Treehouse Analysis: Sample XXXXXXXXX (TH34_1381_S01)

xx/xx/2018

Analyst: **Reviewer:**

Diagnosis XX

Gender XX | **Anatomical Source** XX

Age at Diagnosis XX | **Sample Collected by StanfordClinicians** XX

Age at Relapse XX | **Sequence Received by Treehouse** XX

Relevant Clinical Notes XX

Foundation Medicine

Additional Molecular Testing

Treehouse Primary Categorization

- ☐ RTK: VEGFR/PDGFR/FGFR
- ☐ Cell Cycle
- ☐ JAK/STAT
- ☐ PI3K/AKT/mTOR
- ☐ Other:

Treehouse QC Metrics

	Result	Range	Ok?
RIN	6.9	4.5 - 10.0	PASS
MEND (M)	84.5	> 10.0	PASS
% MEND	59.3	21.3 - 77.3	PASS

Comparative Tumor RNA-Seq Analysis Findings

Molecular Abnormality	Molecular Category	Associated Drugs*	Analyst Summary

a) outlier compared to all tumors (pan-cancer)
b) outlier compared to similar tumors (pan-disease)
c) pathway enrichment in pan-cancer outlier list
d) pathway enrichment in pan-disease outlier list
e) pathway enrichment in overlap outlier list
f) pathway enrichment in top 5% expressed genes
g) tumor similarity analysis
h) literature evidence
i) other molecular support (mutation, fusion, amplification, immunohistochemistry)

*"Associated Drugs" have been identified by Stanford treating oncologists and are included in Stanford IRB Protocol #44179. For more information on these drugs, visit cancer.gov and search for the drug name.

Pathway Summary

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TumorMap

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Treehouse Interpretation Summary

xxx interpretation_analytical_summary xxx

xxx interpretation_clinical_summaries xxx

Appendix to Treehouse Comparative RNA-Seq Analysis Report

Library Construction Note

The RNA-Seq library for this case was constructed using a ribo-deplete protocol. Most RNA-Seq datasets in the Treehouse Reference Compendium are constructed using a polyadenylation protocol, and this library construction method is assumed in our computational analysis. The pathway analysis findings for this case were manually curated to exclude non-polyadenylated transcripts.

Analyst Custom Appendix Goes Here

XXX XXX XXX XXX

Quality Control

This sample meets the quality control standard with 84.5 million MEND reads.

The quality of this sample was assessed by enumerating the number of Mapped Exonic Non-Duplicate (MEND) reads as described at https://github.com/UCSC-Treehouse/mend_qc. We have set a standard of 10 million MEND reads to ensure accurate comparative RNA-Seq analysis based on TumorMap and Gene Expression Outlier analyses.

Versions

Reference Compendium

The compendium used was the Treehouse Reference Compendium Version v11_polya. This reference compendium was constructed in April 2020 and includes 9806 tumors from The Cancer Genome Atlas (TCGA) project, 1190 tumors from the Therapeutically Applicable Research to Generate Effective Treatments (TARGET) project, 395 tumors from the Treehouse data set, and, 1356 tumors from other repository data sets for a total of 12747 tumor samples. The 95th Percentile Correlation Threshold for this Reference Compendium is 0.873.

This Threshold is the correlation value which exceeds 95% of all sample-to-sample Spearman correlations within the Reference Compendium. It is used as a measure of the significance of the focus sample's correlation with other samples.

Protocol

The Treehouse CARE version used was 0.17.1.0. It can be accessed at https://github.com/UCSC-Treehouse/CARE/releases/tag/0.17.1.0 and the Git hash is f2adf596723e15e0dc4abd768a9c3c0915784253.

TumorMap Analysis

The TumorMap for this patient indicates that the tumor is most similar to tumors with the following Diagnoses:

- ependymoma

TumorMap provides a visualization of the genomic similarity among tumor samples (Newton 2017). Each "dot" represents a sample. Samples are laid out in a two-dimensional space based on how similar their RNA-Seq-derived gene expression profiles are to each other.

TumorMap is a research tool and is used to to gain insight into how a given individual's tumor RNA sequencing profile compares to profiles of tumors in the reference cohort. TumorMap should not be used as a stand-alone diagnostic tool.

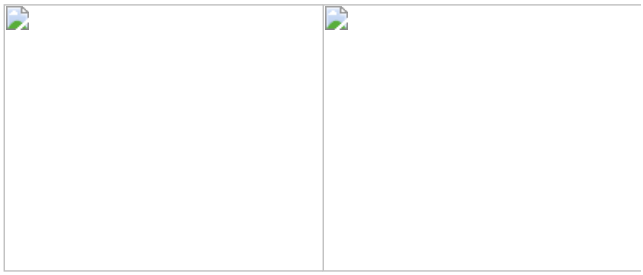
The samples with the profiles most similar to the patient are listed below.

Most Correlated Samples

Sample ID	Score	Disease	Age	Mutations in Cancer Genes
THR24_1805_S01	0.93	ependymoma	no information available	no information available
THR24_1841_S01	0.93	ependymoma	1.7	no information available
THR24_1776_S01	0.93	ependymoma	1.1	no information available
THR24_1771_S01	0.92	ependymoma	3.7	no information available
THR24_1783_S01	0.92	ependymoma	no information available	no information available
THR24_1825_S01	0.92	ependymoma	1.4	no information available

TumorMap Legend

acinar cell carcinoma
acute leukemia
acute leukemia of ambiguous lineage
acute lymphoblastic leukemia
acute megakaryoblastic leukemia
acute myeloid leukemia
acute undifferentiated leukemia
adrenocortical adenoma
adrenocortical cancer
adrenocortical carcinoma
alveolar rhabdomyosarcoma
alveolar soft part sarcoma
angiosarcoma
atypical teratoid/rhabdoid tumor
bladder urothelial carcinoma
breast invasive carcinoma
cervical & endocervical cancer
cholangiocarcinoma
choroid plexus carcinoma
chronic myelogenous leukemia (S02), acute lymphoblastic leukemia (S01)
clear cell carcinoma of cervix
colon adenocarcinoma
craniopharyngioma
dedifferentiated liposarcoma
desmoplastic small round cell tumor
diffuse large B-cell lymphoma
dysembryoplastic neuroepithelial tumor
embryonal rhabdomyosarcoma
embryonal tumor with multilayered rosettes
endometrial stromal sarcoma
ependymoma
epithelioid hemangioendothelioma
epithelioid sarcoma
esophageal carcinoma
Ewing sarcoma
fibrolamellar hepatocellular carcinoma
fibromatosis
follicular neoplasm
ganglioglioma
gastrointestinal stromal tumor
germ cell tumor
glioblastoma multiforme
glioma
gliomatosis cerebri
head & neck squamous cell carcinoma
hepatoblastoma
hepatocellular carcinoma
infantile fibrosarcoma
inflammatory myofibroblastic tumor
INI-deficient soft tissue sarcoma NOS
juvenile myelomonocytic leukemia
kidney chromophobe
kidney clear cell carcinoma
kidney papillary cell carcinoma
leiomyosarcoma
leukemia
lipoblastomatosis
lung adenocarcinoma
lung squamous cell carcinoma
lymphoma
malignant peripheral nerve sheath tumor
medulloblastoma
melanoma
melanotic neuroectodermal tumor
meningioma
mesothelioma
myeloid neoplasm NOS
myeloproliferative neoplasm
myoepithelial carcinoma
myofibromatosis
myxofibrosarcoma
nasopharyngeal carcinoma
neoplasm (uncertain whether benign or malignant)
neuroblastoma
neuroendocrine carcinoma
neurofibroma
neurofibromatosis type 1
NUT midline carcinoma
osteosarcoma
ovarian serous cystadenocarcinoma
pancreatic adenocarcinoma
PEComa
pheochromocytoma & paraganglioma
pineal parenchymal tumor
pleomorphic myxoid liposarcoma
pleuropulmonary blastoma
prostate adenocarcinoma
rectum adenocarcinoma
retinoblastoma
rhabdoid tumor
rhabdomyosarcoma
rosette forming glioneuronal tumor
sarcoma
sclerosing epithelioid fibrosarcoma
Sertoli-Leydig cell tumor, retiform
skin cutaneous melanoma
spindle cell/sclerosing rhabdomyosarcoma
stomach adenocarcinoma
supratentorial embryonal tumor NOS
synovial sarcoma
teratoma
testicular germ cell tumor
thymic carcinoma
thymoma
thyroid carcinoma
undifferentiated hepatic sarcoma
undifferentiated pleomorphic sarcoma
undifferentiated sarcoma NOS
undifferentiated spindle cell sarcoma
uterine carcinosarcoma
uterine corpus endometrioid carcinoma
uveal melanoma
wilms tumor



Identification of Gene Expression Outliers

The full list of pan-cancer and pan-disease outliers of this focus sample are available upon request.

