGA1, PTPRH, STEAP3, AP1S1, KRT80, HN1, BAIAP2L1, GRAMD3, SULF1, BZW2, PSMG3, DBNDD1, ATIC, PKP3, RHOV, SRD5A3, TBL1XR1, TNS4, P2RY6, HKDC1, ADAM28, GPR115, ARNTL2, COL5A1, GMD5, RPL39L, RAMP1, KCNQ3, TRIP13, COL17A1, TMEM156, GAPDH, ADAM12, AIM2, SLC12A7, SERPINB5, ADAMTS12, MYEOV, STEAP2, NFE2L3, MRPL15, EFNA5, EMB, MMP1, PPM1H, FAM83H, BCL9, CPNE7, PERP, FGD6, ADAM9, WISP1, FAM83B, ENO1, ITGA2, CP, POSTN, SYT7, CFB, MFI2, BAIAP2L2, KPNA7, GJB3, KRT6A, TSKU, SPOCK1, MMP13, RPL22L1, CENPM, MUC13, SYT12, KRT15, LYPD1, DUSP4, MET, SPTB, ALDH3B2, EIF4EBP1, HHIPL2, IL23A, PRRX2, GALNT6, FNDC1, HTR3A, SLC7A11, SORL1, PHLDA2, SLC16A3, LY6D, SLAMF7, TCN1, TRIM31, TFF1, IVL, AGR2, LAMC2, TMEM45A, SPRR2D, TSPAN8, CLDN1, TRIM29	ACVRL1, STX11, KANK3, AGER, PDLIM2, S1PR1, WNT3A, CD36, LIN7A, CRTAC1, SPOCK2, EDNRB, PRX, GRK5, EPAS1, TEK, ADAMTS8, NCKAP5, EMCN, CRYAB, RAMP3, ESAM, JAM2, TAL1, TMEM88, PHACTR1, SCUBE1, CLDN5, GLIPR2, DES, TIE1, NPR1, CLEC1A, ADPRH, NECAB1, GDF10, LDB2, KCNK3, CASKIN2, ARHGEF15, CLDN18, LHFP, CNTN6, ST8SIA6, DUOX1, FEZ1, NES, HYAL2, DUOXA1, GRASP, ITIH5, COX7A1, FGR, F10, SOX7, NOTCH4, STARD13, DENND3, ADRB1, MFAP4, FAM150B, CYR1, DACH1, DLC1, SOX17, GRIA1, C5orf38, PKNOX2, SCN4B, TCF21, RHOJ, SLC19A3, NHSL1, PTPRB, CALCRL, WIF1, TNS1, MAMDC2, SEMA6A, PTH1R, LHFPL3, MME, PPP1R14A, ABCG1, PID1, PEAR1, HSPB6, CLEC14A, BCL6B, FOXF1, LTBP4, NDRG2, LRRK2, HHIP, CD34, CDO1, TOX2, C1orf162, AGTR1, ALPL, SLIT2, TOM1L2, MSRB3, FRMD3, CPAMD8, TACC1, SASH1, SPARCL1, ABCA3, FLI1, LAMC3, GJA4, ADCY4, ENG, IRX2, ADAMTS13, GATA2, NDST1, NRN1, SYNM, AQP1, PRKCE, BAALC, RSPO4, DPYSL2, CCBE1, PDLIM1, KANK2, LIMCH1, LMO2, DKK2, JDP2, PRKCZ, SLIT3, FERMT2, PKDCC, SULT1C4, SLC9A3R2, NKD2, NDRG4, GATA6, HYAL1, SORBS1, NEDD9, CLDN11, SEPP1, CBX7, TBX4, CD302, CCDC69, CSF3R, SCD5, ALDH1A2, RBP4, LEPR, SH3BP5, MAPK4, CYB5R3, ALOX5, ITPRIP, ITGA8, KCNJ8, C1orf198, THSD1, SCNN1B, SMAD7, SOSTDC1, ARRB1, SMAD6, RNF122, PLEKHO2, NFAM1, TBX3, KLF13, APBB, FGF2, GSTM5, C2orf40, SSTR1, NFIX, MAP3K8, FPR2, HPCAL1, TUBB6, EFEMP1, TNXB, RXRG, PTGER4, SERPING1, MAL, ITGAL, RSPO2, AMOTL1, NR4A3, BTG2, LIFR, HLF, SPTBN1, F2RL3, RGS16, BMP6, FOXF2, ID3, TDRD10, SOD3, GJA5, RFX2, SEMA6D, C7, NPR3, FGFR2, FIBIN, CDKN1C, CA3, HIF3A, LMO7, PCDH17, FZD4, SLC25A25, ZBTB16, IRX1, DUSP1, SRGN, GPR116, FOXA2, VAMP5, HLA-DPB1, SFRP5, TMPRSS2, SCARA5, PDPN, HAS1, HOPX, EGR2, CFTR, NDUFA4L2, NTM, CLU, AKAP12, SLC26A9

Appendix C9: Summary of the results from the univariate Cox regression analysis in TCGA-LUAD patients

gene	KM.Pvalue	HR	HR.95L	HR.95H	pvalue
BUB1B	0.000625	1.308031	1.12368	1.522626	0.000531
SHCBP1	0.001585	1.443509	1.196051	1.742166	0.00013
RRM2	0.000271	1.339812	1.175718	1.526809	1.14E-05
TRIP13	0.005282	1.192771	1.039981	1.368009	0.011719
GAPDH	0.002148	1.59268	1.325413	1.913842	6.84E-07
ENO1	0.044467	1.406935	1.087539	1.820134	0.009357

Appendix C10: Summary of the results from the multivariate Cox regression analysis in TCGA-LUAD patients

ID	coef	HR	HR.95L	HR.95H	pvalue
RRM2	0.164974	1.179362	1.006266	1.382233	0.04164
GAPDH	0.338623	1.403014	1.124856	1.749957	0.002669

Appendix C11: Clinical information, score, and grouping information related to
TCGA-LUAD patients

ID	futime	fustat	age	gender	stage	T	M	N	RRM2	GAPDH	riskScore	Risk
TCGA-05-4244-01A	0	0	70	male	iv	T2	M1	N2	3.924315	9.964048	4.021465	High
TCGA-05-4249-01A	1523	0	67	male	i	T2	M0	N0	1.798772	8.406302	3.143318	Low
TCGA-05-4250-01A	121	1	79	female	iii	T3	M0	N1	4.885141	9.542872	4.037356	High
TCGA-05-4382-01A	607	0	68	male	i	T2	M0	N0	2.784996	9.684646	3.738895	High
TCGA-05-4384-01A	426	0	66	male	iii	T2	M0	N2	1.821073	9.112219	3.386036	Low
TCGA-05-4389-01A	1369	0	70	male	i	T1	M0	N0	3.712687	9.658092	3.882948	High
TCGA-05-4390-01A	1126	0	58	female	i	T2	M0	N0	4.249345	9.975734	4.079043	High
TCGA-05-4395-01A	0	1	76	male	iii	T4	M0	N2	4.26542	12.21144	4.838755	High
TCGA-05-4396-01A	303	1	76	male	iii	T4	M0	N1	2.477436	8.623859	3.328949	Low
TCGA-05-4397-01A	731	1	65	male	ii	T2	M0	N1	5.483371	9.41279	4.091999	High
TCGA-05-4398-01A	1431	0	47	female	iii	T4	M0	N3	4.061957	11.17554	4.45441	High
TCGA-05-4402-01A	244	1	57	female	iv	T2	M1	NX	3.198369	10.30563	4.017372	High
TCGA-05-4403-01A	578	0	76	male	i	T2	M0	N0	2.82346	9.276899	3.607168	Low
TCGA-05-4405-01A	610	0	74	female	i	T2	M0	N0	2.361295	8.135477	3.144411	Low
TCGA-05-4410-01A	0	0	62	male	i	T2	M0	N0	2.325899	8.825656	3.372283	Low
TCGA-05-4415-01A	91	1	57	male	iii	T4	M0	N2	4.634166	10.98116	4.482991	High
TCGA-05-4417-01A	455	0	51	female	i	T2	M0	N0	2.858344	9.42849	3.664255	Low
TCGA-05-4418-01A	274	1	69	male	iii	T3	M0	N2	3.978039	10.9374	4.359926	High
TCGA-05-4420-01A	912	0	41	male	i	T2	M0	N0	5.280241	9.062578	3.939898	High
TCGA-05-4422-01A	365	0	68	male	i	T2	M0	N0	2.206526	9.141226	3.459448	Low
TCGA-05-4424-01A	913	0	70	male	ii	T3	M0	N0	3.562576	9.424538	3.779097	High
TCGA-05-4425-01A	669	0	70	female	iv	T2	M1	N0	2.914946	8.71334	3.431427	Low
TCGA-05-4426-01A	791	0	71	male	i	T2	M0	N0	3.435127	10.64233	4.170442	High
TCGA-05-4427-01A	791	0	65	female	ii	T2	M0	N1	3.835093	8.854723	3.631102	Low
TCGA-05-4430-01A	761	0	59	female	i	T2	M0	N0	2.825304	9.143135	3.562177	Low
TCGA-05-4432-01A	761	0	66	male	ii	T2	M0	N1	3.771014	8.953401	3.653946	Low
TCGA-05-4433-01A	730	0	82	male	i	T2	M0	N0	3.596754	9.1636	3.696376	Low
TCGA-05-4434-01A	457	1	67	female	iv	T4	M1	N1	4.0851	10.44665	4.211411	High
TCGA-05-5420-01A	457	0	67	male	iii	T2	M0	N2	3.919126	9.132426	3.739002	High
TCGA-05-5423-01A	151	0	65	male	ii	T2	M0	N1	2.322328	8.034552	3.103807	Low
TCGA-05-5425-01A	882	0	68	male	ii	T2	M0	N1	4.344195	9.101102	3.79852	High
TCGA-05-5428-01A	670	0	57	male	ii	T1	M0	N1	4.048244	9.548747	3.901279	High
TCGA-05-5429-01A	275	1	60	male	iii	T3	M0	N2	4.193922	10.00255	4.07898	High
TCGA-05-5715-01A	62	0	69	female	i	T2	M0	N0	3.041032	9.333185	3.662122	Low
TCGA-35-3615-01A	14	0	57	male	i	T2	M0	N0	1.561022	9.357478	3.426185	Low
TCGA-35-4122-01A	225	0	69	male	i	T1	M0	N0	4.66352	10.41087	4.29472	High
TCGA-35-4123-01A	182	0	38	male	i	T1	M0	N0	4.505647	10.72243	4.374176	High
TCGA-35-5375-01A	264	0	61	male	iii	T2	M0	N2	3.983972	10.67265	4.271257	High
TCGA-38-4625-01A	2973	0	66	female	i	T2	M0	N0	4.620372	9.874652	4.106024	High

