

Contents

Glossary	xiii
Acronyms	xiv
1 Introduction and Literature Review	1
1.1 Cancer Research in the Post-Genomic Era	1
1.1.1 Cancer is a Global Health Issue	2
1.1.1.1 The Genetics and Molecular Biology of Cancers	3
1.1.2 The genomic Revolution in Cancer Research	4
1.1.2.1 High-Throughput Technologies	4
1.1.2.2 Bioinformatics and Genomic Data	6
1.1.3 Genomics Projects	6
1.1.3.1 The Cancer Genome Project	6
1.1.3.2 The Cancer Genome Atlas Project	7
1.1.4 Genomic Cancer Medicine	9
1.1.4.1 Cancer Genes and Driver Mutations	9
1.1.4.2 Precision Cancer Medicine	10
1.1.4.3 Molecular Diagnostics and Pan-Cancer Medicine	10
1.1.4.4 Targeted Therapeutics and Pharmacogenomics	10
1.1.5 Systems and Network Biology	11
1.1.5.1 Network Medicine and Polypharmacology	13
1.2 A Synthetic Lethal Approach to Cancer Medicine	14
1.2.1 Synthetic Lethal Genetic Interactions	14
1.2.2 Synthetic Lethal Concepts in Genetics	15
1.2.3 Synthetic Lethality in Model Systems	16
1.2.3.1 Synthetic Lethal Pathways and Networks	16
1.2.3.2 Evolution of Synthetic Lethality	17
1.2.4 Synthetic Lethality in Cancer	18
1.2.5 Clinical Impact of Synthetic Lethality in Cancer	19
1.2.6 High-throughput Screening for Synthetic Lethality	21
1.2.6.1 Synthetic Lethal Screens	22
1.2.7 Computational Prediction of Synthetic Lethality	25
1.2.7.1 Bioinformatics Approaches to Genetic Interactions	25
1.2.7.2 Comparative Genomics	26
1.2.7.3 Analysis and Modelling of Protein Data	29
1.2.7.4 Differential Gene Expression	31

1.2.7.5	Data Mining and Machine Learning	32
1.2.7.6	Mutually Exclusive Bimodality	35
1.2.7.7	Rationale for Further Development	36
1.3	E-cadherin as a Synthetic Lethal Target	36
1.3.1	The <i>CDH1</i> gene and its Biological Functions	36
1.3.1.1	Cytoskeleton	37
1.3.1.2	Extracellular and Tumour Micro-environment	37
1.3.1.3	Cell-Cell Adhesion and Signalling	37
1.3.2	<i>CDH1</i> as a Tumour (and Invasion) Suppressor	38
1.3.2.1	Breast Cancers and Invasion	38
1.3.3	Hereditary Diffuse Gastric Cancer and Lobular Breast Cancer	38
1.3.4	Cell Line Models of <i>CDH1</i> Null Mutations	40
1.4	Summary and Research Direction of Thesis	40
1.4.1	Thesis Aims	42
2	Methods and Resources	43
2.1	Bioinformatics Resources for Genomics Research	43
2.1.1	Public Data and Software Packages	43
2.1.1.1	Cancer Genome Atlas Data	44
2.1.1.2	Reactome and Annotation Data	45
2.2	Data Handling	45
2.2.1	Normalisation	45
2.2.2	Sample Triage	46
2.2.3	Metagenes and the Singular Value Decomposition	46
2.2.3.1	Candidate Triage and Integration with Screen Data	48
2.3	Techniques	49
2.3.1	Statistical Procedures and Tests	49
2.3.2	Gene Set Over-representation Analysis	50
2.3.3	Clustering	50
2.3.4	Heatmap	50
2.3.5	Modeling and Simulations	51
2.3.5.1	Receiver Operating Characteristic (Performance)	52
2.3.6	Resampling Analysis	52
2.4	Pathway Structure Methods	53
2.4.1	Network and Graph Analysis	53
2.4.2	Sourcing Graph Structure Data	54
2.4.3	Constructing Pathway Subgraphs	54
2.4.4	Network Analysis Metrics	55
2.5	Implementation	56
2.5.1	Computational Resources and Linux Utilities	56
2.5.2	R Language and Packages	57
2.5.3	High Performance and Parallel Computing	60

3	Methods Developed During Thesis	62
3.1	A Synthetic Lethal Detection Methodology	62
3.2	Synthetic Lethal Simulation and Modelling	65
3.2.1	A Model of Synthetic Lethality in Expression Data	65
3.2.2	Simulation Procedure	69
3.3	Detecting Simulated Synthetic Lethal Partners	72
3.3.1	Binomial Simulation of Synthetic Lethality	72
3.3.2	Multivariate Normal Simulation of Synthetic Lethality	74
3.3.2.1	Multivariate Normal Simulation with Correlated Genes	77
3.3.2.2	Specificity with Query-Correlated Pathways	84
3.3.2.3	Importance of Directional Testing	84
3.4	Graph Structure Methods	86
3.4.1	Upstream and Downstream Gene Detection	86
3.4.1.1	Permutation Analysis for Statistical Significance	87
3.4.1.2	Hierarchy Based on Biological Context	88
3.4.2	Simulating Gene Expression from Graph Structures	89
3.5	Customised Functions and Packages Developed	93
3.5.1	Synthetic Lethal Interaction Prediction Tool	93
3.5.2	Data Visualisation	94
3.5.3	Extensions to the iGraph Package	97
3.5.3.1	Sampling Simulated Data from Graph Structures	97
3.5.3.2	Plotting Directed Graph Structures	97
3.5.3.3	Computing Information Centrality	98
3.5.3.4	Testing Pathway Structure with Permutation Testing	98
3.5.3.5	Metapackage to Install iGraph Functions	99
4	Synthetic Lethal Analysis of Gene Expression Data	100
4.1	Synthetic Lethal Genes in Breast Cancer	101
4.1.1	Synthetic Lethal Pathways in Breast Cancer	103
4.1.2	Expression Profiles of Synthetic Lethal Partners	104
4.1.2.1	Subgroup Pathway Analysis	107
4.2	Comparing Synthetic Lethal Gene Candidates	110
4.2.1	Primary siRNA Screen Candidates	110
4.2.2	Comparison with Correlation	110
4.2.3	Comparison with Primary Screen Viability	112
4.2.4	Comparison with Secondary siRNA Screen Validation	114
4.2.5	Comparison to Primary Screen at Pathway Level	116
4.2.5.1	Resampling Genes for Pathway Enrichment	118
4.2.6	Integrating Synthetic Lethal Pathways and Screens	121
4.3	Metagene Analysis	123
4.3.1	Pathway Expression	124
4.3.2	Somatic Mutation	126
4.3.3	Synthetic Lethal Pathway Metagenes	130
4.3.4	Synthetic Lethality in Breast Cancer	131
4.4	Replication in Stomach Cancer	132
4.5	Discussion	133

