



CANCER GENOMICS CONSORTIUM

Educating for Best Practices in Clinical Cancer Genomics

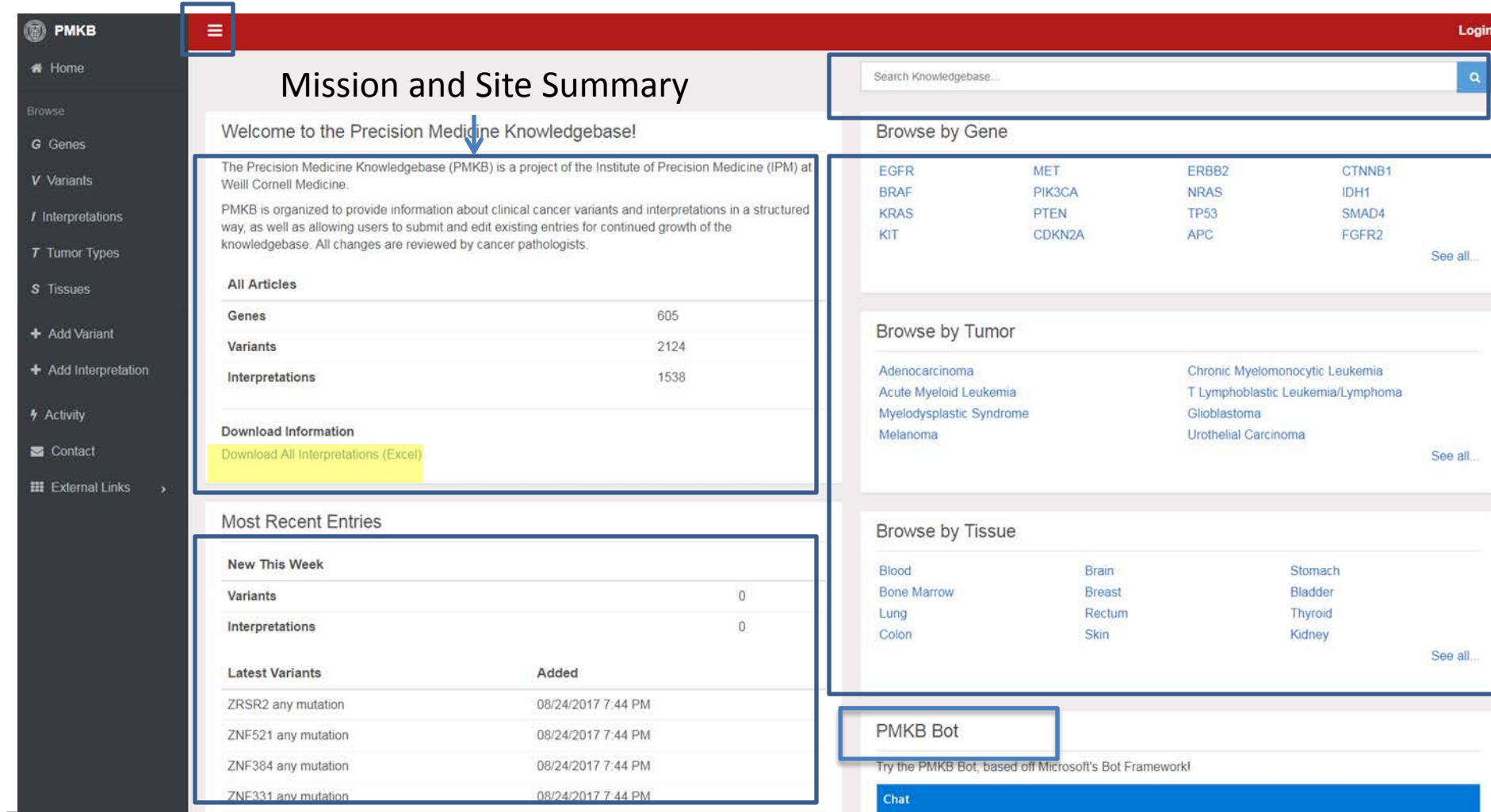
Precision Medicine Knowledgebase (PMKB)

<https://pmkb.weill.cornell.edu/>

<https://academic.oup.com/jamia/article/24/3/513/2418181/The-cancer-precision-medicine-knowledge-base-for>

Click on this to
expand/collapse side menu

Home Page



The screenshot shows the PMKB Home Page with several annotations. A red box highlights the hamburger menu icon in the top left sidebar, with an arrow pointing to it from the text 'Click on this to expand/collapse side menu'. A blue box highlights the 'Mission and Site Summary' section, with an arrow pointing to it from the text 'Click on this to expand/collapse side menu'. Another blue box highlights the 'Most Recent Entries' section, with an arrow pointing to it from the text 'Recent Additions to PMKB'. A third blue box highlights the 'PMKB Bot' chat widget, with an arrow pointing to it from the text 'Recent Additions to PMKB'. The page layout includes a top navigation bar with the PMKB logo and a 'Login' link. The main content area is divided into several sections: 'Mission and Site Summary', 'Browse by Gene', 'Browse by Tumor', 'Browse by Tissue', and 'PMKB Bot'. The 'Mission and Site Summary' section contains a welcome message, a table of statistics, and a download link. The 'Browse by Gene' section lists various genes. The 'Browse by Tumor' section lists various tumor types. The 'Browse by Tissue' section lists various tissues. The 'PMKB Bot' section is a chat widget.

Mission and Site Summary

Welcome to the Precision Medicine Knowledgebase!

The Precision Medicine Knowledgebase (PMKB) is a project of the Institute of Precision Medicine (IPM) at Weill Cornell Medicine.

PMKB is organized to provide information about clinical cancer variants and interpretations in a structured way, as well as allowing users to submit and edit existing entries for continued growth of the knowledgebase. All changes are reviewed by cancer pathologists.

All Articles	
Genes	605
Variants	2124
Interpretations	1538

Download Information

[Download All Interpretations \(Excel\)](#)

Most Recent Entries

New This Week	
Variants	0
Interpretations	0

Latest Variants	Added
ZRSR2 any mutation	08/24/2017 7:44 PM
ZNF521 any mutation	08/24/2017 7:44 PM
ZNF384 any mutation	08/24/2017 7:44 PM
ZNF331 any mutation	08/24/2017 7:44 PM

Browse by Gene

EGFR	MET	ERBB2	CTNNB1
BRAF	PIK3CA	NRAS	IDH1
KRAS	PTEN	TP53	SMAD4
KIT	CDKN2A	APC	FGFR2

[See all...](#)

Browse by Tumor

Adenocarcinoma	Chronic Myelomonocytic Leukemia
Acute Myeloid Leukemia	T Lymphoblastic Leukemia/Lymphoma
Myelodysplastic Syndrome	Glioblastoma
Melanoma	Urothelial Carcinoma

[See all...](#)

Browse by Tissue

Blood	Brain	Stomach
Bone Marrow	Breast	Bladder
Lung	Rectum	Thyroid
Colon	Skin	Kidney


[See all...](#)

PMKB Bot

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Search for Genes


PMKB

Home

Browse

Genes

Variants

Interpretations

Tumor Types

Tissues

+ Add Variant

+ Add Interpretation

Activity

Contact

External Links

Search Knowledgebase...

