OncoKB, MSK's Precision Oncology Knowledge Base

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Comprehensive evidence-based information about cancer variants

www.oncokb.org — 03/01/2022

Welcome to OncoKB

MSK's Precision Oncology Knowledge Base

An FDA-Recognized Human Genetic Variant Database*

687	5707	132	110
Genes	Alterations	Cancer Types	Drugs

Therapeutic Levels | Diagnostic Levels | Prognostic Levels | FDA Levels

Level 1	Level 2	Level 3	Level 4	Level R1/R2
FDA-approved drugs	Standard care	Clinical evidence	Biological evidence	Resistance
43 Genes	20 Genes	26 Genes	25 Genes	11 Genes

An FDA-recognized* human genetic variant database

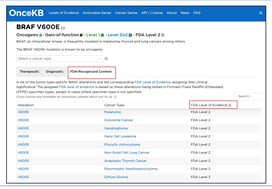
FDA recognizes Memorial Sloan-Kettering database of molecular tumor marker information

"On October 7, 2021, the Food and Drug Administration granted recognition to a partial listing of the Memorial Sloan Kettering Cancer Center's Oncology Knowledge Base (OncoKB) as the first tumor mutation database to be included in the Public Human Genetic Variant Database."

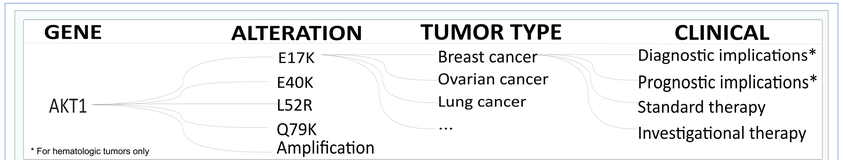
* FDA recognition of OncoKB is for the content that is clearly marked

Scope of OncoKB Recognition

- *Variants curated in OncoKB with an FDA level of evidence*
- *OncoKB's processes for variant evaluation and assertion, data integrity and security, and transparency of evidence*
- *Policies of oversight and governance*
- *Processes for ensuring conflicts of interest are minimized and transparent*

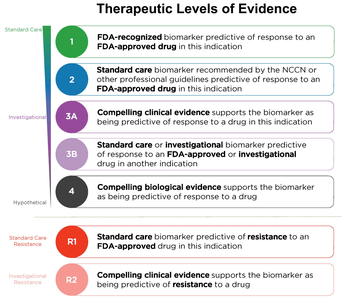


Curation on multiple levels: Gene, Alteration, Tumor Type, MSI/TMB



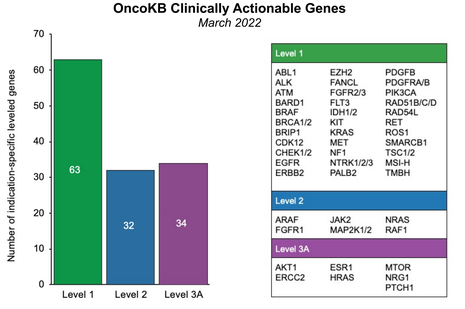
Levels of evidence system for drug sensitivity and resistance

Therapeutic Levels of Evidence



OncoKB Clinically Actionable Genes

March 2022



Level 1

ABL1, ALK, ATM, BARD1, BRAF, BRCA1/2, BRIP1, CDK12, CHEK1/2, EGFR, ERBB2, EZH2, FANCL, FGFR2/3, FLT3, IDH1/2, KIT, KRAS, MET, NF1, NTRK1/2/3, PALB2, PDGFB, PDGFRA/B, PIK3CA, RAD51B/C/D, RAD54L, RET, ROS1, SMARCB1, TSC1/2, MSI-H, TMBH

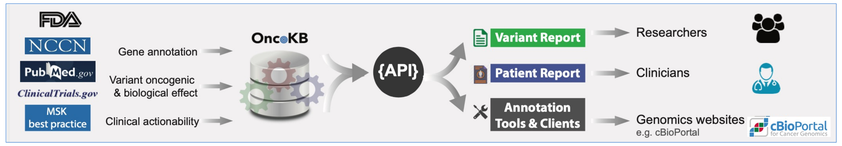
Level 2

ARAF, FGFR1, JAK2, MAP2K1/2, NRAS, RAF1

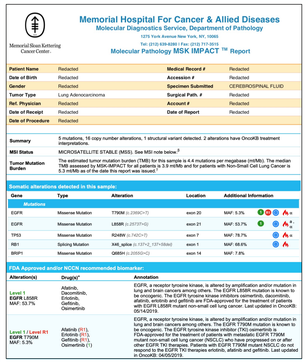
Level 3A

AKT1, ERCC2, ESR1, HRAS, MTOR, NRG1, PTCH1

OncoKB data is available through a high-performance web API



Clinical insight-driven report generation



Memorial Hospital For Cancer & Allied Diseases
Molecular Diagnostics Service, Department of Pathology
1275 York Avenue New York, NY, 10065
Tel: (212) 639-8250 / Fax: (212) 717-3010
Molecular Pathology MSK IMPACT ™ Report