Gene expression outlier analysis uses a statistical test to identify genes with unusual expression levels in the patient's tumor (Jones 2010).

Pan-Cancer Outliers

The pan-cancer analysis is performed by comparing a patient's tumor RNA sequencing profile to the RNA sequencing profiles of all tumors in the Reference Compendium.

Pan-Disease Outliers

This outlier analysis identifies genes that are unusually expressed relative to similar samples. The patient's tumor RNA sequencing profile is compared to the RNA sequencing profiles of four different personalized cohorts of similar tumors, and genes are identified which are outliers relative to at least two of these.
The personalized cohorts are:

- "Focus Sample Diagnosed Disease": all tumor samples annotated with the same diagnosis as the focus sample.
- "First Degree Most Correlated Samples": all samples that have a Spearman correlation with the focus sample which exceeds the Reference Compendium's 95th Percentile Correlation Threshold (see Versions above).
- "First and Second Degree Most Correlated Samples": first degree most correlated samples and in addition each of those samples' first degree most correlated.
- "Diseases of Top Six Most Correlated Samples above Threshold": all tumor samples with the same diagnosis as one or more of the six First Degree Most Correlated Samples which had the greatest correlation with the focus sample.

Diagnosis Composition of Personalized Cohorts

Cohort	Count of Samples in Cohort by Diagnosis
First-Degree MCS	ependymoma — 61 (60%) glioma — 30 (4%) glioblastoma multiforme — 20 (10%) supratentorial embryonal tumor NOS — 2 (10%) **Total —113**
First and Second-Degree MCS	ependymoma — 87 (86%) glioma — 728 (98%) sarcoma — 3 (4%) choroid plexus carcinoma — 3 (11%) testicular germ cell tumor — 3 (1%) skin cutaneous melanoma — 3 (0%) neuroblastoma — 29 (14%) medulloblastoma — 25 (20%) atypical teratoid/rhabdoid tumor — 2 (50%) rhabdomyosarcoma — 2 (3%) malignant peripheral nerve sheath tumor — 2 (22%) leiomyosarcoma — 2 (2%) embryonal tumor with multilayered rosettes — 2 (100%) glioblastoma multiforme — 191 (95%) dysembryoplastic neuroepithelial tumor — 14 (100%) supratentorial embryonal tumor NOS — 13 (68%) undifferentiated sarcoma NOS — 1 (7%) undifferentiated hepatic sarcoma — 1 (50%) infantile fibrosarcoma — 1 (50%) alveolar rhabdomyosarcoma — 1 (2%) undifferentiated pleomorphic sarcoma — 1 (2%) rosette forming glioneuronal tumor — 1 (100%) teratoma — 1 (100%) gliomatosis cerebri — 1 (100%) ganglioglioma — 1 (100%) embryonal rhabdomyosarcoma — 1 (1%) Ewing sarcoma — 1 (1%) uveal melanoma — 1 (1%) pheochromocytoma & paraganglioma — 1 (0%) **Total —1122**
Focus Sample Diagnosed Disease	ependymoma — 101 **Total —101**
Diseases of Top Six Most Correlated Samples above Threshold	ependymoma — 101 **Total —101**

This sample has a diagnosis of **ependymoma**. Of the 101 other ependymoma samples in the compendium, 61 (60%) were among the first degree MCS for this focus sample, and 87 (86%) were among the first and second degree MCS for this sample.

Gene Set Overlap

Genes identified by the outlier analysis are further examined for statistical enrichment of functional categories and signaling pathways using the Molecular Signatures Database (Subramanian 2005) to provide a report on statistically significantly enriched pathways. Significantly enriched pathways containing cancer drug targets as defined by the Drug Gene Interaction Database (Cotto 2017) are tallied below under "Druggable Pathways". Genes whose protein products could be targeted by available therapies are tallied under "Druggable Genes". Druggable genes and pathways may appear in the Pan-Cancer outliers, Pan-Disease outliers, the Overlap set of genes which appear in both outlier sets, or the Top 5% set genes which have expression in the focus sample above the 95th percentile.

Gene Set Overlap Findings

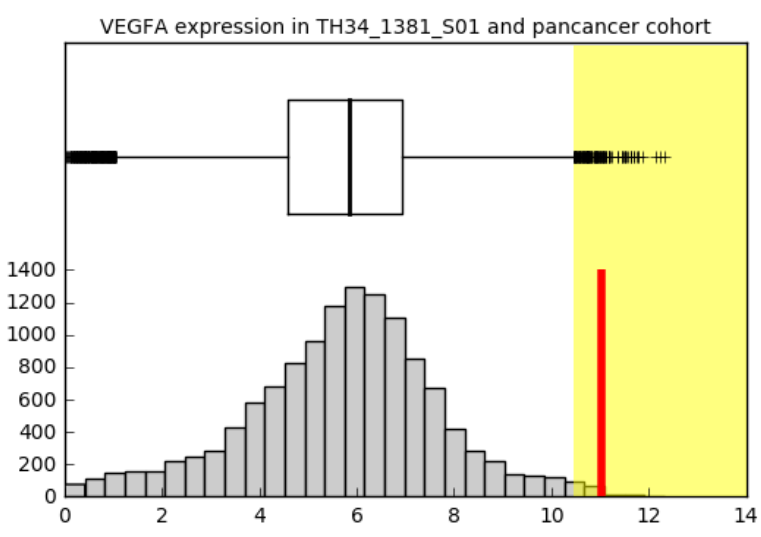
	Pan-Cancer	Pan-Disease	Overlap	Top 5%
Druggable Genes	2	5	0	87
Druggable Pathways	13	52	0	96

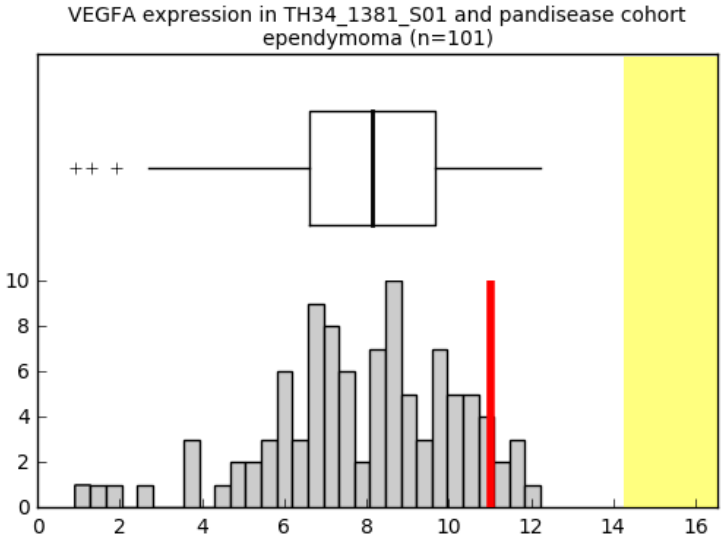
Expression of Druggable Up Outliers

For each up outlier that is considered druggable, we plot the focus sample's expression, red, versus a histogram of the background cohort expression. The two cohorts plotted are the Pan-Cancer cohort and the Diseases of Top Six Most Correlated Samples above Threshold (see Pan-Disease Outliers above for a description of each cohort). The up outlier area for each cohort is shown in yellow.

