

# INTRODUCTION TO Inherited Cancer Genetic Counselling, cBioportal, COSMIC and Somatic Clinvar

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Giảng viên: TS. Lưu Phúc Lợi  
Email: [Luu.p.loi@googlemail.com](mailto:Luu.p.loi@googlemail.com)  
Zalo: 0901802182

# Content of Lecture

1. Cancer Genetic Counselling — Current Practice and Future Challenges

2. cBioportal

- <https://www.personalizedoncogenomics.org/cbioportal/tutorial.jsp>
- [https://www.jax.org/-/media/jaxweb/files/education-and-learning/tutorials/cbioportal-written-tutorials\\_clickable.pdf](https://www.jax.org/-/media/jaxweb/files/education-and-learning/tutorials/cbioportal-written-tutorials_clickable.pdf)

3. COSMIC

- <https://cancer.sanger.ac.uk/cosmic/help/tutorials>

4. Somatic Clinvar

- <https://www.ncbi.nlm.nih.gov/clinvar>



# Cancer Genetic Counseling—Current Practice and Future Challenges

Jaclyn Schienda and Jill Stopfer

Division of Cancer Genetics and Prevention, Dana Farber Cancer Institute, Boston, Massachusetts 02215, USA

*Correspondence:* JillE\_Stopfer@dfci.harvard.edu

Cancer genetic counseling practice is rapidly evolving, with services being provided in increasingly novel ways. Pretest counseling for cancer patients may be abbreviated from traditional models to cover the elements of informed consent in the broadest of strokes. Genetic testing may be ordered by a cancer genetics professional, oncology provider, or primary care provider. Increasingly, direct-to-consumer testing options are available and utilized by consumers anxious to take control of their genetic health. Finally, genetic information is being used to inform oncology care, from surgical decision-making to selection of chemotherapeutic agent. This review provides an overview of the current and evolving practice of cancer genetic counseling as well as opportunities and challenges for a wide variety of indications in both the adult and pediatric setting.

# Cancer Genetic Counselling — Current Practice and Future Challenges

1. CANCER GENETIC COUNSELING — WHERE WE HAVE BEEN AND WHERE WE ARE GOING
2. WHO IS A CANDIDATE FOR CANCER GENETIC COUNSELING AND TESTING?
3. THE PROCESS OF CANCER GENETIC COUNSELING
4. LABORATORY, TEST SELECTION, AND INTERPRETATION ISSUES
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# CANCER GENETIC COUNSELING — WHERE WE HAVE BEEN AND WHERE WE ARE GOING

## CANCER GENETIC COUNSELING—WHERE WE HAVE BEEN AND WHERE WE ARE GOING

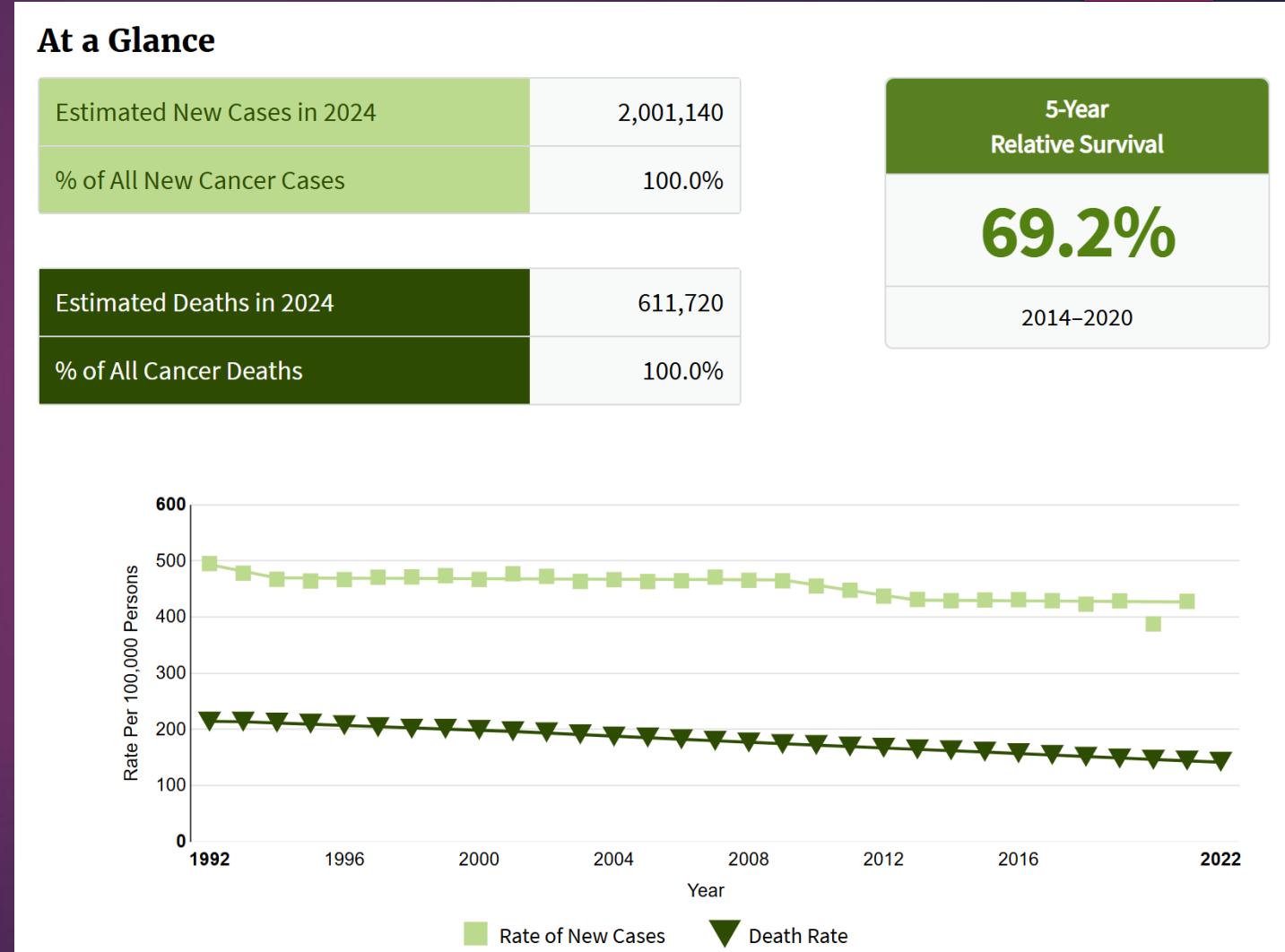
Historically, individuals with known or suspected risk for an inherited mutation in a cancer predisposition gene were likely to be referred for genetic counseling if their care was received at an academic medical center or Comprehensive Cancer Center. As part of a genetic counseling session lasting ~1 h, a three-generation pedigree would be constructed and the prior probability that the patient had inherited a germline mutation calculated. Genetic testing was offered for those having an ~5%–10% chance of having a mutation detected and ordered from a handful of specialty commercial or academic labs. Prior to the 2013 Supreme Court