Appendix C11: continued

TCGA-38-4627-01A	1147	1	64	female	ii	T1	M0	N1	2.740433	9.666989	3.725564	High
TCGA-38-4628-01A	1492	1	65	female	ii	T2	M0	N1	3.527256	8.433282	3.437608	Low
TCGA-38-4629-01A	864	1	68	male	ii	T3	M0	N0	3.489232	10.71511	4.204014	High
TCGA-38-4630-01A	1073	1	75	female	i	T2	M0	N0	5.070905	9.509333	4.056645	High
TCGA-38-4631-01A	354	1	72	female	i	T2	M0	N0	5.430311	10.40949	4.420751	High
TCGA-38-4632-01A	1357	1	42	male	iv	T2	M1	N1	4.395025	9.921225	4.084619	High
TCGA-38-7271-01A	800	1	72	female	i	T1	M0	N0	2.508818	8.541539	3.306251	Low
TCGA-38-A44F-01A	133	0	80	male	i	T2	M0	N0	2.000292	9.470592	3.536956	Low
TCGA-44-2655-01A	1324	0	65	female	i	T1	M0	N0	1.644669	8.213385	3.052569	Low
TCGA-44-2656-01A	1429	0	59	male	i	T2	M0	N0	3.456356	7.727089	3.186778	Low
TCGA-44-2657-01A	1351	0	74	female	i	T2	M0	NX	2.647325	8.570664	3.338963	Low
TCGA-44-2659-01A	1367	0	65	female	ii	T1	M0	N1	1.595682	8.503134	3.142603	Low
TCGA-44-2661-01A	1159	0	69	female	i	T1	M0	N0	2.689429	8.316958	3.259998	Low
TCGA-44-2662-01A	1280	0	65	male	i	T2	M0	N0	4.484388	9.841316	4.072302	High
TCGA-44-2665-01A	1301	0	55	female	ii	T2	M0	N1	2.232904	9.743763	3.667833	Low
TCGA-44-2666-01A	97	1	43	male	i	T2	M0	N0	3.204245	7.818804	3.176243	Low
TCGA-44-2668-01A	761	1	51	male	i	T2	M0	N0	4.065208	10.58508	4.255005	High
TCGA-44-3396-01A	1130	0	74	female	iii	T2	M0	N2	4.175984	9.120243	3.777252	High
TCGA-44-3398-01A	1163	0	77	female	i	T1	M0	N0	3.296832	10.11958	3.970614	High
TCGA-44-3917-01A	1183	0	33	female	i	T2	M0	N0	4.312605	9.020811	3.766121	High
TCGA-44-3918-01A	1036	0	60	female	i	T1	M0	N0	3.470812	7.927348	3.256975	Low
TCGA-44-3919-01A	1026	1	71	female	i	T1	M0	N0	3.617395	9.540547	3.827424	High
TCGA-44-4112-01A	808	1	60	female	i	T2	M0	N0	3.510317	9.993884	3.963269	High
TCGA-44-5643-01A	1013	0	53	male	iii	T2	M0	N2	4.506192	11.51814	4.643709	High
TCGA-44-6145-01A	595	0	62	female	i	T1	M0	N0	3.635435	9.526637	3.82569	High
TCGA-44-6146-01A	728	0	64	male	ii	T3	M0	N0	2.224825	7.711543	2.978344	Low
TCGA-44-6147-01A	845	0	67	female	i	T1	M0	NX	1.863711	7.605092	2.882723	Low
TCGA-44-6148-01A	704	0	60	male	i	T1	M0	N0	0.694646	8.363273	2.946595	Low
TCGA-44-6774-01A	658	0	56	female	iii	T1	M0	N2	3.453834	8.935475	3.595549	Low
TCGA-44-6775-01A	705	0	72	female	i	T2	MX	N0	3.860746	8.548367	3.531595	Low
TCGA-44-6776-01A	2616	0	60	female	i	T1	MX	N0	1.736114	8.531704	3.175445	Low
TCGA-44-6777-01A	987	1	85	female	i	T2	MX	NX	2.784277	9.861928	3.798808	High
TCGA-44-6778-01A	1864	0	59	male	i	T1	MX	N0	3.586818	8.679939	3.530958	Low
TCGA-44-6779-01A	500	1	50	female	ii	T2	MX	N1	4.930516	10.62883	4.412571	High
TCGA-44-7659-01A	691	0	70	male	i	T1	MX	N0	1.477769	8.023573	2.96076	Low
TCGA-44-7660-01A	592	0	72	male	i	T2	MX	N0	3.376744	10.58046	4.139863	High
TCGA-44-7661-01A	557	1	69	female	i	T2	M0	N0	4.429629	10.37881	4.245277	High
TCGA-44-7662-01A	218	0	61	male	i	T2	MX	N0	3.903666	9.51994	3.867673	High
TCGA-44-7667-01A	1097	0	49	female	ii	T3	MX	N0	5.875283	10.86684	4.649028	High
TCGA-44-7669-01A	574	1	59	male	ii	T1	MX	N1	5.503315	10.81355	4.569618	High
TCGA-44-7670-01A	882	0	47	female	ii	T1	M0	N1	5.022158	9.575053	4.070857	High

Appendix C11: continued

TCGA-44-7671-01A	889	0	64	male	i	T2	M0	N0	2.126198	9.630925	3.61202	Low
TCGA-44-7672-01A	719	0	52	female	i	T1	M0	N0	3.624139	10.01555	3.989384	High
TCGA-44-8117-01A	385	0	54	female	i	T2	M0	N0	2.633293	9.343701	3.598417	Low
TCGA-44-8119-01A	285	0	73	male	ii	T3	M0	N0	3.880509	10.12118	4.067447	High
TCGA-44-8120-01A	260	0	58	male	i	T2	M0	N0	1.876807	8.876832	3.315524	Low
TCGA-44-A479-01A	486	0	73	female	i	T2	MX	N0	3.694019	8.592535	3.519046	Low
TCGA-44-A47A-01A	466	0	78	female	i	T2	MX	N0	3.383422	9.599452	3.808771	High
TCGA-44-A47B-01A	287	0	79	male	i	T2	M0	N0	2.782038	8.715636	3.410278	Low
TCGA-44-A47G-01A	351	0	73	female	i	T1	M0	N0	3.748679	9.582713	3.863361	High
TCGA-44-A4SS-01A	415	0	73	male	i	T1	M0	N0	3.845612	9.636701	3.897634	High
TCGA-44-A4SU-01A	409	1	67	female	i	T1	MX	N0	2.663168	8.566548	3.340183	Low
TCGA-49-4486-01A	2318	1	72	male	i	T1	M0	N0	1.094096	9.292904	3.327289	Low
TCGA-49-4487-01A	855	1	72	female	i	T1	M0	N0	4.057785	10.11886	4.095906	High
TCGA-49-4488-01A	869	1	74	female	i	T1	MX	N0	3.524414	9.530548	3.808699	High
TCGA-49-4490-01A	385	1	45	female	iii	T3	M0	N2	2.667354	9.555696	3.675822	Low
TCGA-49-4494-01A	1081	1	77	male	iii	T3	M0	N2	4.281809	10.30178	4.194807	High
TCGA-49-4501-01A	1421	1	67	female	i	T2	M0	N0	2.677808	8.574511	3.345295	Low
TCGA-49-4505-01A	428	1	61	female	ii	T2	M0	N1	1.580691	9.909667	3.616414	Low
TCGA-49-4506-01A	999	1	68	female	ii	T2	M0	N1	4.589772	11.162	4.536903	High
TCGA-49-4507-01A	268	1	73	female	iii	T3	M0	N1	3.940932	11.2074	4.445232	High
TCGA-49-4510-01A	896	1	51	female	ii	T2	M0	N1	0.858442	8.642756	3.068257	Low
TCGA-49-4512-01A	905	1	69	female	iii	T2	MX	N2	2.362683	9.340534	3.552701	Low
TCGA-49-4514-01A	1700	0	79	female	i	T1	M0	N0	3.58765	10.19986	4.045776	High
TCGA-49-6742-01A	488	1	70	male	ii	T2	M0	N1	4.53812	9.357448	3.917318	High
TCGA-49-6743-01A	1621	0	81	female	iii	T1	MX	N2	4.834644	9.271968	3.937291	High
TCGA-49-6744-01A	1683	0	64	female	ii	T2	MX	N1	2.80049	9.185003	3.572261	Low
TCGA-49-6745-01A	522	0	82	male	iii	T2	M0	N2	4.456594	9.37872	3.911071	High
TCGA-49-6761-01A	354	0	68	female	iii	T1	MX	N2	3.203015	9.595311	3.777607	High
TCGA-49-6767-01A	677	0	46	female	ii	T3	MX	N0	4.141578	10.01228	4.07364	High
TCGA-49-AAQV-01A	677	1	63	female	ii	T1	MX	N1	3.929503	9.284152	3.792092	High
TCGA-49-AAR0-01A	4765	0	57	male	i	T1	MX	N0	3.041411	9.311681	3.654902	Low
TCGA-49-AAR2-01A	2224	0	64	male	i	T2	MX	N0	2.970806	9.732464	3.785741	High
TCGA-49-AAR3-01A	1893	0	69	male	ii	T2	MX	N1	4.180534	10.02764	4.085267	High
TCGA-49-AAR4-01A	879	1	51	male	iii	T2	MX	N2	3.683436	9.01336	3.659801	Low
TCGA-49-AAR9-01A	260	1	61	male	ii	T3	MX	N0	5.093135	10.52688	4.404876	High
TCGA-49-AARE-01A	1229	1	51	female	i	T1	MX	N0	4.124853	9.683084	3.959408	High
TCGA-49-AARN-01A	1135	1	56	female	i	T1	MX	N0	3.282712	9.116148	3.628499	Low
TCGA-49-AARO-01A	3759	0	39	female	i	T1	MX	N0	3.176334	10.05735	3.929663	High
TCGA-49-AARQ-01A	6732	0	41	female	i	T2	MX	N0	4.475822	10.47911	4.286862	High
TCGA-49-AARR-01A	4992	0	68	male	i	T1	MX	N0	1.390551	7.904534	2.906062	Low
TCGA-4B-A93V-01A	300	1	52	female	i	T1	M0	N0	2.243105	10.08875	3.786338	High