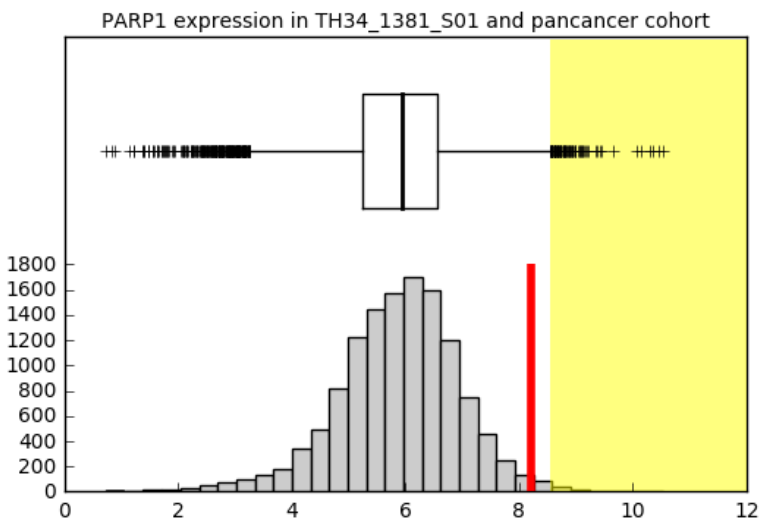
Druggable Up Outliers vs Cohort Expression

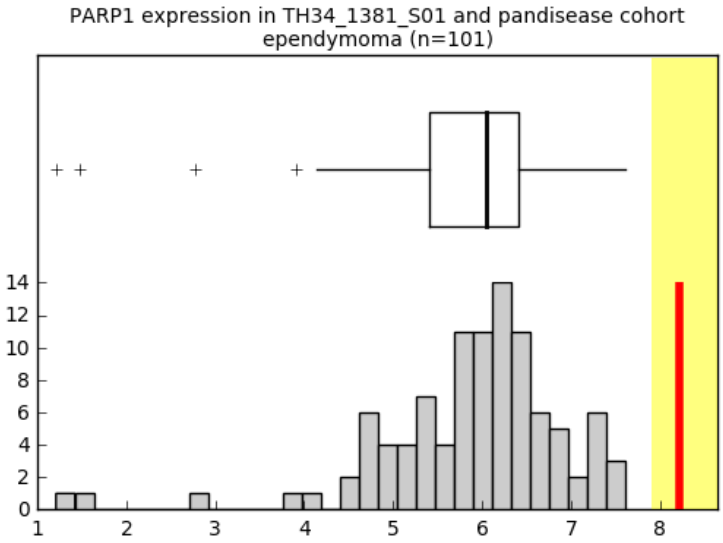
Gene: VEGFA



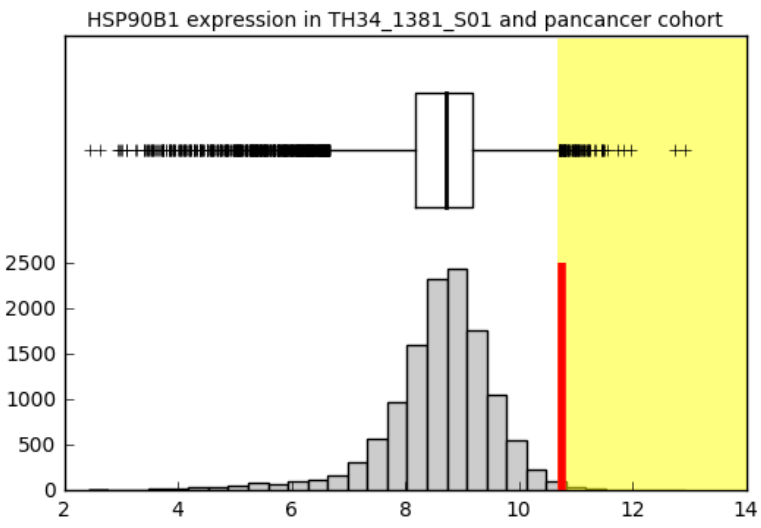


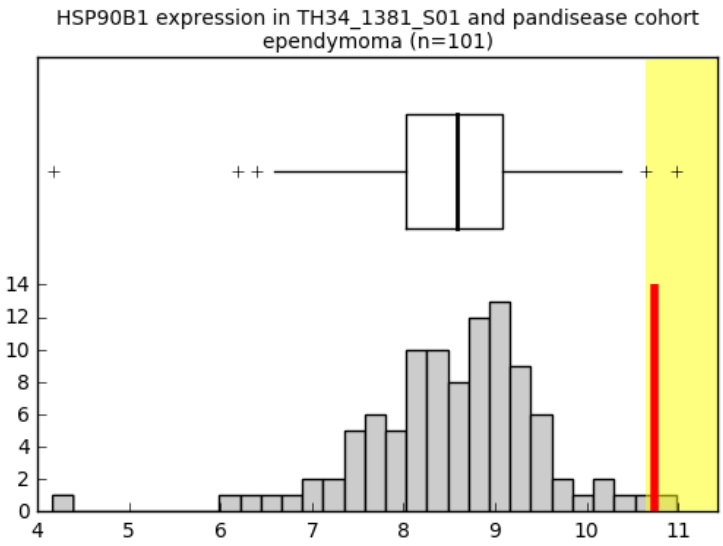
Gene: PARP1





Gene: HSP90B1





Analysis Use of "Associated Drugs"

Associated drugs provided here have been identified by Stanford treating oncologists and are included in Stanford IRB Protocol #44179, PD Sheri Spunt, titled "California Initiative to Advance Precision Medicine, California Kids Cancer Comparison, and Treehouse Childhood Cancer Initiative".

Pathway-Drug Associations

Information about these drugs is provided from www.cancer.gov.

RTK — Pazopanib

Pazopanib is a small molecule inhibitor of multiple protein tyrosine kinases with potential antineoplastic activity. Pazopanib selectively inhibits vascular endothelial growth factor receptors (VEGFR)-1, -2 and -3, c-kit and platelet derived growth factor receptor (PDGF-R), which may result in inhibition of angiogenesis in tumors in which these receptors are upregulated.

Cell Cycle — Ribociclib

Ribociclib is an orally available cyclin-dependent kinase (CDK) inhibitor targeting cyclin D1/CDK4 and cyclin D3/CDK6 cell cycle pathway, with potential antineoplastic activity. Ribociclib specifically inhibits CDK4 and 6, thereby inhibiting retinoblastoma (Rb) protein phosphorylation. Inhibition of Rb phosphorylation prevents CDK-mediated G1-S phase transition, thereby arresting the cell cycle in the G1 phase, suppressing DNA synthesis and inhibiting cancer cell growth. Overexpression of CDK4/6, as seen in certain types of cancer, causes cell cycle deregulation.

PI3K/AKT/mTOR— Everolimus

A derivative of the natural macrocyclic lactone sirolimus with immunosuppressant and anti-angiogenic properties. In cells, everolimus binds to the immunophilin FK Binding Protein-12 (FKBP-12) to generate an immunosuppressive complex that binds to and inhibits the activation of the mammalian Target of Rapamycin (mTOR), a key regulatory kinase. Inhibition of mTOR activation results in the inhibition of T lymphocyte activation and proliferation associated with antigen and cytokine (IL-2, IL-4, and IL-15) stimulation and the inhibition of antibody production.

JAK/STAT — Ruxolitinib

The phosphate salt form of ruxolitinib, an orally bioavailable Janus-associated kinase (JAK) inhibitor with potential antineoplastic and immunomodulating activities. Ruxolitinib specifically binds to and inhibits protein tyrosine kinases JAK 1 and 2, which may lead to a reduction in inflammation and an inhibition of cellular proliferation. The JAK-STAT (signal transducer and activator of transcription) pathway plays a key role in the signaling of many cytokines and growth factors and is involved in cellular proliferation, growth, hematopoiesis, and the immune response; JAK kinases may be upregulated in inflammatory diseases, myeloproliferative disorders, and various malignancies.

References

Scientific articles below are identified by PMID, a unique identifier referring to a published paper. Articles can be searched by PMID at http://www.ncbi.nlm.nih.gov/pubmed.

Newton et al. TumorMap: Exploring the Molecular Similarities of Cancer Samples in an Interactive Portal. Cancer Res. 2017 Nov 1;77(21):e111–e114 (PMID:29092953)

Jones et al. Evolution of an adenocarcinoma in response to selection by targeted kinase inhibitors. Genome Biol 11(8):R82, 2010 (PMID:20696054)

Subramanian, Tamayo, et al. Gene set enrichment analysis: A knowledge-based approach for interpreting genome-wide expression profiles. PNAS 102(43):15545–15550, 2005 (PMID:16199517)

Cotto, et al. DGIdb 3.0: a redesign and expansion of the drug–gene interaction database. Nucleic Acids Research 2017 Nov 17. (DOI:10.1093/nar/gkx1143)

The Cancer Genome Atlas (TCGA): https://cancergenome.nih.gov/

Therapeutically Applicable Research to Generate Effective Treatments (TARGET): https://ocg.cancer.gov/programs/target

Treehouse internal appendix for Treehouse comparative RNA-Seq analysis report

Case Documentation

To be written by the analyst.