4.5.1	Strengths of the SLIPT Methodology	133
4.5.2	Synthetic Lethal Pathways for E-cadherin	134
4.5.3	Replication and Validation	136
4.5.3.1	Integration with short interfering RNA (siRNA) Screen- ing	136
4.5.3.2	Replication across Tissues	137
4.6	Summary	137
5	Synthetic Lethal Pathway Structure	139
5.1	Synthetic Lethal Genes in Reactome Pathways	139
5.1.1	The PI3K/AKT Pathway	140
5.1.2	The Extracellular Matrix	142
5.1.3	G Protein Coupled Receptors	145
5.1.4	Gene Regulation and Translation	145
5.2	Network Analysis of Synthetic Lethal Genes	146
5.2.1	Gene Connectivity and Vertex Degree	147
5.2.2	Gene Importance and Centrality	148
5.2.2.1	Information Centrality	148
5.2.2.2	PageRank Centrality	150
5.3	Relationships between Synthetic Lethal Genes	152
5.3.1	Hierarchical Pathway Structure	152
5.3.1.1	Contextual Hierarchy of PI3K	152
5.3.1.2	Testing Contextual Hierarchy of Synthetic Lethal Genes	152
5.3.2	Upstream or Downstream Synthetic Lethality	156
5.3.2.1	Measuring Structure of Candidates within PI3K	156
5.3.2.2	Resampling for Synthetic Lethal Pathway Structure . .	158
5.4	Discussion	160
5.5	Summary	162
6	Simulation and Modeling of Synthetic Lethal Pathways	164
6.1	Synthetic Lethal Detection Methods	165
6.1.1	Performance of SLIPT and χ^2 across Quantiles	165
6.1.1.1	Correlated Query Genes affects Specificity	169
6.1.2	Alternative Synthetic Lethal Detection Strategies	171
6.1.2.1	Correlation for Synthetic Lethal Detection	171
6.1.2.2	Testing for Bimodality with BiSEp	173
6.2	Simulations with Graph Structures	174
6.2.1	Performance over Graph Structures	175
6.2.1.1	Simple Graph Structures	175
6.2.1.2	Constructed Graph Structures	177
6.2.2	Performance with Inhibitions	180
6.2.3	Synthetic Lethality across Graph Structures	185
6.2.4	Performance within a Simulated Human Genome	189
6.3	Simulations in More Complex Graph Structures	193
6.3.1	Simulations over Pathway-based Graphs	194
6.3.2	Pathway Structures in a Simulated Human Genome	197

6.4	Discussion	200
6.4.1	Simulation Procedure	200
6.4.2	Comparing Methods with Simulated Data	201
6.4.3	Design and Performance of SLIPT	202
6.4.4	Simulations from Graph Structures	204
6.5	Summary	205
7	Discussion	207
7.1	Synthetic Lethality and <i>CDH1</i> Biology	207
7.1.1	Established Functions of <i>CDH1</i>	208
7.1.2	The Molecular Role of <i>CDH1</i> in Cancer	208
7.2	Significance	209
7.2.1	Synthetic Lethality in the Genomic Era	209
7.2.2	Clinical Interventions based on Synthetic Lethality	211
7.3	Future Directions	212
7.4	Conclusions	214
	Bibliography	216
A	Sample Quality	240
A.1	Sample Correlation	240
A.2	Replicate Samples in The Cancer Genome Atlas (TCGA) Breast	242
B	Software Used for Thesis	246
C	Mutation Analysis in Breast Cancer	255
C.1	Synthetic Lethal Genes and Pathways	255
C.2	Synthetic Lethal Expression Profiles	256
C.3	Comparison to Primary Screen	259
C.3.1	Resampling Analysis	261
C.4	Compare Synthetic Lethal Interaction Prediction Tool (SLIPT) genes	263
C.5	Metagene Analysis	265
C.6	Expression of Somatic Mutations	266
C.7	Metagene Expression Profiles	269
D	Intrinsic Subtyping	272
E	Stomach Expression Analysis	274
E.1	Synthetic Lethal Genes and Pathways	274
E.2	Comparison to Primary Screen	278
E.2.1	Resampling Analysis	280
E.3	Metagene Analysis	282
F	Synthetic Lethal Genes in Pathways	283
G	Pathway Connectivity for Mutation SLIPT	291

H	Information Centrality for Gene Essentiality	295
I	Pathway Structure for Mutation SLIPT	298
J	Performance of SLIPT and χ^2	301
	J.1 Correlated Query Genes affects Specificity	307
K	Simulations on Graph Structures	313
	K.0.1 Simulations from Inhibiting Graph Structures	314
	K.1 Simulation across Graph Structures	317
	K.2 Simulations from Complex Graph Structures	321
	K.2.1 Simulations from Complex Inhibiting Graphs	324
	K.3 Simulations from Pathway Graph Structures	330

List of Figures

1.1	Synthetic genetic interactions	15
1.2	Synthetic lethality in cancer	19
2.1	Read count density	47
2.2	Read count sample mean	47
3.1	Framework for synthetic lethal prediction	63
3.2	Synthetic lethal prediction adapted for mutation	64
3.3	A model of synthetic lethal gene expression	66
3.4	Modeling synthetic lethal gene expression	67
3.5	Synthetic lethality with multiple genes	68
3.6	Simulating gene function	70
3.7	Simulating synthetic lethal gene function	70
3.8	Simulating synthetic lethal gene expression	71
3.9	Performance of binomial simulations	73
3.10	Comparison of statistical performance	73
3.11	Performance of multivariate normal simulations	75
3.12	Simulating expression with correlated gene blocks	78
3.13	Simulating expression with correlated gene blocks	79
3.14	Synthetic lethal prediction across simulations	80
3.15	Performance with correlations	81
3.16	Comparison of statistical performance with correlation structure	82
3.17	Performance with query correlations	83
3.18	Statistical evaluation of directional criteria	84
3.19	Performance of directional criteria	85
3.20	Simulated graph structures	89
3.21	Simulating expression from a graph structure	91
3.22	Simulating expression from graph structure with inhibitions	92
3.23	Demonstration of violin plots with custom features	95
3.24	Demonstration of annotated heatmap	95
3.25	Simulating graph structures	98
4.1	Synthetic lethal expression profiles of analysed samples	106
4.2	Comparison of SLIPT to siRNA	110
4.3	Compare SLIPT and siRNA genes with correlation	111
4.4	Compare SLIPT and siRNA genes with correlation	112
4.5	Compare SLIPT and siRNA genes with viability	113

4.6	Compare SLIPT genes with siRNA viability	114
4.7	Resampled intersection of SLIPT and siRNA candidates	118
4.8	Pathway metagene expression profiles	125
4.9	Expression profiles for constituent genes of PI3K	127
4.10	Expression profiles for estrogen receptor related genes	128
4.11	Somatic mutation against the PI3K metagene	129
5.1	synthetic lethality in the PI3K cascade	141
5.2	synthetic lethality in Elastic Fibre Formation	143
5.3	Synthetic lethality in Fibrin Clot Formation	144
5.4	Synthetic lethality and vertex degree	147
5.5	Synthetic lethality and centrality	150
5.6	Synthetic lethality and PageRank	151
5.7	Hierarchical structure of PI3K	153
5.8	Hierarchy score in PI3K against synthetic lethality in PI3K	154
5.9	Structure of synthetic lethality in PI3K	156
5.10	Structure of synthetic lethality resampling in PI3K	157
6.1	Performance of χ^2 and SLIPT across quantiles	167
6.2	Performance of χ^2 and SLIPT across quantiles with more genes	168
6.3	Performance of χ^2 and SLIPT across quantiles with query correlation	169
6.4	Performance of χ^2 and SLIPT across quantiles with query correlation and more genes	170
6.5	Performance of negative correlation and SLIPT	172
6.6	Simple graph structures	175
6.7	Performance of simulations on a simple graph	176
6.8	Performance of simulations is similar in simple graphs	178
6.9	Performance of simulations on a pathway	179
6.10	Performance of simulations on a simple graph with inhibition	181
6.11	Performance is higher on a simple inhibiting graph	182
6.12	Performance of simulations on a constructed graph with inhibition	183
6.13	Performance is affected by inhibition in graphs	185
6.14	Detection of synthetic lethality within a graph structure	187
6.15	Performance of simulations including a simple graph	190
6.16	Performance on a simple graph improves with more genes	191
6.17	Performance on an inhibiting graph improves with more genes	193
6.18	Performance of simulations on the PI3K cascade	196
6.19	Performance of simulations including the PI3K cascade	198
6.20	Performance on pathways improves with more genes	199
A.1	Correlation profiles of removed samples	240
A.2	Correlation analysis and sample removal	241
A.3	Replicate excluded samples	242
A.4	Replicate samples with all remaining	243
A.5	Replicate samples with some excluded	244
C.1	Synthetic lethal expression profiles of analysed samples	257

