GERMLINE PHARMACOGENOMICS TESTING IN FORMALIN-FIXED PARAFFIN-EMBEDDED TUMOURS

by

Shyong Quin Yap

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Abstract

This document provides brief instructions for using the `ubcdiss` class to write a **UBC!**-conformant dissertation in LaTeX. This document is itself written using the `ubcdiss` class and is intended to serve as an example of writing a dissertation in LaTeX. This document has embedded Unique Resource Locators (URLS) and is intended to be viewed using a computer-based Portable Document Format (PDF) reader.

Note: Abstracts should generally try to avoid using acronyms.

Note: at **UBC!** (**UBC!**), both the Graduate and Postdoctoral Studies (GPS) Ph.D. defence programme and the Library's online submission system restricts abstracts to 350 words.

Preface

At **UBC!**, a preface may be required. Be sure to check the GPS guidelines as they may have specific content to be included.

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List of Abbreviations

GPS Graduate and Postdoctoral Studies

PDF Portable Document Format

URL Unique Resource Locator, used to describe a means for obtaining some resource on the world wide web

Acknowledgments

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Chapter 1

Introduction

1.1 Overcoming The Clinical Reality

Germline pharmacogenomic (PGx) variants can influence a patient's response to chemotherapy. Using next-generation sequencing (NGS) technologies, PGx variants can be screened to identify patients who are susceptible to toxicity risk, thereby preventing chemotherapy-associated morbidities. However, clinical NGS testing in oncology is challenging due to the lack of matched normal DNA while tumour biopsies are formalin-fixed paraffin-embedded (FFPE) for histologic examinations. Formalin induces DNA fragmentation and sequence artifacts, specifically C>T/A>G base transitions. Moreover, the ability of NGS approaches to interrogate genomic content at increased depth and breadth can result in detection of variant of unknown significance (VUS) and incidental findings of medical value. At present, there are limited guidelines available for management of these variant categories. Despite these challenges, would it be possible/feasible to harness a clinical targeted NGS panel that only sequence FFPE tumour DNA for germline PGx testing?

The work presented herein aims to address the aforementioned challenges as well as answer this question.

1.2 Genomics-Driven Oncology

1.2.1 Definitions

Genomics-driven oncology is defined as the use of genomic information to provide guidance for disease management and therapeutic intervention in oncologic care. The application of NGS to oncology, or genomics-driven cancer medicine, is conceptually logical and simple: First, the genome of a patients tumor is sequenced, and all genetic differences from the standard human reference genome are identified. Because all human beings have many normal genetic variants that differ from the reference genome, the tumor sequence is compared with the patients constitutional (germline) genome

to determine which alterations in the tumor are somatic (and therefore potentially pathogenic) and which are germline (and probably not cancer-related). Next, the somatic mutation list is filtered through a database of mutations that may render tumors sensitive to established and emerging anticancer drugs. Finally, an annotated list is provided to the treating physician to be used in clinical decision making and clinical research design. However, several technical and ethical challenges must be addressed before real-time application of NGS can become a reality in cancer medicine.

1.2.2 Genomic Alterations in Cancer Pathogenesis

1.2.3 Clinical Deployment of Targeted Cancer Therapies

1.2.4 Advances in DNA Sequencing Technologies

1.3 Next-Generation Sequencing Technologies

The Human Genome Project, which assembled the first human reference genome, was completed in 2003 at an expense of $2.7 billion within 13 years. This was a cost and turn-around time that would not be feasible for routine usage in research and clinical settings, thereby stimulating the advancement of DNA sequencing technologies. As a result, various MPS technologies have emerged and have been adapted to fit the needs of scientific research as well as clinical applications.

1.3.1 Sequencing by Ligation

1.3.2 Sequencing by Synthesis

1.4 Objectives

Current research in cancer genomics primarily focus on somatically acquired mutations that drive malignant transformation through conferring selective growth advantages to cells. These efforts are demonstrated by formation of large-scale collaborations such as the The Cancer Genome Atlas (TCGA) and the International Cancer Genome Consortium (ICGC), which aim to characterize and catalog the genomic landscapes of diverse tumour types. Understanding oncogenic mechanisms underlying driver somatic mutations have led to the development of targeted therapies, which resulted in improved clinical outcomes for various cancer subtypes. However, germline genetic variants can also influence cancer treatment by affecting drug targets and disposition, thereby causing interpatient differences in drug response. These germline variants, known as pharmacogenomic (PGx) variants, can assist with treatment selection, optimal drug dosing, and identifying toxicity risk to reduce cancer therapeutics-associated morbidities.

Advances in massively parallel sequencing (MPS) technologies have revolutionized genetic testing in clinical oncology through enabling surveillance of increased genomic depth and breadth with less DNA in a cost-effective and timely manner. Nevertheless, clinical application of MPS approaches to cancer medicine still encounter several challenges and financial barriers. One of these challenges is caused by formalin fixation of tumour biopsies. Tumour biopsies are routinely formalin-fixed paraffin-embedded (FFPE) to preserve morphology and cellular characteristics for histologic examination. Moreover, most clinical laboratories prefer storage of FFPE blocks at ambient temperature to avoid cost inflicted by maintaining fresh-frozen specimens. However, formalin fixation causes DNA fragmentation and base transition artifacts, which could result in false-negative or false-positive variant calls. These sequence artifacts are particularly concerning in a clinical setting because failure to detect or inaccurate detection of cancer biomarkers could have devastating consequences for patients and their families.

Another challenge in clinical MPS-based testing in oncology practice is the lack of matched normal DNA, which is not commonly collected in the clinic due to increased cost and logistical difficulties. Without matched normal DNA, determining the somatic or germline nature of the variant calls, which is essential for translating MPS data into clinically actionable information, rely heavily on filtering and interpretation using databases such as dbSNP, ExAC, and COSMIC. The bottleneck of MPS data generation to interpretation for clinical use is yet another limiting factor of clinical genomic sequencing. Despite the ability of MPS approaches to screen increased genomic content, these methods lead to higher rates of detecting variants of uncertain significance (VUS) that lack evidence of clinical utility. Conversely, incidental findings with medical value to patient care may arise while there are ethical controversies and very few guidelines on the management of this category of variants.

The main objective of this thesis is to investigate whether germline PGx variants can be accurately and sensitively detected in FFPE tumour DNA sequenced by a clinical targeted MPS panel. To achieve this objective, key challenges in clinical genomic sequencing that were briefly described above were addressed. This introductory chapter is organized into five sections to provide the necessary background knowledge: (1) Describes driving forces that led to emergence of genomics-driven oncology; (2) Introduces different applications of MPS to provide an overview of technologies behind sequence data generation; (3) Introduces bioinformatics pipeline for variant calling, which generated input data analyzed in this thesis; (4) Expands on key challenges in clinical genomic sequencing and potential solutions; (5) Emphasizes on the importance of germline PGx testing in oncology care.

1.5 Genomics-Driven Oncology

1.5.1 Definitions

Genomics-driven oncology is defined as the use of genomic information to provide guidance for disease management and therapeutic intervention in oncologic care. The application of NGS to oncology, or genomics-driven cancer medicine, is conceptually logical and simple: First, the genome of a patients tumor is sequenced, and all genetic differences from the standard human reference genome are identified. Because all human beings have many normal genetic variants that differ from the reference genome, the tumor sequence is compared with the patients constitutional (germline) genome to determine which alterations in the tumor are somatic (and therefore potentially pathogenic) and which are germline (and probably not cancer-related). Next, the somatic mutation list is filtered through a database of mutations that may render tumors sensitive to established and emerging anticancer drugs. Finally, an annotated list is provided to the treating physician to be used in clinical decision making and clinical research design. However, several technical and ethical challenges must be addressed before real-time application of NGS can become a reality in cancer medicine.

1.5.2 Genomic Alterations in Cancer Pathogenesis

1.5.3 Clinical Deployment of Targeted Cancer Therapies

1.5.4 Advances in DNA Sequencing Technologies

The first human reference genome was established in 2003 through completion of the Human Genome Project, which instigated major developments in DNA sequencing technologies and computational tools for large-scale genomic data analysis. As a result, MPS technologies have emerged with increased throughput, sensitivity, and cost efficiency, leading to the genomic characterization of a growing number of tumours. As the application of MPS technologies in cancer genomic studies continued to accelerate the progress of driver gene discoveries and drug development, the clinically feasible features of MPS have led to its rapid integration in oncology practice, giving rise to the genomics-driven oncology framework.

Genomics-driven oncology is defined as the use of genomic information to provide guidance for disease management and therapeutic intervention in oncologic care. One of the driving forces of this emerging approach is the expanding knowledge in tumour biology. A central focus of tumour biology research is elucidating oncogenic mechanisms driven by somatic mutations that confer selective growth advantages to cells. Translation of these findings into targeted therapies have demonstrated pronounced improvement in clinical outcomes, leading to the transition from morphology-based to genetic-based management of cancer. A well-known example is the treatment of BCR-ABL-

translocated chronic myeloid leukemia (CML) with the tyrosine kinase inhibitor imatinib, which targets the constitutively active ABL1 kinase as a result of the BCR-ABL fusion gene.

Several successful applications of targeted therapy ensued the example of imatinib and BCR-ABL-translocated CML such as the use of anti-HER2 monoclonal antibody trastuzumab in treating HER2/neu-amplified breast cancer and BRAF inhibitor vemurafenib in treating advanced BRAF-mutated melanoma. The promising potential of targeted anti-cancer agents accelerated the progress of drug discovery and development as evident by the drastically decreasing timelines between driver mutation discovery and clinical proof-of-concept. For instance, it only took three years for the ALK inhibitor crizotinib to enter Phase II clinical trials since identification of ALK translocations in non-small cell lung carcinoma (NSCLC) whereas the Food and Drug Administration (FDA) approval of imatinib for treatment of BCR-ABL-translocated CML took 41 years since discovery of the Philadelphia chromosome. Consequently, there is an extensive compendium of targeted therapeutics with 19 listed as clinically approved by the National Cancer Institute in 2012 while approximately 150 compounds were listed as clinical candidates.

The enhanced understanding of oncogenic pathways and growing spectrum of targeted therapies have created the perfect opportunity for clinical screening of driver mutations to match patients with targeted treatments. Conversely, patients without specific mutations could be spared treatment-associated toxicities. For example, screening for KRAS mutations in codon 12 or 13 could prevent treating colorectal cancer (CRC) patients with anti-EGFR monoclonal antibody or EGFR inhibitors, which are associated with toxicity risk, as these patients are known to respond poorly. Despite the initial efficacy of targeted treatments, tumours could develop resistant mechanisms causing cancer relapse. One of the crucial realization from proceeding studies is that cancer is a heterogenous disease, in that a tumour can consist of multiple subclonal populations and resistant cancer cells may already exist at an early stage. Hence, treatment resistance occurs after the dominant clone has been wiped out allowing the resistant subclone to proliferate and metastasize. Complexities derived from the vast mutational profiles of tumours and intratumoural heterogeneity revealed that surveillance of multiple cancer genes with increased coverage depth during the course of a disease is essential for positive clinical outcomes. To achieve this, single gene assays using the Sanger method, also known as the dideoxynucleotide chain termination method, are not feasible due to time, labour, and cost constraints.

With the advent of MPS technologies, genome sequencing can be accomplished at a reduced cost of less than $5000 per genome within days. To put this into perspective, the first human reference genome sequenced using the Sanger method was completed at a cost of $2.7 billion over 13 years. Advances in MPS technologies have revolutionized cancer genomics by enabling international consortia such as TCGA and the ICGC to uncover the complex genomic architectures of various tumour types, thereby shedding insights into drug resistant mechanisms and potentiating therapeutic strategies against cancer relapse. The high-throughput nature of MPS and its ability

to generate robust genomic information in a timely and cost-efficient manner are also capable of overcoming the limitations of single gene assays in the clinic. Thus, various MPS approaches, most commonly targeted gene panels, have been rapidly adopted in clinical oncology to inform medical decision-making based on a patient's genomic make-up. Although the path to genomics-driven oncology was paved by a deeper mechanistic understanding of oncogenic pathways and the accelerated progress in targeted therapeutics development, the emergence of MPS technologies played a significant role in providing detailed insights into the cancer genome as well as a feasible method to generate genomic information for clinical use.