Processing Notes

There are no automated processing notes for this sample.

Secondary QC

This sample exceeds the minimum required threshold of 10 million reads.

Read Count Table

MEND	84469102.85
Total_sequences	142557239.0
M	133463458.0
MND	107092811.5
Multimapped_reads	7661400.0

Metrics

Measure	Result	Reference range	In reference range?	n samples
MEND_reads/Total_reads	0.593	0.213 - 0.773	Yes	879
Duplicate_reads/Total_reads	0.2	-0.03 - 0.56	Yes	878
RIN	6.9	4.5 - 10.0	Yes	22
Expressed_genes_(*1000)	32.99	24.76 - 29.7	No	180
Pan-cancer_up_outliers	334	97.04 - 285.05	No	180
95th_percentile_of_genes_in_sample_(log2(TPM)+1)	5.92	4.93 - 5.67	No	180

TumorMap URLs

Focus Sample (calculated)
Most Correlated Samples
Most Correlated Samples Above Threshold

Most Correlated Samples and Focus Sample (calculated)

Leads Identified by Automated Analysis

Assay: druggableUpOutlier HSP90B1
pc, pd

Assay: druggableUpOutlier PARP1
pd

Assay: geneSets_broadCancer PID GLYPICAN 1PATHWAY (pc up (3/27))
druggable: VEGFA (pc) overlap_genes_in_pc_up LAMA1, TGFB2, VEGFA and pd_up NA

Assay: geneSets_nonCancer HALLMARK GLYCOLYSIS (pc up (7/200) and pd up (5/200))
druggable: VEGFA (pc) overlap_genes_in_pc_up COG2, DPYSL4, PGAM2, PPFIA4, SDC3, TKTL1, VEGFA and pd_up COG2, FAM162A, HAX1, SDHC, TKTL1

Assay: geneSets_nonCancer HALLMARK HYPOXIA (pc up (9/200))
druggable: VEGFA (pc) overlap_genes_in_pc_up BCAN, DPYSL4, NCAN, PGAM2, PPFIA4, PYGM, SDC3, TKTL1, VEGFA and pd_up FAM162A, GAPDH, TKTL1

Assay: NA PID INTEGRIN1 PATHWAY (pc up (4/66))
druggable: VEGFA (pc) overlap_genes_in_pc_up COL2A1, ITGA7, LAMA1, VEGFA and pd_up COL2A1

Assay: NA REACTOME REGULATION OF HYPOXIA INDUCIBLE FACTOR HIF BY OXYGEN (pc up (4/25))
druggable: VEGFA (pc) overlap_genes_in_pc_up ARNT, EGLN1, HIF3A, VEGFA and pd_up ARNT, EGLN1

Assay: druggableUpOutlier VEGFA
pc

Assay: geneSets_priority1 HALLMARK MTORC1 SIGNALING (pd up (7/200))
druggable: HSP90B1 (pc and pd) overlap_genes_in_pc_up HSP90B1 and pd_up CACYBP, EPRS, GAPDH, HSP90B1, RIT1, SDF2L1, UCHL5

Assay: geneSets_priority1 KEGG FOCAL ADHESION (pc up (7/201))
druggable: VEGFA (pc) overlap_genes_in_pc_up COL2A1, FLNC, ITGA7, LAMA1, RELN, THBS3, VEGFA and pd_up COL2A1, THBS4

Assay: geneSets_broadCancer HALLMARK EPITHELIAL MESENCHYMAL TRANSITION (pc up (8/200))
druggable: VEGFA (pc) overlap_genes_in_pc_up COPA, CRLF1, ECM2, ELN, LAMA1, MSX1, SCG2, VEGFA and pd_up CADM1, COPA

Assay: geneSets_broadCancer KEGG PATHWAYS IN CANCER (pc up (12/328))
druggable: HSP90B1 (pc and pd), VEGFA (pc) overlap_genes_in_pc_up APC2, ARNT, EGLN1, HSP90B1, LAMA1, PIAS3, RALGDS, STK36, TGFB2, TPR, VEGFA, WNT11 and pd_up ARNT, EGLN1, FH, HSP90B1

Assay: geneSets_broadCancer KEGG RENAL CELL CARCINOMA (pd up (3/70))
druggable: VEGFA (pc) overlap_genes_in_pc_up ARNT, EGLN1, TGFB2, VEGFA and pd_up ARNT, EGLN1, FH

Assay: geneSets_broadCancer NABA MATRISOME (pc up (31/1028))
druggable: VEGFA (pc) overlap_genes_in_pc_up ADAMTS16, BCAN, C1QTNF3, COL27A1, COL2A1, COL9A2, CRLF1, ECM2, EGLN1, ELN, GDF1, GDF10, IL17D, LAMA1, MMP17, NCAN, PLXNA2, PLXNA3, RELN, RSPO2, RSPO4, S100B, SDC3, SEMA5B, SEMA6D, SMOC1, TGFB2, THBS3, VEGFA, VWA3A, WNT11 and pd_up C1QTNF3, COL2A1, EGLN1, PLXNA2, THBS4

Assay: geneSets_broadCancer NABA MATRISOME ASSOCIATED (pc up (17/753))
druggable: VEGFA (pc) overlap_genes_in_pc_up ADAMTS16, C1QTNF3, CRLF1, EGLN1, GDF1, GDF10, IL17D, MMP17, PLXNA2, PLXNA3, S100B, SDC3, SEMA5B, SEMA6D, TGFB2, VEGFA, WNT11 and pd_up C1QTNF3, EGLN1, PLXNA2

TumorMap Legend: Pandisease Cohort Diseases only

alveolar rhabdomyosarcoma
atypical teratoid/rhabdoid tumor
choroid plexus carcinoma
dysembryoplastic neuroepithelial tumor
embryonal rhabdomyosarcoma
embryonal tumor with multilayered rosettes
ependymoma
Ewing sarcoma
ganglioglioma
glioblastoma multiforme
glioma
gliomatosis cerebri
infantile fibrosarcoma
leiomyosarcoma
malignant peripheral nerve sheath tumor
medulloblastoma
neuroblastoma
pheochromocytoma & paraganglioma
rhabdomyosarcoma
rosette forming glioneuronal tumor
sarcoma
skin cutaneous melanoma
supratentorial embryonal tumor NOS
teratoma
testicular germ cell tumor
undifferentiated hepatic sarcoma
undifferentiated pleomorphic sarcoma
undifferentiated sarcoma NOS
uveal melanoma

Most Correlated Samples with Clinical info

Sample ID	Score	Diagnosis (Site's original, Disease)	Histology	Stage	Grade	Subcat	Age	Mutations in Cancer Genes
TH34_1381_S01	1.00	• Ependymoma, anaplastic WHO grade III, RELA fusion negative, Group-! • ependymoma			G3	RELA fusion negative	2.5	no information available
THR24_1805_S01	0.93	• Ependymoma • ependymoma						no information available
THR24_1841_S01	0.93	• Ependymoma; Ependymoma, NOS • ependymoma					1.66	no information available
THR24_1776_S01	0.93	• Ependymoma; Ependymoma, NOS • ependymoma					1.1	no information available
THR24_1771_S01	0.92	• Ependymoma; Ependymoma, NOS • ependymoma					3.7	no information available
THR24_1783_S01	0.92	• Ependymoma • ependymoma						no information available
THR24_1825_S01	0.92	• Ependymoma; Ependymoma, NOS • ependymoma					1.35	no information available

Multiply-Mutated Genes in Most Correlated Samples

No multiply-mutated genes were found in the most correlated samples.

Multiply-Appearing Mutations in Most Correlated Samples

No multiply-appearing mutations were found in the most correlated samples.

Fusions

FusionName	JunctionReadCount	SpanningFragCount
PBX1--SFPQ	1	1

Variants of Focus Sample

Variant calling was run on this sample, but no variants were found.

FLT3-ITD Events

No FLT3-ITD event output file was found for this sample; FLT3-ITD events are unknown.

