Supplemental Table 1: Genes Targeted in OncoPanel

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Full-length exons for detection of SNVs, indels and copy number alterations | | | | | | Genomic regions for structural rearrangements |
| ABL1 | CDK2 | EXT2 | KDM6A | NTRK3 | SETBP1 | ABL1 |
| AKT1 | CDK4 | EZH2 | KDM6B | PALB2 | SETD2 | AKT3 |
| AKT2 | CDK5 | FAM46C | KDR | PARK2 | SF1 | ALK |
| AKT3 | CDK6 | FANCA | KIT | PAX5 | SF3B1 | BCL2 |
| ALK | CDK9 | FANCC | KRAS | PDCD1LG2 | SH2B3 | BCL6 |
| ALOX12B | CDKN1A | FANCD2 | LMO1 | PDGFRA | SMAD2 | BRAF |
| APC | CDKN1B | FANCE | LMO2 | PDGFRB | SMAD4 | CIITA |
| AR | CDKN1C | FANCF | LMO3 | PHF6 | SMARCA4 | EGFR |
| ARAF | CDKN2A | FANCG | MAP2K1 | PHOX2B | SMARCB1 | ETV1 |
| ARID1A | CDKN2B | FAS | MAP2K4 | PIK3C2B | SMC1A | EWSR1 |
| ARID1B | CDKN2C | FBXW7 | MAP3K1 | PIK3CA | SMC3 | FGFR1 |
| ARID2 | CEBPA | FGFR1 | MAPK1 | PIK3R1 | SMO | FGFR3 |
| ASXL1 | CHEK2 | FGFR2 | MCL1 | PIM1 | SOCS1 | FUS |
| ATM | CIITA | FGFR3 | MDM2 | PMS1 | SOX2 | IgH |
| ATRX | CREBBP | FGFR4 | MDM4 | PMS2 | SOX9 | IgK |
| AURKA | CRKL | FH | MECOM | PNRC1 | SRC | IgL |
| AURKB | CRLF2 | FKBP9 | MEF2B | PRAME | SRSF2 | JAK2 |
| AXL | CRTC1 | FLCN | MEN1 | PRDM1 | STAG1 | MLL |
| B2M | CRTC2 | FLT1 | MET | PRF1 | STAG2 | MYC |
| BAP1 | CTNNB1 | FLT3 | MITF | PRKAR1A | STAT3 | NPM1 |
| BCL2 | CUX1 | FLT4 | MLH1 | PRKCI | STAT6 | PAX5 |
| BCL2L1 | CYLD | FUS | MLL | PRKCZ | STK11 | PDGFRA |
| BCL2L12 | DDB2 | GATA3 | MLL2 | PRKDC | SUFU | PDGFRB |
| BCL6 | DDR2 | GATA4 | MPL | PRPF40B | SUZ12 | RAF1 |
| BCOR | DICER1 | GATA6 | MSH2 | PRPF8 | SYK | RARA |
| BCORL1 | DIS3 | GLI1 | MSH6 | PSMD13 | TCF3 | RET |
| BLM | DMD | GLI2 | MTOR | PTCH1 | TCF7L1 | ROS1 |
| BMPR1A | DNMT3A | GLI3 | MUTYH | PTEN | TCF7L2 | TRA |
| BRAF | EGFR | GNA11 | MYB | PTK2 | TERT | TRB |
| BRCA1 | EP300 | GNAQ | MYBL1 | PTPN11 | TET2 | TRG |
| BRCA2 | EPHA3 | GNAS | MYC | RAD21 | TNFAIP3 |  |
| BRD4 | EPHA5 | GPC3 | MYCL1 | RAF1 | TP53 |  |
| BRIP1 | EPHA7 | GSTM5 | MYCN | RARA | TRA |  |
| BUB1B | ERBB2 | H3F3A | MYD88 | RB1 | TRB |  |
| CARD11 | ERBB3 | HNF1A | NBN | RBL2 | TRG |  |
| CBL | ERBB4 | HRAS | NF1 | REL | TSC1 |  |
| CBLB | ERCC2 | ID3 | NF2 | RET | TSC2 |  |
| CCND1 | ERCC3 | IDH1 | NFE2L2 | RFWD2 | U2AF1 |  |
| CCND2 | ERCC4 | IDH2 | NFKBIA | RHPN2 | VHL |  |
| CCND3 | ERCC5 | IGF1R | NFKBIZ | ROS1 | WRN |  |
| CCNE1 | ESR1 | IGH | NKX2-1 | RPL26 | WT1 |  |
| CD274 | ETV1 | IGK | NOTCH1 | RUNX1 | XPA |  |
| CD58 | ETV4 | IGL | NOTCH2 | SBDS | XPC |  |
| CD79B | ETV5 | IKZF1 | NPM1 | SDHAF2 | XPO1 |  |
| CDC73 | ETV6 | IKZF3 | NRAS | SDHB | ZNF217 |  |
| CDH1 | EWSR1 | JAK2 | NTRK1 | SDHC | ZNF708 |  |
| CDK1 | EXT1 | JAK3 | NTRK2 | SDHD | ZRSR2 |  |