1.6 Applications of Massively Parallel Sequencing

1.6.1 Targeted Resequencing

Capture-based, amplicon-based etc.

1.6.2 Whole Exome Sequencing

1.6.3 Whole Genome Sequencing

1.7 Bioinformatics Tools for Variant Calling

1.7.1 Types of Genomic Alterations

There are different types of genomic alterations.

1.7.2 Variant Calling Pipeline

1.7.3 Variant Calling Algorithms

1.7.4 Variant Curation and Interpretation

1.8 Challenges in Clinical Genomics

1.8.1 DNA Damage by Formalin Fixation

- Fragmentation - Transition vs. transversion

1.8.2 Lack of Matched Normal DNA

1.8.3 Variant of Unknown Significance

1.8.4 Incidental Findings

1.9 Pharmacogenomics in Clinical Oncology

Cancer biomarkers, which are central to the genomics-driven oncology approach to medical decision-making, can be classified as diagnostic, prognostic, predictive, and pharmacogenomics (PGx). PGx markers are germline genetic variants that affect genes encoding drug targets as well as drug disposition proteins involved in absorption, distribution, metabolism, and excretion (ADME). Pharmacogenomics (PGx) applies genomic approaches to evaluate the interaction of genetic variants with drug response. These variations affect . The goals of PGx studies are to elucidate biological mechanisms underlying interpatient variability in drug efficacy and toxicity as well as identify PGx biomarkers with clinical utility, which would guide selection of treatment type, optimal dosage, and duration.

Cancer PGx takes into account tumour-associated somatic mutations and germline variants. Somatic mutations in driver genes promote malignant transformation through conferring selective growth advantage to the cells. Characterization of somatic driver mutations has provided an avenue for development of molecularly targeted drugs against specific tumour-defining somatic mutations. Hence, screening for these specific

somatic mutations serving as genomic predictors of tumour response and providing new leads for drug development germline variants optimize cancer drug dosing and predict the susceptibility of patients to the adverse side effects of these drugs - knowledge that can be used to improve benefit:risk ratio of cancer treatment for individual patients

1.9.1 Targeted Therapies

Tamoxifen etc.

1.9.2 Chemotherapy-Associated Morbidities

DPYD, MTHFR, GSTP1, TYMP, TYMS, UGT1A1

1.10 Summary

The advent of MPS technologies has refined analysis of the cancer genome at base-pair resolution,

Chapter 2

Materials and Methods

2.1 Patient Samples

Solid tumour biopsies were collected from 171 consented patients in The Oncopanel Pilot (TOP) study under a protocol approved by the British Columbia Cancer Agency (BCCA) Research Ethics Board (Protocol H12-00292). Details on tumour types are listed in Table 2.1. Excess tissue from tumuor biopsies after pathological evaluation were transported in serum-free medium at ambient temperature followed by washing in PBS with 6.5mM dithiothreitol (DTT). Fat, muscle, and necrotic areas were trimmed and approximately 50-100 mg of specimens were formalin-fixed at 4°C overnight before paraffin-embedding. All specimens were fixed within 2 hours and embedded within 24 hours of collection. For each patient in the TOP cohort, peripheral blood (PB) samples were also collected and processed to serve as germline DNA control for variant calling.

Table 2.1: Summary of FFPE Specimens from 171 TOP Patients

Tumour Type	Number of Specimens	Percentage
Colorectal	85	49.7
Lung	36	21.1
Melanoma	16	9.4
Other	30	17.5
Unknown	6	3.5

2.2 DNA Extraction, Library Preparation, and Illumina Sequencing

Tumour and germline DNA for 171 patients were extracted using the QIAGEN FFPE DNA extraction kit and xx respectively as per manufacturer's instructions. For specimens with sufficient DNA quantity, 250 ng of genomic DNA was used for library preparation. Genomic DNA was sheared

to generate fragment sizes of approximately 3 kbp, followed by PCR primer merging, amplicon generation, and adapter ligation using the RainDance Thunderstorm instrument (Figure 2.1). The complete list of target spaces and primers used to generate the 429 amplicons for 26 genes screened by the OncoPanel are included in Table A.1 and Table A.2 respectively. Six out of 26 genes are PGx genes namely *DPYD*, *GSTP1*, *MTHFR*, *TYMP*, *TYMS*, and *UGT1A1*. Libraries were pooled, ranging from 13-20 libraries per pool, and sequenced with the Illumina MiSeq system for paired end sequencing with a v2 250-bp kit. Pooling of libraries includes libraries from other studies, which is summarized in Figure 2.2.

2.3 Variant Calling Pipeline

Read alignment and variant calling were carried out by the BCCA Centre of Clinical Genomics (CCG) bioinformatics pipeline Figure 2.3. Raw reads from the MiSeq instrument were aligned to the GRCh37 human reference genome (hg19) using BWA (version 0.5.9, mem algorithm) and variant calling was performed using samtools mpileup (version 0.1.18) followed by VarScan2 (version 2.3.6). Variant calling in the six PGx genes were carried out using the following VarScan2 parameters: Variants were annotated as per the Human Genome Variation Society (HGVS) convention and interpreted with databases such as dbSNP, ExAC, COSMIC, and ClinVar using SnpEff (version 4.2). Gene reference models used for HGVS nomenclature are listed in Table A.3.

2.4 Data Analysis and Visualization

Coverage depth was measured using bedtools (version 2.25.0) and per-base metrics were obtained using bam-readcount (https://github.com/genome/). Statistical analyses and data visualization were performed using R (version 3.3.2) and associated open-source packages. Manual review of PGx variants were carried out using the Intergrative Genomics Viewer (IGV, version 2.3). *Note: be more specific on how the data is generated*

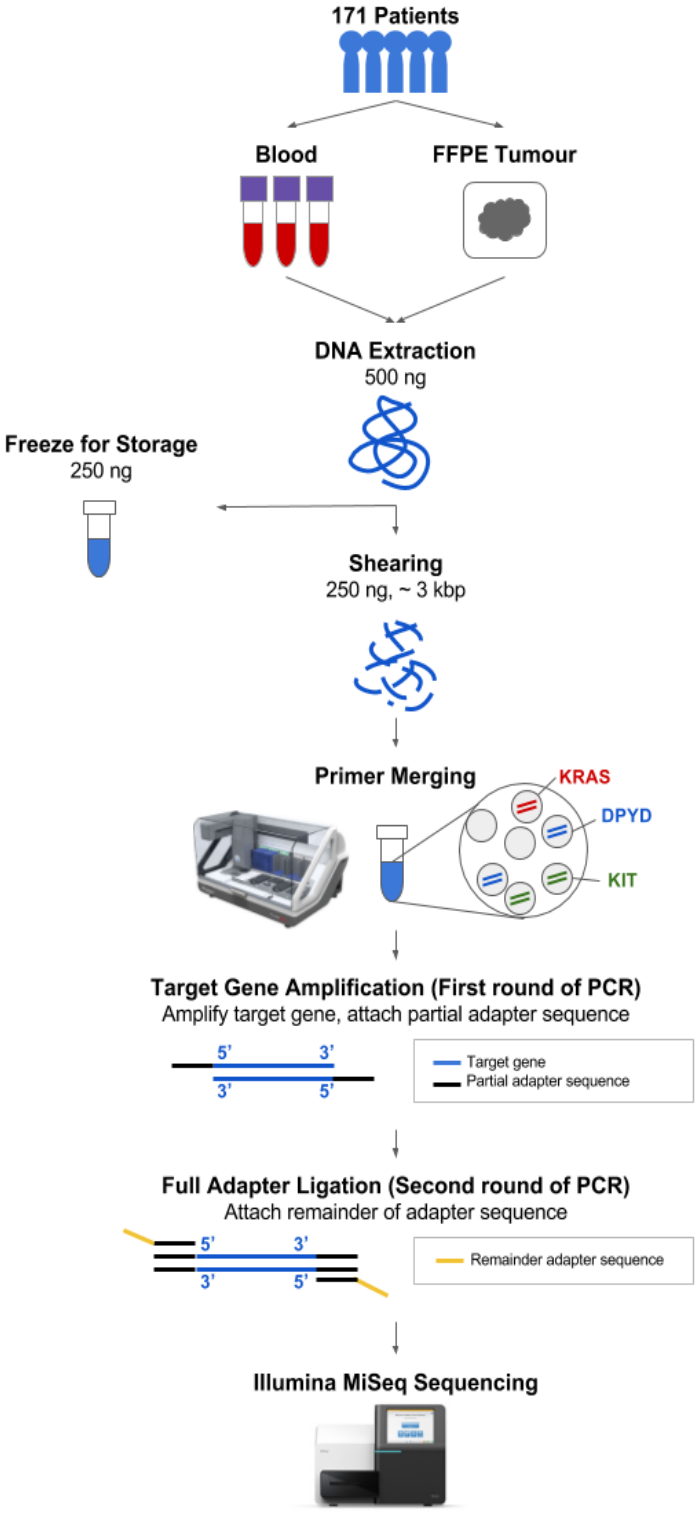

Figure 2.1: Workflow for Sample Processing, Library Preparation, and NGS Sequencing.

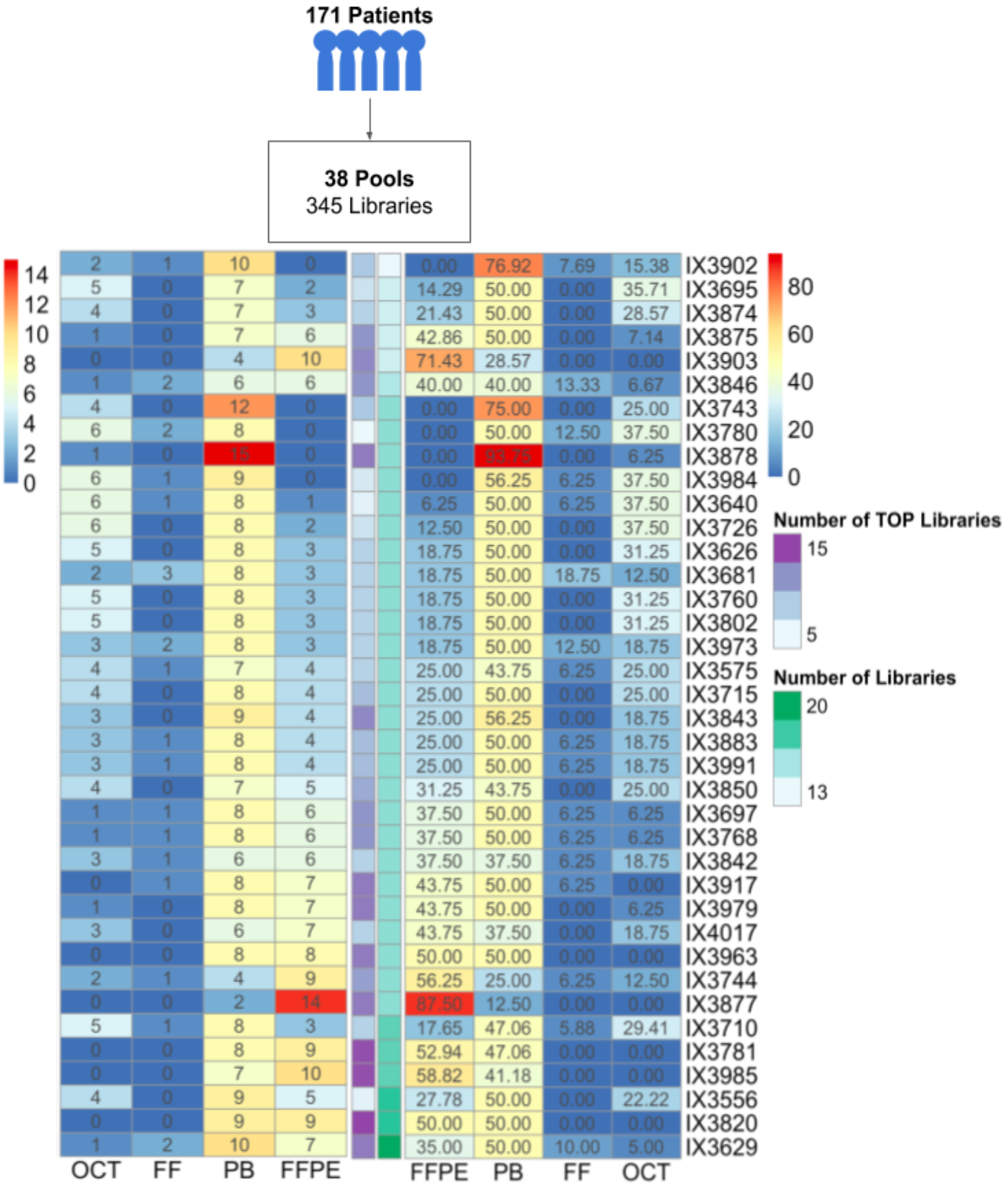

Figure 2.2: 345 TOP Libraries Distributed Across 38 Pools. Number of libraries is presented on the *left* whereas percentage of libraries per total libraries in a pool is presented on the *right*.