All pan-cancer outliers

ACBD6 ADAMTS16 ADCY2 ADCYAP1R1 ADGRA3 ADGRD1 ADRA2A AIFM3 AKAP8L ANGEL2 APC2 APLNR AQP4 ARHGEF11 ARL8A ARMC3 ARNT ATAT1 ATN1 ATP1A2 ATP1B2 ATP2B4 BAIAP3 BCAN BCL9 BOC C10orf105 C1orf194 C1orf198 C1orf226 C1orf35 C1orf61 C1QTNF3 C3orf70 C5orf49 C9orf24 CADM3 CCDC114 CCDC130 CCDC181 CCDC37 CCDC40 CDH23 CERS1 CFAP126 CFAP45 CHD1L CHODL CHTOP CLK2 CNIH2 CNTN1 CNTN2 COG2 COL27A1 COL2A1 COL9A2 COPA CORO2B COX20 CPNE6 CRB1 CRB2 CRLF1 CRTC2 CTD-2297D10.2 CTNND2 CYP4F12 DAW1 DCAF8 DCLK2 DEDD DENND4B DENND6B DFNB31 DMWD DNAH9 DNER DOK5 DPYSL4 DPYSL5 DUSP12 ECM2 EFCAB1 EFNB3 EGLN1 ELN FAM179A FAM189A2 FAM81B FEZ1 FEZ2 FGFRL1 FHAD1 FLNC FMN2 FOXJ1 GALNS GALNT8 GAS8 GDF1 GDF10 GDPD2 GEMIN8 GFAP GGPS1 GNPAT GON4L GORASP1 GPM6A GPM6B GPR162 GPR37L1 GPR89A GRAMD2 GRIA4 GSTM5 HAUS7 HEPACAM HES6 HIF3A HILPDA HNRNPU-AS1 HSD17B7 HSP90B1 IFT140 IGSF1 IL17D INTS3 IPO9 IQCG ITGA7 ITPKB KCNJ10 KIAA0895L KIAA0907 KIF1A KIFAP3 KLHL12 LAMA1 LGR6 LINC00461 LINC00844 LINC01158 LLGL1 LMO3 LRRC4B LRRC71 LRRN1 LRRN2 LSAMP LZTR1 MAB21L2 MAP6 MAPK15 MAPK4 MDM4 MLC1 MMP17 MOK MOXD1 MRPS14 MSTO1 MSX1 MTSS1L NAV1 NBPF15 NCAM1 NCAN NCSTN NDUFS2 NEK11 NFASC NIT1 NKAIN4 NNAT NOS1AP NRBP2 NSL1 NSMF NUCKS1 NUP133 NVL PAQR6 PAX3 PAX6 PDE4DIP PDE8A PDZD4 PDZK1 PEA15 PEX19 PFKFB4 PGAM2 PHYHIPL PI4KAP2 PI4KB PIAS3 PID1 PIGC PIP5K1A PLCD1 PLD2 PLEKHG5 PLXNA2 PLXNA3 PMF1 PNPLA7 POGZ POU3F3 PPFIA4 PPOX PPP1R12B PPP5C PRCC PRPF3 PRRT2 PSD2 PTPRZ1 PYCR2 PYGM RABL2A RABL2B RALGDS RCOR3 REEP2 RELN RFX4 RGS11 RHOBTB2 RMST RMST_10 RNF182 RNF2 ROBO3 RP11-263K19.4 RP11-565P22.6 RP11-632C17__A.1 RP11-734K23.9 RP3-467D16.3 RSPO2 RSPO4 S100B SAP30BP SCG2 SCRIB SDC3 SEMA5B SEMA6D SEPT3 SETDB1 SFI1 SFXN5 SH3BP5L SLC1A3 SLC22A3 SLC38A3 SLC41A1 SLC4A3 SLC6A11 SMG5 SMG7 SMOC1 SMYD3 SNAP47 SNAPIN SOCS2 SOX2 SPA17 SPAG6 SPAG8 SPATA17 SRP9 SSBP3 ST8SIA1 STAC2 STARD3 STK11IP STK36 STX18 SUCO SYNGAP1 SYT11 TADA1 TAGLN3 TARBP1 TARS2 TBCE TCEAL2 TCTEX1D1 TGFB2 THBS3 THEM4 TIMM17A TIPRL TKTL1 TMEM108 TMEM161B-AS1 TMEM231 TMEM59L TNFRSF25 TP53BP2 TPPP3 TPR TSC22D4 TSNAX TTC21A TTLL4 TTYH1 UBAP2L UFC1 USH1C USP21 VANGL2 VEGFA VIPR2 VPS45 VPS72 VWA3A WDR11 WDR90 WNT11 XPR1 YY1AP1 ZBTB18 ZIC1 ZIC2 ZIC4 ZMYND10 ZNF423 ZNF496 ZNF672 ZNF687 ZNF692

All pan-disease outliers

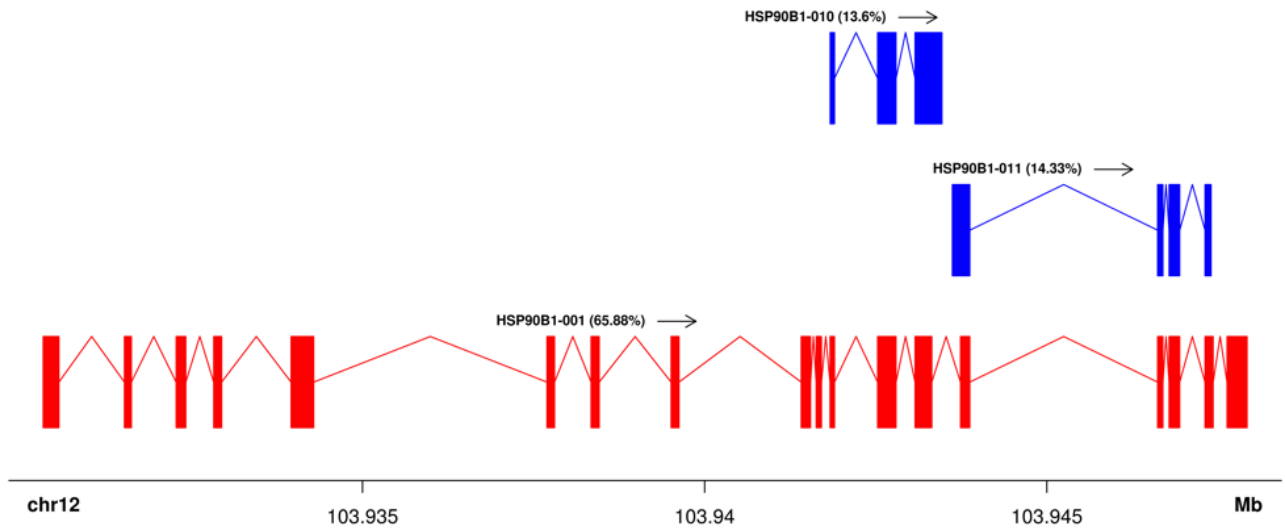
ACBD3 ACBD6 ADRA2A ADSS AL662801.1 ANP32E AP003041.1 APH1A ARF1 ARL8A ARNT ATP2B4 B4GALT3 BCL9 BOLA1 BROX C1orf226 C1orf35 C1orf43 C1QTNF3 CACYBP CADM1 CCT3 CH17-232I21.1 CHD1L CHODL CHTOP CIART COA6 COG2 COL2A1 COPA COX20 CRTC2 DAP DAP3 DCAF6 DEDD DESI2 DUSP12 DUSP23 EGLN1 EIF2D ENSA EPRS FAM162A FDPS FH FLAD1 GAPDH GGPS1 GNPAT GPR89A H3F3A HAX1 HSD17B10 HSD17B7 HSP90B1 HYOU1 IARS2 ILF2 IPO9 ISG20L2 IVNS1ABP JTB KCTD3 KDM5B KIAA0907 KLHL12 KRTCAP2 LAMTOR2 LIX1L MANF MDM4 MEA1 METTL13 METTL5 MGST3 MIA3 MPC2 MRPL24 MRPL55 MRPL9 MRPS14 MSTO1 MTX1 NAV1 NCSTN NDUFS2 NENF NIT1 NME7 NOP10 NOS1AP NSL1 NTPCR NUCKS1 NUP133 NVL PARP1 PBX1 PDIA3 PDZK1 PEX11B PEX19 PFDN2 PFKFB4 PI4KB PIGC PIP5K1A PLXNA2 PMF1 POGK POLR3C PRCC PRKRIR PRPF3 PRRC2C PRUNE PSMB2 PSMB4 PSMD4 RAB29 RBM34 RBM8A RCOR3 RFWD2 RGL1 RIT1 RNF187 RNF2 RNU11 RP11-488L18.4 RP11-565P22.6 RP11-632C17__A.1 RP4-781K5.2 RPRD2 RPS27 SCAMP3 SCCPDH SCNM1 SDF2L1 SDHC SETDB1 SF3B4 SH3BP5L SLC25A44 SMG7 SMYD3 SNAP47 SNAPIN SNRPE SRP9 SSR2 SUCO TADA1 TARS2 TBCE THBS4 TIMM17A TIPRL TKTL1 TMCO1 TMEM9 TSEN15 TSNAX UBAP2L UBQLN4 UCHL5 UFC1 VANGL2 VPS45 VPS72 WDR26 XPR1 Y_RNA YY1AP1 ZNF496 ZNF672 ZNF687