C.2	Comparison of mtSLIPT to siRNA	259
C.3	Compare mtSLIPT and siRNA genes with correlation	263
C.4	Compare mtSLIPT and siRNA genes with correlation	263
C.5	Compare mtSLIPT and siRNA genes with siRNA viability	264
C.6	Somatic mutation against PIK3CA metagene	266
C.7	Somatic mutation against PI3K protein	267
C.8	Somatic mutation against AKT protein	268
C.9	Pathway metagene expression profiles	269
C.10	Expression profiles for p53 related genes	270
C.11	Expression profiles for BRCA related genes	271
E.1	Synthetic lethal expression profiles of stomach samples	276
E.2	Comparison of SLIPT in stomach to siRNA	278
F.1	Synthetic lethality in the PI3K/AKT pathway	283
F.2	Synthetic lethality in the PI3K/AKT pathway in cancer	284
F.3	Synthetic lethality in the Extracellular Matrix	285
F.4	Synthetic lethality in the GPCRs	286
F.5	Synthetic lethality in the GPCR Downstream	287
F.6	Synthetic lethality in the Translation Elongation	288
F.7	Synthetic lethality in the Nonsense-mediated Decay	289
F.8	Synthetic lethality in the 3' UTR	290
G.1	Synthetic lethality and vertex degree	291
G.2	Synthetic lethality and centrality	292
G.3	Synthetic lethality and PageRank	293
H.1	Information centrality distribution	297
I.1	Synthetic lethality and heirarchy score in PI3K	298
I.2	Heirarchy score in PI3K against synthetic lethality in PI3K	299
I.3	Structure of synthetic lethality in PI3K	299
I.4	Structure of synthetic lethality resampling	300
J.1	Performance of χ^2 and SLIPT across quantiles	301
J.2	Performance of χ^2 and SLIPT across quantiles	303
J.3	Performance of χ^2 and SLIPT across quantiles with more genes	305
J.4	Performance of χ^2 and SLIPT across quantiles with query correlation	307
J.5	Performance of χ^2 and SLIPT across quantiles with query correlation	309
J.6	Performance of χ^2 and SLIPT across quantiles with query correlation and more genes	311
K.1	Performance of simulations on a simple graph	313
K.2	Performance of simulations on an inhibiting graph	314
K.3	Performance of simulations on a constructed graph with inhibition	315
K.4	Performance of simulations on a constructed graph with inhibition	316
K.5	Detection of synthetic lethality within a graph structure	317
K.6	Detection of synthetic lethality within an inhibiting graph	319

K.7	Detection of synthetic lethality within an inhibiting graph	320
K.8	Performance of simulations on a branching graph	321
K.9	Performance of simulations on a complex graph	322
K.10	Performance of simulations on a large graph	323
K.11	Performance of simulations on a branching graph with inhibition	324
K.12	Performance of simulations on a branching graph with inhibition	325
K.13	Performance of simulations on a complex graph with inhibition	326
K.14	Performance of simulations on a complex graph with inhibition	327
K.15	Performance of simulations on a large constructed graph with inhibition	328
K.16	Performance of simulations on a large constructed graph with inhibition	329
K.17	Performance of simulations on the $G_{\alpha i}$ signalling pathway	330
K.18	Performance of simulations including the $G_{\alpha i}$ signalling pathway	331

List of Tables

1.1	Methods for predicting genetic interactions	26
1.2	Methods for predicting synthetic lethality in cancer	27
1.3	Methods used by Wu <i>et al.</i> (2014)	28
2.1	Excluded samples by batch and clinical characteristics.	46
2.2	Computers used during thesis	56
2.3	Linux utilities and applications used during thesis	57
2.4	R installations used during thesis	58
2.5	R Packages used during thesis	58
2.6	R packages developed during thesis	60
4.1	Candidate synthetic lethal gene partners of <i>CDH1</i> from SLIPT	102
4.2	Pathways for <i>CDH1</i> partners from SLIPT	104
4.3	Pathways for clusters of <i>CDH1</i> partners from SLIPT	108
4.4	ANOVA for synthetic lethality and correlation with <i>CDH1</i>	112
4.5	Comparing SLIPT genes against secondary siRNA screen	115
4.6	Pathways for <i>CDH1</i> partners from SLIPT and siRNA	117
4.7	Pathways for <i>CDH1</i> partners from SLIPT	120
4.8	Pathways for <i>CDH1</i> partners from SLIPT and siRNA primary screen .	122
4.9	Candidate synthetic lethal metagenes against <i>CDH1</i> from SLIPT	131
5.1	ANOVA for synthetic lethality and vertex degree	148
5.2	ANOVA for synthetic lethality and information centrality	150
5.3	ANOVA for synthetic lethality and PageRank centrality	152
5.4	ANOVA for synthetic lethality and PI3K hierarchy	155
5.5	Resampling for pathway structure of synthetic lethal detection methods	159
B.1	Complete list of R packages used during this thesis	246
C.1	Candidate synthetic lethal gene partners of <i>CDH1</i> from mtSLIPT	255
C.2	Pathways for <i>CDH1</i> partners from mtSLIPT	256
C.3	Pathways for clusters of <i>CDH1</i> partners from mtSLIPT	258
C.4	Pathways for <i>CDH1</i> partners from mtSLIPT and siRNA	260
C.5	Pathways for <i>CDH1</i> partners from mtSLIPT	261
C.6	Pathways for <i>CDH1</i> partners from mtSLIPT and siRNA primary screen	262
C.7	Candidate synthetic lethal metagenes against <i>CDH1</i> from mtSLIPT . .	265
D.1	Comparison of intrinsic subtypes	272

E.1	Synthetic lethal gene partners of <i>CDH1</i> from SLIPT in stomach cancer	274
E.2	Pathways for <i>CDH1</i> partners from SLIPT in stomach cancer	275
E.3	Pathways for clusters of <i>CDH1</i> partners in stomach SLIPT	277
E.4	Pathways for <i>CDH1</i> partners from SLIPT and siRNA	279
E.5	Pathways for <i>CDH1</i> partners from SLIPT in stomach cancer	280
E.6	Pathways for <i>CDH1</i> partners from SLIPT in stomach and siRNA	281
E.7	Synthetic lethal metagenes against <i>CDH1</i> in stomach cancer	282
G.1	ANOVA for synthetic lethality and vertex degree	294
G.2	ANOVA for synthetic lethality and information centrality	294
G.3	ANOVA for synthetic lethality and PageRank centrality	294
H.1	Information centrality for genes and molecules in the Reactome network	296
I.1	ANOVA for synthetic lethality and PI3K hierarchy	298
I.2	Resampling for pathway structure of synthetic lethal detection methods	300

Glossary

E-cadherin	Epithelial cadherin (calcium-dependent adhesion), a cell-adhesion protein encoded by <i>CDH1</i> .
gene expression	A measure of the relative expression of each gene from the mRNA extracted from (pooled) cells.
graph or network	A mathematical structure modelling or depicting the relationships between elements.
metagene	A consistent signal of expression for a collection of genes such as a biological pathway, derived from singular value decomposition.
mutation	A change in DNA sequence that disrupts gene function.
synthetic lethal	Genetic interactions where inactivation of multiple genes is inviable (or deleterious) which are viable if inactivated separately.

