Sema4 Signal®
Hereditary Cancer Panel Guide

Delivered via our Traversa™
Comprehensive Genomic Platform

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1- Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Genetic/Familial High-Risk Assessment: Breast, Ovarian, and Pancreatic V2.2021. National Comprehensive Cancer Network, Inc. 2021©. All rights reserved. Accessed, [5/18/2021]. To view the most recent and complete version of the guidelines, go online to NCCN.org.

Comprehensive options to help guide test selection

This guide provides information about the diseases and genes covered by Sema4 Signal's hereditary cancer testing panels. Sema4 offers a wide range of panels.

Universal Panel
107 genes

This panel includes genes on the Sema4 menu associated with known and possible increased risk for common and rare hereditary cancers across the major organ systems. While some of the genes included in this panel have management guidelines published, there are some with emerging evidence to support association with increased cancer risk.

Comprehensive Panel
73 genes

Given the complexity and overlap of clinical presentation between hereditary cancer syndromes, the Comprehensive Panel is a way to evaluate multiple hereditary cancer conditions in an individual. This panel includes genes associated with hereditary cancers across the major organ systems including breast, ovarian, colon, pancreatic, prostate, renal, brain, and many others.

High Prevalence Panel
38 genes

The High Prevalence Panel is designed to maximize diagnostic yield for individuals with personal and/or family history of cancer. This panel includes genes associated with the most frequent forms of hereditary cancer including breast, colon, ovarian, pancreatic, prostate, renal, uterine and other cancers. Many of these genes have management guidelines published. Most genes included on the panel have clinically actionable interventions.

Pediatric Panel
49 genes

The Pediatric Panel includes genes associated with increased risk for pediatric cancers/tumors, which includes brain and neurological tumors, solid tumors and some hematologic malignancies. This panel may be appropriate for individuals who have clinical manifestations that are suggestive of an inherited childhood onset cancer syndrome.

Ashkenazi Jewish BRCA Panel
3 variants

The Ashkenazi 3-site panel tests for the presence of most common founder variants in individuals of Ashkenazi Jewish descent associated with hereditary breast and ovarian cancer (HBOC). These variants account for up to 99% of identified BRCA mutations in these individuals.There are NCCN Guidelines[1] published which include recommendations for management of HBOC.

***BRCA1* and *BRCA2* Panel**
2 genes

This panel analyzes the *BRCA1* and *BRCA2* genes which are associated with hereditary breast and ovarian cancer (HBOC). HBOC is an autosomal dominant disorder associated with increased risk for breast, ovarian, pancreatic, prostate and other cancers. There are NCCN Clinical Practice Guidelines In Oncology (NCCN Guidelines®)[1] published which include recommendations for management of HBOC. Identification of a pathogenic/likely pathogenic variant in these genes can help estimate cancer risk and guide treatment, screening, and/or prevention decisions for the patient.

Breast Guidelines Panel
11 genes

This panel includes genes associated with increased risk to develop breast cancer, all with NCCN Guidelines® published for risk management. Identification of a pathogenic/likely pathogenic variant in these genes can help estimate cancer risk and guide treatment, screening, and/or prevention decisions for the patient.

Breast & Gynecological Panel
27 genes

The Breast and Gynecological Panel includes genes associated with increased risk for breast, ovarian and uterine cancers. Most of the genes included in this panel have management guidelines published. This panel also includes some genes with emerging evidence supporting cancer risk association. This panel can provide information that may help healthcare providers and patients make more informed decisions regarding treatment and prevention.

Lynch Syndrome Panel
5 genes

The Lynch Syndrome Panel analyzes genes associated with Lynch syndrome, also known as Hereditary Non-Polyposis Colorectal Cancer (HNPCC), the most common hereditary form of colorectal cancer. The NCCN Guidelines[2] for Genetic/Familial High-Risk Assessment: Colorectal can help healthcare providers and patients make decisions regarding surveillance, prevention, and management of specific cancers associated with Lynch.

Colorectal Panel
21 genes

The Colorectal Panel includes genes associated with increased risk for colorectal cancer. This includes genes associated with Lynch Syndrome, Familial Adenomatous Polyposis, *MUTYH*-associated Polyposis, Juvenile Polyposis Syndrome, Cowden Syndrome and Li-Fraumeni Syndrome. While most of the genes included in this panel have management guidelines published, there are some with emerging evidence to support association with cancer predisposition. This panel can provide information that may help healthcare providers and patients make more informed decisions regarding treatment, prevention, and surveillance.