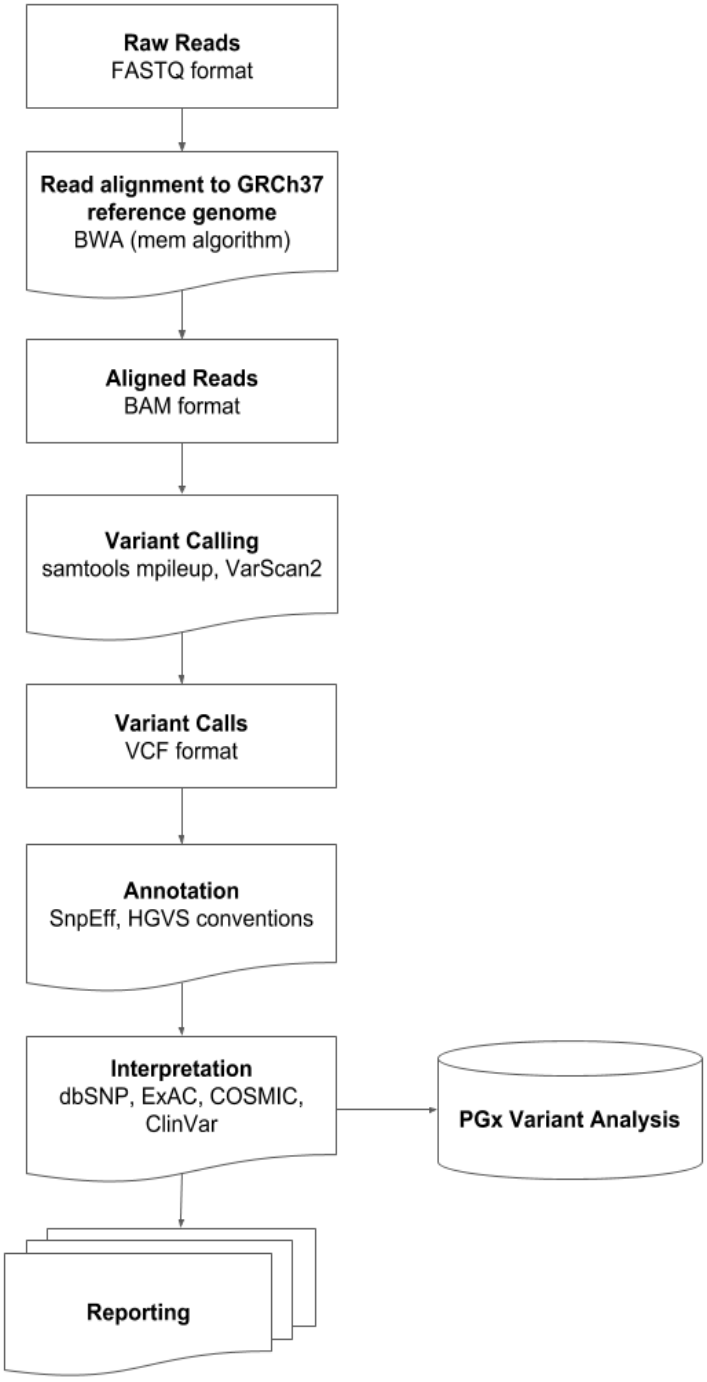

Figure 2.3: OncoPanel Pipeline for Variant Calling. Variants in PGx genes were filtered for downstream analysis.

Chapter 3

Results

3.1 Assessment of DNA Quantity and Quality between Specimen Types

3.2 Sequencing Depth is Comparable between FFPE and FF-PB Samples

Chapter 4

Discussion and Conclusion

Bibliography

Appendix A

Supporting Materials

Table A.1: OncoPanel Genes and Target Spaces.

Gene Target ID	Chr	Target Start	Target End
AKT1_a	14	105246546	105246554
AKT1_b	14	105246450	105246458
ALK_a	2	29445212	29445271
ALK_b	2	29443629	29443703
ALK_c	2	29446148	29448519
BRAF_a	7	140481395	140481418
BRAF_b	7	140453085	140453218
BRAF_b	7	140453129	140453152
DPYD_a	1	97915607	97915621
DPYD_a	1	97915608	97915621
DPYD_b	1	98348855	98349048
DPYD_b	1	98348878	98348892
DPYD_c	1	97981336	97981350
DPYD_c	1	97981418	97981425
DPYD_d	1	97547940	97547954
DPYD_d	1	97547941	97547954
DPYD_e	1	97981417	97981425
DPYD_f	1	98039415	98039423
DPYD_f	1	98039416	98039423
DPYD_g	1	97770916	97770924
DPYD_h	1	98165087	98165095

DPYD_h	1	98165088	98165095
EGFR_18	7	55241599	55241751
EGFR_18	7	55241614	55241736
EGFR_19	7	55242400	55242528
EGFR_19	7	55242415	55242513
EGFR_20	7	55248971	55249186
EGFR_20	7	55248986	55249171
EGFR_21	7	55259397	55259582
EGFR_21	7	55259412	55259567
ERBB2_20	17	37880979	37881164
GSTP1_a	11	67352682	67352696
HRAS_a	11	534281	534293
HRAS_a	11	534282	534293
HRAS_b	11	533870	533884
HRAS_b	11	533871	533884
HRAS_c	11	533549	533557
HRAS_c	11	533550	533557
HRAS_d	11	533462	533470
HRAS_d	11	533463	533470
IDH1_a	2	209113110	209113113
IDH1_a	2	209113111	209113113
IDH2_a	15	90631836	90631839
IDH2_a	15	90631933	90631935
IDH2_b	15	90631837	90631839
IDH2_b	15	90631932	90631935
KIT_9	4	55592008	55592231
KIT_11	4	55593567	55593723
KIT_13	4	55594162	55594302
KIT_14	4	55595486	55595666
KIT_17	4	55599221	55599373
KIT_18	4	55602649	55602790
KRAS_a	12	25398274	25398291
KRAS_a	12	25398275	25398291
KRAS_b	12	25380269	25380283
KRAS_b	12	25380270	25380283

KRAS_c	12	25378554	25378568
KRAS_c	12	25378555	25378568
KRAS_d	12	25378644	25378653
KRAS_d	12	25378645	25378653
MAP2K1_a	15	66727449	66727486
MAP2K1_a	15	66727450	66727486
MAPK1_1	22	22221602	22221740
MAPK1_2	22	22161943	22162145
MAPK1_3	22	22160129	22160338
MAPK1_4	22	22153291	22153427
MAPK1_5	22	22142973	22143107
MAPK1_6	22	22142536	22142687
MAPK1_7	22	22127152	22127281
MAPK1_8	22	22123483	22123619
MTHFR_a	1	11856371	11856385
MTHFR_a	1	11856372	11856385
MTHFR_b	1	11854469	11854483
MTHFR_b	1	11854470	11854483
NRAS_a	1	115258737	115258754
NRAS_a	1	115258738	115258754
NRAS_b	1	115256522	115256536
NRAS_b	1	115256523	115256536
NRAS_c	1	115252286	115252294
NRAS_d	1	115252199	115252207
PDGFRA_12	4	55140993	55141155
PDGFRA_14	4	55144048	55144188
PDGFRA_18	4	55151993	55152145
PIK3CA_a	3	178936047	178936198
PIK3CA_a	3	178936076	178936102
PIK3CA_b	3	178952078	178952092
PIK3CA_b	3	178952079	178952092
PTEN_a	10	89692985	89692999
PTEN_b	10	89717666	89717680
PTEN_b	10	89717667	89717680
PTEN_c	10	89717765	89717785

PTEN_c	10	89717766	89717785
STAT1_0	2	191874592	191874739
STAT1_1	2	191873679	191873843
STAT1_2	2	191872279	191872397
STAT1_3	2	191865790	191865899
STAT1_4	2	191864342	191864440
STAT1_5	2	191862933	191863044
STAT1_6	2	191862572	191862743
STAT1_7	2	191859777	191859955
STAT1_8	2	191855944	191856056
STAT1_9	2	191854331	191854410
STAT1_10	2	191851755	191851804
STAT1_11	2	191851570	191851683
STAT1_11	2	191851755	191851804
STAT1_12	2	191850335	191850396
STAT1_13	2	191849026	191849129
STAT1_14	2	191848358	191848476
STAT1_15	2	191847099	191847254
STAT1_16	2	191845336	191845405
STAT1_17	2	191844488	191844602
STAT1_18	2	191843572	191843737
STAT1_19	2	191841556	191841761
STAT1_20	2	191840528	191840623
STAT1_21	2	191839546	191839668
STAT1_22	2	191835419	191835453
STAT3_0	17	40500397	40500544
STAT3_1	17	40498577	40498741
STAT3_2	17	40497567	40497685
STAT3_3	17	40491322	40491437
STAT3_4	17	40490739	40490840
STAT3_5	17	40489771	40489885
STAT3_6	17	40489443	40489614
STAT3_7	17	40485899	40486077
STAT3_8	17	40485681	40485793
STAT3_9	17	40483480	40483559

STAT3_10	17	40481755	40481804
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STAT3_13	17	40478124	40478227
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STAT3_16	17	40475581	40475653
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STAT3_21	17	40468797	40468929
STAT3_22	17	40467753	40467828
TP53_0	17	7579829	7579922
TP53_1	17	7579690	7579731
TP53_2	17	7579302	7579600
TP53_3	17	7578361	7578564
TP53_4	17	7578162	7578304
TP53_4	17	7578167	7578299
TP53_5	17	7577489	7577618
TP53_6	17	7577009	7577165
TP53_7	17	7576843	7576936
TP53_8	17	7573917	7574043
TP53_9	17	7572917	7573018
TYMP_0	22	50967915	50968148
TYMP_1	22	50967555	50967777
TYMP_2	22	50966931	50967049
TYMP_3	22	50966007	50966156
TYMP_4	22	50965584	50965722
TYMP_5	22	50964995	50965177
TYMP_6	22	50964665	50964915
TYMP_6	22	50964995	50965177
TYMP_7	22	50964420	50964580
TYMP_8	22	50964189	50964357
TYMS_a	18	673437	673451

TYMS_a	18	673438	673451
UGT1A1_a	2	234668807	234668958
UGT1A1_a	2	234668849	234668909
mTOR_0	1	11319295	11319476
mTOR_1	1	11318532	11318660
mTOR_2	1	11316980	11317232
mTOR_3	1	11316039	11316259
mTOR_4	1	11313886	11314040
mTOR_5	1	11307866	11308161
mTOR_6	1	11307672	11307800
mTOR_6	1	11307866	11308161
mTOR_7	1	11303161	11303367
mTOR_8	1	11301600	11301748
mTOR_9	1	11300350	11300614
mTOR_10	1	11298449	11298684
mTOR_11	1	11297890	11298115
mTOR_12	1	11294190	11294332
mTOR_13	1	11293445	11293554
mTOR_14	1	11292483	11292595
mTOR_15	1	11291347	11291501
mTOR_16	1	11290972	11291121
mTOR_17	1	11288715	11288985
mTOR_18	1	11276195	11276301
mTOR_19	1	11273446	11273633
mTOR_20	1	11272843	11272975
mTOR_21	1	11272359	11272541
mTOR_22	1	11270861	11270973
mTOR_23	1	11269359	11269525
mTOR_24	1	11264608	11264770
mTOR_25	1	11259588	11259770
mTOR_26	1	11259305	11259470
mTOR_27	1	11227489	11227584
mTOR_28	1	11217199	11217358
mTOR_29	1	11210173	11210293
mTOR_30	1	11206723	11206858

mTOR_31	1	11205015	11205112
mTOR_32	1	11204695	11204822
mTOR_33	1	11199580	11199725
mTOR_34	1	11199351	11199502
mTOR_35	1	11194398	11194533
mTOR_36	1	11193127	11193264
mTOR_37	1	11190576	11190844
mTOR_38	1	11189785	11189905
mTOR_39	1	11188902	11189018
mTOR_40	1	11188501	11188619
mTOR_41	1	11188051	11188193
mTOR_42	1	11187671	11187873
mTOR_43	1	11187057	11187211
mTOR_44	1	11186669	11186863
mTOR_45	1	11184545	11184700
mTOR_46	1	11182026	11182193
mTOR_47	1	11181293	11181435
mTOR_48	1	11177051	11177153
mTOR_49	1	11175443	11175535
mTOR_50	1	11174860	11174954
mTOR_51	1	11174365	11174520
mTOR_52	1	11172899	11172984
mTOR_53	1	11169696	11169796
mTOR_54	1	11169337	11169437
mTOR_55	1	11168228	11168353
mTOR_56	1	11167532	11167567

Table A.2: OncoPanel Amplicons and RainDance Primers.