Acronyms

ANOVA	Analysis of Variance.
CRAN	comprehensive R archive network.
ER	Estrogen Receptor.
mtSLIPT	Synthetic Lethal Interaction Prediction Tool (against mutation).
PAM50	Prediction Analysis of Microarray 50.
siRNA	Short Interfering RNA.
SLIPT	Synthetic Lethal Interaction Prediction Tool.
TCGA	The Cancer Genome Atlas (genomics project).

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Appendix A

Sample Quality

A.1 Sample Correlation

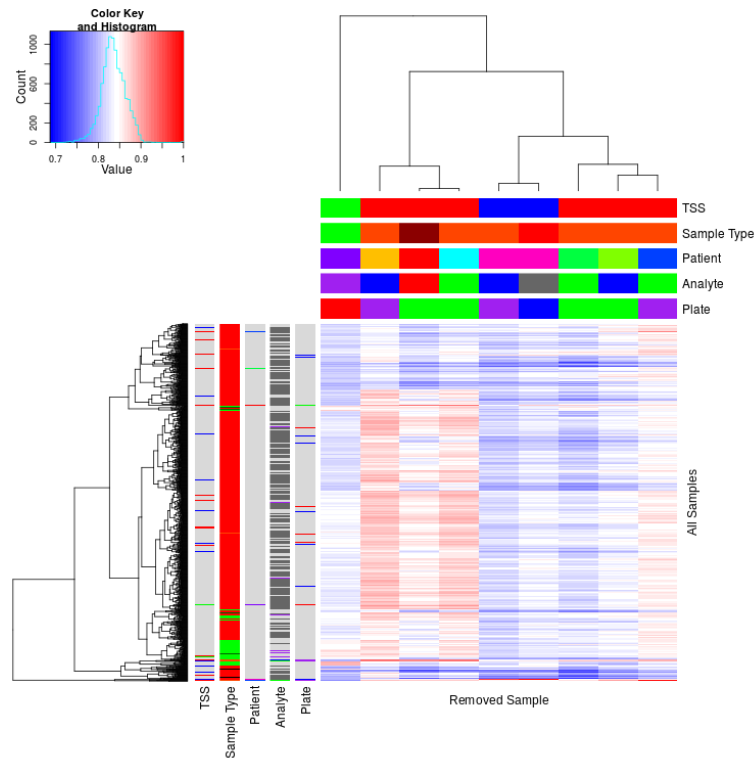


Figure A.1: **Correlation profiles of removed samples.** Heatmap (Euclidean distance) of samples in [TCGA](#) breast cancer dataset (left) clustered for all samples against removed samples (top): tissue source site (TSS), sample type with reds for tumour and greens for normal, patient (A2QH in pink), with varied analyte and plate. Excluded samples clustered at the bottom and annotation (left) show shared properties between samples in the dataset.

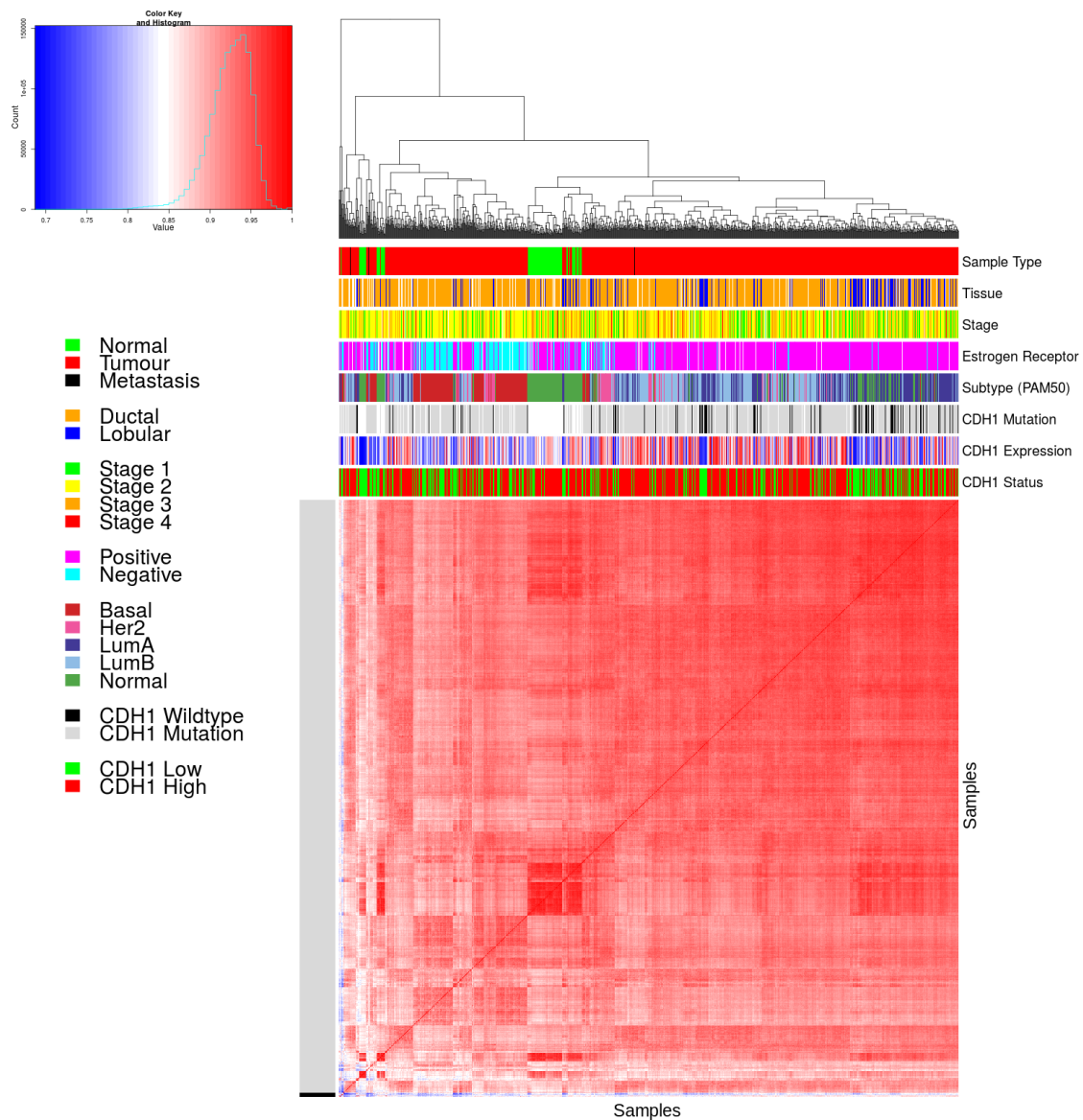


Figure A.2: **Correlation analysis and sample removal.** Correlation matrix heatmap (Euclidean distance) of all samples in TCGA breast cancer dataset against each other annotated for sample clinical data: sample type, tissue type, tumour stage, Estrogen receptor (ER) and intrinsic subtype (from the PAM50 method). *CDH1* somatic mutation, gene expression, and status for SLIPT prediction were also annotated. Discrete variables were coloured as displayed in the legend and continuous variables on a blue–red scale as shown in the colour key. Trimmed samples cluster at the bottom of the heatmap and the colour bars of the left show which were removed for quality concerns.