Appendix C11: continued

TCGA-50-5044-01A	624	1	72	female	iii	T4	M0	N1	4.555746	11.35825	4.597745	High
TCGA-50-5049-01A	3094	0	70	male	i	T2	M0	N0	3.12125	9.172765	3.621034	Low
TCGA-50-5051-01A	478	1	42	female	iii	T2	M0	N2	2.748511	9.193378	3.566521	Low
TCGA-50-5055-01A	1830	1	79	female	ii	T1	M0	N1	3.023923	9.256808	3.633436	Low
TCGA-50-5066-01A	1442	0	72	male	i	T2	M0	N0	4.543977	10.15113	4.187041	High
TCGA-50-5068-01A	1499	1	59	female	ii	T2	MX	N1	3.330667	8.698978	3.495147	Low
TCGA-50-5072-01A	250	1	74	male	iii	T2	M0	N2	4.971997	10.31766	4.314046	High
TCGA-50-5930-01A	282	1	47	male	iii	T2	M0	N2	3.014127	8.999488	3.544686	Low
TCGA-50-5931-01A	434	1	75	female	i	T2	M0	N0	4.343787	10.82162	4.381061	High
TCGA-50-5932-01A	1235	1	75	male	ii	T2	M0	N1	2.359948	8.86048	3.389692	Low
TCGA-50-5933-01A	2393	1	72	male	iii	T4	M0	N2	3.412489	9.479381	3.772908	High
TCGA-50-5935-01A	653	1	86	female	i	T1	M0	N0	1.427584	7.846092	2.892381	Low
TCGA-50-5936-01A	257	1	58	male	iii	T2	M0	N2	3.699123	10.28288	4.092278	High
TCGA-50-5939-01A	460	1	85	male	i	T2	M0	N0	3.949374	11.20852	4.447007	High
TCGA-50-5941-01A	1474	0	55	female	iii	T2	M0	N2	3.579678	10.19823	4.04391	High
TCGA-50-5942-01A	1847	0	67	female	i	T1	M0	N0	0.996174	7.577007	2.730092	Low
TCGA-50-5944-01A	1750	0	69	female	i	T1	M0	N0	2.716903	8.845927	3.443652	Low
TCGA-50-5946-01A	1617	0	62	male	i	T1	MX	N0	5.171253	9.024289	3.908953	High
TCGA-50-6590-01A	1288	1	72	female	i	T2	M0	N0	4.000264	11.31718	4.492195	High
TCGA-50-6591-01A	119	1	63	female	iv	T2	M1	N0	5.047526	10.17012	4.276545	High
TCGA-50-6592-01A	777	1	71	female	i	T2	M0	N0	4.672257	10.26185	4.2457	High
TCGA-50-6593-01A	336	1	49	female	iii	T1	M0	N2	3.088868	9.183349	3.619275	Low
TCGA-50-6594-01A	370	1	79	female	iii	T3	M0	N2	4.850856	9.701761	4.085503	High
TCGA-50-6595-01A	189	1	74	female	iii	T2	M0	N2	4.38721	10.49905	4.278993	High
TCGA-50-6597-01A	1268	1	79	female	i	T2	M0	N0	1.931373	8.92626	3.341263	Low
TCGA-50-6673-01A	22	1	84	female	i	T1	M0	N0	3.497807	9.05932	3.644741	Low
TCGA-50-7109-01A	308	1	60	male	i	T1	M0	N0	3.637533	9.382876	3.777355	High
TCGA-50-8457-01A	1125	0	63	female	i	T1	M0	N0	0.98145	8.20394	2.939957	Low
TCGA-50-8459-01A	1119	0	68	male	ii	T3	M0	N0	1.974515	9.589942	3.573118	Low
TCGA-50-8460-01A	829	0	74	male	i	T1	M0	N0	2.379839	9.755252	3.695964	Low
TCGA-53-7624-01A	1043	1	40	female	iv	T2	M1	N0	4.930855	9.75826	4.117833	High
TCGA-53-7626-01A	929	1	76	female	ii	T1	M0	N1	2.61724	8.521947	3.317503	Low
TCGA-53-7813-01A	424	0	51	female	iii	T4	M0	N0	2.782853	9.223336	3.582331	Low
TCGA-53-A4EZ-01A	1071	0	63	male	ii	T2	MX	N1	4.083506	8.845099	3.668825	Low
TCGA-55-1592-01A	701	1	65	male	i	T2	M0	N0	3.744757	8.802812	3.598621	Low
TCGA-55-1594-01A	1178	0	68	male	iii	T2	M0	N2	5.061809	9.538195	4.064918	High
TCGA-55-1596-01A	2065	0	55	male	ii	T2	M0	N1	4.525977	9.715844	4.036676	High
TCGA-55-6543-01A	435	0	60	female	i	T1	MX	N0	1.925012	9.257307	3.452314	Low
TCGA-55-6642-01A	2449	0	63	male	i	T2	MX	N0	3.548107	9.463377	3.789862	High
TCGA-55-6712-01A	171	1	71	male	ii	T2	MX	N1	3.001906	10.42682	4.025996	High
TCGA-55-6968-01A	1293	1	61	male	iv	T1	M1	N0	5.23561	9.448682	4.063279	High

Appendix C11: continued

TCGA-55-6970-01A	464	1	67	female	iii	T2	MX	N2	4.109825	9.209922	3.796705	High
TCGA-55-6971-01A	1400	0	59	female	i	T2	MX	N0	3.253503	9.517655	3.759639	High
TCGA-55-6972-01A	1632	1	72	male	i	T2	M0	N0	1.662146	8.677874	3.212738	Low
TCGA-55-6975-01A	118	1	61	male	ii	T2	M0	N1	4.924456	10.21173	4.270334	High
TCGA-55-6978-01A	176	1	81	male	ii	T2	MX	N0	4.840876	9.896178	4.149691	High
TCGA-55-6979-01A	237	1	59	female	ii	T2	M0	N1	3.513542	9.033119	3.638464	Low
TCGA-55-6980-01A	2109	0	56	male	i	T1	M0	N0	1.529301	9.609088	3.506153	Low
TCGA-55-6981-01A	1379	1	53	female	iii	T1	M0	N2	3.910829	10.46895	4.190213	High
TCGA-55-6982-01A	995	1	79	female	ii	T2	M0	N1	3.531775	10.17378	4.027727	High
TCGA-55-6983-01A	2823	0	81	male	ii	T2	M0	N1	2.955523	9.292521	3.634245	Low
TCGA-55-6984-01A	760	1	71	female	ii	T2	M0	N1	3.888102	10.74312	4.279303	High
TCGA-55-6985-01A	1233	0	58	female	i	T2	MX	N0	3.484549	9.373239	3.748854	High
TCGA-55-6986-01A	3261	0	74	female	i	T2	M0	N0	2.791989	9.368773	3.633087	Low
TCGA-55-6987-01A	2137	0	77	male	i	T1	M0	N0	3.438944	10.29938	4.054942	High
TCGA-55-7227-01A	952	1	77	male	iii	T3	MX	N1	2.79808	9.071556	3.533447	Low
TCGA-55-7281-01A	872	0	70	female	i	T1	M0	N0	2.40627	9.334965	3.558005	Low
TCGA-55-7283-01A	609	0	76	female	iii	T3	MX	N2	3.187791	8.338629	3.349553	Low
TCGA-55-7284-01B	243	1	74	male	ii	T3	MX	N0	2.075734	8.672986	3.279314	Low
TCGA-55-7570-01A	824	0	60	male	i	T1	MX	N0	4.725512	10.28176	4.261226	High
TCGA-55-7573-01A	487	0	72	female	i	T1	MX	N0	1.529991	8.239036	3.042336	Low
TCGA-55-7574-01A	995	1	64	female	i	T2	M0	N0	2.71888	8.98623	3.491488	Low
TCGA-55-7576-01A	670	0	54	male	i	T2	M0	N0	4.017784	9.948627	4.031663	High
TCGA-55-7724-01A	705	0	76	female	i	T2	MX	N0	3.522996	9.382367	3.758287	High
TCGA-55-7725-01A	442	0	68	female	i	T1	MX	N0	2.103819	8.937783	3.373614	Low
TCGA-55-7726-01A	652	0	72	female	i	T1	MX	N0	3.739621	10.11586	4.042401	High
TCGA-55-7727-01A	119	0	70	male	iii	T1	MX	N2	3.884768	8.480125	3.51245	Low
TCGA-55-7728-01A	704	0	64	female	i	T2	MX	N0	2.172294	9.24928	3.490391	Low
TCGA-55-7815-01A	773	0	76	male	i	T2	MX	N0	3.326732	8.426931	3.402376	Low
TCGA-55-7816-01A	468	1	49	female	iv	TX	MX	NX	1.746946	8.482858	3.160691	Low
TCGA-55-7903-01A	567	0	64	male	i	T1	MX	N0	4.716139	10.43168	4.310445	High
TCGA-55-7907-01A	343	1	77	male	ii	T2	MX	N1	2.998059	9.158825	3.59599	Low
TCGA-55-7910-01A	1040	0	50	female	ii	T2	M0	N0	4.093654	9.425104	3.866903	High
TCGA-55-7911-01A	537	0	70	female	i	T1	MX	N0	5.017449	10.4309	4.359889	High
TCGA-55-7913-01B	561	1	61	female	i	T1	MX	N0	3.677005	9.595314	3.855803	High
TCGA-55-7914-01A	187	1	71	female	ii	T1	MX	N1	3.089507	8.584528	3.416606	Low
TCGA-55-7994-01A	603	0	81	male	ii	T3	MX	N0	5.003131	10.02021	4.218458	High
TCGA-55-7995-01A	889	0	73	female	i	T1	M0	N0	4.181429	10.52991	4.255497	High
TCGA-55-8085-01A	904	0	64	male	i	T1	M0	N0	3.846358	10.19059	4.085317	High
TCGA-55-8087-01A	462	0	59	female	i	T2	MX	N0	0.913459	7.849755	2.808804	Low
TCGA-55-8089-01A	702	1	56	male	i	T1	M0	N0	4.575428	9.971573	4.131429	High
TCGA-55-8090-01A	598	1	80	male	i	T1	M0	N0	3.595592	10.05986	3.999677	High