ruling overturning gene patenting, many genetic tests cost \$3000 or more, and only the rare patient could afford the cost without meeting a strict set of insurance-based criteria. Genetic counseling and testing, including disclosure of results, was typically provided in person as part of a multivisit, multidisciplinary encounter (Hoskins et al. 1995; Resta et al. 2006).

The practice of genetic counseling has been undergoing rapid change in recent years, as increasing numbers of patients require access to genetic testing for treatment decisions, and broader categories of individuals are now considered appropriate candidates for genetic services. This work reviews traditional models for the practice of cancer genetic counseling, and preliminary evidence supporting the inclusion of novel interventions.

# WHO IS A CANDIDATE FOR CANCER GENETIC COUNSELING AND TESTING?

- According to SEER estimates from 2014 to 2016, ~39.3% of men and women will develop cancer in their lifetime, and most will be over the age of 55 years (<https://SEER.cancer.gov/statfacts/html/all.html>).
- Germline pathogenic variants (PVs) in highly penetrant genes play a major role in at least 5%–10% of all cancers and in more than 50 hereditary cancer syndromes.



# WHO IS A CANDIDATE FOR CANCER GENETIC COUNSELING AND TESTING?

**Table 1.** Personal and family history “red flags” suggestive of an underlying hereditary cancer predisposition

History	Examples
<b>Personal</b>	
Early age at diagnosis	Colon cancer at 30
Rare tumor	Male breast cancer, rhabdoid tumor
Tumor associated with known syndrome	Pheochromocytoma, retinoblastoma
Multifocal or bilateral tumors	Bilateral Wilms tumor
Multiple primary tumors	Breast cancer and ovarian cancer
Lack of known environmental factor	Lung cancer in nonsmoker
Excessive toxicity to treatment	Severe toxicity to chemotherapy in Fanconi anemia
Other developmental and physical differences	Large head size, asymmetry, congenital heart defects, etc. (for comprehensive examples, see Kesserwan et al. 2016; Coury et al. 2018)
Pathogenic variant detected in tumor/ abnormal tumor testing	ALK mutation in neuroblastoma, MSH6 absent (IHC) colon cancer
<b>Family</b>	
Multiple generations affected with tumors or cancers (on same side of family)	
Multiple first-degree relatives affected (parent, child, sibling)	
Pattern of cancers suggestive of known syndrome	Osteosarcoma, brain tumor, adrenocortical carcinoma
Known mutation in family member	SDHB mutation in father
Consanguinity	Parents of affected child are first cousins
Ethnicity	Ashkenazi Jewish, Icelandic founder mutations in BRCA1/2

# WHO IS A CANDIDATE FOR CANCER GENETIC COUNSELING AND TESTING?

**Table 2.** Select tumors that warrant genetics evaluation

Tumor	Highly associated syndromes	Gene	Commonly associated tumor/cancer risks
Adrenocortical carcinoma	Li–Fraumeni syndrome	<i>TP53</i>	Breast, sarcoma, brain tumor, adrenocortical carcinoma, many cancer types
Anaplastic rhabdomyosarcoma	Li–Fraumeni syndrome	<i>TP53</i>	See above
Cerebellar hemangioblastoma	von Hippel–Lindau syndrome	<i>VHL</i>	Endolymphatic sac tumor, pancreatic islet cell carcinoma, hemangioblastoma of CNS or retina, renal cell carcinoma, cysts in the liver, kidney, pancreas, or spleen
Choroid plexus carcinoma	Li–Fraumeni syndrome	<i>TP53</i>	See above
Diffuse gastric cancer	Hereditary diffuse gastric cancer	<i>CDH1</i>	Lobular breast cancer, diffuse gastric cancer
Hypodiploid ALL	Li–Fraumeni syndrome	<i>TP53</i>	See above
Medullary thyroid cancer	MEN2	<i>RET</i>	Medullary thyroid cancer, pheochromocytoma, hyperparathyroidism
Medulloblastoma	Familial adenomatous polyposis	<i>APC</i>	Colon, colon polyps, ampullary, small bowel, small bowel polyps, thyroid, desmoid
	Gorlin syndrome	<i>SUFU, PTCH1</i>	Basal cell carcinoma, ovarian fibroma, jaw keratocyst
	Hereditary breast/ovarian cancer	<i>BRCA2, PALB2</i>	Breast, ovarian, pancreatic, prostate, melanoma
	Li–Fraumeni syndrome	<i>TP53</i>	See above

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**Table 2.** Select tumors that warrant genetics evaluation

Tumor	Highly associated syndromes	Gene	Commonly associated tumor/cancer risks
Ovarian cancer	Hereditary breast/ovarian cancer	<i>BRCA1, BRCA2</i>	Breast, ovarian, pancreatic, prostate
	Lynch syndrome	<i>MLH1, MSH2, MSH6, PMS2, EPCAM</i>	Colon, endometrial, colon polyps, small bowel, urinary tract, ovarian
	Epithelial ovarian cancer	<i>BRIP1, RAD51C, RAD51D</i>	Possibly breast
Ovarian Sertoli–Leydig cell tumor	<i>DICER1</i> syndrome	<i>DICER1</i>	Pleuropulmonary blastoma, Sertoli–Leydig cell tumor of the ovary, cystic nephroma, thyroid nodules/cancer
Pancreatic cancer	Familial atypical multiple mole melanoma syndrome	<i>CDKN2A</i>	Melanoma, pancreatic, dysplastic nevi
	Hereditary breast/ovarian cancer	<i>BRCA1, BRCA2, PALB2</i>	Breast, ovarian, pancreatic, prostate, melanoma
	Lynch syndrome	<i>MLH1, MSH2, MSH6, PMS2, EPCAM</i>	Colon, endometrial, colon polyps, small bowel, urinary tract, ovarian