Patient Name	Redacted	Medical Record #	Redacted
Date of Birth	Redacted	Accession #	Redacted
Gender	Redacted	Specimen Submitted	CEREBROSPINAL FLUID
Tumor Type	Lung Adenocarcinoma	Surgical Path. #	Redacted
Ref. Physician	Redacted	Account #	Redacted
Date of Receipt	Redacted	Date of Report	Redacted
Date of Procedure	Redacted		

Summary	5 mutations, 16 copy number alterations, 1 structural variant detected. 2 alterations have OncoKB treatment interpretations.
MSI Status	MICROSATELLITE STABLE (MSS). See MSI note below.‡
Tumor Mutation Burden	The estimated tumor mutation burden (TMB) for this sample is 4.4 mutations per megabase (mt/Mb). The median TMB assessed by MSK-IMPACT for all patients is 3.9 mt/Mb and for patients with Non-Small Cell Lung Cancer is 5.3 mt/Mb as of the date this report was issued.†

Somatic alterations detected in this sample:

Gene	Type	Alteration	Location	Additional Information
Mutations				
EGFR	Missense Mutation	T790M (c.2369C>T)	exon 20	MAF: 5.3%
EGFR	Missense Mutation	L858R (c.2573T>G)	exon 21	MAF: 53.7%
TP53	Missense Mutation	R248W (c.742C>T)	exon 7	MAF: 78.7%
RB1	Splicing Mutation	IVS7_splice (c.1071+2_1071+3delAG)	exon 1	MAF: 88.6%
BRIP1	Missense Mutation	Q855H (c.2564A>C)	exon 14	MAF: 7.8%

FDA Approved and/or NCCN recommended biomarker:

Alteration(s)	Drug(s)*	Annotation
Level 1 EGFR L858R MAF: 53.7%	Afatinib, Dacomitinib, Erlotinib, Gefitinib, Osimertinib	EGFR, a receptor tyrosine kinase, is altered by amplification and/or mutation in lung and brain cancers among others. The EGFR L858R mutation is known to be oncogenic. The EGFR tyrosine kinase inhibitors osimertinib, dacomitinib, afatinib, erlotinib and gefitinib are FDA-approved for the treatment of patients with EGFR L858R mutant non-small cell lung cancer. Last updated in OncoKB: 05/14/2019.
Level 1 / Level R1 EGFR T790M MAF: 5.3%	Afatinib (R1), Erlotinib (R1), Gefitinib (R1), Osimertinib (1)	EGFR, a receptor tyrosine kinase, is altered by amplification and/or mutation in lung and brain cancers among others. The EGFR T790M mutation is known to be oncogenic. The EGFR tyrosine kinase inhibitor (TKI) osimertinib is FDA-approved for the treatment of patients with metastatic EGFR T790M mutant non-small cell lung cancer (NSCLC) who have progressed on or after other EGFR TKI therapies. Patients with EGFR T790M mutant NSCLC do not respond to the EGFR TKI therapies erlotinib, afatinib and gefitinib. Last updated in OncoKB: 04/05/2019.

- >25,000 MSK-IMPACT clinical sequencing reports (solid tumors and heme) annotated over the last two years.
- Reports provide information about the known oncogenicity of all variants (mutations, copy-number alterations and gene fusions), as well as their associated tumor type specific clinical implications.

Variant interpretation in cBioPortal

Samples	Gene	Protein Change	Annotation ▼
❶ ❷	EGFR	*L858R*	
❷	MAP2K1	*K57N*	
❶ ❷	RBM10	*T293Nfs*10*	
❶ ❷	KMT2A	*I3288V*	

EGFR L858R in lung adenocarcinoma

Oncogenic | **Gain-of-function**

EGFR, a receptor tyrosine kinase, is altered by amplification and/or mutation in lung and brain cancers among others.

The EGFR L858R mutation is known to be oncogenic.

The EGFR tyrosine kinase inhibitors osimertinib, dacomitinib, afatinib, erlotinib and gefitinib are FDA-approved for the treatment of patients with EGFR L858R mutant non-small cell lung cancer.