A.2 Replicate Samples in TCGA Breast

Replicate samples were picked where possible from the TCGA breast cancer gene expression data to examine for sample quality. Independent samples of the same tumour were expected to have very high Pearson correlation between their expression profiles unless there were issues with sample collection or preparation and were thus an indicator of sample quality. The log-transformed raw read counts for replicate samples were examined in Figures A.3–A.5. These were examined before normalisation which would be expected to increase sample concordance.

Another consideration was the samples which were removed for quality concerns (in Section 2.2.2). While these were selected by unbiased hierarchical clustering (See Figure A.2), many of the excluded (tumour) samples were performed in replicate despite relatively few replicate samples in the overall dataset. These samples correlate poorly with the rest of the dataset, in addition to correlation with replicate samples.

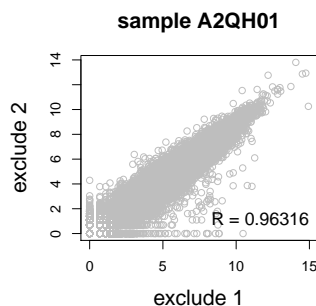


Figure A.3: **Replicate excluded samples.** Both tumour samples of patient A2QH were excluded as they were poorly correlated with other samples, although they were highly similar to each other as shown by Pearson correlation of log-raw counts.

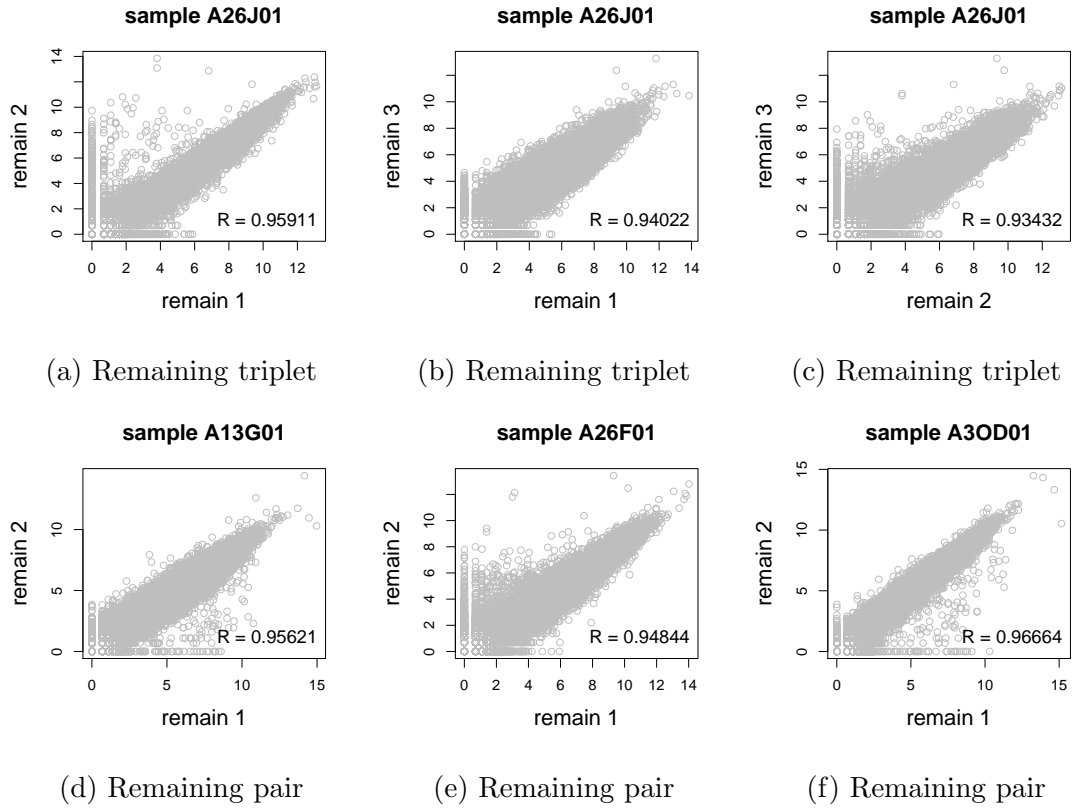


Figure A.4: **Replicate samples with all remaining.** Patient A26J was sampled 3 times and compared pairwise. Pairs of samples were also compared for other patients with replicate samples. In all cases, replicate samples remaining in the dataset were highly concordant, as shown by Pearson correlation of log-raw counts.