# WHO IS A CANDIDATE FOR CANCER GENETIC COUNSELING AND TESTING?

**Table 2.** *Continued*

Tumor	Highly associated syndromes	Gene	Commonly associated tumor/cancer risks
	Peutz–Jeghers syndrome	<i>STK11</i>	Breast, gastrointestinal hamartomatous polyps, mucocutaneous pigmentation, colon, lung, small bowel, stomach, cervix, ovarian, testicular
Paraganglioma/ pheochromocytoma	Hereditary paraganglioma/ pheochromocytoma syndrome  MEN2  von Hippel–Lindau syndrome	<i>SDHA</i> , <i>SDHB</i> , <i>SDHC</i> , <i>SDHD</i> , <i>SDHAF2</i> , <i>MAX</i> , <i>TMEM127</i>  <i>RET</i>  <i>VHL</i>	Paraganglioma, pheochromocytoma, GIST, renal cell cancer, papillary thyroid cancer  Endolymphatic sac tumor, pancreatic islet cell carcinoma, hemangioblastoma of CNS or retina, renal cell carcinoma, cysts in the liver, kidney, pancreas, or spleen
Pleuropulmonary blastoma	<i>DICER1</i> syndrome	<i>DICER1</i>	See above
Retinoblastoma	Hereditary retinoblastoma	<i>RB1</i>	Melanoma, sarcoma, pineoblastoma
Rhabdoid tumor, atypical teratoid/ rhabdoid tumor	Rhabdoid tumor predisposition syndrome	<i>SMARCB1</i> , <i>SMARCA4</i>	Schwannoma, meningioma

(CNS) Central nervous system, (GIST) gastrointestinal stromal tumor.

# WHO IS A CANDIDATE FOR CANCER GENETIC COUNSELING AND TESTING?

Tool	Cancer risks assessed	Mutation probabilities	Notable features	Website
Breast Cancer Risk Assessment Tool, aka Gail Model	Breast cancer 5 yr and lifetime risks	None	Used to determine eligibility for chemoprevention Family history and other risk factors	bcrisktool.cancer.gov
Claus Tables	Breast cancer 10 yr and lifetime risks	None	Risk based on family history, including ages at diagnosis	Breast Cancer Risk Assessment Application (BRisk APP)
Tyrer-Cuzick	Breast cancer 10 yr and lifetime risks	<i>BRCA1, BRCA2</i>	Family history and other risk factors including prior negative genetic testing	<a href="http://www.ems-trials.org/riskevaluator">www.ems-trials.org/riskevaluator</a>
Penn II	None	<i>BRCA1, BRCA2</i>	Based on summary of family history features	<a href="http://pennmodel2.pmacs.upenn.edu/penn2">pennmodel2.pmacs.upenn.edu/penn2</a>
BOADICEA	Breast and ovarian cancer risks	<i>BRCA1, BRCA2, PALB2, CHEK2, ATM</i>	Family history-based Can calculate cancer risks for those with negative genetic testing results	<a href="http://ccge.medschl.cam.ac.uk/boadicea/boadicea-model">ccge.medschl.cam.ac.uk/boadicea/boadicea-model</a>
BRCAPRO	Breast and ovarian cancer risks	<i>BRCA1, BRCA2</i>	Family history and other risk factors, includes contralateral breast cancer risk	<a href="http://projects.iq.harvard.edu/bayesmendel/brcapro">projects.iq.harvard.edu/bayesmendel/brcapro</a>

# WHO IS A CANDIDATE FOR CANCER GENETIC COUNSELING AND TESTING?

Tool	Cancer risks assessed	Mutation probabilities	Notable features	Website
MMRpro	Colon and endometrial cancer risks	<i>MLH1</i> , <i>MSH2</i> , <i>MSH6</i>	Risk for Lynch syndrome	<a href="http://projects.iq.harvard.edu/bayesmendel/brcapro">projects.iq.harvard.edu/bayesmendel/brcapro</a>
MelaPRO	Melanoma	<i>CDKN2A</i>	Risk for <i>CDKN2A</i> -associated melanoma	<a href="http://projects.iq.harvard.edu/bayesmendel/brcapro">projects.iq.harvard.edu/bayesmendel/brcapro</a>
PancPRO	Pancreatic cancer	Dominant pancreatic cancer risk gene	Risk for a putative AD gene for pancreatic cancer risk	<a href="http://projects.iq.harvard.edu/bayesmendel/brcapro">projects.iq.harvard.edu/bayesmendel/brcapro</a>
PREMM5	None	<i>MLH1</i> , <i>MSH2</i> , <i>MSH6</i> , <i>PMS2</i> , <i>EPCAM</i>	Based on personal and family history of Lynch-associated cancers	<a href="http://premm.dfci.harvard.edu">premm.dfci.harvard.edu</a>
ASK2ME	Cancer risks provided in age intervals for mutation carriers	32 high- and moderate-penetrance genes	Risks and summaries of existing management guidelines	<a href="http://ask2me.org/">ask2me.org/</a>

(AD) Autosomal dominant.