Supplemental Table 2: Tumor Diagnoses in the Sequencing Cohort

|  |  |  |  |
| --- | --- | --- | --- |
| **Diagnosis** | **Number** | **Diagnosis** | **Number** |
| **Adrenal Gland** | **20** | **Nasopharynx** | **11** |
| Adenoma | 7 | Adenocarcinoma | 1 |
| Adrenocortical carcinoma | 10 | Carcinoma | 2 |
| Pheochromocytoma | 2 | DLBCL | 1 |
| Primitive neuroectodermal tumor | 1 | Neuroblastoma | 1 |
| **Ampulla of Vater** | **3** | Nut Midline Carcinoma | 1 |
| Adenocarcinoma | 3 | Squamous cell carcinoma | 4 |
| **Anus** | **10** | Undifferentiated carcinoma | 1 |
| Adenocarcinoma | 1 | **Nerve** | **1** |
| Squamous cell carcinoma | 9 | Schwannoma | 1 |
| **Appendix** | **11** | **Nose** | **2** |
| Adenocarcinoma | 3 | Carcinoma | 1 |
| Goblet cell carcinoid | 1 | Neuroblastoma | 1 |
| Mucinous adenocarcinoma | 2 | **Oral Cavity** | **44** |
| Mucinous neoplasm | 2 | Adenoid cystic carcinoma | 1 |
| Neuroendocrine tumor | 3 | Nut Midline Carcinoma | 1 |
| **Bile Duct** | **9** | Squamous cell carcinoma | 42 |
| Cholangiocarcinoma | 9 | **Oropharynx and hypopharynx** | **47** |
| **Bone** | **5** | Adenoid cystic carcinoma | 1 |
| Chondroblastoma | 1 | Squamous cell carcinoma | 46 |
| Chondrosarcoma | 1 | **Other** | **14** |
| Osteosarcoma | 2 | B-cell Lymphoma | 1 |
| Sarcoma | 1 | Blastoma | 1 |
| **Bone Marrow** | **336** | Carcinoma | 1 |
| Acute Leukemia | 58 | Follicular lymphoma | 1 |
| ALL | 10 | Leiomyosarcoma | 2 |
| AML | 64 | Liposarcoma | 2 |
| B-ALL | 37 | Neoplasm | 1 |
| B-cell Lymphoma | 3 | Peripheral nerve sheath tumor | 1 |
| CLL/SLL | 26 | Rhabdomyosarcoma | 1 |
| CML | 14 | Squamous cell carcinoma | 2 |
| CMML | 3 | Wilms tumor | 1 |
| Essential thrombocythemia | 1 | **Ovary** | **191** |
| Hairy cell leukemia | 5 | Adenocarcinoma | 139 |
| Histiocytic Sarcoma | 1 | Borderline serous tumor | 4 |
| Idiopathic hypereosinophilic syndrome | 1 | Carcinoma | 1 |
| Lymphoma | 1 | Carcinosarcoma | 4 |
| Malignancy | 1 | Clear cell carcinoma | 6 |
| Mastocytosis | 1 | Endometrioid adenocarcinoma | 2 |
| Myelodysplastic/myeloproliferative neoplasm | 88 | Granulosa cell tumor | 9 |
| Myeloma | 4 | Mucinous adenocarcinoma | 1 |
| NK/T-cell Lymphoma | 1 | Serous carcinoma | 20 |
| Other | 6 | Sex-cord stromal tumor | 1 |
| Plasmacytoma | 1 | Small cell carcinoma | 1 |
| Polycythemia vera | 2 | Teratoma | 2 |
| Refractory cytopenia | 1 | Undifferentiated carcinoma | 1 |
| T-ALL | 4 | **Pancreas** | **55** |
| T-cell lymphoma | 2 | Adenocarcinoma | 34 |
| T-LGL | 1 | IPMN | 4 |
| **Brain** | **429** | Neuroendocrine carcinoma | 1 |
| Choroid plexus papilloma | 1 | Neuroendocrine tumor | 14 |