Appendix C11: continued

TCGA-55-8091-01A	600	0	74	male	i	T2	MX	N0	2.732663	9.758837	3.755385	High
TCGA-55-8092-01A	154	1	75	male	ii	T3	MX	N0	2.632717	8.85382	3.432437	Low
TCGA-55-8094-01A	541	0	51	male	iv	T2	M1	N0	4.776251	9.960009	4.160644	High
TCGA-55-8096-01A	719	1	67	female	i	T2	MX	N0	2.81834	9.628058	3.725234	High
TCGA-55-8097-01A	476	0	60	female	i	T1	MX	N0	1.015163	7.843897	2.823599	Low
TCGA-55-8203-01A	547	0	69	female	i	T1	M0	N0	3.646523	9.471912	3.808988	High
TCGA-55-8204-01A	515	0	87	female	i	T2	MX	N0	3.978628	10.6079	4.248449	High
TCGA-55-8205-01A	599	0	76	female	ii	T2	M0	N0	5.097378	9.667085	4.114431	High
TCGA-55-8206-01A	888	0	56	male	i	T1	M0	N0	1.486052	7.899575	2.920137	Low
TCGA-55-8207-01A	977	0	73	male	i	T2	MX	N0	1.199941	8.840673	3.191614	Low
TCGA-55-8208-01A	674	0	73	female	i	T1	M0	N0	3.883845	9.341726	3.804056	High
TCGA-55-8299-01A	469	1	61	female	i	T1	MX	N0	3.861527	9.701568	3.922225	High
TCGA-55-8301-01A	534	0	58	male	i	T2	MX	N0	2.984205	9.901825	3.845301	High
TCGA-55-8302-01A	478	0	54	male	i	T2	MX	N0	3.950046	10.48319	4.201502	High
TCGA-55-8505-01A	440	0	62	male	iii	T1	MX	N2	4.195166	10.26741	4.168874	High
TCGA-55-8506-01A	11	0	62	female	ii	T3	MX	N0	2.660062	9.293055	3.585683	Low
TCGA-55-8507-01A	418	0	53	male	i	T1	MX	N0	3.571607	9.143827	3.685531	Low
TCGA-55-8508-01A	617	0	60	female	ii	T2	MX	N1	2.978953	9.581164	3.735852	High
TCGA-55-8510-01A	539	0	55	female	i	T2	MX	N0	2.978561	8.982775	3.533159	Low
TCGA-55-8511-01A	552	0	73	female	i	T2	MX	N0	3.686443	9.029791	3.665861	Low
TCGA-55-8512-01A	607	1	41	male	iv	T1	M1	N1	1.03258	8.148331	2.929561	Low
TCGA-55-8513-01A	791	0	77	female	ii	T3	MX	N0	1.747929	8.263025	3.086413	Low
TCGA-55-8514-01A	520	0	70	female	i	T2	MX	N0	1.067551	8.945362	3.205224	Low
TCGA-55-8614-01A	536	0	76	male	i	T2	MX	N0	2.817472	9.16609	3.568658	Low
TCGA-55-8615-01A	446	0	67	male	iii	T3	MX	N2	2.905377	9.300859	3.628796	Low
TCGA-55-8616-01A	48	0	58	female	i	T2	M0	N0	1.775149	8.809827	3.276063	Low
TCGA-55-8619-01A	416	0	72	female	ii	T3	MX	N0	1.952627	8.645457	3.249683	Low
TCGA-55-8620-01A	375	1	60	male	iv	T1	M1	N1	4.243831	10.21074	4.157713	High
TCGA-55-8621-01A	515	0	75	female	i	T1	MX	N0	2.516175	8.847706	3.41114	Low
TCGA-55-A48X-01A	689	0	63	female	ii	T1	M0	N1	2.94764	8.530727	3.374984	Low
TCGA-55-A48Y-01A	630	0	69	male	ii	T2	M0	N0	2.997252	9.041212	3.55603	Low
TCGA-55-A48Z-01A	651	0	60	female	iii	T1	MX	N3	3.182073	9.63677	3.788191	High
TCGA-55-A490-01A	99	1	78	male	ii	T2	MX	N0	3.278364	10.41779	4.068546	High
TCGA-55-A491-01A	626	0	81	female	i	T1	MX	N0	4.022953	9.539155	3.893859	High
TCGA-55-A492-01A	596	0	70	female	i	T1	MX	N0	1.025683	9.486041	3.381403	Low
TCGA-55-A493-01A	28	0	54	female	i	T2	M0	N0	4.835517	10.5839	4.381685	High
TCGA-55-A494-01A	481	0	61	female	i	T2	MX	N0	4.311954	9.572972	3.952988	High
TCGA-55-A4DF-01A	440	1	88	male	i	T1	MX	N0	4.402024	9.799213	4.044457	High
TCGA-55-A4DG-01A	608	0	71	male	i	T1	MX	N0	1.153295	7.357646	2.681732	Low
TCGA-55-A57B-01A	546	0	80	female	i	T1	M0	N0	2.420021	8.599472	3.311219	Low
TCGA-62-8394-01A	139	1	65	female	iii	T4	M0	N2	4.501756	9.384106	3.920346	High

Appendix C11: continued

TCGA-62-8395-01A	1216	0	80	female	ii	T3	M0	N0	1.555639	9.154869	3.356689	Low
TCGA-62-8397-01A	1289	0	70	female	ii	T3	M0	N0	1.645441	9.913421	3.628367	Low
TCGA-62-8398-01A	444	1	55	male	iii	T2	M0	N2	4.401082	11.06677	4.473527	High
TCGA-62-8399-01A	2696	0	62	male	iii	T2	M0	N2	3.431464	8.946681	3.595653	Low
TCGA-62-8402-01A	1498	1	73	female	iii	T2	M0	N2	4.937291	10.04227	4.215067	High
TCGA-62-A46O-01A	1454	1	65	female	i	T2	M0	N0	5.533939	9.293882	4.060077	High
TCGA-62-A46P-01A	594	1	65	male	i	T2	M0	N0	1.458694	9.023954	3.296365	Low
TCGA-62-A46R-01A	1725	1	54	female	i	T2	M0	N0	3.220027	7.480066	3.064142	Low
TCGA-62-A46S-01A	1653	1	73	male	i	T2	M0	N0	1.850684	8.352171	3.133552	Low
TCGA-62-A46V-01A	2199	0	78	female	i	T2	M0	N0	3.343448	9.375016	3.726177	High
TCGA-62-A46Y-01A	414	1	70	female	iii	T2	M0	N2	3.536858	9.412114	3.770647	High
TCGA-62-A470-01A	1194	1	84	male	i	T2	M0	N0	2.687818	9.331321	3.60322	Low
TCGA-62-A471-01A	1246	0	64	male	ii	T2	M0	N1	4.291959	10.38312	4.224022	High
TCGA-62-A472-01A	910	0	70	male	ii	T3	M0	N0	3.709352	9.786102	3.925745	High
TCGA-64-1676-01A	1728	0	58	male	i	T1	M0	N0	3.18924	9.581063	3.770509	High
TCGA-64-1677-01A	628	1	77	female	iii	T2	M0	N2	4.304276	10.07955	4.12326	High
TCGA-64-1679-01A	2488	0	58	female	iii	T1	M0	N2	3.371692	10.03052	3.952806	High
TCGA-64-1680-01A	1126	0	63	male	iv	T2	M1	N2	3.308153	8.961094	3.580191	Low
TCGA-64-1681-01A	1167	1	61	female	i	T1	M0	N0	2.390177	8.674584	3.33173	Low
TCGA-64-5774-01A	2676	0	60	male	i	T2	M0	N0	5.231526	9.966824	4.23806	High
TCGA-64-5775-01A	62	1	71	male	iii	T4	M0	N0	4.403973	11.144	4.500153	High
TCGA-64-5778-01A	1305	0	60	male	i	T2	M0	N0	3.692558	9.014105	3.661559	Low
TCGA-64-5779-01A	864	0	61	male	iii	T2	M0	N2	3.542881	9.044137	3.647035	Low
TCGA-64-5781-01A	1559	0	55	female	i	T2	M0	N0	4.028966	10.11439	4.089639	High
TCGA-64-5815-01A	866	0	74	male	ii	T2	M0	N1	3.251106	10.53576	4.103998	High
TCGA-67-3770-01A	610	0	70	female	i	T1	M0	N0	2.362696	8.440713	3.248003	Low
TCGA-67-3771-01A	610	0	77	female	i	T1	M0	N0	2.982745	9.16911	3.596946	Low
TCGA-67-3772-01A	573	0	82	female	i	T2	M0	N0	2.359791	9.234022	3.516156	Low
TCGA-67-3773-01A	427	0	84	female	i	T2	M0	N0	2.077526	8.991322	3.387406	Low
TCGA-67-3774-01A	385	0	73	female	i	T2	M0	N0	2.397429	8.107559	3.140919	Low
TCGA-67-6215-01A	174	0	52	female	i	T2	M0	N0	3.302877	9.505694	3.763735	High
TCGA-67-6216-01A	141	0	57	female	i	T1	M0	N0	3.176529	9.774921	3.834057	High
TCGA-67-6217-01A	422	0	73	female	ii	T2	M0	N1	1.196577	8.067567	2.929268	Low
TCGA-69-7760-01A	202	0	73	male	ii	T3	M0	N0	2.987053	9.604264	3.74501	High
TCGA-69-7761-01A	186	0	84	male	i	T2	MX	N0	3.548861	9.158973	3.686908	Low
TCGA-69-7763-01A	690	0	69	male	i	T1	M0	N0	1.998851	8.723429	3.283712	Low
TCGA-69-7764-01A	414	0	75	male	i	T1	M0	N0	3.029458	8.520844	3.385135	Low
TCGA-69-7973-01A	230	0	42	female	i	T2	M0	N0	4.281077	9.574705	3.948481	High
TCGA-69-7974-01A	184	0	54	female	iii	T2	MX	N2	4.370167	9.874465	4.064684	High
TCGA-69-7978-01A	134	0	59	male	ii	T2	MX	N1	2.777548	9.645663	3.724466	Low
TCGA-69-7979-01A	408	0	71	female	i	T2	MX	N0	2.880729	9.432442	3.669287	Low