Q

Browse by Gene

EGFR	MET	ERBB2	CTNNB1
BRAF	PIK3CA	NRAS	IDH1
KRAS	PTEN	TP53	SMAD4
KIT	CDKN2A	APC	FGFR2

[See all...](#)

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[See all...](#)

Browse by Tissue

Blood	Brain	Stomach
Bone Marrow	Breast	Bladder
Lung	Rectum	Thyroid
Colon	Skin	Kidney

[See all...](#)

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Chat

Browse Genes

Genes

Search Knowledgebase...

Browse

AllA B C D E F G H I J K L M N O P Q R S T U V W X Y Z

Search:

HUGO Symbol	↓ Variants	↑ Interpretations
ABL1	16 Variant(s)	5 Interpretation(s)
ABL2	1 Variant(s)	0 Interpretation(s)
AKT1	4 Variant(s)	2 Interpretation(s)
AKT2	1 Variant(s)	1 Interpretation(s)
AKT3	1 Variant(s)	1 Interpretation(s)
ALK	7 Variant(s)	4 Interpretation(s)
APC	16 Variant(s)	9 Interpretation(s)
AR	5 Variant(s)	2 Interpretation(s)
ASXL1	1 Variant(s)	1 Interpretation(s)
ATM	4 Variant(s)	4 Interpretation(s)
AURKA	1 Variant(s)	1 Interpretation(s)
BAP1	1 Variant(s)	1 Interpretation(s)

ABL1

Search Knowledgebase...



Interpretations

By Variant(s)

- [ABL1 any mutation](#)
- [ABL1 D276G](#)
- [ABL1 E255K](#)
- [ABL1 E255V](#)
- [ABL1 G250E](#)
- [ABL1 H396P](#)
- [ABL1 L387M](#)
- [ABL1 M351T](#)
- [ABL1 Q252H](#)
- [ABL1 T315I](#)
- [ABL1 V299L](#)
- [ABL1 Y253F](#)
- [ABL1 Y253H](#)
- [ABL1 F359V](#)
- [ABL1 M244V](#)
- [ABL1 E355G](#)

By Tumor

- Acute Myeloid Leukemia
 - [ABL1 F359V](#)
- B Lymphoblastic Leukemia/Lymphoma
 - [ABL1 any mutation, ABL1 T315I](#)
- Chronic Myeloid Leukemia
 - [ABL1 any mutation, ABL1 T315I](#)
 - [ABL1 F359V](#)
 - [ABL1 E355G](#)
 - [ABL1 M244V](#)
 - [ABL1 F359V](#)
- Other Acute Leukemia
 - [ABL1 F359V](#)
 - [ABL1 E355G](#)
 - [ABL1 M244V](#)

Variants

+ Add New Variant

Show 10 entries

Search:

Gene	Type	Description	COSMIC ID	DNA Change (Coding Nucleotide)	Exon
ABL1	any	ABL1 any mutation			
ABL1	missense	ABL1 D276G	COSM12602	827A>G	5
ABL1	missense	ABL1 E255K	COSM12573	763G>A	4
ABL1	missense	ABL1 E255V	COSM12574	764A>T	4
ABL1	missense	ABL1 G250E	COSM12577	749G>A	4
ABL1	missense	ABL1 H396P	COSM12564	1187A>C	7
ABL1	missense	ABL1 L387M	COSM131574	1159T>A	7
ABL1	missense	ABL1 M351T	COSM12578	1052T>C	6
ABL1	missense	ABL1 Q252H	COSM12609	756G>C	4
ABL1	missense	ABL1 T315I	COSM12560	944C>T	6