| Craniopharyngioma | 1 | Pancreatoblastoma | 1 |
| DLBCL | 10 | Solid pseudopapillary neoplasm | 1 |
| Ependymoma | 8 | **Penis** | **2** |
| Ganglioglioma | 4 | Squamous cell carcinoma | 2 |
| Glioblastoma | 173 | **Peritoneum** | **5** |
| Glioma | 66 | Carcinoma | 1 |
| Hemangioblastoma | 5 | Desmoid | 1 |
| Medulloblastoma | 9 | Liposarcoma | 1 |
| Medullomyoblastoma | 1 | Mesothelioma | 2 |
| Melanocytoma | 1 | **Pituitary** | **32** |
| Meningioma | 34 | Adenoma | 32 |
| Neuroblastoma | 4 | **Pleura** | **55** |
| Neurocytoma | 1 | DLBCL | 1 |
| Neuroepithelial tumor | 1 | Ewing sarcoma | 1 |
| Oligoastrocytoma | 27 | Mesothelioma | 53 |
| Oligodendroglioma | 72 | **Prostate** | **184** |
| Pilocytic astrocytoma | 5 | Adenocarcinoma | 183 |
| Pineoblastoma | 2 | Adenoid cystic carcinoma | 1 |
| Pleomorphic xanthoastrocytoma | 2 | **Retroperitoneum** | **8** |
| Schwannoma | 1 | Leiomyosarcoma | 4 |
| Subependymoma | 1 | Liposarcoma | 3 |
| **Breast** | **298** | Myxoma | 1 |
| Angiosarcoma | 2 | **Salivary gland** | **39** |
| Carcinoma | 291 | Adenocarcinoma | 1 |
| Carcinosarcoma | 1 | Adenoid cystic carcinoma | 15 |
| Neuroendocrine carcinoma | 2 | Carcinoma | 13 |
| Phyllodes tumour | 1 | Carcinoma ex pleomorphic adenoma | 1 |
| Squamous cell carcinoma | 1 | Merkel Cell Carcinoma | 1 |
| **Cervix** | **28** | Mucoepidermoid carcinoma | 1 |
| Adenocarcinoma | 12 | Myoepithelioma | 1 |
| Squamous cell carcinoma | 16 | Neoplasm | 1 |
| **Colon** | **210** | Pleomorphic adenoma | 2 |
| Adenocarcinoma | 209 | Squamous cell carcinoma | 3 |
| Liposarcoma | 1 | **Skin** | **95** |
| **Endometrium** | **168** | Adenocarcinoma | 2 |
| Adenocarcinoma | 148 | Angiosarcoma | 2 |
| Carcinosarcoma | 16 | Apocrine carcinoma | 1 |
| Mucinous adenocarcinoma | 1 | B-cell Lymphoma | 2 |
| Sarcoma | 1 | Carcinoma | 3 |
| Serous carcinoma | 2 | Cutaneous T cell lymphoma | 1 |
| **Esophagus** | **45** | Lymphoma | 2 |
| Adenocarcinoma | 40 | Malignancy | 1 |
| Carcinoma | 1 | Melanoma | 42 |
| Squamous cell carcinoma | 4 | Merkel Cell Carcinoma | 10 |
| **Fallopian Tube** | **30** | Other | 1 |
| Adenocarcinoma | 30 | Squamous cell carcinoma | 19 |
| **Female genital tract** | **167** | T-cell lymphoma | 9 |
| Adenocarcinoma | 73 | **Small intestine** | **14** |
| Adenosarcoma | 1 | Adenocarcinoma | 4 |
| Borderline serous tumor | 6 | Gastrointestinal Stromal Tumor | 1 |
| Carcinoma | 3 | Leiomyosarcoma | 1 |
| Carcinosarcoma | 10 | Neuroendocrine carcinoma | 1 |
| Choriocarcinoma | 1 | Neuroendocrine tumor | 7 |
| Endometrioid adenocarcinoma | 4 | **Soft tissue** | **130** |