Gene Target ID	Chr	Amplicon Start	Amplicon End	Forward Primer	Reverse Primer
AKT1_a	14	105246546	105246554	TCTTGAGGAGGAAGTAGCGT	AGGCACATCTGTCCTGG
AKT1_b	14	105246450	105246458	GCCACAGAGAAGTTGTTGAG	GTACATCAAGACCTGGCGG
ALK_a	2	29445212	29445271	GGAGATATCGATCTGTTAGAAACC	CCCACCCTCCCCTTCTC
ALK_b	2	29443629	29443703	GGACTTGAGGTCTCCCC	CTTTGTATCCTGTTCCTCCC
ALK_c	2	29446148	29446365	CCCATAGGGAGGGCTCTG	GCACCAGGAGCTGCAA
ALK_c	2	29446336	29446587	GGAGCTTGCTCAGCTTGTA	CCATATATCTGATTTTTAGCTTTGCAT
ALK_c	2	29446519	29446774	CTGAGCTCTGAACCTTTCCA	TACTTGCAACACAGTCTGCT
ALK_c	2	29446696	29446959	ACTGGAGATGGGATTAGACC	CCCAATGGCTGAGCAC
ALK_c	2	29446940	29447186	CCATGACTCCCAGGAATTGG	GAAACTGCAGTCCAAAGAGG
ALK_c	2	29447129	29447369	AATTGGTGTCTGGGGATCTG	TTTGCCTTCCAGAACATCCT
ALK_c	2	29447344	29447591	CCTAAAGAGCTCTACCAATGTG	GCTAACACTTGTTGCATGGT
ALK_c	2	29447522	29447779	CCTCCTCTATGCAATGGACC	CTCTTACTGCTGGCAGAGAC
ALK_c	2	29447745	29447987	CTCAAGAGCCTTTCCCTCTG	TTCTAGCTCCCACATGCTTC
ALK_c	2	29447910	29448162	TCCTATCTCTCTGCCTGGAG	CAAGCCAAAACGGAAGCTC
ALK_c	2	29448101	29448366	AGGAGGATACACACGGGG	GGTGACCTCTGCCCTC
ALK_c	2	29448288	29448519	ACACTATTCAGTCCTGCCTT	AAGTGTGACAAGGTCTCCAG
BRAF_a	7	140481395	140481418	ACTTACCATGCCACTTTCCC	TCGAGTGATGATTGGGAGAT
BRAF_b	7	140453085	140453218	AAAATAGCCTCAATTCTTACCATC	TCATAATGCTTGCTCTGATAGG
BRAF_b	7	140453129	140453152	ATGGATCCAGACAACTGTTC	TTTTCCTTTACTTACTACACCTCA
DPYD_a	1	97915607	97915621	TCACCAACTTATGCCAATTCT	GAAAACGGCTGCATATTGGT

DPYD_a	1	97915608	97915621	ACATTCACCAACTTATGCCAA	CTGGACAAAGCTCCTTTCTG
DPYD_b	1	98348855	98349021	CAGTGGTACTTACAAAGCAGTT	GACAAAGTGAGAGAGACCGT
DPYD_b	1	98348878	98348892	TCTTGTCTAATTTCTTGGCCG	CCTGGGTGACAAAGTGAG
DPYD_c	1	97981336	97981350	AAAGTTTTGGTGAGGGCAAA	CTCCAGCCACCAGCAC
DPYD_c	1	97981418	97981425	GGTGAGGGCAAAACCCC	GCAGTCACAATATGGAGCTT
DPYD_d	1	97547940	97547954	AGCCAGAATCATTACAGGTCA	TGAGCAACGTAGAGCAAGTT
DPYD_d	1	97547941	97547954	TTCCAGCAGGATTCTTACCT	CAACGTAGAGCAAGTTGTGG
DPYD_e	1	97981417	97981425	CGAATCATTGATGTGCTGGT	TTTCTGCCAAGCCTGAACTA
DPYD_f	1	98039415	98039423	CCAGCACTGTACCTTTAGGA	TTGCTATGCAGTTTGTTCGG
DPYD_f	1	98039416	98039423	GCTCCCAGCACTGTACC	AGGTGGGAGAATTGTTGCTA
DPYD_g	1	97770916	97770924	AATCCCATCAGACCTGAGAC	TTTTTCTGGGATGTGAGGGT
DPYD_h	1	98165087	98165095	CAACTTATACTTGCAGGCCC	ACCATGACAATTGATTTCCCC
DPYD_h	1	98165088	98165095	AGGCCCAGCACCAAAAAG	ATTTTAACCATGACAATTGATTTCC
EGFR_18	7	55241599	55241751	GAGGTGACCCTTGTCTCTG	AGACCATGAGAGGCCCTG
EGFR_18	7	55241614	55241733	TGACCCTTGTCTCTGTGTTC	TGCCAGGGACCTTACCTT
EGFR_18	7	55241646	55241736	TTACACCCAGTGGAGAAGC	TATACAGCTTGCAAGGACTC
EGFR_19	7	55242400	55242528	CAGCATGTGGCACCATC	GCCATGGACCCCCACA
EGFR_19	7	55242415	55242513	GCATGTGGCACCATCTC	CCCCACACAGCAAAGCA
EGFR_20	7	55248971	55249186	CCTCCTTCTGGCCACC	GATCCTGGCTCCTTATCTCC
EGFR_20	7	55248986	55249101	CACTGACGTGCCTCTCC	CTTTGTGTTCCCGGACATAG
EGFR_20	7	55249054	55249171	GGCATCTGCCTCACCTC	GGATCCTGGCTCCTTATCTC
EGFR_21	7	55259397	55259582	CCCATGATGATCTGTCCCTC	CTGGTCCCTGGTGTCAG
EGFR_21	7	55259412	55259545	CCCATGATGATCTGTCCCTC	GCCTCCTTCTGCATGGTAT

EGFR_21	7	55259508	55259567	CAGCATGTCAAGATCACAGAT	CCCAGAATGTCTGGAGAGC
ERBB2_20	17	37880979	37881136	CTCAGCGTACCCTTGTCC	TCTGCATACACCAGTTCAGC
ERBB2_20	17	37881030	37881164	CATATGTCTCCCGCCTTCTG	CAAAGAGCCCAGGTGCATA
GSTP1_a	11	67352682	67352696	TGAATGACGGCGTGGAG	GCCCCTTTCTTTGTTCAGC
HRAS_a	11	534281	534293	TCACCTCTATAGTGGGGTCG	ACGGAATATAAGCTGGTGGT
HRAS_a	11	534282	534293	GGGTCGTATTCGTCCACA	GGAGCGATGACGGAATATAAG
HRAS_b	11	533870	533884	TACTGGTGGATGTCCTCAAA	GTGGTCATTGATGGGGAGAC
HRAS_b	11	533871	533884	CATGTACTGGTCCCGCAT	GATTCCTACCGGAAGCAGG
HRAS_c	11	533549	533557	AGGTCTCGATGTAGGGGATG	GATCAAACGGGTGAAGGACT
HRAS_c	11	533550	533557	TAGCTTCGGGCGAGGT	TCAAACGGGTGAAGGACTC
HRAS_d	11	533462	533470	GTCAAGGGAGAGGGTCAGT	GCATCCCCTACATCGAGAC
HRAS_d	11	533463	533470	GTCAGTGAGTGCTGCTCC	CTGTGGAATCTCGGCAGG
IDH1_a	2	209113110	209113113	ACATGACTTACTTGATCCCCA	CCAAATGGCACCATACGAAA
IDH1_a	2	209113111	209113113	ACATGACTTACTTGATCCCCA	TGGAAATCACCAAATGGCAC
IDH2_a	15	90631836	90631839	TGTACTGCAGAGACAAGAGG	AAAAACATCCCACGCCTAGT
IDH2_a	15	90631933	90631935	ACTAGGCGTGGGATGTTTTT	TGCAGTGGGACCACTATTAT
IDH2_b	15	90631837	90631839	AAAGTCTGTGGCCTTGTACT	GACCAAGCCCATCACCAT
IDH2_b	15	90631932	90631935	ACTAGGCGTGGGATGTTTTT	CTCTGTCCTCACAGAGTTCA
KIT_9	4	55592008	55592160	TATGCCACATCCCAAGTGTT	AGAAGTCTTGCCCACATCG
KIT_9	4	55592096	55592231	CACCGTTTGGAAAGCTAGTG	GACAGAGCCTAAACATCCCC
KIT_11	4	55593567	55593723	AGAGTGCTCTAATGACTGAGA	ACCCAAAAAGGTGACATGGA
KIT_11	4	55593567	55593723	TTACAGGTAACCATTTATTTGTTCT	GTGTACCCAAAAAGGTGACA
KIT_13	4	55594162	55594302	GCCAGTTGTGCTTTTTGCTA	ACCTGACAGACAATAAAAGGC

KIT_14	4	55595486	55595636	ATGACCACCCTTGGGTATTT	TCTTACCAGGAAGACTCCTTT
KIT_14	4	55595486	55595666	ATCTCACCTTCTTTCTAACCTTT	CCCCATGAACTGCCTGTC
KIT_14	4	55595612	55595666	GGAAGATCATGCAGAAGCTG	TGCCTGTCAACAGCTAACTA
KIT_17	4	55599221	55599371	AAAATGAATTTAAATGGTTTTCTTTTCT	GCAGGACTGTCAAGCAGAG
KIT_17	4	55599270	55599373	CTTGGCAGCCAGAAATATCC	GTGTGATATCCCTAGACAGGA
KIT_18	4	55602649	55602790	GAGCTTCTGAATTAACATTATTGAC	AGAAGATGCTCTGAGTCTAATG
KRAS_a	12	25398274	25398291	TGCATATTAAAACAAGATTTACCTCTAT	GCCTGCTGAAAATGACTGA
KRAS_a	12	25398275	25398291	TGCATATTAAAACAAGATTTACCTCTATT	AAGGCCTGCTGAAAATGACT
KRAS_b	12	25380269	25380283	ATACACAAAGAAAGCCCTCC	GGAGAAACCTGTCTCTTGGA
KRAS_b	12	25380270	25380283	ATACACAAAGAAAGCCCTCC	GGAGAAACCTGTCTCTTGGA
KRAS_c	12	25378554	25378568	TCTGTATTTATTTCAGTGTTACTTACC	ACAAAACAGGCTCAGGACTT
KRAS_c	12	25378555	25378568	TCTGTATTTATTTCAGTGTTACTTACC	GTAGACACAAAACAGGCTCA
KRAS_d	12	25378644	25378653	TGTCTACTGTTCTAGAAGGCAA	AGTTGTGGACAGGTTTTGAA
KRAS_d	12	25378645	25378653	GTGTCTACTGTTCTAGAAGGC	TGTGGACAGGTTTTGAAAGA
MAP2K1_a	15	66727449	66727486	AGCGAAAGCGCCTTGA	AGCCCCCAGCTCACTG
MAP2K1_a	15	66727450	66727486	GAGCTAGAGCTTGATGAGCA	GGAGACCTTGAACACCACA
MAPK1_1	22	22221602	22221638	GTGAAGTCCGGGTTCGAG	CTACACCAACCTCTCGTACAT
MAPK1_1	22	22221602	22221645	GCGGTGAAGTCCGGG	GCGCTACACCAACCTCT
MAPK1_1	22	22221611	22221673	GGTCGCGGACACTCA	CGCGGGCAGGTGTTC
MAPK1_1	22	22221620	22221687	GGACACTCACCACACCAT	GCCCGGAGATGGTCC
MAPK1_1	22	22221653	22221740	GCCGATGTACGAGAGGTT	AGAGCTGAGCGGCGG
MAPK1_1	22	22221658	22221740	GATGTACGAGAGGTTGGTGT	CGACAAGAGCTGAGCGG
MAPK1_2	22	22161943	22162075	AAGGTTACCAAGCAGTGGAA	CAAGAAAATCAGCCCCTTTGA