Isoform Report

HSP90B1 isoforms, ordered by IsoPct

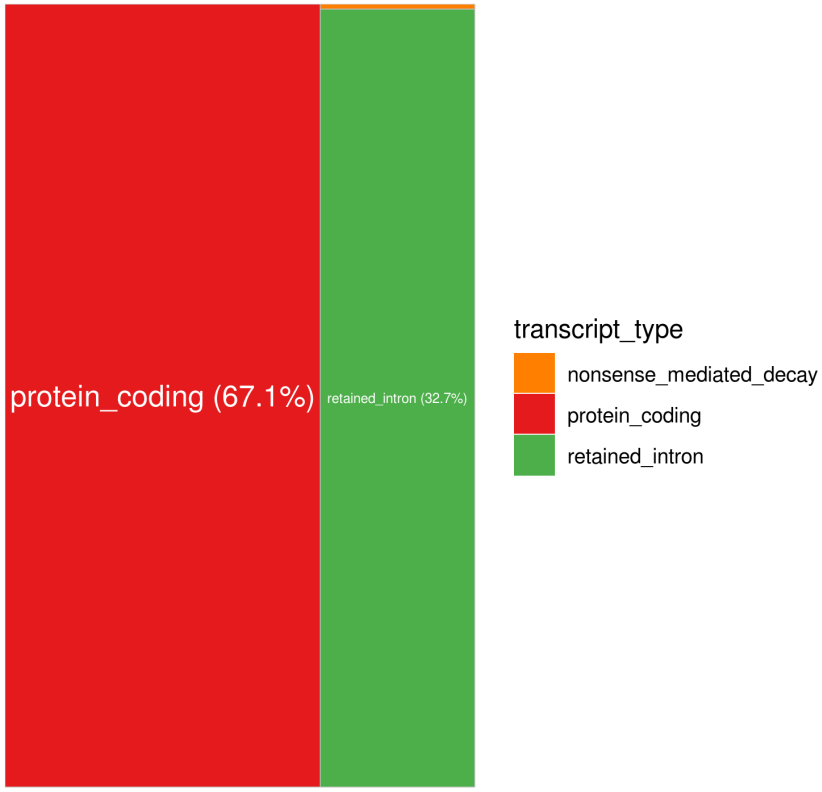
transcript_name	length	log2TPM1	strand	IsoPct	transcript_type	transcript_id	gene_name
HSP90B1-001	2858	10.15	+	65.88	protein_coding	ENST00000299767.9	HSP90B1
HSP90B1-011	581	7.95	+	14.33	retained_intron	ENST00000552051.1	HSP90B1
HSP90B1-010	728	7.88	+	13.6	retained_intron	ENST00000551983.1	HSP90B1
HSP90B1-007	839	5.47	+	2.52	retained_intron	ENST00000548622.1	HSP90B1
HSP90B1-009	698	4.84	+	1.6	retained_intron	ENST00000550479.1	HSP90B1
HSP90B1-012	694	4.43	+	1.2	protein_coding	ENST00000550595.1	HSP90B1
HSP90B1-003	3032	3.6	+	0.65	retained_intron	ENST00000548462.5	HSP90B1
HSP90B1-008	590	2.19	+	0.21	nonsense_mediated_decay	ENST00000540297.6	HSP90B1
HSP90B1-006	581	0.2	+	0.01	protein_coding	ENST00000549334.5	HSP90B1
HSP90B1-201	1338	0.15	+	0.01	protein_coding	ENST00000614327.1	HSP90B1

Expressed HSP90B1 isoforms in TH34_1381_S01



Colored by isoform percent, also reported in label

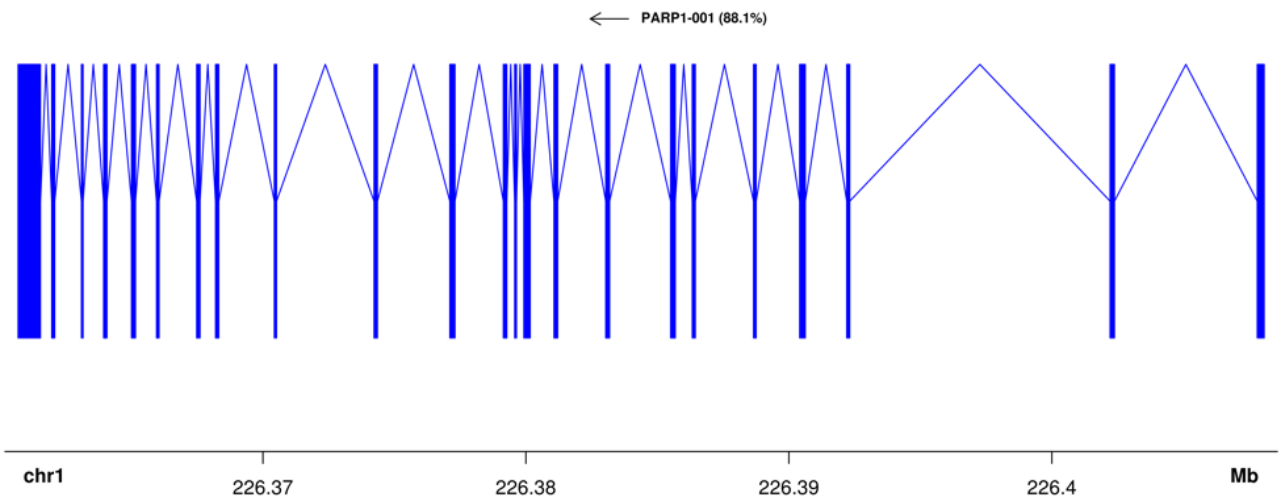
Frequency of HSP90B1 transcript biotypes in TH34_1381_S