Pancreatic Panel
21 genes

The Pancreatic Panel includes genes that are associated with increased pancreatic cancer. This panel may provide information that may help healthcare providers and patients make more informed medical decisions.

Pancreatic Plus Panel
27 genes

The Pancreatic Plus Panel includes genes associated with increased risk for pancreatic cancer and additional genes associated with increased risk for pancreatitis. Chronic pancreatitis has been reported as a risk factor for pancreatic cancer.

Customizable panels available to fit your needs

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2- Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Genetic/Familial High-Risk Assessment: Colorectal V1.2021. National Comprehensive Cancer Network, Inc. 2021©. All rights reserved. Accessed, [5/18/2021]. To view the most recent and complete version of the guidelines, go online to NCCN.org.

Prostate Panel
15 genes

The Prostate Panel includes genes associated with increased lifetime risk for prostate cancer. While most of the genes included in this panel have management guidelines published, there are some with emerging evidence to support association with cancer predisposition. This panel can provide information that may help healthcare providers and patients make more informed decisions regarding treatment and/or screening.

Brain/Neurological Panel
32 genes

The Brain and Neurological Tumor Panel includes genes that are associated with inherited forms of brain and/or neurological cancers such as Lynch Syndrome, Familial Adenomatous Polyposis, Neurofibromatosis, Cowden Syndrome, Li-Fraumeni Syndrome, and other syndromes.

Melanoma Panel
9 genes

The Melanoma Panel includes genes associated with increased lifetime risk of developing melanoma. While most of the genes included in this panel have management guidelines published, there are some with emerging evidence to support association with cancer predisposition. This panel can provide information that may help healthcare providers and patients make more informed medical decisions.

Endocrine Tumor Panel
21 genes

The Endocrine Tumor Panel includes genes associated with inherited forms of endocrine tumors/cancers including hereditary paraganglioma-pheochromocytoma syndrome, multiple endocrine neoplasia, and thyroid cancer. These genes have published management guidelines which can help healthcare providers and patients to make informed medical decisions.

Renal/Urinary Panel
25 genes

The Renal and Urinary Panel includes genes associated with increased lifetime risk of developing cancers of the kidneys, renal pelvis, ureters or bladder. These individuals are also at risk of developing these cancers at an earlier age compared to the general population.

High-quality genetic testing for your practice

- Our hereditary cancer testing technologies are >99% accurate
- Large selection of targeted and comprehensive panels with 16 sub-panels, single gene testing, and customizable panel options
- Reflex and re-requisition options to meet your needs

Genes covered by Sema4 Signal

Gene	Universal Panel 107 genes	Comprehensive Panel 73 genes	High Prevalence Panel 38 genes	Pediatric Panel 49 genes	Ashkenazi Jewish BRCA Panel 3 variants	*BRCA1 & BRCA2* Panel 2 genes	Breast Guidelines Panel 11 genes	Breast & Gynecological Panel 27 genes	Lynch Syndrome Panel 5 genes	Colorectal Panel 21 genes	Pancreatic Panel 21 genes	Pancreatic+ Plus Panel 27 genes	Prostate Panel 15 genes	Brain/ Neurological Panel 32 genes	Melanoma Panel 9 genes	Endocrine Tumor Panel 21 genes	Renal/Urinary Panel 25 genes
AIP	✓	✓												✓		✓	
ALK	✓	✓		✓										✓			
APC	✓	✓	✓	✓						✓	✓	✓		✓		✓	
ATM	✓	✓	✓	✓			✓	✓		✓	✓	✓	✓				
AXIN2	✓	✓	✓							✓							
BAP1	✓	✓												✓	✓		✓
BARD1	✓	✓	✓				✓	✓						✓			
BLM	✓	✓		✓													
BMPR1A	✓	✓	✓	✓						✓	✓	✓					
BRCA1	✓	✓	✓		✓‡	✓	✓	✓			✓	✓	✓				
BRCA2	✓	✓	✓		✓‡	✓	✓	✓			✓	✓	✓		✓		
BRIP1	✓	✓	✓					✓									
CASR	*											✓					
CDC73	✓			✓												✓	✓
CDH1	✓	✓	✓				✓	✓		✓							
CDK4	✓	✓	✓								✓	✓			✓		
CDKN1B	✓	✓												✓		✓	
CDKN1C	✓			✓													
CDKN2A	✓	✓	✓								✓	✓		✓	✓		
CEBPA	✓	✓		✓													
CFTR	*											✓					
CHEK2	✓	✓	✓				✓	✓		✓			✓			✓	
CPA1	*											✓					
CTC1	✓																
CTRC	*											✓					
DDB2	✓																
DICER1	✓	✓	✓	✓				✓						✓		✓	✓
DIS3L2	✓			✓													✓
DKC1	✓																