MAPK1_2	22	22161943	22162113	AAGGTTACCAAGCAGTGGAA	GCTCTGCTTATGATAATGTCAAC
MAPK1_2	22	22161979	22162145	TTCATTTGCTCGATGGTTGG	GAGGGCTGTTTTTAATGCCA
MAPK1_2	22	22162037	22162145	GTCTGAAGCGCAGTAAGATT	CTGAGGGCTGTTTTTAATGC
MAPK1_3	22	22160129	22160157	ACATGTTTTTGGGTATTTCTGGT	TTCCAACCTGCTGCTCAA
MAPK1_3	22	22160143	22160266	AAATAACCTGGCTGACCTTG	CTTGAAGACACAACACCTCA
MAPK1_3	22	22160241	22160338	AACCCTCTGAGGATCTGGTA	TGTGACCAGCTAATTGGTGT
MAPK1_4	22	22153291	22153399	CAGAAAGTTCTCTTACTTACTGGA	AGATCTGTGACTTTGGCCTG
MAPK1_4	22	22153291	22153427	TTACTGGATTTCTTTTTATGCAAAC	TGATGTTTTGATATGAAAGGTTAGA
MAPK1_4	22	22153365	22153427	GCCACATATTCTGTCAGGAAC	ATGCCCAGAAAGTATCTGCC
MAPK1_5	22	22142973	22143079	GATGTAAGCTGTACAAACTTGAG	GGGCTACACCAAGTCCATT
MAPK1_5	22	22143071	22143107	CCAGAATGCAGCCTACAGA	GCACCTGTCATACAGGAAGA
MAPK1_6	22	22142536	22142645	TCAGGCTAGTGACCTAACAAT	CCCCATCACAAGAAGACCTG
MAPK1_6	22	22142536	22142687	GCGAAGCTAAGCCTAAGAAA	GACTCAGAGTTGATGGTGTG
MAPK1_6	22	22142567	22142687	TTTGGAGTCAGCATTTGGGA	CAGAGTTGATGGTGTGTAGTC
MAPK1_7	22	22127152	22127281	CTGGCTGATCTATGTCCCTG	TCTGCTCTCACTACTGCAAA
MAPK1_7	22	22127152	22127281	CTGGCTGATCTATGTCCCTG	CTCTCACTACTGCAAAACCT
MAPK1_8	22	22123483	22123602	CCTTGCTAGAGCTCACTGTAT	TGTTTTCTTTTAAAGCCCATCG
MAPK1_8	22	22123483	22123619	CTCACTGTATTAAACTCCAGGT	ACCCATAACAACTTTGACTGTT
MAPK1_8	22	22123520	22123619	CTGTATCCTGGCTGGAATCT	ATCTGAGCAGTGGTCATTTT
MTHFR_a	1	11856371	11856385	AAAGAAAAGCTGCGTGATGA	AAGCAGGGAGCTTTGAGG
MTHFR_a	1	11856372	11856385	TCAAAGAAAAGCTGCGTGAT	ACTGTCATCCCTATTGGCAG
MTHFR_b	1	11854469	11854483	GGTTCTCCCGAGAGGTAAAG	GAGGAGCTGCTGAAGATGT
MTHFR_b	1	11854470	11854483	GGTTCTCCCGAGAGGTAAAG	GGAGCTGAAGGACTACTACC

NRAS_a	1	115258737	115258754	TGGATTAGCTGGATTGTCAGT	ACTGGTTTCCAACAGGTTCT
NRAS_a	1	115258738	115258754	ATCCGACAAGTGAGAGACAG	ACTGAGTACAAACTGGTGGT
NRAS_b	1	115256522	115256536	ATTGGTCTCTCATGGCACTG	AGATGGTGAAACCTGTTTGTT
NRAS_b	1	115256523	115256536	TCCGCAAATGACTTGCTATT	AGATGGTGAAACCTGTTTGTT
NRAS_c	1	115252286	115252294	TGGAATCCCGTAACTCTTGG	AAGCGAGTAAAAGACTCGGA
NRAS_d	1	115252199	115252207	GCAAACTCTTGCACAAATGC	TACAAAACAAGCCCACGAAC
PDGFRA_12	4	55140993	55141155	GCACTGGGACTTTGGTAATTC	AAGGGAAAAGGGAGTCTTGG
PDGFRA_14	4	55144048	55144188	AGCTCAGCTGGACTGATATG	ACATGTGTCCAGTGAAAATCC
PDGFRA_18	4	55151993	55152145	AGATGGCTTGATCCTGAGTC	GAAGGAGGATGAGCCTGAC
PIK3CA_a	3	178936047	178936198	ACAGACTAGCTAGAGACAATGA	CATGTAAATTCTGCTTTATTTATTCCAA
PIK3CA_a	3	178936076	178936102	AGCTCAAAGCAATTTCTACAC	GCTGAGATCAGCCAAATTCA
PIK3CA_b	3	178952078	178952092	AAAACTGAGCAAGAGGCTTT	TGTGTGGAAGATCCAATCCAT
PIK3CA_b	3	178952079	178952092	AGCAAGAGGCTTTGGAGTAT	CATGCTGTTTAATTGTGTGGA
PTEN_a	10	89692985	89692999	GGGCAAATTTTTAAAGGCACA	AGATCCAGGAAGAGGAAAGG
PTEN_b	10	89717666	89717680	TGGTATGTATTTAACCATGCAGA	GTAACGGCTGAGGGAACT
PTEN_b	10	89717667	89717680	GTATGTATTTAACCATGCAGATCC	ACCACACACAGGTAACGG
PTEN_c	10	89717765	89717785	GCCGTTACCTGTGTGTGG	GCTTTTAATCTGTCCTTATTTTGG
PTEN_c	10	89717766	89717785	TCTTCCACAAACAGAACAAGA	CACCTGCAGATCTAATAGAAAACA
STAT1_0	2	191874592	191874698	GGCCCCAAGTCACTTAATCA	GTACGAACTTCAGCAGCTTG
STAT1_0	2	191874634	191874739	TCTAACCACTGTGCCAGGTA	GGCTTTCTTTGGAGCTATGG
STAT1_1	2	191873679	191873783	GCCTTCCATAAACATGAGAACA	CACCATCCGTTTTCATGACC
STAT1_1	2	191873679	191873843	TGAAGAAAACTGCCTTCCAT	AGTTCTAGAATGAAATGTGTAAATGTT
STAT1_1	2	191873719	191873843	ACGCTTGCTTTTCCTTATGTT	GTCTGTTTTACATAGACATTTAGTTC

STAT1_2	2	191872279	191872357	ATCATTGCTTTGACATGGGC	AGGAAGACCCAATCCAGATG
STAT1_2	2	191872279	191872397	TGACATGGGCCCTAATAGT	ACACAATAAAGTAAACATTCTGCAT
STAT1_2	2	191872352	191872367	CCTTCAGACAGCTGTAAATGAT	AGGATAATTTTCAGGAAGACCC
STAT1_2	2	191872368	191872397	GTAAATGATCATAGACATCTGGATT	ACAAATTCATATCAACTTACAATACAC
STAT1_3	2	191865790	191865899	CCCCTACAGAAAGTTTCAGAATAA	ACACACCCTGAAGAAAACGA
STAT1_3	2	191865790	191865899	CCCAAGCAATTGAAACCTTTTT	CCTGAAGAAAACGATGGCTA
STAT1_4	2	191864342	191864440	AACGGGCACCACTTCA	AAGTCTTTGGAAGTTGCTGA
STAT1_4	2	191864342	191864440	AACGGGCACCACTTCA	AGTCTTTGGAAGTTGCTGAT
STAT1_5	2	191862933	191863044	GTGGCATGCTATTCTGGAAA	TGGCTTTTGTTGGTTTTGTCT
STAT1_5	2	191862933	191863044	TGGCTATAATTTTTCCTCTCTTCTA	AATCTTGGCTTTTGTTGGTTT
STAT1_6	2	191862572	191862689	CAGTCAGCTGCCAGTTTTC	GTTGCTGAATGTCACTGAACT
STAT1_6	2	191862671	191862743	TCCACTCCACTAGTTCATCATT	CTTAGAGCCCCAGTTGAGAA
STAT1_6	2	191862689	191862743	TTAATCAGGGCATTCTGGGT	AGCCCCAGTTGAGAATGAAA
STAT1_7	2	191859777	191859908	AGACCGATTACAGAAGGTACAA	AGTCTGCAGCAAGTTCGG
STAT1_7	2	191859777	191859942	AGACCGATTACAGAAGGTACAA	GTCTTGTGTCTTCCCAGGTT
STAT1_7	2	191859820	191859955	GCTGGAAAAGACTGAAGGTG	GCTTCTGGACTGTTTCTCATAG
STAT1_7	2	191859821	191859955	CTGGAAAAGACTGAAGGTGC	CTGCTTCTGGACTGTTTCTC
STAT1_8	2	191855944	191856056	TGACAGGTGATGTATGGGAT	TCATTGTGATTGCCTCAACC
STAT1_8	2	191855944	191856056	GACAGGTGATGTATGGGATG	CCTTAATGGAAATGCTAACTTATCT
STAT1_9	2	191854331	191854393	CAGCTAGAAATCTGCTTATTTAGT	TTTTATTTTTCTTTCCAGACTGTTG
STAT1_9	2	191854331	191854410	TCTGTGCTTGAGTAACAAAATC	ACGTTAATAGGGAATTGGCAT
STAT1_9	2	191854395	191854410	TCAGCTCTTGCAATTTCACC	ACTGGAGGGGGAGTAGTTTA
STAT1_10	2	191851755	191851781	CCCAAAATGTTGAACTTCCTAAA	TTTTTGCAGAGATGTGAATGAG

STAT1_10	2	191851755	191851804	GAAATGCTGAAAAGTCTTCCAA	TTACACTCTTATGCTCTTATACTCT
STAT1_10	2	191851799	191851804	TTCTCTCATTCACATCTCTGC	CTTACACTCTTATGCTCTTATACTCT
STAT1_11	2	191851570	191851602	CAATGTGCCAAAAAGGGCT	AGTCCACCAATGGCAGTC
STAT1_11	2	191851596	191851649	TACCAGGTGCCGAAATTCA	TTAGGAAGTTCAACATTTTGGG
STAT1_11	2	191851755	191851779	GTGGACTCCTCCATGTTCA	TGCAGAGATGTGAATGAGAG
STAT1_12	2	191850335	191850396	TGGGCCCATTCACAACATAA	GACCATTACCATGGTGTTTACT
STAT1_13	2	191849026	191849127	CAATTAAAAGTAAAAATAATGAAGTTTTCCA	AATTATATTCTTTTCTTCTTTCCTTTTCT
STAT1_13	2	191849026	191849129	TTTCCAACTCGGGACCAT	TTTGAAAGTTTTAGGATCTGTGAAT
STAT1_13	2	191849091	191849129	TGGGTTTCAAAACTAAGGGAG	TCTTCAGACTTGCCACTGAT
STAT1_14	2	191848358	191848459	CTCTGCTTAACCCTGGGAC	TGTCATCCTTTAGACGACCT
STAT1_14	2	191848377	191848476	GTTTTCCATACCCTGGGTTC	AGCAGTTATCTGAAGGTGACA
STAT1_15	2	191847099	191847201	GCAGAGGGGAAAAGAGCAA	ATGTGCACGATGGGCTC
STAT1_15	2	191847099	191847252	AGAGGGGAAAAGAGCAATTAGA	ACCCTTAGATTTTGGGTGTTTT
STAT1_15	2	191847199	191847254	CCAACTCAGCACTTCTGAAA	TACTGTGAAAGCACCTGTGT
STAT1_16	2	191845336	191845405	ACTTAGAGAGCATAAAACCCAG	AACCAAAGCTTTAGAATCAGTTT
STAT1_17	2	191844488	191844591	ATACTGAAGCTGGACTCAGG	GTCTGCATTTGTATACTTTCAGG
STAT1_17	2	191844488	191844602	ACCTCGCAGCACTAAAAATA	CCATGGTAAGTCATTGTTTTAGATT
STAT1_17	2	191844574	191844602	CCAAAGCCAGAAGGGAAAAT	CTTTGCAAATGATGGTGGGA
STAT1_18	2	191843572	191843706	AAGAGGGACTTCACACACAT	GCATCATGGGCTTCATCAG
STAT1_18	2	191843622	191843737	TCCACCCATGTGAATGTGAT	AAAGCCCATCCGTCCATC
STAT1_19	2	191841556	191841670	CCCTCATCAGGAAAGACTGT	CCTGACATCATTCGCAATTACA
STAT1_19	2	191841556	191841734	CCCCTCATCAGGAAAGACTG	TAGAACCTGACTTCCATGCG
STAT1_19	2	191841652	191841761	CTTCAGGGGATTCTCAGGAATA	TCTGTCCTCTTTCATTTTGGG