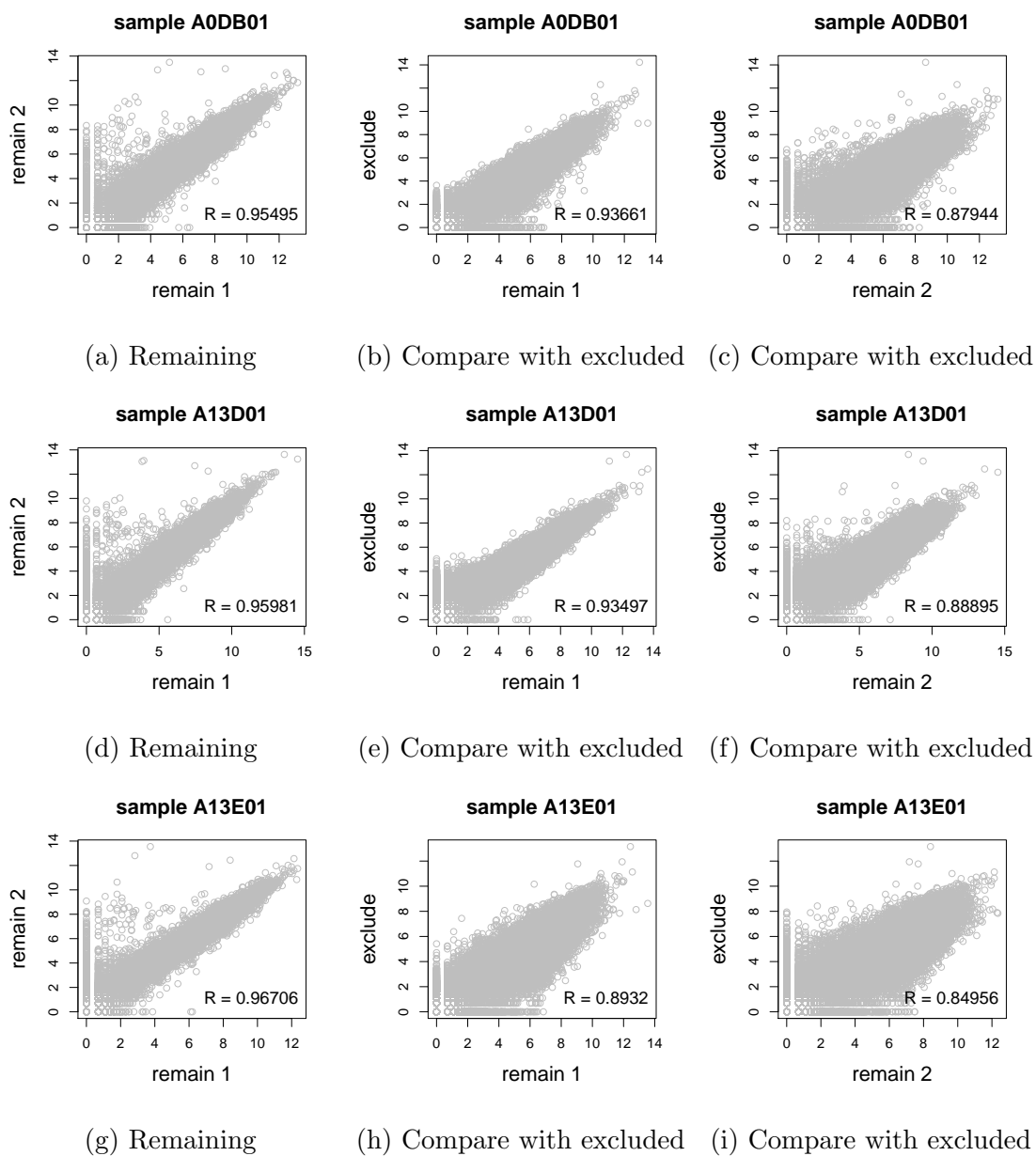


Figure A.5: **Replicate samples with some excluded.** (continued on next page)

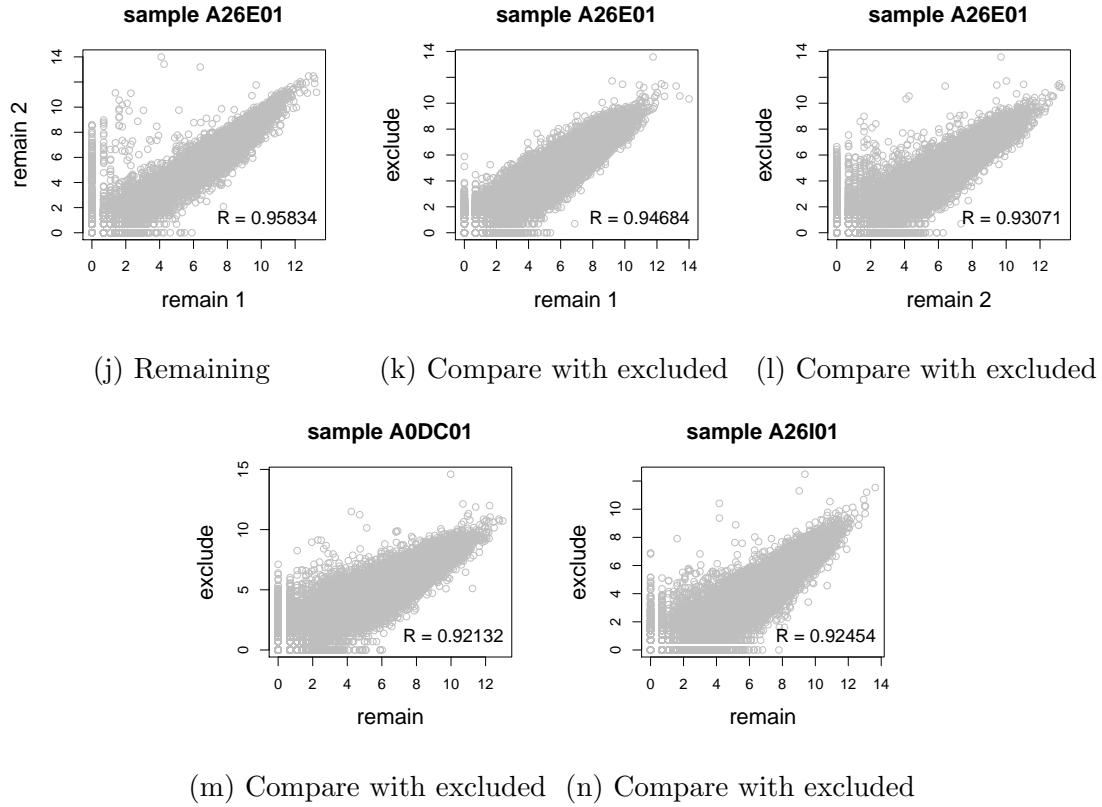


Figure A.5: **Replicate samples with some excluded.** Patients A0DB, A13D, A13E, and A26E were each sampled 3 times and compared pairwise. Pairs of samples were also compared for other patients with replicate samples. In all cases, the replicate samples remaining in the dataset more were highly concordant than those excluded from the analysis, as shown by Pearson correlation of log-raw counts.

Appendix B

Software Used for Thesis

Table B.1: Complete list of R packages used during this thesis

Package	Repository	Laptop	Lab	Server	NeSI
base	base	3.3.2	3.3.2	3.3.1	3.3.0
abind	CRAN		1.4-5		1.4-3
acepack	CRAN		1.4.1		1.3-3.3
ade4	CRAN		1.7-5		
annaffy	Bioconductor		1.46.0		
AnnotationDbi	Bioconductor		1.36.0	1.36.0	1.34.4
apComplex	CRAN		2.40.0		
ape	CRAN		4		3.4
arm	CRAN		1.9-3		
assertthat	CRAN	0.1	0.1	0.1	0.1
backports	CRAN	1.0.5	1.0.4	1.0.5	1.0.2
base64	CRAN			2	2
base64enc	CRAN		0.1-3		0.1-3
beanplot	CRAN		1.2	1.2	1.2
BH	CRAN	1.60.0-2	1.62.0-1	1.62.0-1	1.60.0-2
Biobase	Bioconductor		2.34.0	2.34.0	2.32.0
BiocGenerics	Bioconductor		0.20.0	0.20.0	0.18.0
BiocInstaller	Bioconductor		1.24.0	1.20.3	1.22.3
BiocParallel	Bioconductor		1.8.1	1.8.1	
Biostings	Bioconductor		2.42.1	2.42.0	
BiSEp	Bioconductor		2.0.1	2.0.1	2.0.1