Showing 1 to 10 of 16 entries

First Previous 2 Next Last

Interpretations

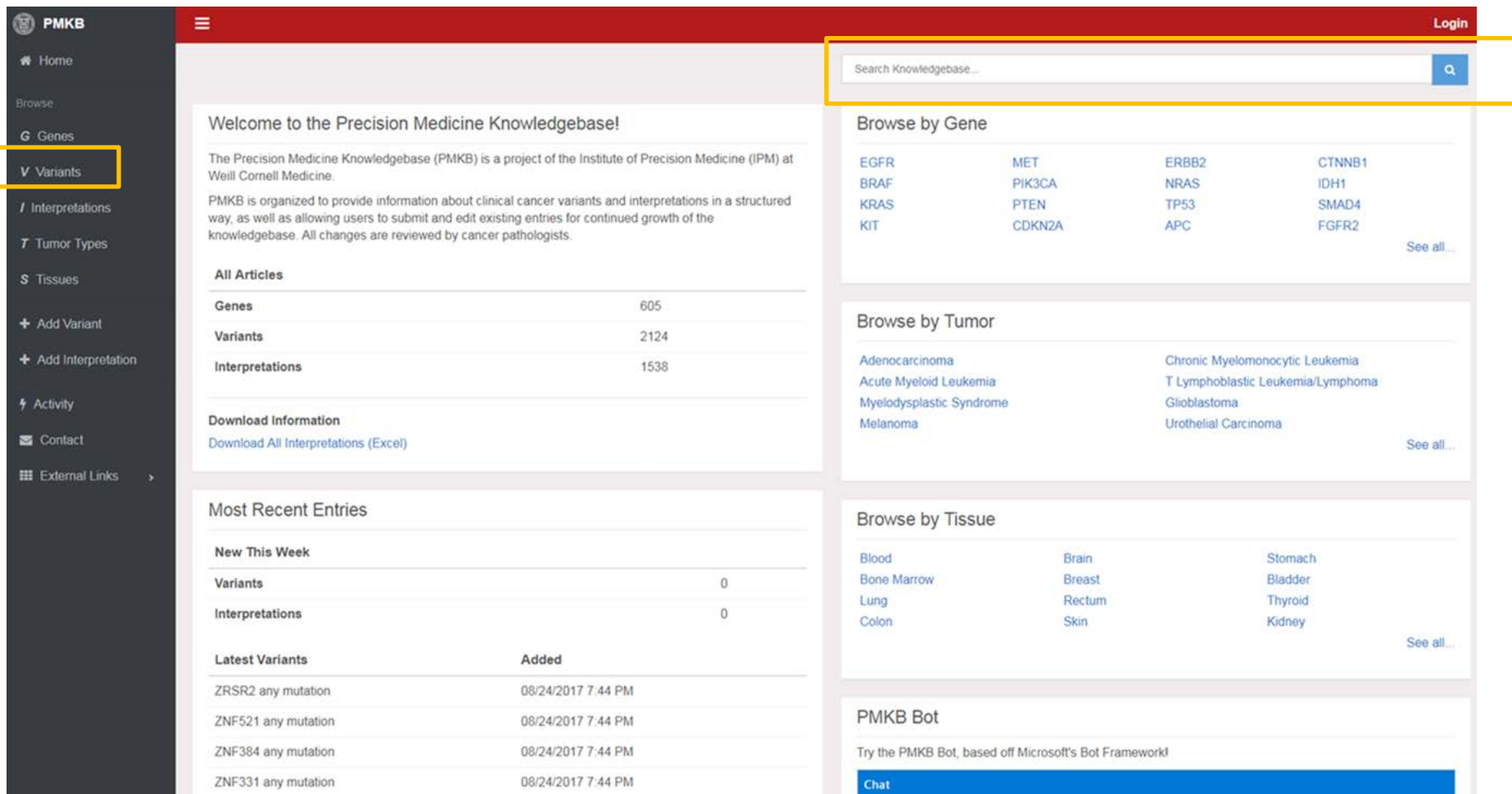
+ Add New Interpretation

Show 10 entries

Search:

Tumor	Tissue	Variants	Interpretation
Chronic Myeloid Leukemia	Blood	ABL1 F359V	The p.F359V mutation in the context of the BCR-ABL1 translocation may associated with resistance to ABL kinase inhibitors.
Acute Myeloid Leukemia	Bone Marrow		
Other Acute Leukemia			
Chronic Myeloid Leukemia	Blood	ABL1 any mutation	ABL1 kinase domain mutations in Philadelphia chromosome positive acute lymphoblastic leukemia and chronic myelogenous leukemia are associated with resistance to some types of tyrosine kinase inhibitor therapy. The various mutations span several hundred amino acids (M237 thru E507) and vary in their
B Lymphoblastic	Bone Marrow		

Search for Variants



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ZNF331 any mutation	08/24/2017 7:44 PM

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- Either search by variants through the gene page or on their own using either of the boxed regions above. Includes some copy number variants.

Browse Variants

Variants							
Search Knowledgebase...							
Variants							
Show 10 entries							
Search:							
Gene	Type	Description	COSMIC ID	DNA Change (Coding Nucleotide)	Exon		
ABL1	any	ABL1 any mutation					
ABL1	missense	ABL1 D276G	COSM12602	827A>G	5		
ABL1	missense	ABL1 E255K	COSM12573	763G>A	4		
ABL1	missense	ABL1 E255V	COSM12574	764A>T	4		
ABL1	missense	ABL1 G250E	COSM12577	749G>A	4		
ABL1	missense	ABL1 H396P	COSM12564	1187A>C	7		
ABL1	missense	ABL1 L387M	COSM131574	1159T>A	7		
ABL1	missense	ABL1 M351T	COSM12578	1052T>C	6		

- 513 Variants described in PMKB



Variant Page

ERBB2

Interpretations

By Variant(s)

[ERBB2 D769H](#)
[ERBB2 D769Y](#)
[ERBB2 E321G](#)
[ERBB2 G309A](#)
[ERBB2 G309E](#)
[ERBB2 L755S](#)
[ERBB2 R896C](#)
[ERBB2 S310F](#)
[ERBB2 S310Y](#)
[ERBB2 T733I](#)
[ERBB2 V659E](#)
[ERBB2 V777L](#)
[ERBB2 V842I](#)
[ERBB2 G776delinsVC](#)
[ERBB2 exon\(s\) 20 insertion](#)
[ERBB2 R157W](#)
[ERBB2 copy number gain](#)
[ERBB2 L755P](#)
[ERBB2 S295F](#)
[ERBB2 L869R](#)
[ERBB2 T798I](#)

By Tumor

- Adenocarcinoma
 - [ERBB2 G776delinsVC](#)
 - [ERBB2 V842I](#)
 - [ERBB2 V842I](#)
 - [ERBB2 S310F, ERBB2 S310Y, ERBB2 R157W](#)
 - [ERBB2 L755S](#)
 - [ERBB2 copy number gain](#)

Search Knowledgebase...

q

ERBB2 exon(s) 20 insertion

InformationView HistorySuggested Revisions

Gene	ERBB2
Variant	insertion
Transcript ID (GRCh37/hg19)	ENST00000269571
Exon(s)	20
Genomic Coordinates (GRCh37/hg19)	17:37880979-37881164
Germline/Somatic?	Somatic

Coordinates for exon 20

Pertinent Negative In

Tumor	Tissue
Adenosarcoma	Lung

Interpretations

+ Add New Interpretation

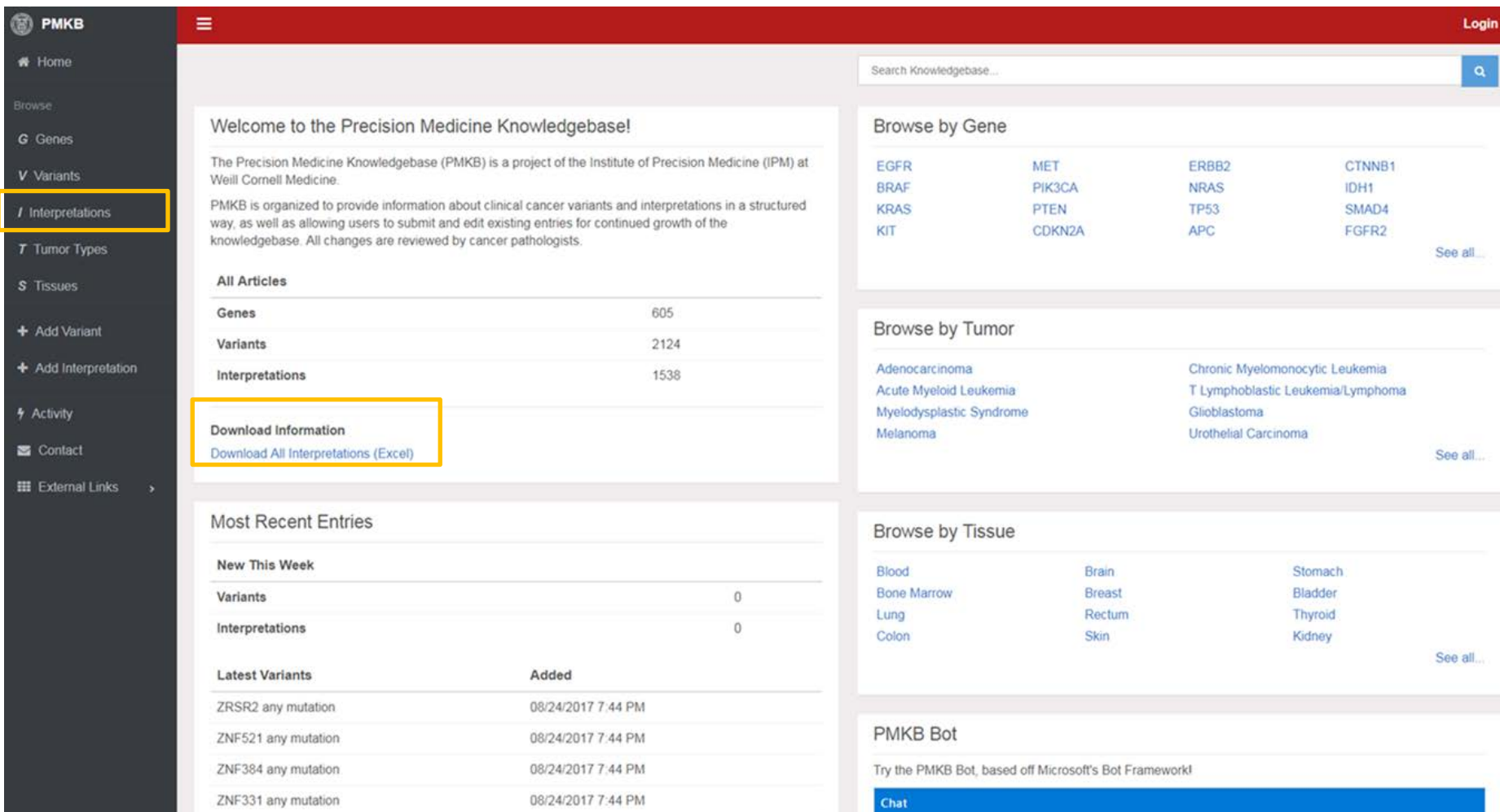
Search:

Showing 1 to 1 of 1 entries

Tumor	Tissue	Variants	Interpretation
Adenosarcoma	Lung	ERBB2 exon(s) 20 insertion	ERBB2 exon 20 insertions occur within exon 20, which encodes part of the kinase domain. These mutations occur with a frequency of approximately 2–4% of all NSCLC. Overall, in-frame ERBB2 insertions in exon 20 have been reported in approximately 6% of cases of lung adenocarcinoma which are negative for EGFR, KRAS, ALK alterations and these variants are more frequent in patients who were never-smokers. Mutations in ERBB2 do not have an independent prognostic value in lung adenocarcinoma, according to a recent study. In vitro studies have shown that this specific variant is associated with constitutive kinase activation and is associated with sensitivity to some ERBB2 inhibitors and therefore, it may represent a targetable mutation in some clinical settings. Please refer to clinicaltrials.gov for additional information. Recommend correlation with other clinical and laboratory findings.

FirstPreviousNextLast

Interpretations



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↓ Scroll down to view latest interpretations

View Latest Interpretations

Latest Intepretations			
Variants	Tumortypes	Tumorsites	Added
KRAS G13D	Adenocarcinoma	Colon Rectum	03/24/2017 2:09 PM
BRAF codon(s) 594 any	Adenocarcinoma	Lung	03/15/2017 5:04 PM
BRAF G464V BRAF codon(s) 464 any	Melanoma	Skin	03/15/2017 4:54 PM
FOXL2 C134W	Sex Cord Stromal Tumor	Ovary	03/12/2017 6:47 PM
ERBB2 T798I	Adenocarcinoma	Breast	03/08/2017 4:32 PM