Appendix C11: continued

TCGA-69-7980-01A	411	0	70	female	i	T1	M0	N0	3.71928	9.687707	3.894064	High
TCGA-69-8253-01A	426	0	59	female	ii	T1	MX	N1	1.279957	9.651712	3.479451	Low
TCGA-69-8255-01A	129	0	71	male	i	T1	M0	N0	4.714252	10.39819	4.298794	High
TCGA-69-8453-01A	813	0	77	male	ii	T3	MX	N0	3.053847	9.261473	3.639952	Low
TCGA-69-A59K-01A	591	0	60	female	ii	T3	M0	N0	3.933586	10.37382	4.161753	High
TCGA-71-6725-01A	256	0	48	female	i	T2	M0	N0	2.220605	8.478707	3.237427	Low
TCGA-71-8520-01A	210	1	60	female	i	T2	M0	N0	4.230346	9.057274	3.764897	High
TCGA-73-4658-01A	1600	1	80	female	i	T2	M0	N0	2.9268	9.642368	3.747973	High
TCGA-73-4659-01A	711	1	66	male	iii	T2	M0	N2	4.398244	9.984935	4.106723	High
TCGA-73-4662-01A	2515	0	65	female	i	T1	M0	N0	2.641554	8.402874	3.281193	Low
TCGA-73-4666-01A	800	0	52	female	iv	T1	M1	N0	5.193806	11.0151	4.586808	High
TCGA-73-4668-01A	467	0	66	female	ii	T2	M0	N1	3.782411	9.450833	3.824268	High
TCGA-73-4670-01A	131	0	69	female	iv	T2	M1	N0	4.98933	11.33231	4.66049	High
TCGA-73-4675-01A	922	1	59	male	iii	T3	M0	N1	2.730483	10.03085	3.847134	High
TCGA-73-4676-01A	281	1	45	male	ii	T2	M0	N1	5.468585	9.951452	4.271963	High
TCGA-73-7498-01A	1189	0	58	female	i	T1	M0	N0	0.968843	8.086545	2.898124	Low
TCGA-73-7499-01A	1531	1	81	female	i	T2	M0	N0	4.493689	8.792666	3.718739	Low
TCGA-73-A9RS-01A	340	1	41	male	ii	T3	M0	N0	6.034703	9.581358	4.240036	High
TCGA-78-7143-01A	4961	1	62	female	i	T2	M0	N0	4.001763	8.82269	3.647751	Low
TCGA-78-7145-01A	826	1	52	female	iv	T4	M1	N1	5.028279	9.341854	3.992901	High
TCGA-78-7146-01A	173	1	71	female	iii	T2	M0	N2	4.553495	10.95513	4.460866	High
TCGA-78-7147-01A	586	1	67	female	ii	T2	M0	N1	3.775161	9.135861	3.716415	Low
TCGA-78-7148-01A	626	1	71	male	ii	T2	M0	N1	3.992116	10.07847	4.071396	High
TCGA-78-7149-01A	3940	0	71	male	iii	T4	M0	N0	1.452826	9.422965	3.430511	Low
TCGA-78-7150-01A	666	1	59	male	ii	T2	M0	N1	5.053222	11.0075	4.561042	High
TCGA-78-7152-01A	1215	1	65	male	i	T2	M0	N0	2.610867	8.924243	3.452679	Low
TCGA-78-7153-01A	3635	0	65	female	i	T2	M0	N0	1.625666	8.548938	3.163059	Low
TCGA-78-7154-01A	593	1	72	male	iii	T3	M0	N2	3.992603	10.56882	4.23752	High
TCGA-78-7155-01A	1171	1	68	male	i	T2	M0	N0	5.282828	8.920661	3.892269	High
TCGA-78-7156-01A	976	1	62	male	iv	T4	M1	N1	1.422035	8.611447	3.150633	Low
TCGA-78-7158-01A	179	1	59	female	iii	T4	M0	N2	2.610074	9.291427	3.576885	Low
TCGA-78-7159-01A	1974	0	60	female	i	T1	M0	NX	3.413759	9.556314	3.799168	High
TCGA-78-7160-01A	697	1	61	male	iv	T4	M1	N2	4.418561	9.428178	3.921544	High
TCGA-78-7161-01A	291	1	69	female	ii	T3	M0	N0	1.629477	8.997719	3.315656	Low
TCGA-78-7162-01A	3169	1	75	male	i	T1	M0	N0	1.834253	8.293991	3.11114	Low
TCGA-78-7163-01A	7248	0	60	male	i	T2	M0	N0	1.724817	9.569198	3.5249	Low
TCGA-78-7166-01A	258	1	84	male	ii	T2	M0	N1	3.720294	10.65351	4.221273	High
TCGA-78-7167-01A	2681	1	77	male	iv	T2	M1	N0	0.552501	8.907378	3.107392	Low
TCGA-78-7220-01A	807	1	53	female	iii	T2	M0	N2	5.208941	9.672825	4.134779	High
TCGA-78-7535-01A	949	1	45	male	i	T2	M0	N0	2.877929	9.318331	3.630184	Low
TCGA-78-7536-01A	244	1	69	male	iii	T2	M0	N2	4.369835	10.08557	4.136115	High

Appendix C11: continued

TCGA-78-7537-01A	1622	1	72	male	i	T2	M0	N0	1.264366	8.51438	3.091752	Low
TCGA-78-7539-01A	791	0	75	female	ii	T2	M0	N0	1.417285	8.555977	3.131066	Low
TCGA-78-7540-01A	1197	1	66	female	i	T2	M0	N0	2.413951	8.547926	3.292763	Low
TCGA-78-7542-01A	321	1	56	male	i	T2	M0	N0	4.501632	10.88371	4.428125	High
TCGA-78-7633-01A	1528	1	67	male	i	T2	M0	N0	1.95212	8.37738	3.158822	Low
TCGA-78-8640-01A	7062	0	59	male	ii	T1	M0	N1	3.984005	11.17528	4.441464	High
TCGA-78-8648-01A	1209	1	58	female	ii	T3	M0	N0	3.104487	9.100345	3.593745	Low
TCGA-78-8655-01A	2360	0	77	female	i	T1	M0	N0	2.875399	9.283781	3.618067	Low
TCGA-78-8660-01A	321	1	69	male	ii	T2	M0	N1	4.650855	10.95979	4.478505	High
TCGA-78-8662-01A	3361	1	53	female	i	T2	M0	N0	3.453543	10.13172	4.000576	High
TCGA-83-5908-01A	824	0	59	female	i	T1	M0	N0	5.261525	8.566357	3.768779	High
TCGA-86-6562-01A	376	1	52	male	ii	T2	M0	N1	4.240446	9.774275	4.009357	High
TCGA-86-6851-01A	179	0	73	female	ii	T1	M0	N1	3.231184	9.648284	3.800192	High
TCGA-86-7701-01A	947	0	66	male	iv	T2	M1	N0	3.787948	9.94871	3.993774	High
TCGA-86-7711-01A	1046	1	70	male	ii	T2	M0	N1	5.353285	10.39083	4.401727	High
TCGA-86-7713-01A	1157	0	70	male	ii	T2	M0	N0	3.502155	9.301683	3.727527	High
TCGA-86-7714-01A	625	1	61	female	iii	T1	M0	N2	1.998503	9.143739	3.425981	Low
TCGA-86-7953-01A	997	0	69	female	i	T1	M0	N0	4.367088	9.344259	3.884636	High
TCGA-86-7954-01A	605	0	68	female	i	T2	M0	N0	3.711023	9.371889	3.785759	High
TCGA-86-7955-01A	1072	0	62	male	i	T2	M0	N0	4.653371	10.66084	4.377689	High
TCGA-86-8054-01A	1148	0	61	male	ii	T2	M0	N1	5.797469	9.68979	4.237616	High
TCGA-86-8055-01A	124	1	79	male	ii	T2	M0	N1	3.992166	9.790229	3.973799	High
TCGA-86-8056-01A	139	0	63	female	iii	T4	M0	N0	1.967955	8.207489	3.103906	Low
TCGA-86-8073-01A	740	0	58	male	i	T2	M0	N0	2.558576	7.957296	3.116621	Low
TCGA-86-8074-01A	24	0	62	female	ii	T1	M0	N1	3.956157	9.235848	3.780132	High
TCGA-86-8075-01A	694	1	66	female	i	T2	M0	N0	4.00262	9.5548	3.895802	High
TCGA-86-8076-01A	993	0	42	male	i	T1	M0	N0	1.898978	9.910662	3.66926	Low
TCGA-86-8278-01A	944	0	63	female	ii	T2	M0	N1	3.661836	9.439811	3.800644	High
TCGA-86-8279-01A	949	0	46	male	ii	T2	M0	N1	2.692811	9.527219	3.670379	Low
TCGA-86-8280-01A	701	0	54	female	ii	T2	M0	N0	2.700953	9.123959	3.535169	Low
TCGA-86-8281-01A	0	0	75	male	i	T1	M0	NX	1.357507	8.609031	3.139169	Low
TCGA-86-8358-01A	653	0	44	male	i	T2	M0	N0	6.165825	9.628557	4.27765	High
TCGA-86-8359-01A	444	1	52	male	iii	T3	M0	N2	2.563004	8.60419	3.336405	Low
TCGA-86-8585-01A	353	0	57	male	i	T2	M0	N0	2.937267	10.58495	4.06888	High
TCGA-86-8668-01A	423	0	61	female	i	T1	M0	N0	1.869134	8.820477	3.295175	Low
TCGA-86-8669-01A	938	0	64	male	i	T1	M0	N0	2.206787	9.349374	3.529975	Low
TCGA-86-8671-01A	839	0	72	female	ii	T2	M0	N1	2.755462	8.754069	3.418908	Low
TCGA-86-8672-01A	19	1	59	male	ii	T3	M0	N0	3.070149	10.23134	3.971062	High
TCGA-86-8673-01A	862	0	61	male	i	T2	M0	N0	3.491023	9.412642	3.763264	High
TCGA-86-8674-01A	806	0	50	male	ii	T2	M0	N1	2.68561	9.759209	3.747748	High
TCGA-86-A456-01A	896	0	78	female	i	T1	M0	N0	2.26515	8.661736	3.306753	Low