Biological Effect | Therapeutic Implications

FDA-recognized biomarker predictive of response to an FDA-approved drug in this indication

Level	Alteration(s)	Drug(s)	Level-associated cancer type(s)
1	Exon 19 deletion, L858R	Erlotinib	Non-Small Cell Lung Cancer
1	Exon 19 deletion, L858R	Erlotinib + Ramucirumab	Non-Small Cell Lung Cancer
1	Exon 19 deletion, L858R	Afatinib	Non-Small Cell Lung Cancer
1	Exon 19 deletion, L858R	Gefitinib	Non-Small Cell Lung Cancer
1	Exon 19 deletion, L858R	Osimertinib	Non-Small Cell Lung Cancer

EGFR L858R in lung adenocarcinoma

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Biological Effect | Therapeutic Implications

EGF receptor gene mutations are common in lung cancers from "never smokers" and are associated with sensitivity of tumors to gefitinib and erlotinib.
Pao W et al. Proc Natl Acad Sci U S A. 2004 — PMID: 15329413

Activating mutations in the epidermal growth factor receptor underlying responsiveness of non-small-cell lung cancer to gefitinib.
Lynch TJ et al. N Engl J Med. 2004 — PMID: 15118073

EGFR mutations in lung cancer: correlation with clinical response to gefitinib therapy.
Paez JG et al. Science. 2004 — PMID: 15118125

Structure-based classification predicts drug response in EGFR-mutant NSCLC.
Robichaux JP et al. Nature. 2021 — PMID: 34526717

The information above is intended for research purposes only and should not be used as a substitute for professional diagnosis and treatment.

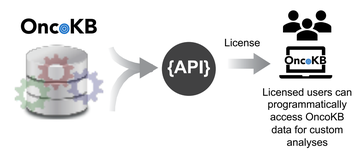
OncoKB — Feedback

Licensed users have access to the OncoKB API

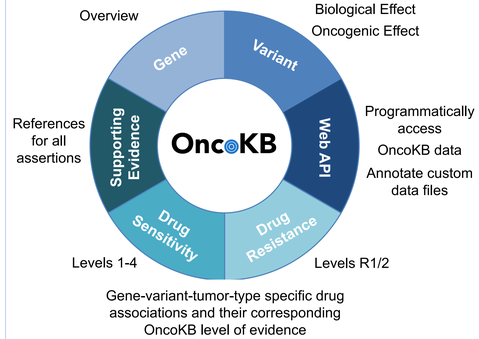
OncoKB License Types

Research use in an academic setting	Research use in a commercial setting*
Use in a commercial product*	Use for patient services or reports in hospital care/clinical setting*

*Fee required



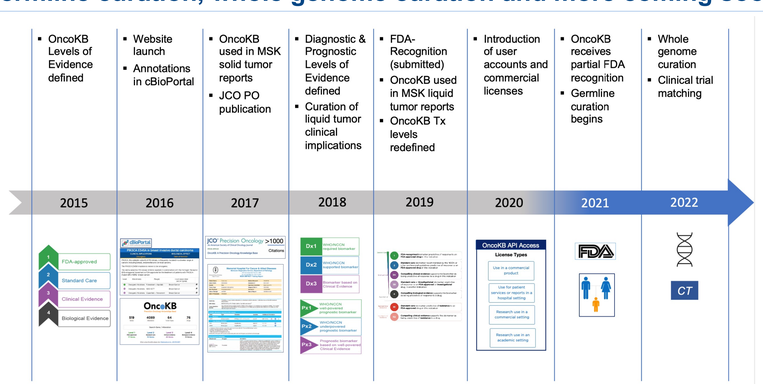
Current Data Includes



OncoKB Features

- *Powered by the clinical expertise of Memorial Sloan Kettering physicians and physician-scientists*
- *Insights from MSK's FDA-approved targeted tumor sequencing test (MSK-IMPACT) provides a rich dataset for variant discovery*
- *OncoKB Levels of Evidence align 1:1 with the Levels of Evidence developed by AMP/ASCO/CAP*
- *OncoKB annotations can be incorporated into a local instance of cBioPortal for Cancer Genomics providing a custom and dynamic web-based platform for exploring patient sequencing data*
- *High-performance API for variant annotation*
- *Support from OncoKB scientists*

Germline curation, whole genome curation and more coming soon



Resources

- OncoKB website: www.oncokb.org
- Licensing information: www.oncokb.org/APIaccess
- Email us: contact@OncoKB.org
- cBioPortal for Cancer Genomics: www.cbioportal.org
- Oncotree: www.oncotree.mskcc.org/#/home
- Follow us: @OncoKB