# WHO IS A CANDIDATE FOR CANCER GENETIC COUNSELING AND TESTING?

**Table 4.** Cancer and genetics resources and societal guidelines for hereditary cancer predisposition evaluation

Category	Resources	Website	Societal guidelines/ policies	Reference	Content summary
Genetics	American College of Medical Genetics and Genomics (ACMG)	www.acmg.net	A practice guideline from the ACMG and the NSGC: referral indications for cancer predisposition assessment	10.1038/gim.2014.147 (Hampel et al. 2015)	Recommendations for referral for cancer genetics evaluation—not guidelines for testing; includes tables of cancer types with personal and family history; features suggestive of specific syndromes; provides description of syndromes and rationale for referral
	National Society of Genetic Counselors (NSGC)	www.nscc.org			Comprehensive reviews of genetic conditions
	GeneReviews	www.ncbi.nlm.nih.gov/books/NBK1116/			Information about genes and genetic conditions
	Genetics Home Reference	ghr.nlm.nih.gov			Comprehensive information about cancer and support for families
	American Cancer Society (ACS)	www.cancer.org			Recommendations for use of multigene panels, somatic testing, and direct-to-consumer testing in clinical care; includes detailed table of informed consent/pretest education
	American Society of Clinical Oncology (ASCO)	www.asco.org	ASCO Policy Statement Update: Genetic and Genomic Testing for Cancer Susceptibility	10.1200/JCO.2015.63.0996 (Robson et al. 2015)	Recommendations address inclusion of moderate- and low-penetrance genes and direct-to-consumer testing, not in updated version
			ASCO policy statement update: genetic and genomic testing for cancer susceptibility	10.1200/JCO.2009.27.0660 (Robson et al. 2010)	Guidelines for referral for cancer genetics evaluation; includes criteria for genetic testing, criteria for clinical diagnosis, and management guidelines
	National Comprehensive Cancer Network (NCCN)	www.nccn.org	NCCN Guidelines: Breast/Ovarian, Colon, Gastric, Neuroendocrine and Adrenal Tumors, Myelodysplastic Syndromes	www.nccn.org/professionals/physician_gls/default.aspx	

# WHO IS A CANDIDATE FOR CANCER GENETIC COUNSELING AND TESTING?

**Table 4.** *Continued*

Category	Resources	Website	Societal guidelines/ policies	Reference	Content summary
Breast/ ovarian	National Cancer Institute (NCI)	<a href="http://www.cancer.gov">www.cancer.gov</a>	NCI Cancer Genetics Risk Assessment and Counseling (PDQ)– Health Professional Version. <a href="http://www.cancer.gov/about-cancer/causes-prevention/genetics/risk-assessment-pdq">www.cancer.gov/about-cancer/causes-prevention/genetics/risk-assessment-pdq</a>	<a href="http://www.cancer.gov/about-cancer/causes-prevention/genetics/risk-assessment-pdq">www.cancer.gov/about-cancer/causes-prevention/genetics/risk-assessment-pdq</a>	Comprehensive information about cancer for patients and providers; directory for cancer genetics services
	Familial Cancer Database Online (FaCD)	<a href="http://www.facd.info">www.facd.info</a>			Very detailed review of process and content for cancer genetic risk assessment and counseling
	The American College of Obstetricians and Gynecologists (ACOG)	<a href="http://www.acog.org">www.acog.org</a>	Committee Opinion: Hereditary Cancer Syndromes and Risk Assessment	10.1097/01. AOG.0000466373.71146.51 (2015)	Database that associates cancer types and syndromes; useful for creating differential diagnosis
Other	The American Society of Breast Surgeons (ASBrS)	<a href="http://www.breastsurgeons.org">www.breastsurgeons.org</a>	Practice Bulletin No 182: Hereditary Breast and Ovarian Cancer Syndrome	10.1097/AOG.0000000000002296 (Committee on Practice Bulletins– Gynecology 2017)	Recommendations for obtaining a family history, medical history, and referral for a cancer genetics evaluation; review of common hereditary syndromes with gynecologic cancers
			ASBrS: Consensus Guideline on Genetic Testing for Hereditary Breast Cancer	<a href="http://www.breastsurgeons.org/docs/statements/Consensus-Guideline-on-Genetic-Testing-for-Hereditary-Breast-Cancer.pdf">www.breastsurgeons.org/docs/statements/Consensus-Guideline-on-Genetic-Testing-for-Hereditary-Breast-Cancer.pdf</a>	Guidelines for genetic counseling, testing, and management for hereditary breast and ovarian cancer syndrome

# WHO IS A CANDIDATE FOR CANCER GENETIC COUNSELING AND TESTING?

**Table 4.** *Continued*

Category	Resources	Website	Societal guidelines/policies	Reference	Content summary
Endocrine	Society of Gynecologic Oncology (SGO)	www.sgo.org	SGO statement on risk assessment for inherited gynecologic cancer predispositions	10.1016/j.ygyno.2014.09.009 (Lancaster et al. 2015)	Recommendations for referral criteria for genetic counseling and offering testing for hereditary breast and ovarian cancer and Lynch syndrome
	U.S. Preventive Services Task Force (USPSTF)	www.uspreventiveservicestaskforce.org	Draft Recommendation Statement BRCA-Related Cancer: Risk Assessment, Genetic Counseling, and Genetic Testing	www.uspreventiveservicestaskforce.org/Page/Document/draft-recommendation-statement/brcarelated-cancer-risk-assessment-genetic-counseling-and-genetic-testing1	Recommendations for risk assessment, genetic counseling, and genetic testing for <i>BRCA1</i> and <i>BRCA2</i>
	American Thyroid Association (ATA)	www.thyroid.org	Revised ATA for the Management of Medullary Thyroid Carcinoma Guidelines	10.1089/thy.2014.0335 (Wells et al. 2015)	Recommendations for <i>RET</i> genetic testing and management of hereditary MTC and MEN2 based on genotype
	Endocrine Society (ENDO)	www.endocrine.org	Pheochromocytoma and Paraganglioma: An Endocrine Society Clinical Practice Guideline	10.1210/jc.2014-1498 (Lenders et al. 2014)	Guidelines for genetic testing and management for hereditary paraganglioma and pheochromocytoma
Gastrointestinal	American College of Gastroenterology (ACG)	www.gi.org	ACG Clinical Guideline: Genetic Testing and Management of Hereditary Gastrointestinal Cancer Syndromes	10.1038/ajg.2014.435 (Syngal et al. 2015)	Guidelines for genetic testing and management for hereditary gastrointestinal cancer syndromes
	American Gastroenterological Association (AGA)	www.gastro.org	AGA Institute Guideline on the Diagnosis and Management of Lynch Syndrome	10.1053/j.gastro.2015.07.036 (Rubenstein et al. 2015)	Guidelines for diagnosis and management of Lynch syndrome

