Table. Clinical indications for hereditary cancer single-gene tests

Test Name	Gene	Test Code	Clinical Indication	Additional information
APC Sequencing and Deletion/Duplication	APC	93797	Personal or family history of ≥ 20 cumulative colorectal adenomas, colorectal cancer, duodenal adenomas, duodenal cancer, papillary thyroid cancer, hepatoblastoma, desmoid tumor, or multifocal congenital hypertrophy of the retinal pigment epithelium (CHRPE)	
ATM Sequencing and Deletion/Duplication	ATM	38802	Personal and/or family history of female breast cancer, prostate cancer, pancreatic cancer	Also associated with autosomal recessive Ataxia-telangiectasia.
BAP1 Sequencing and Deletion/Duplication	BAP1	38803	Personal and/or family history of uveal melanoma, cutaneous melanoma, malignant mesothelioma, atypical Spitz tumors, renal cell carcinoma, or basal cell carcinoma	
BLM Sequencing and Deletion/Duplication	BLM	38804	Individuals with a suspected diagnosis of Bloom syndrome or those with a personal or family history of colorectal cancer	Bloom syndrome is an autosomal recessive condition.
CDH1 Sequencing and Deletion/Duplication	CDH1	92568	Personal or family history of diffuse gastric cancer or lobular breast cancer	
CDKN2A Sequencing and Deletion/Duplication	CDKN2A	93939	Personal or family history of melanoma (especially multiple or early-onset) or pancreatic cancer	
CHEK2 Sequencing and Deletion/Duplication	CHEK2	93940	Personal or family history of breast cancer, colon cancer, prostate cancer, stomach cancer, thyroid cancer, renal cancer, or melanoma	
FH Gene Sequencing and Deletion/Duplication	FH	38805	Personal history of multiple cutaneous leiomyomas, symptomatic and/or multiple uterine leiomyomas <40 years, renal cell carcinoma <40 years, or a close relative with any of these features	Also associated with autosomal recessive fumarate hydratase deficiency.

Test Name	Gene	Test Code	Clinical Indication	Additional information
FLCN Sequencing and Deletion/Duplication	FLCN	38806	Individuals with either 1 major clinical feature or 2 or more minor features of BHD syndrome. Major criteria • At least 5 fibrofolliculomas or trichodiscomas, at least 1 histologically confirmed, of adult onset Minor criteria • Multiple lung cysts: bilateral basally located lung cysts with no other apparent cause, with or without spontaneous primary pneumothorax • Renal cancer: early onset (<50 years) or multifocal or bilateral renal cancer, or renal cancer of mixed chromophobe and oncocytic histology • A first-degree relative with BHD	
HOXB13 Sequencing and Deletion/Duplication	HOXB13	38807	Personal history or family history of prostate cancer	
MEN1 Sequencing and Deletion/Duplication	MEN1	93942	Personal history of two or more of the following: • Multi-gland parathyroid hyperplasia • Pancreatic neuroendocrine tumor (PanNET) (also known as pancreatic islet cell tumor) • Pituitary tumors, including pituitary adenomas • Lung/thymus neuroendocrine carcinoid tumors In addition, MEN1 may also be associated with neuroendocrine tumors of the lung or thymus, of adrenal adenomas or carcinomas, thyroid adenomas, multiple lipomas, cutaneous angiomas	
MITF Gene Analysis	MITF	38808	Individuals with a personal or family history of cutaneous melanoma or renal cancer	Test only includes analysis of the c.952G>A variant.

Test Name	Gene	Test Code	Clinical Indication	Additional information
Lynch Syndrome, MLH1 Sequencing and Deletion/Duplication	MLH1	91460	Personal history of a Lynch syndrome-related cancer when IHC analysis of mismatch repair proteins has been performed on the tumor and is suggestive of an inherited mutation in the *MLH1* gene. Lynch syndrome-related cancers include colorectal, endometrial, gastric, ovarian, pancreas, ureter and renal pelvis, brain (usually glioblastoma), biliary tract, small intestinal cancers, in addition to sebaceous carcinomas and keratoacanthomas in Muir-Torre syndrome.	This gene is most often ordered as part of the Lynch Syndrome Panel, test code 91461. Also associated with autosomal recessive constitutional mismatch repair deficiency (CMMRD).
Lynch Syndrome, MSH2 Sequencing and Deletion/Duplication (Including EPCAM)	MSH2 (including EPCAM)	91471	Personal history of a Lynch syndrome-related cancer when IHC analysis of mismatch repair proteins has been performed on the tumor and is suggestive of an inherited mutation in the *MSH2* gene. Lynch syndrome-related cancers include colorectal, endometrial, gastric, ovarian, pancreas, ureter and renal pelvis, brain (usually glioblastoma), biliary tract, small intestinal cancers, in addition to sebaceous carcinomas and keratoacanthomas in Muir-Torre syndrome	This gene is most often ordered as part of the Lynch Syndrome Panel, test code 91461. For *EPCAM*, only CNV's are analyzed and reported. Also associated with autosomal recessive constitutional mismatch repair deficiency (CMMRD).
Lynch Syndrome, MSH6 Sequencing and Deletion/Duplication	MSH6	91458	Personal history of a Lynch syndrome-related cancer when IHC analysis of mismatch repair proteins has been performed on the tumor and is suggestive of an inherited mutation in the *MSH6* gene. Lynch syndrome-related cancers include colorectal, endometrial, gastric, ovarian, pancreas, ureter and renal pelvis, brain (usually glioblastoma), biliary tract, small intestinal cancers, in addition to sebaceous carcinomas and keratoacanthomas in Muir-Torre syndrome	This gene is most often ordered as part of the Lynch Syndrome Panel, test code 91461. Also associated with autosomal recessive constitutional mismatch repair deficiency (CMMRD).
MUTYH Sequencing and Deletion/Duplication	MUTYH	93944	Personal or family history of ≥20 cumulative colorectal adenomas, colorectal cancer, or other GI cancer	*MUTYH*-associated polyposis (MAP) is an autosomal recessive condition.