bitops	CRAN	1.0-6	1.0-6	1.0-6	1.0-6
boot	base	1.3-18	1.3-18	1.3-18	1.3-18
brew	CRAN	1.0-6	1.0-6	1.0-6	1.0-6
broom	CRAN	0.4.1			
caTools	CRAN	1.17.1	1.17.1	1.17.1	1.17.1
cgdsr	CRAN		1.2.5		
checkmate	CRAN		1.8.2		1.7.4
chron	CRAN	2.3-47	2.3-48	2.3-50	2.3-47
class	base	7.3-14	7.3-14	7.3-14	7.3-14
cluster	base	2.0.5	2.0.5	2.0.5	2.0.4
coda	CRAN		0.19-1		0.18-1
codetools	base	0.2-15	0.2-15	0.2-15	0.2-14
colorRamps	CRAN		2.3		
colorspace	CRAN	1.2-6	1.3-2	1.3-2	1.2-6
commonmark	CRAN	1.1		1.2	
compiler	base	3.3.2	3.3.2	3.3.1	3.3.0
corpcor	CRAN		1.6.8	1.6.8	1.6.8
Cprob	CRAN		1.2.4		
crayon	CRAN	1.3.2	1.3.2	1.3.2	1.3.2
crop	CRAN		0.0-2	0.0-2	
curl	CRAN	1.2	2.3	2.3	0.9.7
d3Network	CRAN		0.5.2.1		
data.table	CRAN	1.9.6	1.10.0	1.10.1	1.9.6
data.tree	CRAN		0.7.0	0.7.0	
datasets	base	3.3.2	3.3.2	3.3.1	3.3.0
DBI	CRAN	0.5-1	0.5-1	0.5-1	0.5-1
dendextend	CRAN	1.4.0	1.4.0	1.4.0	
DEoptimR	CRAN	1.0-8	1.0-8	1.0-8	1.0-4
desc	CRAN	1.1.0		1.1.0	
devtools	CRAN	1.12.0	1.12.0	1.12.0	1.12.0
DiagrammeR	CRAN		0.9.0	0.9.0	
dichromat	CRAN	2.0-0	2.0-0	2.0-0	2.0-0
digest	CRAN	0.6.10	0.6.11	0.6.12	0.6.9
diptest	CRAN	0.75-7	0.75-7	0.75-7	
doParallel	CRAN	1.0.10	1.0.10	1.0.10	1.0.10

dplyr	CRAN	0.5.0	0.5.0	0.5.0	0.5.0
ellipse	CRAN		0.3-8	0.3-8	0.3-8
evaluate	CRAN		0.1	0.1	0.9
fdrtool	CRAN		1.2.15		
fields	CRAN		8.1		
flexmix	CRAN	2.3-13	2.3-13	2.3-13	
forcats	CRAN	0.2.0			
foreach	CRAN	1.4.3	1.4.3	1.4.3	1.4.3
foreign	base	0.8-67	0.8-67	0.8-67	0.8-66
formatR	CRAN		1.4	1.4	1.4
Formula	CRAN		1.2-1		1.2-1
fpc	CRAN	2.1-10	2.1-10	2.1-10	
futile.logger	CRAN		1.4.3	1.4.3	1.4.1
futile.options	CRAN		1.0.0	1.0.0	1.0.0
gdata	CRAN	2.17.0	2.17.0	2.17.0	2.17.0
geepack	CRAN		1.2-1		
GenomeInfoDb	Bioconductor		1.10.2	1.10.1	
GenomicAlignments	Bioconductor		1.10.0	1.10.0	
GenomicRanges	Bioconductor		1.26.2	1.26.1	
ggm	CRAN		2.3		
ggplot2	CRAN	2.1.0	2.2.1	2.2.1	2.1.0
git2r	CRAN	0.15.0	0.18.0	0.16.0	0.15.0
glasso	CRAN		1.8		
GO.db	Bioconductor		3.4.0	3.2.2	3.3.0
GOSemSim	Bioconductor		2.0.3	1.28.2	1.30.3
gplots	CRAN	3.0.1	3.0.1	3.0.1	3.0.1
graph	Bioconductor		1.52.0		
graphics	base	3.3.2	3.3.2	3.3.1	3.3.0
graphsim	GitHub TomKellyGenetics	0.1.0	0.1.0	0.1.0	0.1.0
grDevices	base	3.3.2	3.3.2	3.3.1	3.3.0
grid	base	3.3.2	3.3.2	3.3.1	3.3.0
gridBase	CRAN	0.4-7	0.4-7	0.4-7	0.4-7
gridExtra	CRAN	2.2.1	2.2.1	2.2.1	2.2.1
gridGraphics	CRAN		0.1-5		

gtable	CRAN	0.2.0	0.2.0	0.2.0	0.2.0
gtools	CRAN	3.5.0	3.5.0	3.5.0	3.5.0
haven	CRAN	1.0.0			
heatmap.2x	GitHub TomKellyGenetics	0.0.0.9000	0.0.0.9000	0.0.0.9000	0.0.0.9000
hgu133plus2.db	Bioconductor		3.2.3		
highr	CRAN		0.6	0.6	0.6
Hmisc	CRAN		4.0-2	4.0-2	3.17-4
hms	CRAN	0.2	0.3		
htmlTable	CRAN		1.8	1.9	
htmltools	CRAN	0.3.5	0.3.5	0.3.5	0.3.5
htmlwidgets	CRAN		0.8	0.8	
httpuv	CRAN	1.3.3		1.3.3	
httr	CRAN	1.2.1	1.2.1	1.2.1	1.1.0
huge	CRAN		1.2.7		
hunspell	CRAN		2.3		2
hypergraph	CRAN		1.46.0		
igraph	CRAN	1.0.1	1.0.1	1.0.1	1.0.1
igraph.extensions	GitHub TomKellyGenetics	0.1.0.9001	0.1.0.9001	0.1.0.9001	0.1.0.9001
influenceR	CRAN		0.1.0	0.1.0	
info.centraliity	GitHub TomKellyGenetics	0.1.0	0.1.0	0.1.0	0.1.0
IRanges	Bioconductor		2.8.1	2.8.1	2.6.1
irlba	CRAN	2.1.1	2.1.2	2.1.2	2.0.0
iterators	CRAN	1.0.8	1.0.8	1.0.8	1.0.8
jpeg	CRAN		0.1-8		
jsonlite	CRAN	1.1	1.2	1.3	0.9.20
KEGG.db	Bioconductor		3.2.3		
kernlab	CRAN	0.9-25	0.9-25	0.9-25	
KernSmooth	base	2.23-15	2.23-15	2.23-15	2.23-15
knitr	CRAN		1.15.1	1.15.1	1.14
labeling	CRAN	0.3	0.3	0.3	0.3
lambda.r	CRAN		1.1.9	1.1.9	1.1.7
lattice	base	0.20-34	0.20-34	0.20-34	0.20-33

latticeExtra	CRAN		0.6-28		0.6-28
lava	CRAN		1.4.6		
lavaan	CRAN		0.5-22		
lazyeval	CRAN	0.2.0	0.2.0	0.2.0	0.2.0
les	CRAN		1.24.0		
lgtdl	CRAN		1.1.3		
limma	Bioconductor		3.30.7	3.30.3	
lme4	CRAN		1.1-12		1.1-12
lubridate	CRAN	1.6.0			
magrittr	CRAN	1.5	1.5	1.5	1.5
maps	CRAN		3.1.1		
markdown	CRAN		0.7.7	0.7.7	0.7.7
MASS	base	7.3-45	7.3-45	7.3-45	7.3-45
Matrix	base	1.2-7.1	1.2-7.1	1.2-8	1.2-6
matrixcalc	CRAN	1.0-3	1.0-3	1.0-3	1.0-3
mclust	CRAN	5.2	5.2.1	5.2.2	5.2
memoise	CRAN	1.0.0	1.0.0	1.0.0	1.0.0
methods	base	3.3.2	3.3.2	3.3.1	3.3.0
mgcv	base	1.8-16	1.8-16	1.8-17	1.8-12
mi	CRAN		1		
mime	CRAN	0.5	0.5	0.5	0.4
minqa	CRAN		1.2.4		1.2.4
mnormt	CRAN	1.5-5	1.5-5		1.5-4
modelr	CRAN	0.1.0			
modeltools	CRAN	0.2-21	0.2-21	0.2-21	
multtest	Bioconductor		2.30.0	2.30.0	
munsell	CRAN	0.4.3	0.4.3	0.4.3	0.4.3
mvtnorm	CRAN	1.0-5	1.0-5	1.0-6	1.0-5
network	CRAN		1.13.0		
nlme	base	3.1-128	3.1-128	3.1-131	3.1-128
nloptr	CRAN		1.0.4		1.0.4
NMF	CRAN	0.20.6	0.20.6	0.20.6	0.20.6
nnet	base	7.3-12	7.3-12	7.3-12	7.3-12
numDeriv	CRAN		2016.8-1		2014.2-1
openssl	CRAN	0.9.4	0.9.6	0.9.6	0.9.4