STAT1_19	2	191841698	191841761	GCGAATGATGTCAGGGAAAG	TCTGTCCTCTTTCATTTTGGG
STAT1_20	2	191840528	191840623	GAGGTTTGTAAACATGTCACTCT	GTTGATGGAAAGCGTACACA
STAT1_21	2	191839546	191839668	CTGAGCACACACACTTATTGA	CTCAGATGTTGACATTGCTCT
STAT1_21	2	191839546	191839668	CTTATTGAGAGCTACACACAGG	CTCAGATGTTGACATTGCTCT
STAT1_22	2	191835419	191835453	CTGTCGCCAGAGAAGATGAA	TGAGTCTGCATTTCACAAGAT
STAT3_0	17	40500397	40500497	ATGGAACAGCAAGGCATGA	CTACAGCAGCTTGACACAC
STAT3_0	17	40500432	40500544	TTGACTCTCAATCCAAGGGG	TTGTTTACCCCTACTGGGAC
STAT3_1	17	40498577	40498688	AGAACACTAACACCCGACTC	CACATGCCACTTTGGTGTTT
STAT3_1	17	40498577	40498728	AGAACACTAACACCCGACTC	CATTCTTCCTTTTCCTAGGGC
STAT3_1	17	40498670	40498741	CGGCTATACTGCTGGTCAA	GCATCAGGTTTGCTTTGTTT
STAT3_1	17	40498713	40498741	ACCAAAGTGGCATGTGATTC	GCATCAGGTTTGCTTTGTTT
STAT3_2	17	40497567	40497685	CCAGACCAGGGATTTGTTTT	ACAGTTCAGTCCACATCTCC
STAT3_2	17	40497567	40497685	CCCAGACCAGGGATTTGTTT	TGGTCTGCTGCTGATTTTTA
STAT3_3	17	40491322	40491430	TTAATGAAAGCTCCCTGCC	TGCATTGACCTCCTTTTTGG
STAT3_3	17	40491334	40491437	GCTTGTAACTTGCATCACCT	TTCACATGTGCATTGACCTC
STAT3_4	17	40490739	40490840	ACTCAACAACACAAACTCACTT	TTTCTGTTCCCAAGGAAATCT
STAT3_4	17	40490739	40490840	CCGCCCGCCTTAAGAT	ATTTTCTGTTCCCAAGGAAATC
STAT3_5	17	40489771	40489885	GCCACAAGACGCTGAAATC	TCCCTCAGGTCAAGGAGTTT
STAT3_5	17	40489771	40489885	GCAAGTGAGCGAGACAC	CCCTCAGGTCAAGGAGTTTT
STAT3_6	17	40489443	40489544	GTACCAATTCTGTGGGCCT	AGTACGTGCAGAAAACTCTC
STAT3_6	17	40489443	40489614	AGCTTTCGAGAAAGAAAGGAA	TGGTTAGAGACAGTCTGAGG
STAT3_6	17	40489511	40489614	CCAATGCAGGCAATCTGTT	TCCTGCTCTGGAGTTGACTA
STAT3_7	17	40485899	40486023	ACTCTACCACGTGAGTCTTT	ACTTCAGACCCGTCAACAAA

STAT3_7	17	40485899	40486051	ACTCTACCACGTGAGTCTTT	GCAGGATAACGTCATTAGCA
STAT3_7	17	40485946	40486077	AAACAGCTCCACGATTCTCT	TGTAGTGGTCTCCATGTCTTC
STAT3_7	17	40485981	40486077	TGCTGTACAATGGGGTCC	GTATTTCCTTCCCCTTCTCCA
STAT3_8	17	40485681	40485786	CCTAACAGTGTCCCTCAGTAA	GAGCCCATCTTCTCTTTCCT
STAT3_8	17	40485717	40485793	TTAGTAGTGAACTGGACGCC	ACTCACGTGGTAGAGTGAGA
STAT3_9	17	40483480	40483559	TGTCTGTCAAAGTTCTCATTTTTC	TTATGGGAGAGTTACTGACTTTT
STAT3_10	17	40481755	40481804	CGGAACAAAAGGAAGCCT	TGAAGAAACACAGAGCCTATT
STAT3_10	17	40481755	40481804	GTAGCCGGAGGATGAAGTTA	GGTGGTCAAAGTAGGCTTTT
STAT3_11	17	40481562	40481672	CAGGTGTCCTGTGAGGC	CATAGTTGATTGTTCCCCTGT
STAT3_11	17	40481562	40481675	CCAGAGGCCCTTTGTGAA	TGGTCACCTACATAGTTGATTG
STAT3_11	17	40481653	40481675	GTGTTTGTGCCCAGAATGTT	TCTCAGAGGGTAAGTTCAGC
STAT3_12	17	40481418	40481485	CTCTCTCCCTCAAGGAAAAC	CAGGACACCTGCCTTTTT
STAT3_12	17	40481418	40481485	TTTACCCCTCTCTCCCTCAA	ACAGGACACCTGCCTTTTT
STAT3_13	17	40478124	40478227	GTTTTTGTCCTGAGTCACCC	ACCACACCTGGCCTAAGA
STAT3_14	17	40476971	40477089	GGGCACCAACTAAAAGGAGG	AGAGATTTCCAAGGCTGTGA
STAT3_14	17	40476971	40477089	GGGGCACCAACTAAAAGGA	TCCCCAGCTCAGTCCC
STAT3_15	17	40476719	40476762	CAGTAGACATGGCCCAAATG	AAGCGAGGACTGAGCATC
STAT3_15	17	40476719	40476874	CCGGATCCCTTTTCTGGG	GAGCACCATCCCTCATCTAA
STAT3_15	17	40476735	40476874	TGAAATGCGGACCCAAGA	AATGAGCACCATCCCTCATC
STAT3_16	17	40475581	40475653	GGTGAGCATTCCCATTCC	CCCAAGCTGAAAATGTACTACT
STAT3_17	17	40475268	40475382	CAGGGGACTTGGTTACATCT	AGTAGACTTGGCTTTCCCATT
STAT3_18	17	40475012	40475170	GTGGGGTGGGTGGGA	ACAACATTGTTCCTCCTCCT
STAT3_18	17	40475051	40475171	CCTTCTCCACCCAAGTGAAA	TGGATGCCCTGTTAGCAAT

STAT3_19	17	40474290	40474390	TCCTCCAAGGATCCCAAAAT	ATATCCTGGTGTCTCCACTG
STAT3_19	17	40474290	40474460	TCCTCCAAGGATCCCAAAAT	CAAAGCAGCAGCTGAACAA
STAT3_19	17	40474350	40474522	TCTCTGGCCGACAATACTTT	TGACCTAGCTGTAGGTTCCA
STAT3_19	17	40474364	40474495	TACTTTCCGAATGCCTCCTC	CAGGTAAGACCCAGATCCAG
STAT3_19	17	40474489	40474522	CTGCTGCTTTGTGTATGGTT	TCCCCTTCGAGGAAAGAAAA
STAT3_20	17	40469190	40469252	AGGGATAACTGAGGATATTAGAAAT	TCACAGTCAGTAAGAAAACTGG
STAT3_20	17	40469190	40469252	AGAAATGAAGGCAAAACGGG	TCCAGCTCTGCTTACTGAAT
STAT3_21	17	40468797	40468897	GTGAGAGCATCACACAAAGG	CGACCTGCAGCAATACCATT
STAT3_21	17	40468883	40468929	AATGAATCTAAAGTGCGGGG	AGACCAGAGTTTGATGGCTT
STAT3_22	17	40467753	40467828	GTCGTATCTTTCTGCAGCTT	AGGGTGGACAACTGAACT
TP53_0	17	7579829	7579922	AGGGGGCTGGGGTTG	TTGCAGCAGCCAGACT
TP53_0	17	7579829	7579922	GGCCTGCCCTTCCAAT	CTGGATCCCCACTTTTCCTC
TP53_1	17	7579690	7579731	GCATCAAATCATCCATTGCTT	TGGGACTGACTTTCTGCT
TP53_1	17	7579690	7579731	GGTGAAAAGAGCAGTCAGAG	ATTCCATGGGACTGACTTTC
TP53_2	17	7579302	7579440	GGCATTGAAGTCTCATGGAA	CAGCAGCTCCTACACCG
TP53_2	17	7579399	7579514	TAGGTTTTCTGGGAAGGGAC	ACAATGGTTCACTGAAGACC
TP53_2	17	7579461	7579598	GTGTAGGAGCTGCTGGTG	CTGACTGCTCTTTTCACCC
TP53_3	17	7578361	7578483	CCTGGGCAACCAGCC	GCAGCTGTGGGTTGATTC
TP53_3	17	7578437	7578564	CCGTCATGTGCTGTGACT	TTGTGCCCTGACTTTCAACT
TP53_4	17	7578162	7578304	CAAATAAGCAGCAGGAGAAAG	CCAGGGTCCCCAGGC
TP53_4	17	7578167	7578259	CAGCAGGAGAAAGCCCC	TCCTCAGCATCTTATCCGAG
TP53_4	17	7578259	7578299	CCACACGCAAATTTCCTTCC	GGTCCCCAGGCCTCT
TP53_5	17	7577489	7577618	CAGGCCAGTGTGCAGG	CTGGCCTCATCTTGGGC

TP53_6	17	7577009	7577042	CTCCTCCACCGCTTCTTG	AGCCTCACCACGAGC
TP53_6	17	7577009	7577165	CCTCCACCGCTTCTTGT	AGGTAGGACCTGATTTCCTTA
TP53_6	17	7577014	7577045	CGCTTCTTGTCCTGCTTG	GGGAGCCTCACCACG
TP53_6	17	7577057	7577165	AGCTCGTGGTGAGGC	GGACAGGTAGGACCTGATTT
TP53_7	17	7576843	7576936	GCATTTTGAGTGTTAGACTGG	TTATGCCTCAGATTCACTTTTATC
TP53_8	17	7573917	7574043	CCAACCTAGGAAGGCAGG	CTTACTTCTCCCCCTCCTCT
TP53_8	17	7573917	7574043	AGTAGGGCCAGGAAGGG	TGTGTATATACTTACTTCTCCCCC
TP53_9	17	7572917	7573018	CCCAAAACCCAAAATGGCA	TGATGTCATCTCTCCTCCCT
TP53_9	17	7572917	7573018	GCTGTCAGTGGGGAACAA	GTGATGTCATCTCTCCTCCC
TYMP_0	22	50967915	50968030	GGGACCCAAAGTCTCTCG	CAGAGCCCAAGCAGCTC
TYMP_0	22	50967989	50968121	CCCCTGATGTCCGCTTC	GATGGCAGCCTTGATGAC
TYMP_0	22	50968098	50968148	CGGAGAAGTCACCAGGC	GGAGAGACACGGGAAAGG
TYMP_1	22	50967555	50967682	GACTGGTTGCTGCATGTG	TGGCTCAGTCGGGACA
TYMP_1	22	50967623	50967765	CTGACCTTGTCACCCACA	TACCCCCACATACCAGGG
TYMP_1	22	50967738	50967777	GTCTCCTCCAGATCCATGC	GTCAGCCCGAGAGACTTTG
TYMP_2	22	50966931	50967042	CCACCAGTGATCTTTTAGTGA	CTCAGCATCCCTGACCAC
TYMP_2	22	50966997	50967049	AGACTCCAGCTTATCCAAGG	CTAGCCAGGGAAGGTGAAG
TYMP_3	22	50966007	50966156	GTGAACATGCAGAAGCAGG	AAGTCACTGAGAACAGGGGA
TYMP_4	22	50965584	50965722	GCATCAAGACGCTTGCC	ATTGTCTCCAACCTCCTCTG
TYMP_5	22	50964995	50965108	CCTCCGCTCCCCTACA	CTGACCGCCATGGACAA
TYMP_5	22	50965033	50965177	GTGACCAGGTCCCTTAAGTC	GGTCCACGCTGAGCC
TYMP_5	22	50965126	50965177	TTGTCCATGGCGGTCAG	ACTTCACTCGTGTCTCTTCC
TYMP_6	22	50964665	50964793	CGGGAAGGGAAGGGGAT	GCTTCGAGCGGATGCT