Appendix C11: continued

TCGA-86-A4D0-01A	116	1	48	male	ii	T2	M0	N0	4.211076	9.933859	4.05855	High
TCGA-86-A4JF-01A	737	1	56	male	ii	T3	M0	N0	4.767976	10.01349	4.177388	High
TCGA-86-A4P7-01A	415	0	63	female	i	T2	M0	N0	2.773147	8.525232	3.344336	Low
TCGA-86-A4P8-01A	805	0	59	female	iii	T1	MX	N2	0.96595	7.56921	2.722465	Low
TCGA-91-6828-01A	323	0	70	male	i	T1	M0	N0	2.726507	8.107621	3.195229	Low
TCGA-91-6829-01A	1258	1	78	male	i	T2	MX	N0	3.205783	9.270626	3.668117	Low
TCGA-91-6830-01A	60	0	65	female	ii	T1	MX	N1	3.042996	10.13755	3.934824	High
TCGA-91-6831-01A	310	0	66	male	i	T2	MX	N0	5.25663	9.748941	4.168421	High
TCGA-91-6835-01A	79	0	81	female	i	T1	M0	N0	3.645482	8.306224	3.414087	Low
TCGA-91-6836-01A	417	0	52	female	i	T2	MX	N0	6.067079	9.944652	4.368396	High
TCGA-91-6840-01A	372	0	59	female	i	T1	M0	N0	3.229818	8.161343	3.296454	Low
TCGA-91-6847-01A	842	0	62	female	i	T2	MX	N0	4.185577	10.22668	4.153498	High
TCGA-91-6848-01A	224	0	59	male	iii	T2	MX	N2	4.769573	9.667637	4.060538	High
TCGA-91-6849-01A	35	0	75	female	iii	T2	MX	N2	1.418304	8.944707	3.262867	Low
TCGA-91-7771-01A	492	0	62	male	ii	T3	MX	N0	2.446788	9.31893	3.55926	Low
TCGA-91-8496-01A	505	0	63	female	i	T2	MX	NX	1.496022	8.465125	3.113291	Low
TCGA-91-8497-01A	434	1	75	female	i	T1	MX	N0	1.372247	8.696969	3.171379	Low
TCGA-91-8499-01A	36	0	76	female	i	T1	MX	N0	4.164407	10.74227	4.324596	High
TCGA-91-A4BC-01A	44	0	59	male	ii	T2	MX	N0	3.376711	8.881826	3.564659	Low
TCGA-91-A4BD-01A	603	0	78	male	ii	T1	MX	N1	1.700095	9.127227	3.37116	Low
TCGA-93-7347-01A	683	0	76	female	i	T1	MX	N0	2.419822	8.876316	3.404932	Low
TCGA-93-7348-01A	531	0	75	female	i	T1	MX	N0	2.696887	8.111729	3.191734	Low
TCGA-93-8067-01A	186	0	77	male	i	T2	MX	N0	3.690342	10.62418	4.206402	High
TCGA-93-A4JN-01A	718	0	71	male	iv	T2	M1	N0	4.147491	8.640563	3.610121	Low
TCGA-93-A4JO-01A	33	1	70	male	i	T1	MX	N0	2.461613	9.717825	3.696781	Low
TCGA-93-A4JP-01A	578	0	64	male	iv	TX	M1	NX	2.552662	8.249586	3.214622	Low
TCGA-93-A4JQ-01A	526	0	49	male	i	T1	MX	N0	3.370099	9.146318	3.653131	Low
TCGA-95-7039-01A	1272	0	54	female	ii	T3	MX	N0	4.097773	10.33076	4.174257	High
TCGA-95-7043-01A	503	1	63	female	i	T1	MX	N0	4.098995	9.412131	3.863391	High
TCGA-95-7562-01A	87	1	71	male	ii	T2	M0	N1	4.507708	10.64328	4.347714	High
TCGA-95-7567-01A	568	0	61	male	ii	T2	M0	N1	3.230832	9.799856	3.851459	High
TCGA-95-7944-01A	377	0	71	male	i	T1	M0	N0	3.43754	10.22054	4.028015	High
TCGA-95-7947-01A	477	0	67	male	i	T1	M0	N0	3.333402	9.499787	3.76677	High
TCGA-95-7948-01A	476	0	42	female	i	T2	M0	N0	2.319982	8.735016	3.340614	Low
TCGA-95-8039-01A	830	0	72	male	i	T1	MX	N0	3.006557	8.957171	3.529107	Low
TCGA-95-8494-01A	84	0	67	male	ii	T2	M0	N1	4.463053	10.4018	4.258575	High
TCGA-95-A4VK-01A	651	0	74	female	iii	T2	M0	N2	2.974184	9.00837	3.541104	Low
TCGA-95-A4VN-01A	553	0	62	female	ii	T2	M0	N1	4.809307	9.636694	4.056616	High
TCGA-95-A4VP-01A	605	0	66	female	iii	T2	M0	N2	2.704862	8.863637	3.447663	Low
TCGA-97-7546-01A	1285	0	76	female	i	T1	MX	N0	1.668647	7.715989	2.888094	Low
TCGA-97-7547-01A	1965	0	67	female	i	T2	MX	N0	1.265209	8.127756	2.960972	Low

Appendix C11: continued

TCGA-97-7552-01A	1932	0	70	male	i	T2	MX	N0	2.561929	8.607342	3.337295	Low
TCGA-97-7553-01A	1870	0	58	female	i	T1	MX	N0	3.286083	8.573031	3.445143	Low
TCGA-97-7554-01A	775	0	83	female	iii	T2	M0	N2	2.959329	8.825398	3.476695	Low
TCGA-97-7937-01A	564	0	65	male	i	T2	MX	N0	2.299588	9.314672	3.533534	Low
TCGA-97-7938-01A	18	1	76	female	i	T1	MX	N0	1.600643	6.891001	2.597516	Low
TCGA-97-7941-01A	484	0	72	female	i	T1	MX	N0	1.824925	9.211881	3.42042	Low
TCGA-97-8171-01A	568	0	81	male	iv	T2	M1	N2	2.887625	9.612081	3.731254	High
TCGA-97-8172-01A	545	0	75	female	i	T2	M0	N0	1.294422	8.376879	3.05015	Low
TCGA-97-8174-01A	164	1	67	male	ii	T2	M0	N0	1.2154	8.234305	2.988834	Low
TCGA-97-8175-01A	551	0	55	female	i	T2	M0	N0	3.398126	10.41501	4.087365	High
TCGA-97-8176-01A	468	1	63	male	iii	T3	M0	N1	4.231399	10.47796	4.24615	High
TCGA-97-8177-01A	499	0	59	female	i	T2	M0	N0	2.713055	9.773775	3.757208	High
TCGA-97-8179-01A	435	0	72	male	i	T1	M0	N0	2.559335	8.915338	3.441162	Low
TCGA-97-8547-01A	657	0	78	female	iii	T2	MX	N2	2.993675	9.921731	3.853604	High
TCGA-97-8552-01A	626	0	55	female	i	T1	MX	N0	1.279892	8.149829	2.970868	Low
TCGA-97-A4LX-01A	614	0	81	male	i	T2	M0	N0	3.330821	9.277267	3.690994	Low
TCGA-97-A4M0-01A	652	0	60	female	i	T2	M0	N0	1.72147	9.134384	3.37711	Low
TCGA-97-A4M1-01A	601	0	52	female	i	T1	M0	N0	1.141568	7.640744	2.775661	Low
TCGA-97-A4M2-01A	624	0	66	male	i	T1	M0	N0	1.254365	8.163324	2.971227	Low
TCGA-97-A4M3-01A	540	0	69	female	i	T1	M0	N0	1.834548	9.136762	3.39657	Low
TCGA-97-A4M5-01A	634	0	83	male	i	T1	M0	N0	2.002675	8.666919	3.265207	Low
TCGA-97-A4M6-01A	568	0	45	female	i	T1	M0	N0	2.658364	8.505794	3.318818	Low
TCGA-97-A4M7-01A	629	0	74	male	i	T1	M0	N0	2.412669	8.95382	3.429996	Low
TCGA-99-7458-01A	747	0	74	female	iii	T4	M0	N0	2.374619	9.144388	3.48825	Low
TCGA-99-8025-01A	1060	0	72	female	iii	T3	M0	N2	2.829489	8.974239	3.505675	Low
TCGA-99-8028-01A	1118	0	50	female	i	T1	M0	N0	2.638256	9.493606	3.649996	Low
TCGA-99-8032-01A	44	0	61	male	i	T1	M0	N0	2.87459	9.613268	3.729506	High
TCGA-99-8033-01A	656	1	74	female	iv	TX	M1	NX	3.863486	10.74173	4.27477	High
TCGA-99-AA5R-01A	658	0	70	female	i	T1	M0	N0	1.914159	8.101906	3.059278	Low
TCGA-J2-8192-01A	739	0	65	female	ii	T2	MX	N1	2.3294	8.904776	3.399652	Low
TCGA-J2-8194-01A	724	0	69	female	ii	T3	MX	N0	1.545451	9.428533	3.447677	Low
TCGA-J2-A4AD-01A	550	1	61	female	i	T1	MX	N0	3.633575	9.894987	3.950115	High
TCGA-J2-A4AE-01A	1079	0	77	female	i	T1	MX	N0	2.57772	8.087187	3.163764	Low
TCGA-J2-A4AG-01A	988	0	66	female	i	T1	MX	N0	2.139153	8.471338	3.221494	Low
TCGA-L4-A4E5-01A	578	0	48	female	i	T1	M0	N0	4.371322	10.01094	4.111089	High
TCGA-L4-A4E6-01A	435	0	67	male	i	T1	M0	N0	1.419039	7.983988	2.937666	Low
TCGA-L9-A443-01A	193	1	63	female	i	T1	MX	N0	2.581589	9.194513	3.539368	Low
TCGA-L9-A444-01A	307	0	60	female	i	T1	MX	N0	2.976687	8.985533	3.533783	Low
TCGA-L9-A50W-01A	442	1	75	male	ii	T1	MX	N1	1.782565	9.008194	3.344458	Low
TCGA-L9-A5IP-01A	58	1	40	female	iv	T3	M1	N2	4.408481	9.795951	4.044418	High
TCGA-L9-A743-01A	664	0	56	male	ii	T2	M0	N1	3.380054	8.898562	3.570878	Low