- At bottom of home page

Excel of All Interpretations Available for Download

Gene	Tumor Type(s)	Tissue Type(s)	Variant(s)	Tier	Interpretations	Citations
CSF3R	Myeloproliferative Neoplasm, Chronic Neutrophilic Leukemia, Atypical Chronic Myeloid Leukemia	Blood, Bone Marrow	CSF3R T618I, CSF3R any nonsense, CSF3R any frameshift	1	The activating missense membrane-proximal mutation in CSF3R (p.T618I) has been reported to occur in approximately 83% of cases of chronic neutrophilic leukemia, some reports indicate this mutation may be present in cases of atypical chronic myeloid leukemia as well. The CSF3R T618I mutation has been associated with response to JAK2 inhibitors but not dasatinib. A germline activating CSF3R mutation (p. T617N) has been described in autosomal dominant hereditary neutrophilia associated with splenomegaly and increased circulating CD34-positive myeloid progenitors. Nonsense and/or frameshift somatic mutations truncating the cytoplasmic domain of CSF3R have been described in approximately 40% of patients with severe congenital neutropenia and in the context of mutations in other genes may be associated with progression to acute myeloid leukemia. These activating truncating mutations have also been found in patients with chronic neutrophilic leukemia or atypical chronic myeloid leukemia. Some of these cytoplasmic truncating mutations have been associated with responses to dasatinib but not JAK2 inhibitors.	Pardanani A, et al. CSF3R T618I is a highly prevalent and specific mutation in chronic neutrophilic leukemia. <i>N Engl J Med</i> 2013;368(9):1870-3
MPL	Myeloproliferative Neoplasm, Essential Thrombocythemia, Primary Myelofibrosis	Blood, Bone Marrow	MPL codon(s) 515 missense, MPL W515L, MPL W515K	1	Somatic activating mutation in MPL (W515L, W515K) has been reported in approximately 1%-10% of cases of JAK2 Val617Phe-negative myelofibrosis, essential thrombocythemia, a subset of cases of acute megakaryoblastic leukemia and has been associated with sensitivity to JAK inhibitors. The W515 mutations are typically not observed in polycythemia vera or other myeloid disorders (chronic myelomonocytic leukemia, myelodysplastic syndrome). A Ser505Asn activating mutation has also been described in familial essential thrombocythemia.	Pikman Y, et al. MPLW515L is a novel somatic activating mutation in myelofibrosis with myeloid metaplasia. <i>PLoS Med</i> 2006;3(7):e270
JAK1	T Lymphoblastic Leukemia/Lymphoma, Acute Myeloid Leukemia	Blood, Bone Marrow	JAK1 any mutation	1	Activating mutations in JAK1 SH2, pseudokinase and kinase domains have been reported in approximately 5-20% of cases of T-Cell Acute Lymphoblastic Leukemia and less than 1% of Acute Myeloid Leukemia. Some, but not all, of these mutations have been shown to be inhibitable by ATP-competitive JAK inhibitors or Type I interferon.	Flex E, et al. Somatic acquired JAK1 mutations in adult acute lymphoblastic leukemia. <i>J Exp Med</i> 2008;205(4):751-8
NRAS	Acute Myeloid Leukemia, Chronic Myelomonocytic Leukemia, Myelodysplastic Syndrome, B Lymphoblastic Leukemia/Lymphoma, MDS/MPN	Blood, Bone Marrow	NRAS any mutation	1	Mutations in codons 12, 13, and 61 of NRAS have been reported in 7-12% of acute myeloid leukemia and may not be responsive to some MEK inhibitors according to some studies. Mutations in these codons of NRAS have also been reported in 10-30% of chronic myelomonocytic leukemia and 4-10% of myelodysplastic syndromes and may be associated with a worse prognosis according to some but not all studies. In addition, NRAS mutations have been described in approximately 15% of cases of B-ALL and, interestingly, some cases of ALL may show more than one abnormality in this pathway.	Jain N, et al. Phase II study of the oral MEK inhibitor selumetinib in advanced acute myelogenous leukemia: a University of Chicago phase II consortium trial. <i>Clin Cancer Res</i> 2014;20(2):490-8
NOTCH2	Marginal Zone B Cell Lymphoma, Diffuse Large B Cell Lymphoma	Blood, Bone Marrow	NOTCH2 any mutation, NOTCH2 I2304fs, NOTCH2 exon(s) 34 frameshift	1	NOTCH2 gain of function mutations have been reported in approximately 25% of splenic marginal zone lymphomas and are thought to be rare in non-splenic marginal zone lymphomas. These mutations are typically located near the C-terminal PEST domain and lead to protein truncation or, more rarely, are nonsynonymous substitution mutations affected the extracellular heterodimerization domain. NOTCH2 mutations may be associated with a worse prognosis among cases of splenic marginal zone lymphoma. In addition, NOTCH2 PEST domain mutations have been reported in approximately 8% of diffuse large B cell lymphomas and in vitro systems have demonstrated these PEST domain mutant NOTCH2 receptors have increased activity compared to wild type NOTCH2. In addition, copy number gain has been reported in a subset of DLBCL cases with NOTCH2 mutations.	Lee SY, et al. Gain-of-function mutations and copy number increases of Notch2 in diffuse large B-cell lymphoma. <i>Cancer Sci</i> 2009;100(5):920-6
RIT1	Acute Myeloid Leukemia, Myelodysplastic Syndrome, Chronic Myelomonocytic Leukemia	Blood, Bone Marrow	RIT1 any mutation	1	Ras-like-without-CAAX-1 (RIT1) gene is a member of the RAS gene family. Recurrent somatic mutations of RIT1 have been reported in approximately 7% of cases of chronic myelomonocytic leukemia, and less than 5% of cases of myelodysplastic syndrome and less than 5% of acute myeloid leukemia. The mutations typically occur in the Switch II effector domain, and the affected residues are close to codon Q79, which is analogous to amino acid Q61 of NRAS or KRAS where mutations frequently occur in cancer. Moreover, the experimental Q79L mutation in RIT1 has been reported to confer constitutive activation of the protein. RIT1 mutations are typically mutually exclusive of mutations in other RAS family members. In addition, RIT1 maps to the minimal common amplified region (1q21-22) in 1q gains frequently found in other cancers. 1q amplification involving the RIT1 locus has been reported in 4-18% of cases of myelofibrosis as well as less than 5% of chronic myelomonocytic leukemia, less than 5% of myelodysplastic syndromes and less than 5% of acute myeloid leukemia. In rare cases mutations and amplifications of RIT1 may coexist. In general, RIT1 has been reported to increased phosphorylation of AKT and activate proliferation through the mitogen activated protein kinase pathway.	Gómez-Seguí I, et al. Novel recurrent mutations in the RAS-like GTP-binding gene RIT1 in the myeloid malignancies. <i>Leukemia</i> 2013;27(9):1943-6
DNMT3A	Myeloproliferative Neoplasm, Acute Myeloid Leukemia, T Lymphoblastic Leukemia/Lymphoma, Myelodysplastic Syndrome, Chronic Myelomonocytic Leukemia	Blood, Bone Marrow	DNMT3A any mutation	1	DNMT3A is a DNA methyltransferase. Recurrent, somatic, heterozygous mutations in DNMT3A have been reported in approximately 18-25% of cases of acute myeloid leukemia, 8% of cases of myelodysplastic syndrome, up to 15% of myeloproliferative neoplasms and less than 5% of cases of chronic myelomonocytic leukemia. Mutations in DNMT3A have been reported to occur together with mutations in other genes including JAK2, FLT3, IDH1/IDH2, ASXL1, TET2 and NPM1. DNMT3A mutations have been associated with reduced enzymatic activity or altered histone binding, as well as reduced DNA methylation in various genomic regions and altered gene expression in some models. DNMT3A mutations may be associated with adverse prognosis. In addition to myeloid disorders, mutations in DNMT3A have also been reported in approximately 15% of cases of adult, early T cell precursor acute lymphoblastic leukemia.	Larsson CA, et al. The changing mutational landscape of acute myeloid leukemia and myelodysplastic syndrome. <i>Mol Cancer Res</i> 2013;11(8):815-27

- Columns include Genes, Tumor types, Variants, Tier, Interpretations, and Citations
- Each row represents an interpretation

Browse Interpretations

Interpretations

+ Add New Interpretation

Show10entries

Search:

Tumor	Tissue	Variants	Interpretation
Acute Myeloid Leukemia	Blood	NPM1 codon(s) 288 frameshift	Mutations of NPM1 have been reported in approximately 25-35% of cases of acute myeloid leukemia (AML). The mutations of NPM1 are frameshift mutations in the C-terminus of the protein that alter the C-terminal amino acid sequence and are associated with aberrant cytoplasmic localization of the protein. NPM1 mutations in AML are typically associated with a normal karyotype and may co-exist with FLT3 mutations. The presence of NPM1 mutations has been associated with improved complete remission rates, but not necessarily overall survival, in multivariate analysis including assesement of the variety of more recently discovered mutations that may be present in AML. In addition, cytogenetically normal AML with mutated NPM1, without FLT3 ITD or mutated DNMT3A, has been considered to be a favorable genetic risk group according to some studies, although other studies suggest that coexistent mutations in IDH1 or IDH2 may be required for the favorable risk effect of NPM1.
	Bone Marrow	NPM1 codon(s) 290 frameshift	
Acute Myeloid Leukemia	Blood	WT1 any mutation	WT1 mutations have been reported in approximately 7-12% of cytogenetically normal acute myeloid leukemia and most frequently occur in exon 7 or exon 9. WT1 mutations are typically putative loss of funtion mutations (frameshift, missense and nonsense mutations) ; in some cases two mutations in WT1 may occur. In addition, WT1 mutations may coexist with mutations in NPM1, FLT3, among others. In general, WT1 mutations have been associated with a poor prognosis although, the strength of this association is variable and may depend on other concomitant factors, as such, WT1 mutation may not impact outcome as a single molecular marker. In addition, a synonymous WT1 SNP rs16745 located in exon 7 has been described and corresponds to adenine (A) or guanine (G) containing alleles, the frequency of which varies between ethnic groups(G is the minor allele in Western – and the major allele in Asian – populations). The presence of the G allele has been associated with improved prognosis in some studies but not in others .
	Bone Marrow		
Acute Myeloid Leukemia	Blood	CEBPA any mutation	Mutations of the transcription factor CEBPA (CCAAT/enhancer binding protein alpha) have been reported in approximately 13-19% of patients with acute myeloid leukemia (AML) and a normal karyotype. Two types of mutations have been reported: N-terminal changes which result in a truncated dominant negative isoform lacking one of the N terminal domain transactivation domains and C-terminal mutations which are in-frame insertions or deletions affecting the leucine zipper and preventing dimerization and DNA binding. Patients may carry both N- and C-terminal mutations affecting different alleles. There appears to be a beneficial prognostic effect of CEBPA mutation, but may be limited to patients with two different CEBPA mutations, so-called double mutant CEBPA(biallelic mutations) rather than patients with a single CEBPA mutation.
	Bone Marrow		
Acute Myeloid	Blood	GATA1 any mutation	The GATA1 transcription factor is important in the development of erythroid and megakaryocytic lineages. Amino-terminal, small

- Each interpretation is within disease context and may be specific to a variant(s).
- Click on interpretation to see interpretation page w/citations and more information.