PARP1 isoforms, ordered by IsoPct

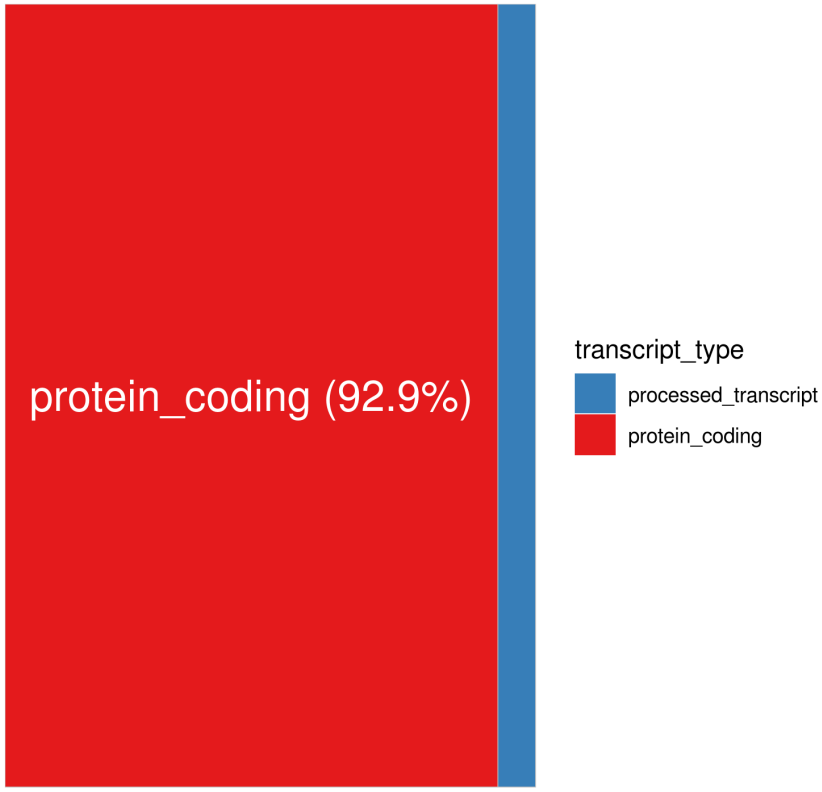
transcript_name	length	log2TPM1	strand	IsoPct	transcript_type	transcript_id	gene_name
PARP1-001	3958	8.03	-	88.1	protein_coding	ENST00000366794.9	PARP1
PARP1-201	477	3.85	-	4.52	protein_coding	ENST00000629232.1	PARP1
PARP1-006	628	3.26	-	2.89	processed_transcript	ENST00000498787.1	PARP1
PARP1-007	830	2.71	-	1.87	processed_transcript	ENST00000463968.5	PARP1
PARP1-009	416	2.2	-	1.21	processed_transcript	ENST00000491816.1	PARP1
PARP1-002	3165	1.48	-	0.6	processed_transcript	ENST00000490921.5	PARP1
PARP1-008	438	1.32	-	0.5	processed_transcript	ENST00000468608.1	PARP1
PARP1-003	570	0.86	-	0.28	protein_coding	ENST00000366790.3	PARP1
PARP1-004	542	0.14	-	0.03	processed_transcript	ENST00000469663.1	PARP1

Expressed PARP1 isoforms in TH34_1381_S01



Colored by isoform percent, also reported in label

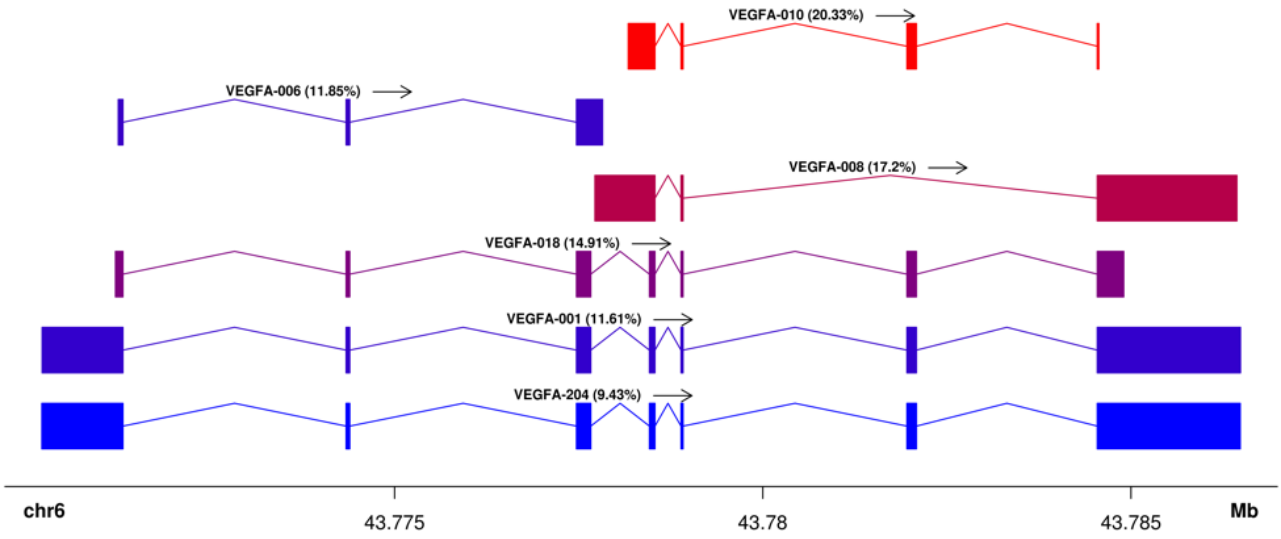
Frequency of PARP1 transcript biotypes in TH34_1381_S01



VEGFA isoforms, ordered by IsoPct

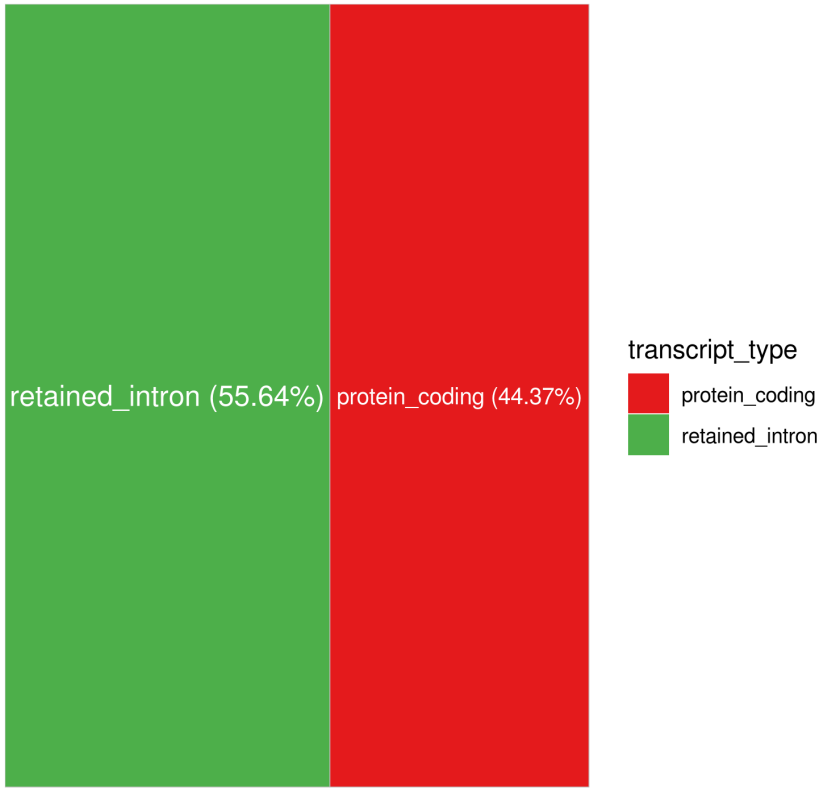
transcript_name	length	log2TPM1	strand	IsoPct	transcript_type	transcript_id	gene_name
VEGFA-010	551	8.74	+	20.33	retained_intron	ENST00000493786.2	VEGFA
VEGFA-008	2746	8.5	+	17.2	retained_intron	ENST00000497139.5	VEGFA
VEGFA-018	954	8.29	+	14.91	protein_coding	ENST00000523950.5	VEGFA
VEGFA-006	475	7.96	+	11.85	retained_intron	ENST00000512683.1	VEGFA
VEGFA-001	3535	7.93	+	11.61	protein_coding	ENST00000372067.7	VEGFA
VEGFA-204	3536	7.63	+	9.43	protein_coding	ENST00000621747.4	VEGFA
VEGFA-020	1199	6.59	+	4.57	protein_coding	ENST00000520948.5	VEGFA
VEGFA-005	1683	6.29	+	3.69	retained_intron	ENST00000476772.5	VEGFA
VEGFA-202	3404	6.17	+	3.39	protein_coding	ENST00000615393.4	VEGFA
VEGFA-007	12167	5.16	+	1.66	retained_intron	ENST00000480614.1	VEGFA
VEGFA-017	535	4.32	+	0.91	retained_intron	ENST00000518538.5	VEGFA
VEGFA-023	630	2.13	+	0.16	protein_coding	ENST00000518689.5	VEGFA
VEGFA-203	3374	1.99	+	0.14	protein_coding	ENST00000617771.4	VEGFA
VEGFA-009	993	1.01	+	0.05	protein_coding	ENST00000230480.10	VEGFA
VEGFA-012	1197	1.1	+	0.05	protein_coding	ENST00000413642.7	VEGFA
VEGFA-016	336	1.04	+	0.05	protein_coding	ENST00000520265.1	VEGFA
VEGFA-025	541	0.23	+	0.01	protein_coding	ENST00000523125.5	VEGFA