# WHO IS A CANDIDATE FOR CANCER GENETIC COUNSELING AND TESTING?

**Table 4.** *Continued*

Category	Resources	Website	Societal guidelines/policies	Reference	Content summary
	American Society of Clinical Oncology (ASCO)	<a href="http://www.asco.org">www.asco.org</a>	Hereditary Colorectal Cancer Syndromes: ASCO Clinical Practice Guideline Endorsement of the Familial Risk-Colorectal Cancer: European Society for Medical Oncology Clinical Practice Guidelines Evaluating Susceptibility to Pancreatic Cancer: ASCO Provisional Clinical Opinion	10.1200/JCO.2014.58.1322 (Stoffel et al. 2015) 10.1200/JCO.18.01489 (Stoffel et al. 2019a)	Guidelines for genetic testing and management for hereditary colon cancer syndromes Recommendations for genetic testing and management for hereditary pancreatic cancer syndromes
Hematologic	American Society of Hematology (ASH)	<a href="http://www.hematology.org">www.hematology.org</a>			
Pediatric	American Association for Cancer Research (AACR)	<a href="http://www.aacr.org">www.aacr.org</a>	Clinical Cancer Research: Pediatric Oncology Series by AACR	<a href="http://clincancerres.aacrjournals.org/pediatricseries">clincancerres.aacrjournals.org/pediatricseries</a>	Series of articles summarizing cancer predisposition syndromes in childhood and providing expert consensus guidelines for management
	American Academy of Pediatrics (AAP)	<a href="http://www.aap.org">www.aap.org</a>	POLICY STATEMENT: Ethical and Policy Issues in Genetic Testing and Screening of Children	10.1542/peds.2012-3680 (BIOETHICS et al. 2013)	Recommendations about when genetic testing should be offered in different clinical scenarios
	The American Society of Pediatric Hematology/Oncology (ASPHO)	<a href="http://www.aspbo.org">www.aspbo.org</a>			
	Children's Oncology Group (COG)	<a href="http://www.childrensoncologygroup.org">www.childrensoncologygroup.org</a>			Clinical trials group for childhood cancer; provides support for families and connects researchers and clinicians

# THE PROCESS OF CANCER GENETIC COUNSELING

- Genetic counseling is “the process of helping people understand and adapt to the medical, psychological, and familial implications of genetic contributions to disease” (Resta et al. 2006).
- Genetic counseling was proposed as a key component of the cancer risk assessment process in the 1990s (Peters and Stopfer 1996; Stopfer 2000)
- Empowering patients to make informed decisions regarding
  - screening,
  - prevention, and
  - genetic testing through provision of pertinent genetic and medical information and **tailored psychological counseling** remain core goals

# THE PROCESS OF CANCER GENETIC COUNSELING

- The Cancer Genetics Studies Consortium (CSGC) Task Force was among the first groups in the oncology setting to develop **consensus guidelines** for the process and content of **informed consent** (Geller et al. 1997).
- This multidisciplinary group first considered why informed consent for genetic testing requires special consideration and acknowledged the following issues:
  - (1) Genetic information affects an entire family,
  - (2) genetic information can present unique challenges for medical professionals as it is probabilistic in nature, and
  - (3) genetic information can lead to the reclassification of patients from healthy to high risk.
- At that time, the authors described the primary risks and benefits as psychological and social rather than physical or medical because the efficacy of preventive and therapeutic strategies in PV carriers had not yet been substantiated.

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# Genetic Testing for Inherited Cancer Risk

- What is genetic testing for inherited cancer risk?
- How is genetic testing done?
- Who should consider genetic testing for inherited cancer risk?
- What genetic tests are available for inherited cancer risk?
- What do the results of genetic testing mean?
- When should repeat genetic testing be considered?
- What is the role of genetic counseling in genetic testing for inherited cancer risk?
- What are the health implications of genetic test results for blood relatives?
- What are the benefits and downsides of genetic testing for cancer risk?
- Who has access to a person's genetic test results?
- Can at-home or direct-to-consumer (DTC) genetic tests be used to test for cancer risk?
- How are genetic testing labs regulated?
- What research is being done to improve genetic testing for inherited cancer risk?

**cBioPortal**  
FOR CANCER GENOMICS

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Looking for AACR Project GENIE, the largest public clinicogenomic cancer dataset? It's available here. [\[link\]](#)

**PanCancer Studies**

PanCancer Studies	11	Quick select: TCGA PanCancer Atlas Studies Curated set of non-redundant studies Help [link]
Pediatric Cancer Studies	15	Looking for AACR Project GENIE, the largest public clinicogenomic cancer dataset? It's available here. [link]
Immunogenomic Studies	8	
Cell lines	3	
PreCancerous Studies	1	
Adrenal Gland	3	
Ampulla of Vater	1	
Biliary Tract	16	
Bladder/Urinary Tract	22	
Bone	4	
Bowel	25	
Breast	31	