Appendix C11: continued

TCGA-L9-A7SV-01A	565	0	69	male	ii	T2	M0	N1	3.093283	7.389552	3.012583	Low
TCGA-L9-A8F4-01A	476	0	64	female	i	T2	MX	N0	3.679593	9.141755	3.702645	Low
TCGA-MN-A4N1-01A	827	0	60	male	ii	T2	M0	N1	4.422068	10.22514	4.191992	High
TCGA-MN-A4N4-01A	1175	0	57	male	i	T1	M0	N0	1.739345	10.00653	3.675387	Low
TCGA-MN-A4N5-01A	84	0	63	male	i	T1	M0	N0	4.039814	9.066678	3.736649	High
TCGA-MP-A4SV-01A	2620	1	67	male	i	T2	M0	N0	3.666504	9.684278	3.884196	High
TCGA-MP-A4SW-01A	1778	1	53	male	ii	T2	M0	N1	3.126145	9.521619	3.739971	High
TCGA-MP-A4SY-01A	1501	1	61	male	ii	T2	M0	N1	3.429564	10.40914	4.090561	High
TCGA-MP-A4T4-01A	2617	1	68	female	ii	T2	M0	N1	3.871333	9.139666	3.733569	High
TCGA-MP-A4T6-01A	1790	1	76	female	iii	T1	MX	N2	1.673001	8.880717	3.283216	Low
TCGA-MP-A4T7-01A	167	1	75	female	iv	T2	M1	N0	3.450122	10.11964	3.995922	High
TCGA-MP-A4T8-01A	161	1	68	male	iii	T2	M0	N2	3.339025	9.888724	3.899401	High
TCGA-MP-A4T9-01A	1265	1	54	female	iii	T2	MX	N2	3.942044	8.787725	3.626059	Low
TCGA-MP-A4TA-01A	950	1	75	female	i	T1	M0	N0	4.120932	9.207178	3.797608	High
TCGA-MP-A4TC-01A	74	1	77	male	iii	T1	M0	N2	3.560283	9.428335	3.780004	High
TCGA-MP-A4TD-01A	307	1	71	male	iii	T2	M0	N2	2.193046	9.275233	3.502602	Low
TCGA-MP-A4TE-01A	896	1	56	male	ii	T2	MX	N0	2.861152	10.4445	4.008762	High
TCGA-MP-A4TF-01A	336	1	58	female	ii	T2	M0	N0	4.303156	10.72242	4.340765	High
TCGA-MP-A4TH-01A	741	0	70	female	i	T1	M0	N0	1.413651	7.997094	2.941216	Low
TCGA-MP-A4TI-01A	429	1	72	male	ii	T2	M0	N1	3.804212	10.62631	4.225907	High
TCGA-MP-A4TJ-01A	339	1	62	female	i	T1	M0	N0	3.386002	8.923451	3.580287	Low
TCGA-MP-A4TK-01A	582	1	56	female	ii	T2	MX	N1	3.88386	9.210656	3.759675	High
TCGA-MP-A5C7-01A	2248	0	76	female	i	T2	M0	N0	1.326084	8.297983	3.028657	Low
TCGA-NJ-A4YF-01A	2161	0	50	female	i	T1	M0	N0	2.824948	9.115922	3.552903	Low
TCGA-NJ-A4YG-01A	2261	0	65	male	i	T2	M0	N0	1.898885	8.86729	3.315935	Low
TCGA-NJ-A4YI-01A	4	1	87	female	iii	T2	M0	N2	2.09424	8.553164	3.241793	Low
TCGA-NJ-A4YP-01A	50	0	52	male	i	T2	M0	N0	2.97884	9.494317	3.706425	Low
TCGA-NJ-A4YQ-01A	1432	0	69	female	i	T1	M0	N0	3.903737	9.670758	3.918755	High
TCGA-NJ-A55A-01A	15	0	76	female	i	T2	M0	N0	2.008524	7.804915	2.974278	Low
TCGA-NJ-A55O-01A	13	0	56	female	ii	T1	M0	N1	3.079817	9.51307	3.729433	High
TCGA-NJ-A55R-01A	603	0	67	male	i	T1	MX	N0	2.852981	9.737081	3.767867	High
TCGA-NJ-A7XG-01A	617	0	49	male	iii	T4	M0	N1	1.261012	8.984201	3.250291	Low
TCGA-O1-A52J-01A	1798	1	74	female	i	T1	MX	N0	2.115893	8.095636	3.090435	Low
TCGA-S2-AA1A-01A	513	0	68	female	i	T1	M0	N0	1.690707	8.932979	3.303835	Low

Appendix C12: Information on survival time, survival status, risk score, and grouping of LUAD patients in the GSE31210 cohort

ID	futime	fustat	RRM2	GAPDH	riskScore	risk
GSM773540	437	1	2183.513	19815.83	7070.318	High Risk
GSM773541	743	0	2552.547	21406.63	7669.881	High Risk
GSM773542	2601	0	2382.527	24163.53	8575.384	High Risk
GSM773543	1173	0	3425.058	17756.18	6577.695	High Risk
GSM773544	2369	0	638.7321	19496.25	6707.254	High Risk
GSM773545	1879	0	1383.579	15227.13	5384.512	High Risk
GSM773546	606	0	3418.775	18344.93	6776.022	High Risk
GSM773547	300	1	891.9826	19022.66	6588.663	High Risk
GSM773548	1919	0	1616.804	14749.36	5261.204	High Risk
GSM773549	1835	0	888.5214	16047.34	5580.581	High Risk
GSM773550	1828	0	937.9267	14952.07	5217.848	High Risk
GSM773551	1841	1	911.9627	12325.94	4324.296	High Risk
GSM773552	639	1	11276.44	25578.05	10521.63	High Risk
GSM773553	1311	1	3236.748	14200.8	5342.696	High Risk
GSM773554	1098	0	1894.934	11641.53	4254.704	High Risk
GSM773555	1189	0	8761.688	17248.59	7286.217	High Risk
GSM773558	1856	0	7172.269	24561.27	9500.247	High Risk
GSM773559	3067	0	11583.34	30992.86	12405.84	High Risk
GSM773560	1142	0	8144.796	18754.72	7694.458	High Risk
GSM773562	1610	0	12503.62	12207.13	6196.384	High Risk
GSM773563	2014	0	9248.728	15185.04	6667.802	High Risk
GSM773564	1826	0	1089.26	13504.5	4752.634	High Risk
GSM773565	2191	0	6581.664	19734.54	7768.372	High Risk
GSM773566	3342	0	1845.921	13196.27	4773.09	High Risk
GSM773568	2925	0	2648.691	17345.07	6310.406	High Risk
GSM773570	1724	0	1621.376	11799.73	4263.145	High Risk
GSM773571	2765	0	1175.682	17495.76	6118.425	High Risk
GSM773572	1529	0	5038.598	15090.49	5941.223	High Risk
GSM773573	221	1	6702.686	28348.08	10705.08	High Risk
GSM773574	546	1	4233.117	14374.62	5565.931	High Risk

Appendix C12: continued

GSM773575	346	1	2624.56	18927.15	6842.154	High Risk
GSM773576	853	1	800.3239	12807.43	4468.923	High Risk
GSM773578	817	0	2825.411	17211.5	6294.327	High Risk
GSM773579	425	1	2908.168	13935.79	5198.751	High Risk
GSM773580	1281	0	1553.186	13122.92	4699.958	High Risk
GSM773581	1044	0	5679.134	21695.32	8283.442	High Risk
GSM773582	565	0	7694.678	23275.05	9150.887	High Risk
GSM773583	1059	1	4457.677	18070.2	6854.385	High Risk
GSM773584	1625	1	2948.8	16588.83	6103.836	High Risk
GSM773585	1695	1	5084.338	21662.03	8174.046	High Risk
GSM773586	2976	0	8811.655	20752.45	8480.948	High Risk
GSM773587	1143	1	3535.337	11236.27	4388.096	High Risk
GSM773588	1682	0	1392.308	13913.84	4941.241	High Risk
GSM773589	1242	1	2910.242	19218.62	6987.981	High Risk
GSM773590	2252	0	2385.476	13960.71	5120.957	High Risk
GSM773591	943	1	5466.545	19208.06	7406.129	High Risk
GSM773592	1346	1	3597.136	15481.07	5835.68	High Risk
GSM773593	1482	1	4010.646	14093.26	5433.953	High Risk
GSM773597	259	1	1597.853	12183.23	4389.125	High Risk
GSM773598	2289	0	1878.804	21367.45	7545.465	High Risk
GSM773599	1916	0	3498.291	14798.63	5588.284	High Risk
GSM773600	2048	0	4509.907	12854.3	5096.779	High Risk
GSM773601	1475	0	8419.987	23304.97	9280.676	High Risk
GSM773603	636	0	7306.324	18965.44	7627.486	High Risk
GSM773604	1275	0	7262.816	19136.42	7678.205	High Risk
GSM773610	729	0	1077.095	12149.94	4291.942	High Risk
GSM773613	2009	0	11681.46	13660.48	6552.886	High Risk
GSM773615	3411	0	979.8915	14674.61	5130.816	High Risk
GSM773616	1806	0	14186.97	24122.19	10508.81	High Risk
GSM773617	1937	0	1170.806	14837.49	5217.467	High Risk
GSM773621	1597	0	6140.201	17595.08	6971.072	High Risk
GSM773627	2050	0	1733.335	13575.95	4883.083	High Risk

Appendix C12: continued

GSM773628	1256	0	5888.029	10355.5	4477.981	High Risk
GSM773630	1154	0	16318.91	14743.47	7684.669	High Risk
GSM773633	1596	0	5280.411	10577.5	4452.912	High Risk
GSM773636	1637	0	1476.256	17272.49	6092.407	High Risk
GSM773637	2034	0	1443.681	11927.11	4276.965	High Risk
GSM773639	779	1	4155.286	18984.63	7114.145	High Risk
GSM773640	540	1	1337.57	17379.15	6105.646	High Risk
GSM773641	1317	0	1693.081	14983.7	5353.138	High Risk
GSM773642	1980	0	1625.432	16701.13	5923.541	High Risk
GSM773643	702	1	2647.885	14930.62	5492.684	High Risk
GSM773644	564	1	1467.637	13047.51	4660.31	High Risk
GSM773645	788	1	2735.576	16510.17	6042.022	High Risk
GSM773646	1463	0	1852.758	14949.39	5367.865	High Risk
GSM773647	1345	1	1328.729	12300.2	4384.336	High Risk
GSM773649	2687	0	5469.236	19355.08	7456.357	High Risk
GSM773651	2668	0	5758.982	22956.8	8723.78	High Risk
GSM773652	1936	0	1192.122	16962	5940.392	High Risk
GSM773654	2671	0	2305.678	12968.12	4771.679	High Risk
GSM773655	1482	0	1007.621	11888.46	4191.936	High Risk
GSM773658	1229	1	10178.97	23686.17	9699.946	High Risk
GSM773659	2263	1	5929.145	21707.05	8328.662	High Risk
GSM773660	1770	0	2458.313	17377.77	6290.072	High Risk
GSM773661	1433	1	3595.089	19873.34	7322.667	High Risk
GSM773663	1988	0	743.013	14866.97	5156.876	High Risk
GSM773665	630	1	3961.766	19446.18	7238.513	High Risk
GSM773666	1537	0	3532.829	14328.63	5434.828	High Risk
GSM773667	1429	1	2981.175	13085.61	4922.903	High Risk
GSM773669	2486	0	1523.482	14850.31	5279.993	High Risk
GSM773673	1017	0	4531.141	14690.92	5722.204	High Risk
GSM773674	1041	0	7053.833	18379.04	7387.263	High Risk
GSM773675	1859	0	2026.61	13076.17	4762.23	High Risk
GSM773676	1717	0	2938.351	15259.61	5652.007	High Risk