Expressed VEGFA isoforms in TH34_1381_S01

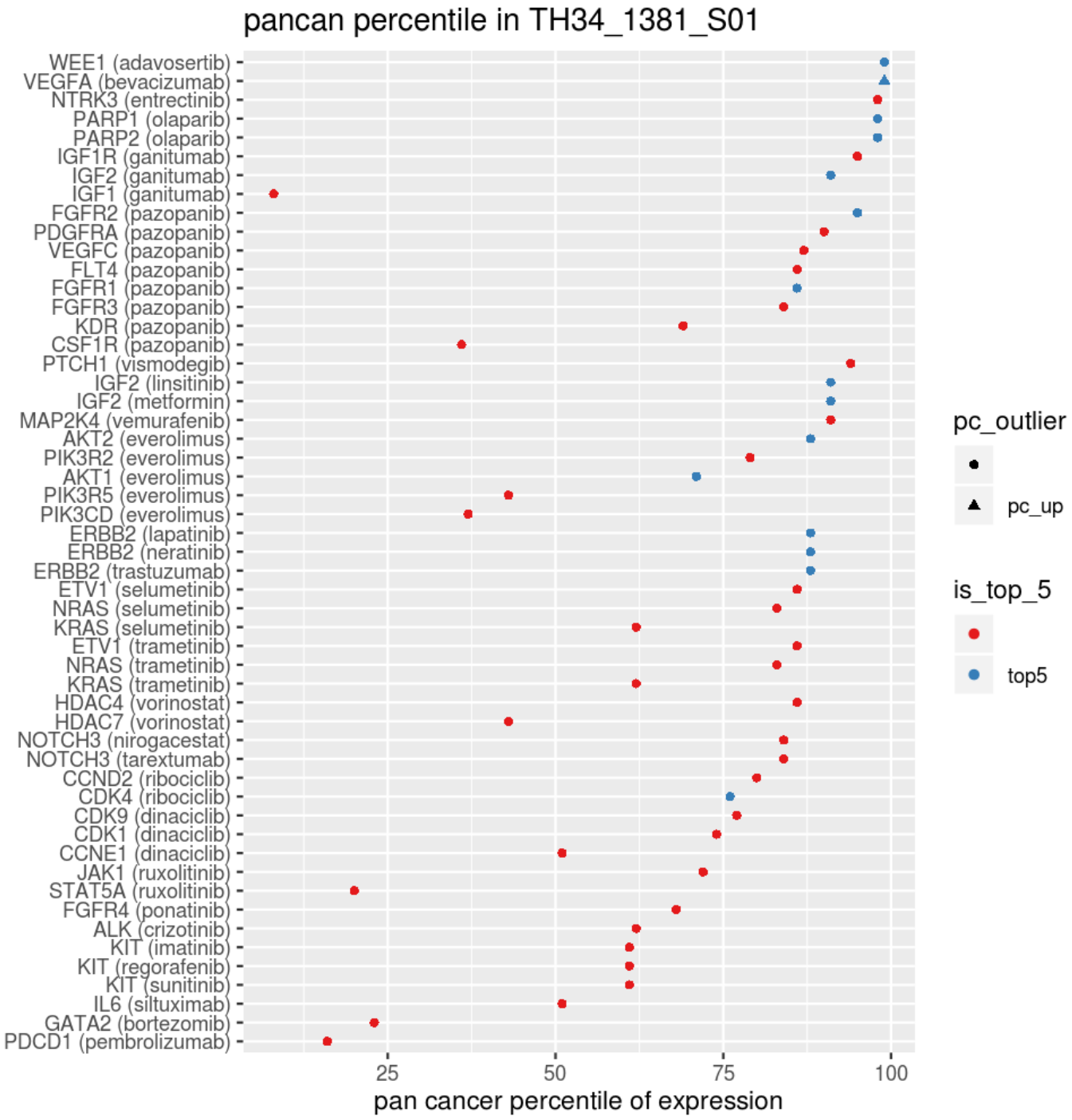


Colored by isoform percent, also reported in label

Frequency of VEGFA transcript biotypes in TH34_1381_S01



Expression of all drug targets identified as leads in the CKCC2 project.



Gene	drug	sample	is_top_5	pc_low	pc_median	pc_high	pc_outlier	pd_outlier	pc_percentile
WEE1	adavosertib	6.68	top5	0.94	4.18	7.31			99
VEGFA	bevacizumab	11.03	top5	1.05	5.85	10.45	pc_up		99
NTRK3	entrectinib	5.74		-1.85	0.44	3.41			98
PARP1	olaparib	8.22	top5	3.26	5.94	8.55		pd_up	98
PARP2	olaparib	5.93	top5	1.92	4.12	6.38			98
IGF1R	ganitumab	5.35		-0.19	3.28	6.65			95
IGF2	ganitumab	9.69	top5	-3.64	2.89	9.97			91
IGF1	ganitumab	0.08		-2.28	1.28	5.26			8
FGFR2	pazopanib	6.03	top5	-3.42	3.17	9.13			95
PDGFRA	pazopanib	5.1		-3.36	2.25	7.86			90
VEGFC	pazopanib	3.82		-1.69	2.02	5.8			87
FLT4	pazopanib	3.29		-1.07	1.8	4.81			86
FGFR1	pazopanib	6.57	top5	-0.04	4.62	9.24			86
FGFR3	pazopanib	5.27		-4.36	2.7	9.62			84
KDR	pazopanib	3.1		-1.59	2.36	6.28			69
CSF1R	pazopanib	3.17		-0.65	3.74	8.12			36
PTCH1	vismodegib	4.65		-1.13	2.15	5.59			94
IGF2	linsitinib	9.69	top5	-3.64	2.89	9.97			91
IGF2	metformin	9.69	top5	-3.64	2.89	9.97			91
MAP2K4	vemurafenib	4.48		1.48	3.54	5.52			91
AKT2	everolimus	7.22	top5	3.9	6.11	8.31			88
PIK3R2	everolimus	5.67		2.53	4.98	7.35			79
AKT1	everolimus	6.78	top5	4.32	6.38	8.36			71
PIK3R5	everolimus	1.57		-1.44	1.77	5.15			43
PIK3CD	everolimus	2.16		-0.9	2.57	6.13			37
ERBB2	lapatinib	6.86	top5	-0.19	5.22	10.09			88
ERBB2	neratinib	6.86	top5	-0.19	5.22	10.09			88
ERBB2	trastuzumab	6.86	top5	-0.19	5.22	10.09			88
ETV1	selumetinib	4.69		-2.84	2.09	7.34			86
NRAS	selumetinib	5.06		1.81	4.28	6.66			83
KRAS	selumetinib	3.86		1.3	3.59	5.87			62
ETV1	trametinib	4.69		-2.84	2.09	7.34			86
NRAS	trametinib	5.06		1.81	4.28	6.66			83
KRAS	trametinib	3.86		1.3	3.59	5.87			62
HDAC4	vorinostat	3.69		-0.35	2.35	5.2			86
HDAC7	vorinostat	4.88		2.68	5.01	7.32			43

NOTCH3	nirogacestat	5.9		-0.46	4.38	9			84
NOTCH3	tarextumab	5.9		-0.46	4.38	9			84
CCND2	ribociclib	5.49		-1.86	3.59	9.34			80
CDK4	ribociclib	7.34	top5	4.51	6.74	8.96			76
CDK9	dinaciclib	5.8		3.6	5.31	7.04			77
CDK1	dinaciclib	5.31		-1.14	4.25	9.2			74
CCNE1	dinaciclib	2.6		-1.35	2.52	6.46			51
JAK1	ruxolitinib	5.83		2.82	5.32	7.74			72
STAT5A	ruxolitinib	2.97		0.9	3.89	6.86			20
FGFR4	ponatinib	2.88		-3.31	1.76	7.73			68
ALK	crizotinib	0.26		-0.81	0.14	1.42			62
KIT	imatinib	2.04		-2.42	1.57	5.89			61
KIT	regorafenib	2.04		-2.42	1.57	5.89			61
KIT	sunitinib	2.04		-2.42	1.57	5.89			61
IL6	siltuximab	1.26		-2.78	1.22	5.81			51
GATA2	bortezomib	1		-2.17	2	6.44			23
PDCD1	pembrolizumab	0.21		-1.44	0.73	3.26			16