**PanCancer Studies**

<input type="checkbox"/> MSK-CHORD (MSK, Nature 2024)	25040 samples	<a href="#">[link]</a> <a href="#">[link]</a> <a href="#">[link]</a>
<input type="checkbox"/> MSK-IMPACT Clinical Sequencing Cohort (MSK, Nat Med 2017)	10945 samples	<a href="#">[link]</a> <a href="#">[link]</a> <a href="#">[link]</a>
<input type="checkbox"/> Metastatic Solid Cancers (UMich, Nature 2017)	500 samples	<a href="#">[link]</a> <a href="#">[link]</a> <a href="#">[link]</a>
<input type="checkbox"/> MSS Mixed Solid Tumors (Broad/Dana-Farber, Nat Genet 2018)	249 samples	<a href="#">[link]</a> <a href="#">[link]</a> <a href="#">[link]</a>
<input type="checkbox"/> SUMMIT - Neratinib Basket Study (Multi-Institute, Nature 2018)	141 samples	<a href="#">[link]</a> <a href="#">[link]</a> <a href="#">[link]</a>
<input type="checkbox"/> TMB and Immunotherapy (MSK, Nat Genet 2019)	1661 samples	<a href="#">[link]</a> <a href="#">[link]</a> <a href="#">[link]</a>
<input type="checkbox"/> Tumors with TRK fusions (MSK, Clin Cancer Res 2020)	106 samples	<a href="#">[link]</a> <a href="#">[link]</a> <a href="#">[link]</a>
<input type="checkbox"/> Cancer Therapy and Clonal Hematopoiesis (MSK, Nat Genet 2020)	24146 samples	<a href="#">[link]</a> <a href="#">[link]</a> <a href="#">[link]</a>
<input type="checkbox"/> China Pan-cancer (OrigMed, Nature 2022)	10194 samples	<a href="#">[link]</a> <a href="#">[link]</a> <a href="#">[link]</a>
<input type="checkbox"/> Pan-cancer analysis of whole genomes (ICGC/TCGA, Nature 2020)	2922 samples	<a href="#">[link]</a> <a href="#">[link]</a> <a href="#">[link]</a>
<input type="checkbox"/> MSK MetTropism (MSK, Cell 2021)	25775 samples	<a href="#">[link]</a> <a href="#">[link]</a> <a href="#">[link]</a>

**Pediatric Cancer Studies**

<input type="checkbox"/> Pediatric Preclinical Testing Consortium (CHOP, Cell Rep 2019)	261 samples	<a href="#">[link]</a> <a href="#">[link]</a> <a href="#">[link]</a>
<input type="checkbox"/> Pediatric Acute Lymphoid Leukemia - Phase II (TARGET, 2018)	1978 samples	<a href="#">[link]</a> <a href="#">[link]</a> <a href="#">[link]</a>
<input type="checkbox"/> Pediatric Rhabdoid Tumor (TARGET, 2018)	72 samples	<a href="#">[link]</a> <a href="#">[link]</a> <a href="#">[link]</a>

478 studies available (313984 samples) [Query By Gene](#) OR [Explore Selected Studies](#)

**What's New** @cbioportal [\[link\]](#)

- Added data consisting of 34,904 samples from 9 studies:
  - MSK-CHORD (MSK, Nature 2024) 25040 samples
  - MSK ctDNA Sequencing Cohort (MSK, Nature Med 2024) 5567 samples
  - Prostate Cancer (MSK, Clin Cancer Res 2024) 2260 samples
  - Hepatocellular Carcinoma (MSK, Clin Cancer Res 2024) 1370 samples
  - Pancreatic Cancer (MSK, Cancer Cell 2024) 395 samples
  - Metastatic Pancreatic Neuroendocrine Tumor (MSK, JCO Precis Oncol 2018) 96 samples

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**Example Queries**

- Primary vs. metastatic prostate cancer
- RAS/RAF alterations in colorectal cancer
- BRCA1 and BRCA2 mutations in ovarian cancer
- POLE hotspot mutations in endometrial cancer
- TP53 and MDM2/4 alterations in GBM
- PTEN mutations in GBM in text format
- Patient view of an endometrial cancer case
- All TCGA Pan-Cancer
- MSK-IMPACT clinical cohort, Zehir et al. 2017
- Histone mutations across cancer types

# Lung cancer: EGFR



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Metastatic Non-Small Cell Lung Cancer (MSK, Nature Medicine 2022)

Samples with mutation and CNA data (2621 samples / 1127 patients) - EGFR

Queried gene is altered in • 320 (28%) of queried patients  
• 683 (26%) of queried samples