TYMP_6	22	50964665	50964876	CGGAAGGACGGGGACT	CTGGCTCAGCGGACAC
TYMP_6	22	50964757	50964915	GGACTTCCCGAGCACAG	GCCGCGCCTAAGACC
TYMP_6	22	50964995	50965016	CCAGCATCCGCTCGAA	CCAGACTTAAGGGACCTGG
TYMP_7	22	50964420	50964526	GCGAGGGGCTGTTAGAG	CTGGCGCTGGTGCTG
TYMP_7	22	50964420	50964570	GCGAGGGGCTGTTAGAG	CCCCTCTCCCCGCAG
TYMP_7	22	50964465	50964580	CACGTCGACCAGCAGC	ATCCCCTTCCCTTCCCG
TYMP_8	22	50964189	50964333	CCGCCCAAGCACTGAC	GGGACCCCCTGGCTC
TYMP_8	22	50964204	50964357	GCGGCAAAGGAGCTTTATT	CGCGGCCTCTAACAGC
TYMS_a	18	673437	673451	TTTCACAAGCTATTCCCTCAA	ACGAATGCAGAACACTTCTTT
TYMS_a	18	673438	673451	TTTCACAAGCTATTCCCTCAA	AGAATGAACAAAGCGTGGAC
UGT1A1_a	2	234668807	234668958	CTGAAAGTGAACTCCCTGCT	TCAACAGTATCTTCCCAGCAT
UGT1A1_a	2	234668807	234668958	CTGAAAGTGAACTCCCTGCT	GCAGGCCCAGGACAAG
UGT1A1_a	2	234668849	234668909	TTGTGGACTGACAGCTTTT	GTCCGCCCTGGGACT
mTOR_0	1	11319295	11319413	CACACATCCCACAATGACTG	CTGCCACCACATCTAGCAA
mTOR_0	1	11319381	11319476	TTTCCTCATTCCGGCTCTTT	TGACCAGGGCCATAAGTAAA
mTOR_0	1	11319424	11319476	GACGCTCACATTGCTAGATG	GTGACCAGGGCCATAAGTAA
mTOR_1	1	11318532	11318632	CACAAAGGTGAGTGTGTTGT	CAGATGAGTCAAGAGGAGTCT
mTOR_1	1	11318570	11318660	AAGATGCCACCTTTCCTCTC	AATCTTTAGATGCCAGCCCA
mTOR_2	1	11316980	11317112	ATGACACCATCGTTCCCC	TTGTCATGGAAATGGCATCC
mTOR_2	1	11316980	11317147	AGGAAGCAAAAGACCCCC	CTATCTTCGGAACCTCCTCC
mTOR_2	1	11317060	11317200	CTCGCTTCACCTCAAATTCC	GCCTCATAGGAGTGGAAGG
mTOR_2	1	11317080	11317232	ACGTACTCAGCGGTAAAAGT	TGAAGTCTGCGTACTTTCCT
mTOR_2	1	11317143	11317232	TCCATGACAACTGGGTCATT	GAAGTCTGCGTACTTTCCTG

mTOR_3	1	11316039	11316161	TTTAGGCCAGGTGATTCTCT	TGACAACATTTTTGTGGCCG
mTOR_3	1	11316039	11316196	CCTTTAGGCCAGGTGATTCT	CCTACCTTCTTCTTCCAGCA
mTOR_3	1	11316119	11316259	AATCAGACAGGCACGAAGG	AATGAGAGTTCTCGGTTTGC
mTOR_3	1	11316182	11316259	CGGCCACAAAAATGTTGTCA	CTAGAAGAGTGAGCAAGCCT
mTOR_4	1	11313886	11313987	TCGCTCACAGAATGGTACAC	GGGATTTGATGAGACCTTGG
mTOR_4	1	11313941	11314040	ACCAGCTCGTTAAGGATCAA	CTCTAATGAAGGCACCCTGT
mTOR_5	1	11307866	11307970	AAGTGAGGTGTGGAGCTTAG	GGGTACAGCTCTCACCAAG
mTOR_5	1	11307966	11308116	GGAGGTCCCAAATCCCAT	ATGGAAGAAATCACACAGCA
mTOR_5	1	11308015	11308161	CCCACCAAGGCATTTGAC	TGTAGAATCCACAGTGCCC
mTOR_5	1	11308056	11308161	AAACTGGTGAAGGGGGTAAT	TGTAGAATCCACAGTGCCC
mTOR_6	1	11307672	11307799	CTGTTCCCTGTTTACCCTGA	CTGCCAACCCTTTATCCTTC
mTOR_6	1	11307866	11307891	CGGGGCAACAAATTAAGGAT	TGTTGCAGAGACTTGATGGA
mTOR_7	1	11303161	11303298	TTCCTCTCCAACCAAATGGA	GCTGTGTCAAGAAGGAGAAG
mTOR_7	1	11303161	11303349	CCAACCAAATGGAGTGGAAG	TTCTGTGCTCAGATACCCAG
mTOR_7	1	11303234	11303367	GCACGCGAGGCAAATAG	TAGACCCTAACCCTGACCTG
mTOR_8	1	11301600	11301728	CAAGCCTCACGCTGATACA	TTCTCTACAGGAGGCAGAAG
mTOR_8	1	11301656	11301748	CAGCAGCTCCTTGATATCCT	CCAAGGTGATTTTGAGGTGG
mTOR_9	1	11300350	11300487	AAGTTTCCAGCATCTCTCAC	CTTATGCACAAACCCCTTCG
mTOR_9	1	11300350	11300513	CTTTCCCAAAGTTTCCAGCA	GGCTACTGAAAATGCTGTCC
mTOR_9	1	11300407	11300614	AGGGCAAGAGTGATGCTG	CAGCCCTTATGTGACTTGTTT
mTOR_9	1	11300412	11300571	AAGAGTGATGCTGCCCAC	CAGTGCTCTACGACCTGAG
mTOR_9	1	11300515	11300614	GTTTGTGCATAAGGACCAGG	TCTTCCCAAGAACAGACTGA
mTOR_10	1	11298449	11298553	CCCAATTGTCCTAAGCTCCT	ACACCCTCCATCCACCT

mTOR_10	1	11298494	11298652	CAACTACGAGCAGTTTGCTA	CACTCTCTGACCCAATTTGT
mTOR_10	1	11298629	11298684	TCTCCTTGTGCTCACTGTTC	AGACCTACCTGTCTACAGCA
mTOR_11	1	11297890	11298007	TCCTCAAGCAGTTCTCACAG	GCCTTGTTTGTGGCTCTG
mTOR_11	1	11297890	11298044	TTCCTCAAGCAGTTCTCACA	CTTTGATGCACACCTGGC
mTOR_11	1	11297952	11298108	AAAGGCAGGGTTCATGCTA	CAAAGGCTCCATTGCTCTTG
mTOR_11	1	11297959	11298115	AGGGTTCATGCTACTGAGTC	GGAAATGTTCAAAGGCTCCA
mTOR_11	1	11298035	11298115	CAAACAAGGCCTGCAAGTT	TCTGGAATCTTCCCACTACG
mTOR_12	1	11294190	11294300	TCCCCATATGAGCTGATGAC	TTTGACAGAGTTGGAGCACA
mTOR_12	1	11294200	11294332	AGCCTCTCGGTTTGTGTTAC	TCTCTCTAGAATGTCTTCTGCC
mTOR_13	1	11293445	11293550	CCCTATCTCCGCTATGGAAA	GCATTCATTTTCTCATAACTTCTTT
mTOR_13	1	11293445	11293554	CCCTATCTCCGCTATGGAA	AGAGTCTAATCTGCATTCATTTTC
mTOR_13	1	11293523	11293554	GTTTGGATCAGGGTCTGGAT	ACTGAGATGGTCTCTTGGGT
mTOR_14	1	11292483	11292594	GGGGTCTGTCTTGCTCAATC	TTTCTGCCACCCTCTTTTTC
mTOR_14	1	11292499	11292595	GCAGTAATACTCACCTGCCT	TTTCTAACCCTTTCTGCCAC
mTOR_15	1	11291347	11291465	AATGCTGCAACCATCTCTCT	TGGACCCTGGGACAGTT
mTOR_15	1	11291347	11291501	CTCTTGCCATCGTCCCA	GCTCATTGAATCGTGTTCTTG
mTOR_15	1	11291416	11291501	ATTCAGTAGCACCTCAAGCA	TCTTTTCTCTCGTACTGGCT
mTOR_16	1	11290972	11291087	GGCTCTGTGAGTGAGAACTT	TCCGTGTGTTAGGGCTTTTA
mTOR_16	1	11291016	11291121	GACTTGGATTCTGACAGGCT	CCTGAGAGGAGTATCCGTGA
mTOR_17	1	11288715	11288817	AAGAGAAGGATTGGGGTTTG	AGGCCATCACCTTCATCTTC
mTOR_17	1	11288803	11288918	GCAGGAACTGCACACATTT	AAACTTGCCTCTGGATGAGT
mTOR_17	1	11288886	11288985	GACTGGTCTCGGAAGATCC	TTACTAACCATGCTCTGCCT
mTOR_18	1	11276195	11276296	TTCAAACTTGCTTCTGAGCC	CTGGTTGACCTCTTGTCCAT

mTOR_18	1	11276275	11276301	CAAAGGACACCAACATTCCC	ACCCATTCCATAGTTGCCTT
mTOR_19	1	11273446	11273548	TTTAGCTGATCACCCAGGGA	AAATTGTGGTAGCTCTTGGG
mTOR_19	1	11273446	11273633	AGAAAATCTCTCTGGAGGATGA	TGACTCAGCTCCTCTGACTT
mTOR_19	1	11273543	11273633	GGGGCAGGTAGAGCTTAAA	TCATCAGAAAGGGACCTGAC
mTOR_20	1	11272843	11272955	GCTTAAAGATTGCTAGTCCCA	CCTTTTGCAGTTACTGGCTG
mTOR_20	1	11272892	11272975	CTTCAGGGGCATCAAACAAC	GCTGCGTGTCCTTAGATACT
mTOR_21	1	11272359	11272507	CAGAAGAGCACCTGTCTGT	GCTAGAGACTGTGGACCG
mTOR_21	1	11272430	11272541	CTGTGGAGCGCAGTTCT	CACGTCTCTTCCTTGGAGAT
mTOR_22	1	11270861	11270963	ACACAAACTCCCATAGCCAA	TCTTCCCCCTCCTGTTTTAG
mTOR_22	1	11270861	11270973	GACAACAGGGACTTCAGAAC	ACTCTCCAAAATGATAGTTTCTCA
mTOR_22	1	11270922	11270973	CGCTGATGATTGATTCGGTG	TATCACAGAGCTAGCCACAA
mTOR_23	1	11269359	11269490	GAGCTCTCCTTTCCCAGT	CACACTTGCTGATGAAGAGG
mTOR_23	1	11269359	11269520	GAGCTCTCCTTTCCCAGT	AGGTGTTTCCTATAAATCTTTGGT
mTOR_23	1	11269435	11269525	TTTCCACTGGTCCACTAGC	TCTACCAGGTCTGCACCTC
mTOR_24	1	11264608	11264708	CCAGCCCCTTGATTATTACTTC	CTGGCTGGAATGGCTGA
mTOR_24	1	11264608	11264770	GCTGATCTTCTCCACCCG	TCAATTGGCCCTTGAAACTG
mTOR_24	1	11264689	11264770	GGCGATGATGAGTCCTTCAG	TCAATTGGCCCTTGAAACTG
mTOR_25	1	11259588	11259723	CCAGCTGGTTCCCTGTC	ATTTGTGTCCTGCTGGTCT
mTOR_25	1	11259642	11259770	AGCCAAGTTTAAGAGGGTCT	AGGTCTCTCCATTTTCCACC
mTOR_26	1	11259305	11259461	AGGCAGCAATTAAAAAGGGT	TGAGGTTTTGCTCTTCTCCA
mTOR_26	1	11259305	11259470	GTCATTTTGCATGAAGGCAG	CATTTTCCTGTGCTGTGAGG
mTOR_26	1	11259320	11259470	GGGTTTATGGCCTACCTGAT	CCTGTGCTGTGAGGTTTTG
mTOR_27	1	11227489	11227584	CAAGTCTCTACCTCCTGCTT	TGAGTGTAACTACCTTTTCCCT