org.Hs.eg.db	Bioconductor		3.1.2		3.3.0
org.Sc.sgd.db	Bioconductor		3.4.0		
parallel	base	3.3.2	3.3.2	3.3.1	3.3.0
pathway.structure	GitHub				
.permutation	TomKellyGenetics	0.1.0	0.1.0	0.1.0	0.1.0
pbivnorm	CRAN		0.6.0		
PGSEA	Bioconductor		1.48.0		
pkgmaker	CRAN	0.22	0.22	0.22	0.22
PKI	CRAN		0.1-3		
plogr	CRAN		0.1-1	0.1-1	
plot.igraph	GitHub				
	TomKellyGenetics	0.0.0.9001	0.0.0.9001	0.0.0.9001	0.0.0.9001
plotrix	CRAN		3.6-4		
plyr	CRAN	1.8.4	1.8.4	1.8.4	1.8.3
png	CRAN		0.1-7		0.1-7
prabclus	CRAN	2.2-6	2.2-6	2.2-6	
praise	CRAN	1.0.0	1.0.0		1.0.0
pROC	CRAN		1.8	1.9.1	
prodlm	CRAN		1.5.7		
prof.tree	CRAN		0.1.0		
proftools	CRAN		0.99-2		
progress	CRAN			1.1.2	
psych	CRAN	1.6.12	1.6.12		
purrr	CRAN	0.2.2	0.2.2	0.2.2	0.2.2
qgraph	CRAN		1.4.1		
quadprog	CRAN		1.5-5	1.5-5	1.5-5
R.methodsS3	CRAN		1.7.1		1.7.1
R.oo	CRAN		1.21.0		1.20.0
R.utils	CRAN		2.5.0		
R6	CRAN	2.1.3	2.2.0	2.2.0	2.1.3
RBGL	CRAN		1.50.0		
RColorBrewer	CRAN	1.1-2	1.1-2	1.1-2	1.1-2
Rcpp	CRAN	0.12.7	0.12.9	0.12.9	0.12.7
RcppArmadillo	CRAN			0.7.700.0.0	0.6.700.6.0
RcppEigen	CRAN		0.3.2.9.0		0.3.2.8.1

RCurl	CRAN		1.95-4.8	1.95-4.8	1.95-4.8
reactome.db	Bioconductor		1.52.1	1.52.1	
reactometree	GitHub TomKellyGenetics		0.1		
readr	CRAN	1.0.0	1.0.0		
readxl	CRAN	0.1.1			
registry	CRAN	0.3	0.3	0.3	0.3
reshape2	CRAN	1.4.1	1.4.2	1.4.2	1.4.1
rgexf	CRAN		0.15.3	0.15.3	
rgl	CRAN			0.97.0	0.95.1441
Rgraphviz	CRAN		2.18.0		
rjson	CRAN		0.2.15		
RJSONIO	CRAN		1.3-0		
rmarkdown	CRAN		1.3	1.3	1
Rmpi	CRAN		0.6-6		0.6-5
rngtools	CRAN	1.2.4	1.2.4	1.2.4	1.2.4
robustbase	CRAN	0.92-7	0.92-7	0.92-7	0.92-5
ROCR	CRAN	1.0-7	1.0-7	1.0-7	1.0-7
Rook	CRAN		1.1-1	1.1-1	
roxygen2	CRAN	6.0.1	5.0.1	6.0.1	5.0.1
rpart	base	4.1-10	4.1-10	4.1-10	4.1-10
rprojroot	CRAN	1.2	1.1	1.2	
Rsamtools	Bioconductor		1.26.1	1.26.1	
rsconnect	CRAN		0.7		
RSQLite	CRAN		1.1-2	1.1-2	1.0.0
rstudioapi	CRAN	0.6	0.6	0.6	0.6
rvest	CRAN	0.3.2			
S4Vectors	Bioconductor		0.12.1	0.12.0	0.10.3
safe	Bioconductor		3.14.0	3.10.0	
scales	CRAN	0.4.0	0.4.1	0.4.1	0.4.0
selectr	CRAN	0.3-1			
sem	CRAN		3.1-8		
shiny	CRAN	0.14		1.0.0	
slipt	GitHub TomKellyGenetics	0.1.0	0.1.0	0.1.0	0.1.0

sm	CRAN	2.2-5.4	2.2-5.4		
sna	CRAN		2.4		
snow	CRAN	0.4-1	0.4-2	0.4-2	0.3-13
sourcetools	CRAN	0.1.5		0.1.5	
SparseM	CRAN		1.74		1.7
spatial	base	7.3-11	7.3-11	7.3-11	7.3-11
splines	base	3.3.2	3.3.2	3.3.1	3.3.0
statnet.common	CRAN		3.3.0		
stats	base	3.3.2	3.3.2	3.3.1	3.3.0
stats4	base	3.3.2	3.3.2	3.3.1	3.3.0
stringi	CRAN	1.1.1	1.1.2	1.1.2	1.0-1
stringr	CRAN	1.1.0	1.1.0	1.2.0	1.0.0
Summarized Experiment	Bioconductor		1.4.0	1.4.0	
survival	base	2.39-4	2.40-1	2.40-1	2.39-4
tcltk	base	3.3.2	3.3.2	3.3.1	3.3.0
testthat	CRAN	1.0.2	1.0.2		1.0.2
tibble	CRAN	1.2	1.2	1.2	1.2
tidyr	CRAN	0.6.1	0.6.1	0.6.1	
tidyverse	GitHub hadley	1.1.1			
timeline	CRAN		0.9		
tools	base	3.3.2	3.3.2	3.3.1	3.3.0
tpr	CRAN		0.3-1		
trimcluster	CRAN	0.1-2	0.1-2	0.1-2	
Unicode	CRAN	9.0.0-1	9.0.0-1	9.0.0-1	
utils	base	3.3.2	3.3.2	3.3.1	3.3.0
vioplot	CRAN		0.2		
vioplotx	GitHub TomKellyGenetics	0.0.0.9000	0.0.0.9000		
viridis	CRAN	0.3.4	0.3.4	0.3.4	
visNetwork	CRAN		1.0.3	1.0.3	
whisker	CRAN	0.3-2	0.3-2	0.3-2	0.3-2
withr	CRAN	1.0.2	1.0.2	1.0.2	1.0.2
XML	base	3.98-1.3	3.98-1.1	3.98-1.5	3.98-1.4

xml2	CRAN	1.1.1		1.1.1	1.0.0
xtable	CRAN	1.8-2	1.8-2	1.8-2	1.8-2
XVector	Bioconductor		0.14.0	0.14.0	
yaml	CRAN		2.1.14	2.1.14	2.1.13
zlibbioc	CRAN		1.20.0	1.20.0	
zoo	CRAN	1.7-13	1.7-14		1.7-13