Oncoprint

Cancer Types Summary

Plots

Mutations

Structural Variants **Beta!**

Comparison/Survival

CN Segments

Pathways

Download

Tracks ▾ Sort ▾ Mutations ▾ View ▾ Download ▾ 37 %

# Samples per P...



EGFR



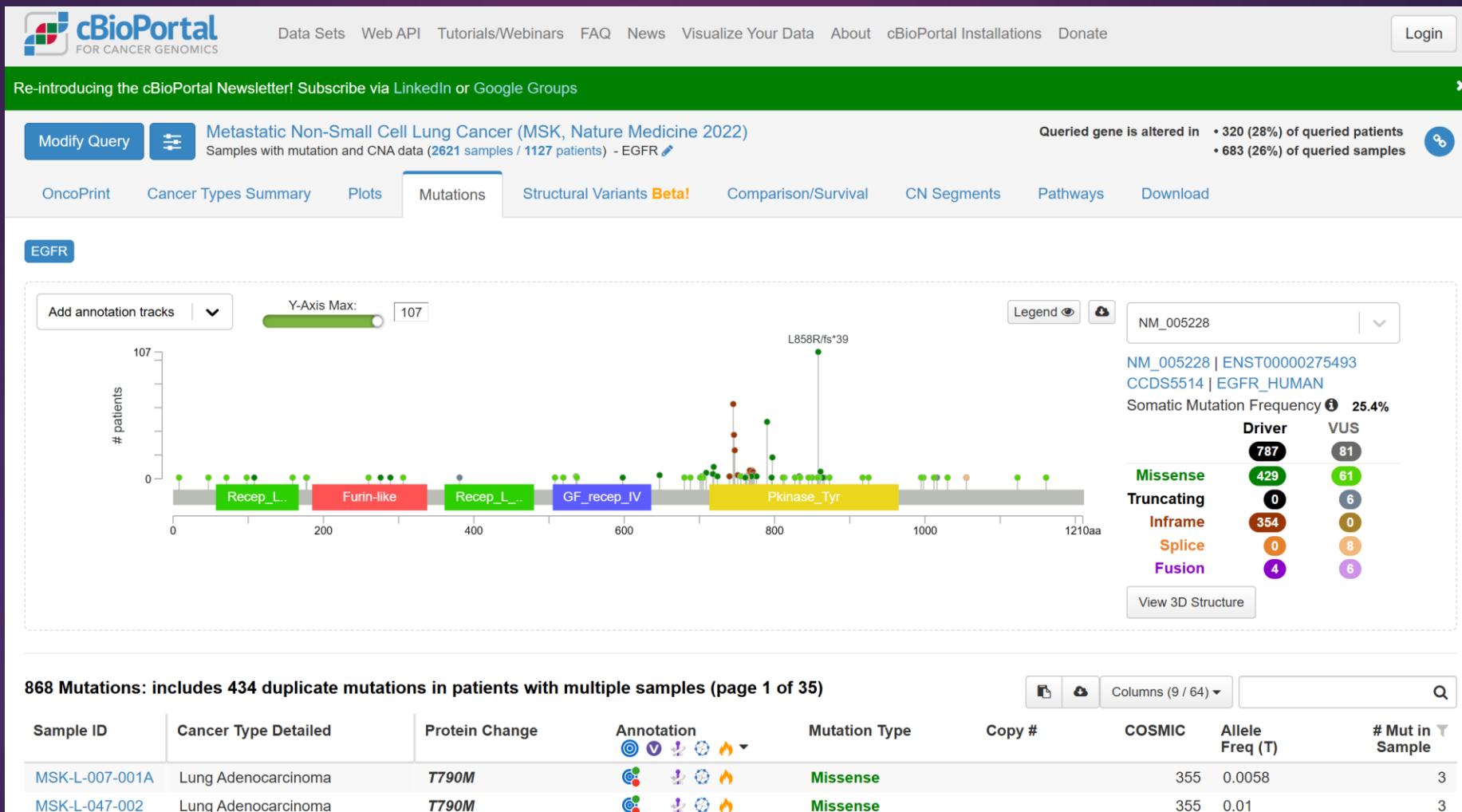
Genetic Alteration

Inframe Mutation (putative driver) Missense Mutation (putative driver) Missense Mutation (unknown significance)  
 Splice Mutation (unknown significance) Truncating Mutation (unknown significance) Structural Variant (putative driver)  
 Structural Variant (unknown significance) Amplification No alterations

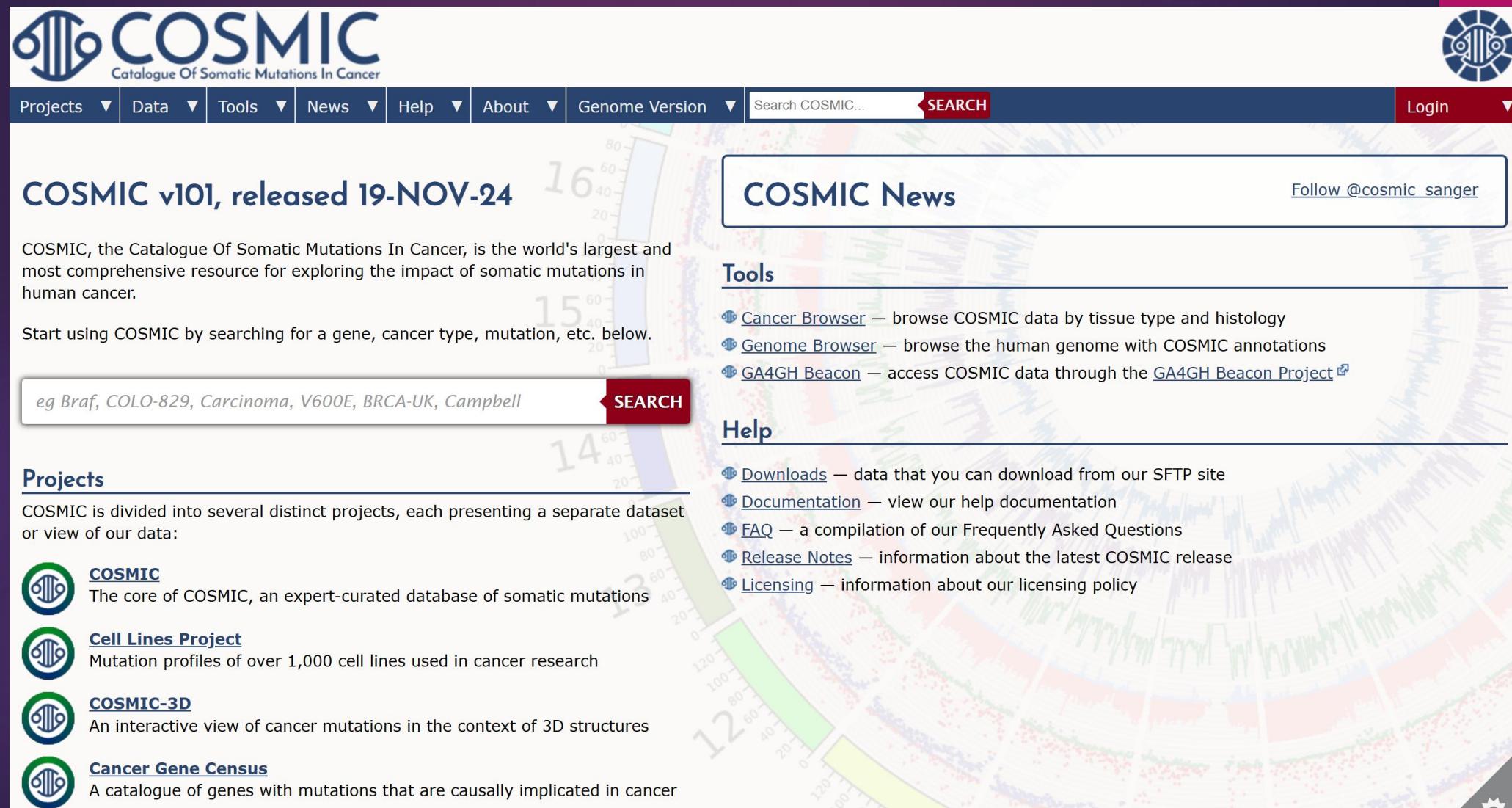
# Samples per Patient



# Lung cancer: EGFR



# COSMIC (<https://cancer.sanger.ac.uk/cosmic>)



The screenshot shows the COSMIC website interface. At the top, there is a navigation bar with links for Projects, Data, Tools, News, Help, About, Genome Version, a search bar, and a login link. A banner at the top left announces "COSMIC v101, released 19-NOV-24". Below the banner, there is a search bar with placeholder text "eg Braf, COLO-829, Carcinoma, V600E, BRCA-UK, Campbell" and a red "SEARCH" button. The main content area is divided into sections: "Projects" (listing COSMIC, Cell Lines Project, COSMIC-3D, and Cancer Gene Census), "Tools" (listing Cancer Browser, Genome Browser, and GA4GH Beacon), and "Help" (listing Downloads, Documentation, FAQ, Release Notes, and Licensing). The "COSMIC News" section on the right includes a "Follow @cosmic\_sanger" link.