| Ewing sarcoma | 1 | Alveolar rhabdomyosarcoma | 1 |
| Leiomyoma | 1 | Angiosarcoma | 3 |
| Leiomyosarcoma | 11 | Chondrosarcoma | 2 |
| Malignancy | 1 | Chondrosarcoma, extraskeletal myxoid | 1 |
| Mesothelioma | 1 | Dermatofibrosarcoma protuberans | 1 |
| Mucinous adenocarcinoma | 2 | Desmoid | 3 |
| Sarcoma | 2 | Desmoplastic small round cell tumor | 1 |
| Serous carcinoma | 47 | Ewing sarcoma | 1 |
| Solitary fibrous tumor | 1 | Gastrointestinal Stromal Tumor | 31 |
| Squamous cell carcinoma | 1 | Giant cell tumor | 2 |
| Trophoblastic tumor | 1 | Glomus tumor | 1 |
| **Gall Bladder** | **5** | Hemangioendothelioma | 2 |
| Adenocarcinoma | 1 | Leiomyosarcoma | 17 |
| Merkel Cell Carcinoma | 1 | Lipomatous tumor | 1 |
| **Ganglion** | **1** | Liposarcoma | 15 |
| Neuroblastoma | 1 | Lymphangioma | 1 |
| **Gastrointestinal tract** | **7** | Myoepithelioma | 1 |
| Adenocarcinoma | 5 | Myxofibrosarcoma | 2 |
| Gastrointestinal Stromal Tumor | 1 | Myxoma | 1 |
| Tumor | 1 | Osteosarcoma | 3 |
| **Head and neck** | **1** | Perineurioma | 1 |
| Squamous cell carcinoma | 1 | Peripheral nerve sheath tumor | 3 |
| **Ileum** | **1** | Rhabdomyosarcoma | 3 |
| Neuroepithelial tumor | 1 | Sarcoma | 20 |
| **Kidney** | **107** | Schwannoma | 2 |
| Angiomyolipoma | 1 | Small round cell tumor | 1 |
| Angiosarcoma | 1 | Solitary fibrous tumor | 5 |
| Clear cell sarcoma | 1 | Synovial sarcoma | 3 |
| Myelolipoma | 1 | Tumor | 1 |
| Neoplasm | 1 | Wilms tumor | 1 |
| Oncocytoma | 6 | **Soft tissue** | **2** |
| Renal cell carcinoma | 88 | Myxofibrosarcoma | 1 |
| Sarcoma | 1 | Synovial sarcoma | 1 |
| Urothelial neoplasm | 2 | **Spinal Cord** | **4** |
| Wilms tumor | 5 | Astroblastoma | 1 |
| **Larynx** | **6** | Ependymoma | 1 |
| Adenoid cystic carcinoma | 1 | Hemangioma | 1 |
| Squamous cell carcinoma | 5 | Neurofibroma | 1 |
| **Liver** | **21** | **Spleen** | **1** |
| Adenocarcinoma | 1 | Lymphoma | 1 |
| Cholangiocarcinoma | 6 | **Stomach** | **31** |
| Hepatoblastoma | 2 | Adenocarcinoma | 21 |
| Hepatocellular carcinoma | 11 | Gastrointestinal Stromal Tumor | 9 |
| Liposarcoma | 1 | Leiomyosarcoma | 1 |
| **Lung** | **661** | **Testis** | **42** |
| Adenocarcinoma | 495 | Germ cell tumor | 24 |
| Adenoid cystic carcinoma | 1 | Leydig cell tumor | 2 |
| Atypical carcinoid | 2 | Liposarcoma | 1 |
| B-cell Lymphoma | 1 | Seminoma | 13 |
| Carcinoid-adenocarcinoma | 1 | Serous carcinoma | 1 |
| Carcinoma | 34 | Sertoli cell tumor | 1 |
| Hemangioma | 1 | **Throat** | **1** |
| Lymphoma | 2 | Squamous cell carcinoma | 1 |
| Neuroendocrine carcinoma | 8 | **Thymus** | **15** |
| Neuroendocrine tumor | 11 | Carcinoma | 11 |