Interpretation Page

NPM1

Search Knowledgebase...

Interpretations

By Variant(s)

[NPM1 any mutation](#)

[NPM1 codon\(s\) 288 frameshift](#)

[NPM1 codon\(s\) 290 frameshift](#)

By Tumor

- Acute Myeloid Leukemia
 - [NPM1 codon\(s\) 288 frameshift, NPM1 codon\(s\) 290 frameshift](#)

Interpretation 28

Information View History Suggested Revisions

Variant(s)	NPM1 codon(s) 288 frameshift NPM1 codon(s) 290 frameshift
Tumor(s)	Acute Myeloid Leukemia
Tissue(s)	Blood Bone Marrow
Tier	1

Interpretation

Mutations of NPM1 have been reported in approximately 25-35% of cases of acute myeloid leukemia (AML). The mutations of NPM1 are frameshift mutations in the C-terminus of the protein that alter the C-terminal amino acid sequence and are associated with aberrant cytoplasmic localization of the protein. NPM1 mutations in AML are typically associated with a normal karyotype and may co-exist with FLT3 mutations. The presence of NPM1 mutations has been associated with improved complete remission rates, but not necessarily overall survival, in multivariate analysis including assessment of the variety of more recently discovered mutations that may be present in AML. In addition, cytogenetically normal AML with mutated NPM1, without FLT3 ITD or mutated DNMT3A, has been considered to be a favorable genetic risk group according to some studies, although other studies suggest that coexistent mutations in IDH1 or IDH2 may be required for the favorable risk effect of NPM1.

Citations

Falini B, et al. Cytoplasmic nucleophosmin in acute myelogenous leukemia with a normal karyotype. *N Engl J Med* 2005;352(3):254-66

Suzuki T, et al. Clinical characteristics and prognostic implications of NPM1 mutations in acute myeloid leukemia. *Blood* 2005;106(8):2854-61

Kihara R, et al. Comprehensive analysis of genetic alterations and their prognostic impacts in adult acute myeloid leukemia patients. *Leukemia* 2014;28(8):1586-95

Patel JP, et al. Prognostic relevance of integrated genetic profiling in acute myeloid leukemia. *N Engl J Med* 2012;366(12):1079-89

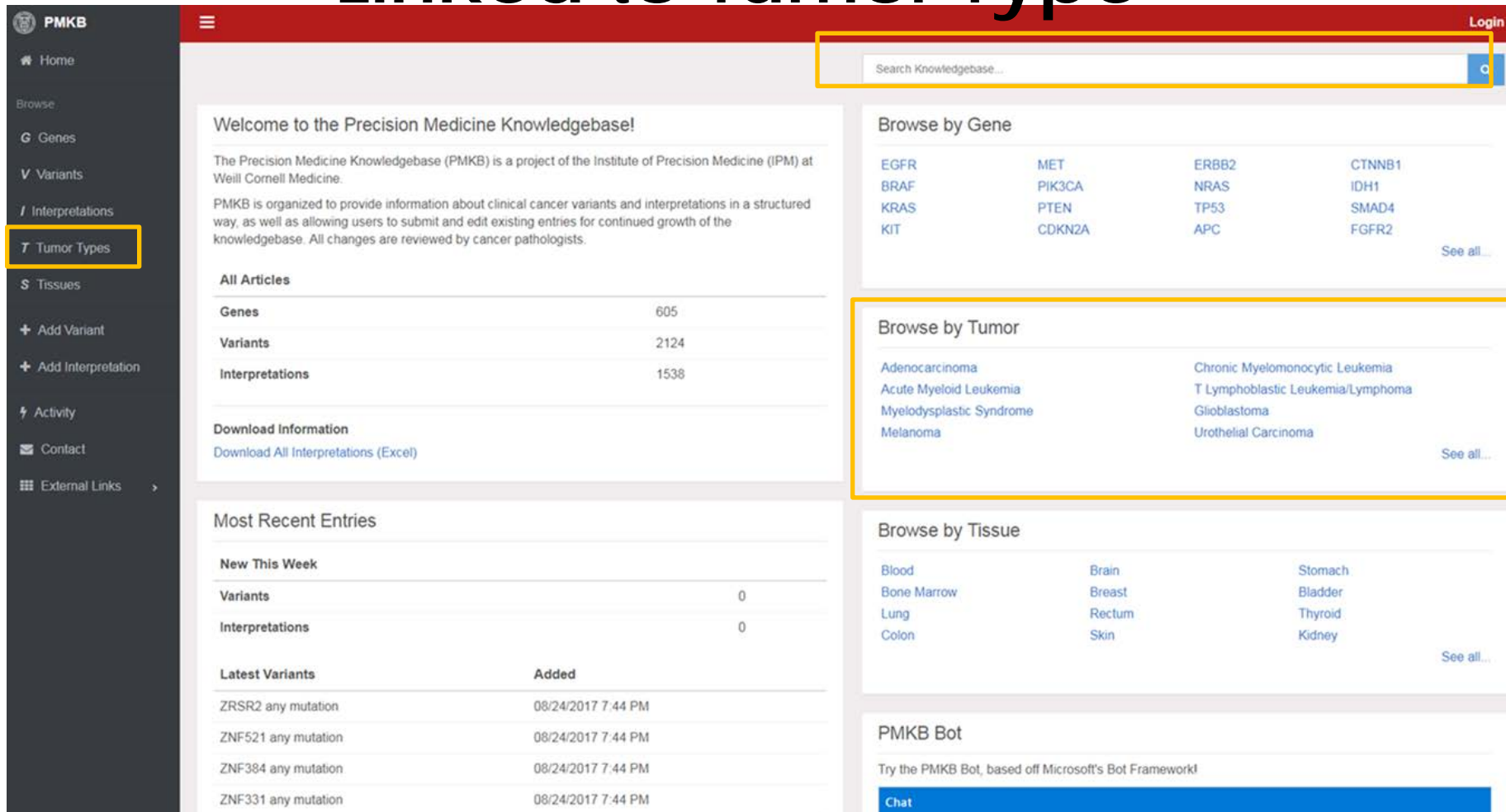
[Edit Interpretation](#)

Links to PubMed

Tier Definitions

- **Tier 1** - Clinical utility has been demonstrated - Actionable / Clinically Relevant variants. Variants in genes with approved therapeutic implications in specified tumors.
- **Tier 2** - Clinical utility/actionability has diagnostic, prognostic or therapeutic implications. Variants with potential diagnostic/classification, prognostic implications. Variants with approved therapeutic implications in a different tumor type. Novel variants in genes that have approved therapeutic implications. Variants associated with Clinical trials.
- **Tier 3** - Variants of Unknown Significance.