**COSMIC** Catalogue Of Somatic Mutations In Cancer

Projects ▾ Data ▾ Tools ▾ News ▾ Help ▾ About ▾ Genome Version ▾ Search COSMIC... **SEARCH** Login ▾

**COSMIC v101, released 19-NOV-24**

COSMIC, the Catalogue Of Somatic Mutations In Cancer, is the world's largest and most comprehensive resource for exploring the impact of somatic mutations in human cancer.

Start using COSMIC by searching for a gene, cancer type, mutation, etc. below.

eg Braf, COLO-829, Carcinoma, V600E, BRCA-UK, Campbell **SEARCH**

**Projects**

COSMIC is divided into several distinct projects, each presenting a separate dataset or view of our data:

- COSMIC**  
The core of COSMIC, an expert-curated database of somatic mutations
- Cell Lines Project**  
Mutation profiles of over 1,000 cell lines used in cancer research
- COSMIC-3D**  
An interactive view of cancer mutations in the context of 3D structures
- Cancer Gene Census**  
A catalogue of genes with mutations that are causally implicated in cancer

**COSMIC News** Follow @cosmic\_sanger

**Tools**

- Cancer Browser** — browse COSMIC data by tissue type and histology
- Genome Browser** — browse the human genome with COSMIC annotations
- GA4GH Beacon** — access COSMIC data through the [GA4GH Beacon Project](#)

**Help**

- Downloads** — data that you can download from our SFTP site
- Documentation** — view our help documentation
- FAQ** — a compilation of our Frequently Asked Questions
- Release Notes** — information about the latest COSMIC release
- Licensing** — information about our licensing policy

# Clinvar (<https://www.ncbi.nlm.nih.gov/clinvar>)

**ClinVar** Genomic variation as it relates to human health

Search by gene symbols, location, HGVS expressions, c-dot, p-dot [Search ClinVar](#) [?](#)

[Advanced search](#)

About    Access    Submit    Stats    FTP    Help    Were new search queries using location, c-dot, and p-dot helpful?

**NM\_000051.4(ATM):c.2251-10T>G**

Cite    Follow    Print    Download

**Germline**

Classification Pathogenic  
★☆☆☆ (1) criteria provided, single submitter [?](#)

**Somatic**

Clinical impact Tier I - Strong for Malignant tumor of breast  
★☆☆☆ (3) criteria provided, multiple submitters [?](#)

Somatic Oncogenicity Oncogenic  
★☆☆☆ (1) reviewed by expert panel [?](#)

# Clinvar (<https://www.ncbi.nlm.nih.gov/clinvar>)

Graphical view of search results ▾

► GRCh37

Gene 

Pathogenic

Likely pathogenic

Uncertain significance

Likely benign

Benign

Conflicting

Not provided

other

ATM (+)  
NC\_000011.9  
Q\_108093794-108239829

Transcripts  
[NM\\_001351835.2](#)  
[NM\\_001351834.2](#)  
[NM\\_000051.4](#)  
[NM\\_001351836.2](#)

108100K 108120K 108140K 108160K 108180K 108200K 108220K

Search results

Filters activated: Somatic, Pathogenic. [Clear all](#) to show 17468 items.

Variation	Gene (Protein Change)	Type (Consequence)	Condition	Classification, Review status
<input type="checkbox"/> <a href="#">NM_000051.4(ATM):c.2135C&gt;G (p. Ser712Ter)</a>	ATM (S712*)	Single nucleotide variant (nonsense)	Hereditary cancer-predisposing syndrome +2 more	 Pathogenic/Likely pathogenic ★★  Oncogenic ★
<input type="checkbox"/> <a href="#">NM_000051.4(ATM):c.2921+1G&gt;A</a>	ATM	Single nucleotide variant (splice donor variant)	Ataxia-telangiectasia syndrome +5 more	 Pathogenic/Likely pathogenic ★★  Oncogenic ★

# Clinvar: NM\_000051.4(ATM):c.2921+1G>A

**NM\_000051.4(ATM):c.2921+1G>A**

Cite Follow Print Download

**Germine**

Classification     (23) **Pathogenic/Likely pathogenic**  
criteria provided, multiple submitters, no conflicts

**Somatic**

No data submitted for somatic clinical impact **Oncogenicity**     (1) **Oncogenic**  
criteria provided, single submitter

**Variant Details** 

<b>Identifiers:</b>	NM_000051.4(ATM):c.2921+1G>A  Variation ID: 141182 Accession: VCV000141182.56		
<b>Type and length:</b>	single nucleotide variant, 1 bp		
<b>Location:</b>	Cytogenetic: 11q22.3 11: 108271147 (GRCh38) [ <a href="#">NCBI</a> <a href="#">UCSC</a> ] 11: 108141874 (GRCh37) [ <a href="#">NCBI</a> <a href="#">UCSC</a> ]		
<b>Timeline in ClinVar:</b>	<b>First in ClinVar</b>  Mar 29, 2015	<b>Last submission</b>  Dec 22, 2024	<b>Last evaluated</b>  Oct 10, 2024
	Germline		
	Somatic - Oncogenicity	Aug 11, 2024	Jul 31, 2024



# Xin chân thành cảm ơn!

LUU PHUC LOI, PHD

ZALO: 0901802182

EMAIL: LUU.P.LOI@GOOGLEMAIL.COM