| Non-small cell carcinoma | 12 | Thymoma | 4 |
| Small cell carcinoma | 18 | **Thyroid** | **104** |
| Squamous cell carcinoma | 75 | Anaplastic thyroid carcinoma | 5 |
| **Lymph node** | **22** | Carcinoma | 1 |
| B-cell Lymphoma | 6 | Follicular adenoma | 1 |
| Burkitt Lymphoma | 1 | Follicular thyroid carcinoma | 9 |
| DLBCL | 4 | Medullary thyroid carcinoma | 5 |
| Follicular lymphoma | 4 | Papillary thyroid carcinoma | 81 |
| Hodgkin lymphoma | 1 | Poorly differentiated carcinoma | 1 |
| Langerhans cell sarcoma | 1 | Undifferentiated carcinoma | 1 |
| Lymphoma | 2 | **Unknown** | **22** |
| NK/T-cell Lymphoma | 1 | Adenocarcinoma | 3 |
| Sarcoma | 1 | Carcinoma | 10 |
| T-cell lymphoma | 1 | Malignancy | 2 |
| **Mediastinum** | **4** | Sarcoma | 1 |
| Carcinoma | 1 | Squamous cell carcinoma | 6 |
| DLBCL | 1 | **Urinary tract** | **127** |
| Liposarcoma | 1 | Adenocarcinoma | 4 |
| Squamous cell carcinoma | 1 | Bladder Carcinoma | 1 |
| **Nasopharynx** | **11** | Ewing sarcoma | 1 |
| Adenocarcinoma | 1 | Leiomyosarcoma | 1 |
| Carcinoma | 2 | Paget's disease | 1 |
| DLBCL | 1 | Sarcoma | 3 |
| Neuroblastoma | 1 | Small cell carcinoma | 2 |
| Nut Midline Carcinoma | 1 | Urothelial carcinoma | 113 |
| Squamous cell carcinoma | 4 | Urothelial neoplasm | 1 |
| Undifferentiated carcinoma | 1 | **Vagina** | **1** |
| **Nerve** | **1** | Melanoma | 1 |
| Schwannoma | 1 | **Vulva** | **11** |
| **Nose** | **2** | Melanoma | 1 |
| Carcinoma | 1 | Squamous cell carcinoma | 9 |
| Neuroblastoma | 1 | Yolk sac tumor | 1 |
|  |  | **Grand Total** | **3892** |

Supplemental Table 3. OncoPanel assay performance for detection of KRAS point mutations and EGFR insertion-deletion mutations.





Supplemental Table 4. OncoPanel assay performance for detection of low and high copy number changes.

\* In one case with a complex karyotype, segmental 1p loss and monosomy 19 was detected by Oncopanel but not by clinical aCGH. In another case, monosomy 19 was detected by Oncopanel but not by clinical aCGH.

†In one case, low mean target coverage and high signal dispersion (noise) precluded accurate copy calls by Oncopanel.

Supplemental Table 5. OncoPanel assay performance for detection of ALK rearrangements.



\*One case considered a false negative by Oncopanel was estimated to have <20% tumor content and thus was below the limit of detection for this assay.

†After elimination of one tumor with a concurrent KRAS activating mutation considered falsely positive by FISH, and inclusion of one tumor originally called negative by FISH but found to have ALK rearrangement by OncoPanel as well as ALK protein overexpression.