mTOR_28	1	11217199	11217356	GCCACACATGCCATCATTC	ACAGCAGTCTTTCTTTCCCA
mTOR_28	1	11217199	11217358	GCCACACATGCCATCATTC	TGTACCTCACAGCAGTCTTT
mTOR_28	1	11217284	11217358	TCCTTGTTGGTGTCCATTTTC	GTGAAGTGTCATGCGTACAG
mTOR_29	1	11210173	11210293	ACAGGGTGCCTGTGAG	GCAGGAGAGGAAGATTGGT
mTOR_29	1	11210173	11210293	ACAGGGTGCCTGTGAG	TGGTAGTTTAAGGAGATTTGGAT
mTOR_30	1	11206723	11206839	TTCCTCACTGAGAGATCTGG	TGTGTGTATAGGTCAGTGGG
mTOR_30	1	11206763	11206858	AAGGAGAAGAGGTCCTGATG	ACCTATTTGAGATGCTGCCT
mTOR_31	1	11205015	11205112	CCTCAAAAATGACAATGTGCAG	CCAGAGCTCAGTCCCAAG
mTOR_32	1	11204695	11204822	GTAGGGGTAGGTGGGTGAA	TGGATTGTTCGTGCAGTAAT
mTOR_32	1	11204695	11204822	GGTGAACTGGGGCTTTCT	TGGATTGTTCGTGCAGTAAT
mTOR_33	1	11199580	11199712	CCTGCCCATGTGGGTG	ACTTCTGAATGTTCCAGGGC
mTOR_33	1	11199636	11199725	TTGCATACTTGAGCCAGGTT	GACTCTGCCACAAAAACAATG
mTOR_34	1	11199351	11199473	ATTCTGGAGAAGGTGGTCTG	AGGCTCTTGCTCATAAAACTT
mTOR_34	1	11199351	11199502	GGAGAAGGTGGTCTGTTCTG	TCCAGTTCTGTCTATAACCCAG
mTOR_34	1	11199432	11199502	GTGAACTGTTGGCAGAGGAT	AGGCTGGTGAGTGACAAC
mTOR_35	1	11194398	11194513	TGACAGGGCTGGAATATGAC	CCTGTTACAGATCGATGCCT
mTOR_35	1	11194456	11194533	TATGCTGCTGGTCCTCAGTA	ATTCTGTTTGGAGAGGGGTT
mTOR_36	1	11193127	11193233	TGTAACCACGAGCACACAG	TGCTTCCTGAAACTTGGAGA
mTOR_36	1	11193145	11193264	GCTTCTGATCACCTTGTACC	TTGAGGAGGGAATGTCATGG
mTOR_37	1	11190576	11190648	CACTTCAGATACAGCCTCAG	AGGGCAGCAACAGTGAG
mTOR_37	1	11190576	11190748	TTCCATTTCTCAGAGAGCCT	CGCGATGAGAAGAAGAAACT
mTOR_37	1	11190635	11190792	GGGGCTGTTCTCGGTG	TGAACTTCGAAGCTGTGCTA
mTOR_37	1	11190662	11190844	TCGCTCTCACTGTTGCTG	CTCCAGTGTCTGTCCTTGC

mTOR_37	1	11190680	11190844	TCGGTGCTGGCAGTG	GTGTCTGTCCTTGCCTTTC
mTOR_38	1	11189785	11189886	CCTACCAGAGTTGCATCCTT	TGTTCCAACAGGATCTGTCC
mTOR_38	1	11189849	11189905	AGGAGATGGAACGGAAGAAG	AAAGCAGAGGCAAGAGTG
mTOR_39	1	11188902	11189018	ACACAGAAGAGAGACTTGGA	AGGCAAAAACTGGGAAACTA
mTOR_39	1	11188902	11189018	CCACCTTCACCTGTAACCA	CAGGCAAAAACTGGGAAAC
mTOR_40	1	11188501	11188619	GGTTAGATGAGAAACTGCCC	AGTTGTTTCAAGTCTCATATGCT
mTOR_40	1	11188501	11188619	GGTTAGATGAGAAACTGCCC	AAAGAATTGATCTTTGCCTAGAAG
mTOR_41	1	11188051	11188177	AAGGGACCAGGGTCTATGAA	GTTTTTCCCTCAGGCCCTC
mTOR_41	1	11188111	11188193	GTGCTCACACATGTTCTTCA	ATGTCACACTCACCACTTGT
mTOR_42	1	11187671	11187806	GGCAGAATATTTCTACAGGGTT	GAGATGTGGCATGAAGGC
mTOR_42	1	11187671	11187860	ACAGGGTTATGTCCTTTCGT	TCTTCTCTTGGCTTCAGGTG
mTOR_42	1	11187765	11187873	GCACCTCAAACATGCCTTT	TAGTACCTCCTGTGTCTCCA
mTOR_42	1	11187776	11187873	CATGCCTTTCACGTTCCTTT	TTCCTCTGACTGCTGGAAAT
mTOR_43	1	11187057	11187173	GGACTATAATGACAGTTAACCCTG	TCGAGATTTAATGGAGGCCC
mTOR_43	1	11187104	11187211	AGATTCGTCGGAACACATGA	CTGGGTTGGTTGAGACTTTG
mTOR_44	1	11186669	11186769	GAGAAGTGGGTGACAGAAGT	CTGTGCCAGGAACATATGAC
mTOR_44	1	11186754	11186863	TGCTATGGACTGAATGCGAA	CCTGGAGGCAGAACACTAA
mTOR_45	1	11184545	11184691	CAAATTGTTGCCATTTCAGGG	GCTCCCACTGTTCCTTACA
mTOR_45	1	11184548	11184700	TGTTGCCATTTCAGGGTTTC	CTGATGTACACTCACCGCT
mTOR_46	1	11182026	11182145	GGAAGGGGCACTAGCTCT	TCATCCCTTTATCGACCAACT
mTOR_46	1	11182047	11182193	ATCACATACCCGCAACATGA	CGGTACACTAACCCTGCTTT
mTOR_47	1	11181293	11181428	TATTGCGAGTGGGGGTTC	TGAACAGTTGTGTCCTGATG
mTOR_47	1	11181362	11181435	GTCGTCCCCAGCTGTATTAT	TTTCTTCCTGGACCCAAACT

mTOR_48	1	11177051	11177133	ACCATTCAGGAAAACTACAATGG	CTGTGTTCTAGGTGTGGTTTG
mTOR_48	1	11177051	11177153	AAAACTACAATGGAGAAAGAAGAC	TCCAGAACCGTAGTTCACAT
mTOR_48	1	11177133	11177148	CGGGTATAATTGGTTCTTCGG	TTCACATGCACTCCTGTGT
mTOR_48	1	11177144	11177153	GTTCTTCGGTCAAACCACAC	AGACTCGGTCTCAAAAGTACA
mTOR_49	1	11175443	11175535	GAAGATGAGGTTGGGGTTCTA	ATCTCTGTTGATCCCTCCCT
mTOR_50	1	11174860	11174954	GATCCCATTTGGAAGCAGC	AACATTGATTTGGCTTTTCCC
mTOR_51	1	11174365	11174511	AGCTCCCAGGCACTTGA	GTGGCTCTGTCCCATTTCTA
mTOR_51	1	11174387	11174520	ATACTCACTGTCCATCAGCC	TGCTTTGGGTGGAGAGTTAG
mTOR_52	1	11172899	11172984	TTGCGACCTCCCGTG	ATAACCAAGTTTCTTTCAAGTCAA
mTOR_52	1	11172899	11172984	CTTTGCGACCTCCCGTG	ATAACCAAGTTTCTTTCAAGTCAA
mTOR_53	1	11169696	11169796	GCTGCTATTTTCTTAATGAGCTA	GGCTTTTTGGTGTTTGAATTTT
mTOR_53	1	11169696	11169796	AGTCACTGGTGCGGTT	GGCTTTTTGGTGTTTGAATTTT
mTOR_54	1	11169337	11169437	TGCTCAGATTTTATGTCCCTTTT	CACCCATTGAACCTGTTGT
mTOR_54	1	11169337	11169437	TGCTCAGATTTTATGTCCCTTTT	GTATTGCTCCCATTCTTACAGT
mTOR_55	1	11168228	11168342	GCTTGGGACCTGATTGCTTA	TTTGTTCCTCCTGTGCTAGG
mTOR_55	1	11168251	11168353	CACTCACCAGCCAATATAGC	TAGACAGTTAAGCCCACAGG
mTOR_56	1	11167532	11167567	TTTCTCACCATGGTTTCAGT	GTCAGACCTTGGCCTTTTC
mTOR_56	1	11167532	11167567	TCACCATGGTTTCAGTTTAGTG	TGTAAACCTTTGAAGAAGCTCAA

Table A.3: Gene Reference Models for HGVS Nomenclature. PGx genes are highlighted in blue.

Gene	Protein	Reference Model
AKT1	Protein kinase B	NM_001014431.1
ALK	Anaplastic lymphoma receptor tyrosine kinase	NM_004304.3
BRAF	Serine/threonine-protein kinase B-Raf	NM_004333.4
DPYD	Dihydropyrimidine dehydrogenase	NM_000110.3
EGFR	Epidermal growth factor receptor	NM_005228.3
ERBB2	Receptor tyrosine-protein kinase erbB-2	NM_001005862.1
GSTP1	Glutathione S-rransferase pi 1	NM_000852.3
HRAS	GTPase HRas	NM_005343.2
IDH1	Isocitrate dehydrogenase 1	NM_005896.2
IDH2	Isocitrate dehydrogenase 2	NM_002168.2
KIT	Tyrosine-protein kinase Kit	NM_000222.2
KRAS	KRas proto-oncogene GTPase	NM_033360.2
MAPK1	Mitogen-activated protein kinase 1	NM_002745.4
MAP2K1	Mitogen-activated protein kinase kinase 1	NM_002755.3
MTHFR	Methylenetetrahydrofolate reductase	NM_005957.4
MTOR	Serine/threonine-protein kinase mTOR	NM_004958.3
NRAS	Neuroblastoma RAS viral oncogene homolog	NM_002524.3
PDGFRA	Platelet-derived growth factor receptor alpha	NM_006206.4
PIK3CA	Phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit alpha	NM_006218.2
PTEN	Phosphatase and tensin homolog	NM_000314.4
STAT1	Signal transducer and activator of transcription 1	NM_007315.3
STAT3	Signal transducer and activator of transcription 3	NM_139276.2
TP53	Tumor protein P53	NM_000546.5
TYMP	Thymidine phosphorylase	NM_001113755.2
TYMS	Thymidylate synthetase	NM_001071.2
UGT1A1	Uridine diphosphate (UDP)-glucuronosyl transferase 1A1	NM_000463.2