Test Name	Gene	Test Code	Clinical Indication	Additional information
NF1 Sequencing and Deletion/Duplication	NF1	93941	To help confirm a suspected diagnosis of NF1 under certain circumstances, such as when only one diagnostic feature is observed in a young child. A diagnosis of NF1 syndrome is made for individuals with 2 or more of the following features: • Six or more café au lait macules >5 mm in greatest diameter in prepubertal individuals, or >15 mm in greatest diameter in post-pubertal individuals • Two or more neurofibromas of any type, or 1 plexiform neurofibroma • Freckling in the axillary or inguinal regions • Optic glioma • Two or more Lisch nodules (iris hamartomas) • A distinctive osseous lesion such as sphenoid dysplasia or tibial pseudarthrosis • A first-degree relative (parent, sib, or offspring) with NF1 as defined by the above criteria	
PALB2 Sequencing and Deletion/Duplication	PALB2	92571	Personal or family history of breast cancer or pancreatic cancer	Associated with autosomal recessive Fanconi anemia.
Lynch Syndrome, PMS2 Sequencing and Deletion/Duplication	PMS2	91457	Personal history of a Lynch syndrome-related cancer when IHC analysis of mismatch repair proteins has been performed on the tumor and is suggestive of an inherited mutation in the *PMS2* gene. Lynch syndrome-related cancers include colorectal, endometrial, gastric, ovarian, pancreas, ureter and renal pelvis, brain (usually glioblastoma), biliary tract, small intestinal cancers, in addition to sebaceous carcinomas and keratoacanthomas in Muir-Torre syndrome	This gene is most often ordered as part of the Lynch Syndrome Panel, test code 91461. Also associated with autosomal recessive constitutional mismatch repair deficiency (CMMRD)

Test Name	Gene	Test Code	Clinical Indication	Additional information
PTEN Sequencing and Deletion/Duplication	PTEN	92566	Individuals with one or more of the following: Major features • Breast cancer • Endometrial cancer • Follicular thyroid cancer • Multiple gastrointestinal hamartomas or ganglioneuromas • Lhermitte-Duclos disease • Macrocephaly • Macular pigmentation of the glans penis • Mucocutaneous lesions such as trichilemmomas, palmoplantar keratosis, oral mucosal papillomatosis, or cutaneous facial papules Minor features • Autism spectrum disorder • Colon cancer • Three or more esophageal glycogenic acanthoses • Lipomas • Intellectual disability • Papillary or follicular variant of papillary thyroid cancer • Thyroid structural lesions such as adenoma, nodules, or goiter • Renal cell carcinoma • Single gastrointestinal hamartoma or ganglioneuroma • Testicular lipomatosis • Vascular anomalies	
RET Sequencing and Deletion/Duplication	RET	93796	Individuals with a clinical diagnosis of MEN2, medullary thyroid cancer, or primary C-cell hyperplasia	
SMARCA4 Sequencing and Deletion/Duplication	SMARCA4	38809	Personal or family history of rhabdoid tumors, including small cell carcinoma of the ovary, hypercalcemic type, or SCCOHT	

Test Name	Gene	Test Code	Clinical Indication	Additional information
STK11 Sequencing and Deletion/Duplication	STK11	92565	This test may be appropriate for individuals with • Multiple hamartomatous polyps of the gastrointestinal tract • Mucocutaneous hyperpigmentation of the mouth, lips, nose, eyes, genitalia, or fingers • Family history of Peutz-Jeghers syndrome	
Li-Fraumeni Syndrome, TP53 Sequencing and Deletion/Duplication	TP53	92560	Individuals who meet the Chompret criteria, summarized below: • Individual with a tumor from the LFS spectrum (soft tissue sarcoma, osteosarcoma, central nervous system tumor, breast cancer, adrenocortical carcinoma) diagnosed before age 46, and a first- or second-degree relative with a tumor from the LFS spectrum diagnosed before age 56, or • Individual with multiple primary LFS tumors (except multiple breast tumors), two of which belong to the LFS tumor spectrum with the initial cancer occurring before age 46, or • Individual with adrenocortical carcinoma, choroid plexus carcinoma, or rhabdomyosarcoma diagnosed at any age, or • Individual with breast cancer diagnosed before age 31	This test is frequently mis-ordered in place of test code 16515, TP53 somatic mutation, Prognostic.
VHL Sequencing and Deletion/Duplication	VHL	93943	Personal or family history of retinal angioma, spinal or cerebellar hemangioblastoma, clear cell renal carcinoma, pancreatic cysts, renal cysts, pheochromocytomas, endolymphatic sac tumors, or pancreatic neuroendocrine tumors	