Appendix C12: continued

GSM773677	1494	0	2131.179	15677.43	5660.328	High Risk
GSM773679	2364	0	1505.272	15324.18	5437.45	High Risk
GSM773680	1733	0	1028.987	13702.17	4809.625	High Risk
GSM773683	2913	0	5628.561	17056.83	6704.399	High Risk
GSM773688	1964	0	1415.796	12173.98	4355.959	High Risk
GSM773697	1998	0	5987.94	11968.9	5040.796	High Risk
GSM773702	3189	0	1705.581	12662.16	4569.074	High Risk
GSM773708	1412	0	734.6344	12322.61	4293.913	High Risk
GSM773713	1426	0	2307.207	11840.91	4390.233	High Risk
GSM773714	1674	0	1751.899	15492.82	5535.242	High Risk
GSM773716	1856	0	4617.449	15990.66	6176.564	High Risk
GSM773720	1114	0	770.9567	13412.82	4669.079	High Risk
GSM773723	1726	0	1867.19	13236.47	4790.21	High Risk
GSM773724	1629	0	1934.824	12907.56	4689.991	High Risk
GSM773727	1446	0	2008.242	13300.9	4835.299	High Risk
GSM773746	1947	0	2488.329	13212.97	4884.727	High Risk
GSM773749	2409	0	1924.021	11341	4157.737	High Risk
GSM773751	2430	0	2584.794	15410.05	5644.62	High Risk
GSM773756	1849	0	2543.053	13594.66	5023	High Risk
GSM773556	3863	0	2278.36	9695.859	3659.111	Low Risk
GSM773557	1475	0	2597.018	9741.436	3727.114	Low Risk
GSM773561	1825	0	662.3989	7550.712	2666.123	Low Risk
GSM773567	1328	0	1402.841	10531.07	3797.495	Low Risk
GSM773569	2880	0	1760.214	8768.159	3259.49	Low Risk
GSM773577	2661	1	2240.158	6467.617	2559.651	Low Risk
GSM773594	2386	0	378.1273	8553.192	2958.689	Low Risk
GSM773595	1560	0	691.7334	8493.741	2990.294	Low Risk
GSM773596	1001	1	428.345	8199.847	2847.323	Low Risk
GSM773602	1539	0	457.301	9260.665	3211.317	Low Risk
GSM773605	2005	0	1899.746	11240.73	4119.779	Low Risk
GSM773606	1965	0	286.3409	8848.169	3043.433	Low Risk
GSM773607	2425	0	606.755	7230.334	2548.456	Low Risk

Appendix C12: continued

GSM773608	1566	0	340.4119	8027.501	2774.456	Low Risk
GSM773609	990	0	538.6639	7750.908	2713.501	Low Risk
GSM773611	2354	0	601.7399	9069.609	3170.45	Low Risk
GSM773612	818	0	3235.666	9797.54	3851.473	Low Risk
GSM773614	2549	0	664.6868	10637.46	3711.745	Low Risk
GSM773618	1520	0	885.6568	8928.845	3169.623	Low Risk
GSM773619	1375	0	1051.194	11536.53	4079.954	Low Risk
GSM773620	1756	0	416.6226	7237.145	2519.396	Low Risk
GSM773622	1714	0	256.6318	7996.502	2750.137	Low Risk
GSM773623	1637	0	514.0172	5277.043	1871.728	Low Risk
GSM773624	1653	0	751.0739	7955.447	2817.805	Low Risk
GSM773625	1196	0	661.8991	8870.019	3112.789	Low Risk
GSM773626	1702	0	1331.233	7962.764	2915.994	Low Risk
GSM773629	818	0	509.5877	8778.146	3056.551	Low Risk
GSM773631	3058	0	1425.952	8571.931	3137.898	Low Risk
GSM773632	1941	0	2073.937	7964.348	3039.057	Low Risk
GSM773634	2450	0	942.5596	8377.001	2992.143	Low Risk
GSM773635	1881	0	937.1546	8768.98	3123.985	Low Risk
GSM773638	2134	0	221.0073	6018.91	2074.602	Low Risk
GSM773648	832	0	1698.139	9221.185	3402.654	Low Risk
GSM773650	1122	1	783.4527	11277.24	3947.984	Low Risk
GSM773653	871	0	1373.466	8321.28	3044.363	Low Risk
GSM773656	1128	0	1127.871	10847.32	3859.22	Low Risk
GSM773657	1042	1	923.4096	9686.949	3432.563	Low Risk
GSM773662	1823	0	568.7181	11811.1	4093.334	Low Risk
GSM773664	1434	0	820.347	5428.987	1973.716	Low Risk
GSM773668	1038	1	1050.54	6604.684	2409.81	Low Risk
GSM773670	740	0	875.2963	10029.42	3540.594	Low Risk
GSM773671	1042	0	901.4685	6391.72	2313.102	Low Risk
GSM773672	1267	0	1644.96	10277.57	3751.596	Low Risk
GSM773678	754	0	1337.587	10977.96	3938.056	Low Risk
GSM773681	1941	0	233.457	6032.149	2081.139	Low Risk

Appendix C12: continued

GSM773682	774	0	832.9404	11353.22	3981.875	Low Risk
GSM773684	1803	0	743.507	8977.392	3162.611	Low Risk
GSM773685	1912	0	623.6043	7647.86	2692.62	Low Risk
GSM773686	1481	0	619.5579	6109.621	2171.069	Low Risk
GSM773687	1231	0	686.2375	9153.297	3212.729	Low Risk
GSM773689	3352	0	520.4593	7943.85	2775.833	Low Risk
GSM773690	2158	0	1009.86	11322.71	4000.732	Low Risk
GSM773691	3466	0	761.1533	7004.107	2497.322	Low Risk
GSM773692	3263	0	699.737	7607.816	2691.62	Low Risk
GSM773693	1823	0	640.2124	7461.559	2632.274	Low Risk
GSM773694	1856	0	2636.881	10408.3	3959.507	Low Risk
GSM773695	2449	0	723.7404	9870.694	3461.843	Low Risk
GSM773696	1859	0	299.7207	4568.786	1596.542	Low Risk
GSM773698	1852	0	1011.534	9354.112	3334.394	Low Risk
GSM773699	1894	0	669.7923	5125.254	1846.027	Low Risk
GSM773700	1861	0	1077.376	8384.213	3016.827	Low Risk
GSM773701	1669	0	1022.523	8355.91	2998.193	Low Risk
GSM773703	1822	0	2896.931	8212.222	3258.765	Low Risk
GSM773704	1809	0	728.2268	5388.08	1944.666	Low Risk
GSM773705	2552	0	1009.549	8809.174	3149.538	Low Risk
GSM773706	2968	0	268.6807	6068.238	2099.171	Low Risk
GSM773707	3066	0	812.7386	11680.72	4089.44	Low Risk
GSM773709	1317	0	1137.309	5844.244	2166.622	Low Risk
GSM773710	1180	0	610.9787	6255.416	2219.024	Low Risk
GSM773711	1688	0	452.2593	8322.686	2892.864	Low Risk
GSM773712	1417	0	488.5992	3660.649	1320.186	Low Risk
GSM773715	1848	0	1546.068	10805.82	3914.159	Low Risk
GSM773717	1780	0	2457.809	8289.456	3212.475	Low Risk
GSM773718	2084	0	580.8934	7637.865	2682.189	Low Risk
GSM773719	1879	0	422.2543	5833.199	2044.917	Low Risk
GSM773721	2806	0	616.5497	7902.774	2777.776	Low Risk
GSM773722	1663	0	877.6795	10484.42	3695.06	Low Risk

Appendix C12: continued

GSM773725	2179	0	1279.155	10343.73	3713.651	Low Risk
GSM773726	1917	0	821.1773	11342.62	3976.345	Low Risk
GSM773728	1162	0	698.5386	7798.798	2756.093	Low Risk
GSM773729	1231	0	1255.164	9032.086	3265.541	Low Risk
GSM773730	941	0	1236.777	11154.79	3981.305	Low Risk
GSM773731	1623	0	862.2058	6710.05	2414.419	Low Risk
GSM773732	1855	0	535.0821	4055.68	1461.621	Low Risk
GSM773733	1404	0	919.2522	6783.489	2448.698	Low Risk
GSM773734	2221	0	522.2342	4400.162	1576.151	Low Risk
GSM773735	849	0	568.113	6712.17	2366.619	Low Risk
GSM773736	831	0	823.2625	7505.094	2677.214	Low Risk
GSM773737	3219	0	2121.102	6391.263	2514.155	Low Risk
GSM773738	2585	0	1155.67	4430.864	1691.048	Low Risk
GSM773739	2442	0	355.5437	8284.165	2863.864	Low Risk
GSM773740	1910	0	2307.99	9369.332	3553.429	Low Risk
GSM773741	1834	0	639.57	9266.977	3243.524	Low Risk
GSM773742	2918	0	2545.503	6616.29	2660.369	Low Risk
GSM773743	2285	0	967.1256	7134.338	2575.401	Low Risk
GSM773744	2149	0	381.4822	5296.857	1856.572	Low Risk
GSM773745	2561	0	3175.365	8715.413	3475.091	Low Risk
GSM773747	1841	0	470.0926	10695.6	3699.329	Low Risk
GSM773748	1971	0	674.7801	5665.924	2029.933	Low Risk
GSM773750	1624	0	535.5624	6432.619	2266.587	Low Risk
GSM773752	1856	0	452.1499	5670.711	1994.826	Low Risk
GSM773753	1516	0	1084.858	8232.772	2966.779	Low Risk
GSM773754	1819	0	1134.03	10946.75	3893.908	Low Risk
GSM773755	2413	0	548.4941	7928.772	2775.352	Low Risk
GSM773757	2181	0	662.9781	9962.128	3482.78	Low Risk
GSM773758	2168	0	395.0383	8971.808	3103.232	Low Risk
GSM773759	2154	0	487.217	5850.392	2061.456	Low Risk
GSM773760	2073	0	584.1912	8856.486	3095.386	Low Risk
GSM773761	1994	0	743.02	8168.766	2888.711	Low Risk

Appendix C12: continued

GSM773762	2137	0	577.4151	7527.626	2644.286	Low Risk
GSM773763	1998	0	593.3719	8121.011	2847.852	Low Risk
GSM773764	1908	0	1714.741	10489.92	3835.016	Low Risk
GSM773765	1660	0	532.8082	7308.202	2562.625	Low Risk