Search for Variants Linked to Tumor Type



PMKB

Home

Browse

Genes

Variants

Interpretations

Tumor Types

Tissues

+ Add Variant

+ Add Interpretation

Activity

Contact

External Links

Search Knowledgebase...

Welcome to the Precision Medicine Knowledgebase!

The Precision Medicine Knowledgebase (PMKB) is a project of the Institute of Precision Medicine (IPM) at Weill Cornell Medicine.

PMKB is organized to provide information about clinical cancer variants and interpretations in a structured way, as well as allowing users to submit and edit existing entries for continued growth of the knowledgebase. All changes are reviewed by cancer pathologists.

All Articles

Genes	605
Variants	2124
Interpretations	1538

Download Information

[Download All Interpretations \(Excel\)](#)

Most Recent Entries

New This Week

Variants	0
Interpretations	0

Latest Variants

Added	
ZRSR2 any mutation	08/24/2017 7:44 PM
ZNF521 any mutation	08/24/2017 7:44 PM
ZNF384 any mutation	08/24/2017 7:44 PM
ZNF331 any mutation	08/24/2017 7:44 PM

Browse by Gene

EGFR	MET	ERBB2	CTNNB1
BRAF	PIK3CA	NRAS	IDH1
KRAS	PTEN	TP53	SMAD4
KIT	CDKN2A	APC	FGFR2

[See all...](#)

Browse by Tumor

Adenocarcinoma	Chronic Myelomonocytic Leukemia
Acute Myeloid Leukemia	T Lymphoblastic Leukemia/Lymphoma
Myelodysplastic Syndrome	Glioblastoma
Melanoma	Urothelial Carcinoma

[See all...](#)

Browse by Tissue

Blood	Brain	Stomach
Bone Marrow	Breast	Bladder
Lung	Rectum	Thyroid
Colon	Skin	Kidney

[See all...](#)

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Browse Tumor Types

Tumors

Search Knowledgebase...

Browse

All A B C D E F G H I J K L M N O P Q R S T U V W X Y Z

Search:

Name	Interpretations
Acinar Cell Carcinoma	0 Interpretation(s)
Acinic Cell Carcinoma	0 Interpretation(s)
Acute Myeloid Leukemia	50 Interpretation(s)
Adenocarcinoma	148 Interpretation(s)
Adenoid Cystic Carcinoma	0 Interpretation(s)
Adenosarcoma	1 Interpretation(s)
Ameloblastic Tumor	0 Interpretation(s)
Anaplastic Large Cell Lymphoma	0 Interpretation(s)
Angioimmunoblastic T-Cell Lymphoma	1 Interpretation(s)
Angiomatoid Fibrous Histiocytoma	0 Interpretation(s)
Angiomatosis	0 Interpretation(s)
Angiomyolipoma	0 Interpretation(s)
Angiosarcoma	0 Interpretation(s)
Astrocytoma, Anaplastic	3 Interpretation(s)
Astrocytoma, Pilocytic	0 Interpretation(s)
Atypical Chronic Myeloid Leukemia	3 Interpretation(s)

- Click on tumor type to see all associated interpretations.
- 143 tumor types listed – not all have interpretations.

Tumor-Specific Page of Interpretations

Chronic Myelomonocytic Leukemia

Search Knowledgebase...

Interpretations

Show 10 entries

Search:

Tumor

Tissue

Variants

Interpretation

Acute Myeloid Leukemia

Chronic Myeloid Leukemia

Myelodysplastic Syndrome

Chronic Myelomonocytic Leukemia

Blood

Bone Marrow

GATA2 any mutation

GATA2 is a member of the GATA transcription factors which play a role in hematopoiesis. GATA2 mutations in the zinc finger domains have been described in accelerated phase and blasts phase chronic myelogenous leukemia as well as 5-10% of acute myeloid leukemia and familial syndromes with a predisposition to acute myeloid leukemia and myelodysplastic syndromes. Mutations in ASXL1 have been reported in a subset of patients with mutations in GATA2 and are believed to represent an important step in myeloid transformation, particularly to chronic myelomonocytic leukemia in young female patients. Other reports suggest that in cases of AML, GATA2 mutations have a higher prevalence among cases with biallelic CEBPA mutations and were not observed in cases with monoallelic CEBPA mutations. In general, the GATA2 mutations are believed to result in impairment of granulocyte differentiation. GATA2 mutations have not been reported in juvenile myelomonocytic leukemia or acute lymphoblastic leukemia. In AML, GATA2 mutations may be associated with a better prognosis according to some studies.

Acute Myeloid Leukemia

Chronic Myelomonocytic Leukemia

Myelodysplastic Syndrome

B Lymphoblastic Leukemia/Lymphoma

MDS/MPN

Blood

Bone Marrow

NRAS any mutation

Mutations in codons 12, 13, and 61 of NRAS have been reported in 7-12% of acute myeloid leukemia and may not be responsive to some MEK inhibitors according to some studies. Mutations in these codons of NRAS have also been reported in 10-30% of chronic myelomonocytic leukemia and 4-10% of myelodysplastic syndromes and may be associated with a worse prognosis according to some but not all studies. In addition, NRAS mutations have been described in approximately 15% of cases of B-ALL and, interestingly, some cases of ALL may show more than one abnormality in this pathway.

Acute Myeloid Leukemia

Chronic Myelomonocytic Leukemia

Myelodysplastic Syndrome

B Lymphoblastic Leukemia/Lymphoma

T Lymphoblastic Leukemia/Lymphoma

Blood


Bone Marrow

KRAS any mutation

KRAS codon(s) 12, 13, 61, 117, 146 any

KRAS is a well known proto-oncogene that belongs to the small GTPase family. Pathogenic mutations in KRAS typically occur in codons 12-13 of exon 2 and codon 61 of exon 3; however, other, non-canonical, pathogenic mutations in KRAS have also been reported in acute myeloid leukemia. KRAS mutations have been described in approximately 3-15% of acute myeloid leukemia, 8-20% of chronic myelomonocytic leukemia, 4% of patients with myelodysplastic syndrome, 12% of B cell acute lymphoblastic leukemia (often associated with MLL rearrangement) and 1-2% of T cell acute lymphoblastic leukemia. Investigation into the targetability of this pathway in leukemia has been attempted in some disease models.

Search for Tissue type


PMKB

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Q

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Lung	Rectum	Thyroid
Colon	Skin	Kidney

[See all...](#)

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Chat

Browse Tissue Types

Tissues

Search Knowledgebase...

Browse

All A B C D E F G H I J K L M N O P Q R S T U V W X Y Z

Search:

Name	Interpretations
Adrenal Gland	0 Interpretation(s)
Ampulla (Pancreaticobiliary Duct)	3 Interpretation(s)
Anus	3 Interpretation(s)
Appendix	3 Interpretation(s)
Bladder	21 Interpretation(s)
Blood	104 Interpretation(s)
Blood Vessel	0 Interpretation(s)
Bone	2 Interpretation(s)
Bone Marrow	102 Interpretation(s)
Brain	28 Interpretation(s)
Brain, Infratentorial	12 Interpretation(s)
Brain, Supratentorial	13 Interpretation(s)
Breast	30 Interpretation(s)

- 68 tissue types listed – not all have interpretations.

PMKB Bot

- Type in a gene name, disease, tissue, or variant
- PMKB Bot will output interpretations that fit your criteria.
- Click anywhere in the interpretation or the image above the interpretation to see the gene page housing that interpretation.

PMKB Bot

Try the PMKB Bot, based off Microsoft's Bot Framework!


Chat

PMKB at 2:44:02 PM


Find KIT

You


Found 18 interpretations for kit





Interpretation for KIT
 Tumors(Acute Myeloid Leukemia,Mast Cell Neoplasm) Tissues(Blood,Bone Marrow)
 Variants(KIT any mutation,KIT D816V,KIT exon(s))



Interpretation for KIT
 Tumors(Gastrointestinal Stromal Tumor,Other Tumor Type) Tissues(Small Intestine,Stomach)
 Variants(KIT M541L)



Inter
 Tumo
 Tissue
 E554k


Type your message...


Scenario #1

- You are a laboratory professional putting together a Pan Cancer gene list.
 - Browse Genes and add all
 - OR add only genes with interpretations

Browse Genes and sort genes by the number of associated interpretations.

Genes

Search Knowledgebase...

Browse

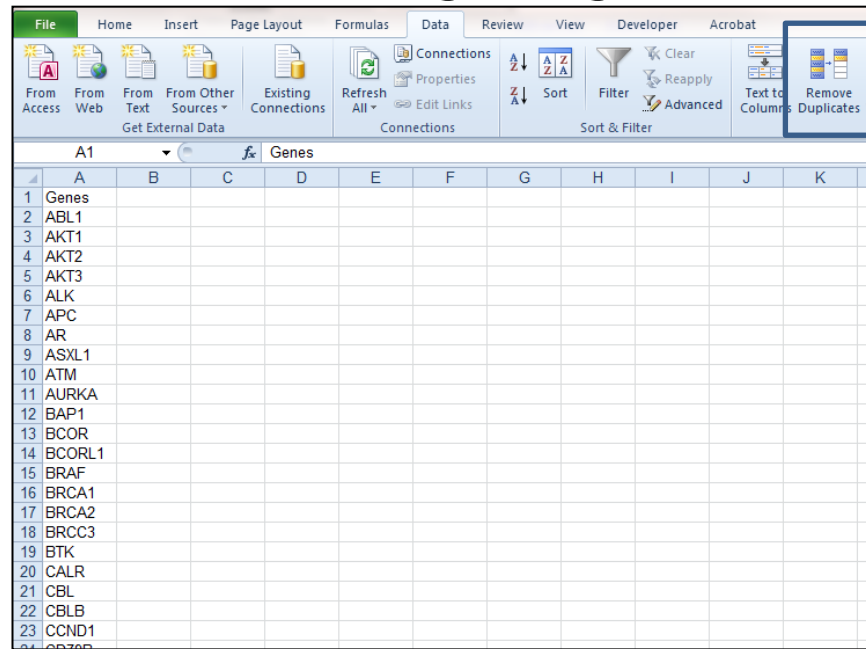
All
A
B
C
D
E
F
G
H
I
J
K
L
M
N
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P
Q
R
S
T
U
V
W
X
Y
Z

Search:

HUGO Symbol	<div> <div></div> <div>↑↓</div> </div> Variants	<div> <div></div> <div>↑↓</div> </div> Interpretations	<div> <div></div> <div>↑↓</div> </div>
APC	16 Variant(s)	9 Interpretation(s)	
CTNNB1	9 Variant(s)	9 Interpretation(s)	
NRAS	18 Variant(s)	9 Interpretation(s)	
IDH1	6 Variant(s)	8 Interpretation(s)	
SMAD4	3 Variant(s)	8 Interpretation(s)	
FGFR1	2 Variant(s)	6 Interpretation(s)	
FGFR2	5 Variant(s)	6 Interpretation(s)	
HRAS	4 Variant(s)	6 Interpretation(s)	
ABL1	16 Variant(s)	5 Interpretation(s)	
FGFR3	5 Variant(s)	5 Interpretation(s)	
ALK	7 Variant(s)	4 Interpretation(s)	
ATM	4 Variant(s)	4 Interpretation(s)	

Another way to compile the same list of genes with interpretations is to download the Excel file of all interpretations, sort by gene name, and expect duplicates for genes with >1 interpretation. I like to copy the gene column over to another worksheet/tab.

- One you have the gene list in Excel (or similar), go to Data/Remove Duplicates to have a full list of candidate genes.
- I like to alphabetize before integrating with other lists/resources.



Scenario #2

- You are putting together a list for a potential AML NGS panel. Using PMKB, what genes might you consider including?
 - Search for AML Tumor Type (see slides 14-16)
 - Filter spreadsheet for rows/interpretations related to AML
 - Copy Information over to new unprotected worksheet
 - Filter Tumor Type(s) column by “Contains” criteria for “Acute Myeloid Leukemia”

Scenario #3

- Your laboratory is interpreting a small NGS panel for a patient with lung adenocarcinoma. How can PMKB aid in interpretation?
- Abnormal genes
 - EGFR L858R
 - RET V804M
- Normal genes
 - ALK
 - ERBB2
 - KRAS
 - PIK3CA
 - BRAF

PMKB Relevant Interpretations

- EGFR: **positive** for L858R mutation
<https://pmkb.weill.cornell.edu/variants/115>
- ERBB2: **pertinent negative!**
<https://pmkb.weill.cornell.edu/genes/95/variants/366>
- KRAS: **pertinent negative!**
<https://pmkb.weill.cornell.edu/genes/50/variants/368>
- PIK3CA: **pertinent negative!**
<https://pmkb.weill.cornell.edu/genes/19/variants/367>

Future Features: Coming Soon!

- Shared API
- Opportunities for Crowd-sourcing:
 - Addition of variants
 - Addition of interpretation

Contacts

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