*Available on Universal Plus Panel

‡ Variants: *BRCA1* (c.5266dupC), *BRCA1* (c.68_69delAG), *BRCA2* (c.5946delT)

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EGFR	✓	✓															
EPCAM	✓	✓	✓	✓				✓	✓	✓	✓	✓	✓	✓			✓
ERCC2	✓																
ERCC3	✓																
ERCC4	✓																
ERCC5	✓																
FANCA	✓																
FANCB	✓																
FANCC	✓							✓									
FANCD2	✓																
FANCE	✓																
FANCF	✓																
FANCG	✓																
FANCI	✓																
FANCL	✓																
FANCM	✓																
FH	✓	✓		✓												✓	✓
FLCN	✓	✓															✓
GATA2	✓	✓		✓													
GPC3	✓			✓										✓			
GREM1	✓	✓	✓							✓							
HOXB13	✓	✓	✓										✓				
HRAS	✓	✓		✓										✓			
KIT	✓	✓															
MAX	✓	✓		✓												✓	
MEN1	✓	✓		✓							✓	✓		✓		✓	
MET	✓	✓															✓
MITF	✓	✓						✓							✓		✓
MLH1	✓	✓	✓	✓				✓	✓	✓	✓	✓	✓	✓			✓
MRE11A	✓							✓									
MSH2	✓	✓	✓	✓				✓	✓	✓	✓	✓	✓	✓			✓
MSH3	✓	✓	✓							✓							
MSH6	✓	✓	✓	✓				✓	✓	✓	✓	✓	✓	✓			✓
MUTYH	✓	✓	✓					✓		✓							

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NBN	✓	✓	✓	✓				✓					✓	✓			
NF1	✓	✓	✓	✓			✓	✓			✓	✓		✓		✓	
NF2	✓	✓		✓										✓			
NHP2	✓																
NOP10	✓																
NTHL1	✓	✓	✓							✓							
PALB2	✓	✓	✓				✓	✓			✓	✓	✓				
PDGFRA	✓	✓															
PHOX2B	✓	✓		✓										✓			
PMS2	✓	✓	✓	✓				✓	✓	✓	✓	✓	✓	✓			✓
POLD1	✓	✓	✓							✓							
POLE	✓	✓	✓							✓							
POLH	✓																
POT1	✓	✓												✓	✓		
PRKAR1A	✓	✓		✓										✓		✓	
PRSS1	*											✓					
PTCH1	✓	✓		✓										✓			
PTEN	✓	✓	✓	✓			✓	✓		✓				✓	✓	✓	✓
RAD50	✓							✓									
RAD51C	✓	✓	✓					✓					✓				
RAD51D	✓	✓	✓					✓					✓				
RB1	✓	✓		✓										✓	✓		
RECQL4	✓			✓												✓	
RET	✓	✓		✓													
RTEL1	✓																
RUNX1	✓	✓		✓													
SDHA	✓	✓		✓												✓	✓
SDHAF2	✓	✓		✓												✓	
SDHB	✓	✓		✓												✓	✓
SDHC	✓	✓		✓												✓	✓
SDHD	✓	✓		✓												✓	✓
SLX4	✓																
SMAD4	✓	✓	✓							✓	✓	✓					

*Available on Universal Plus Panel

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SMARCA4	✓	✓	✓	✓				✓						✓			✓
SMARCB1	✓	✓		✓										✓			✓
SPINK1	*											✓					
STK11	✓	✓	✓	✓			✓	✓		✓	✓	✓					
SUFU	✓	✓		✓										✓			
TERC	✓			✓													
TERT	✓			✓													
TINF2	✓																
TMEM127	✓	✓		✓												✓	
TP53	✓	✓	✓	✓			✓	✓		✓	✓	✓	✓	✓	✓	✓	✓
TSC1	✓	✓	✓	✓							✓	✓		✓			✓
TSC2	✓	✓	✓	✓							✓	✓		✓			✓
VHL	✓	✓	✓	✓							✓	✓		✓		✓	✓
WT1	✓	✓		✓													✓
XPA	✓																
XPC	✓																
XRCC2	✓	✓						✓									

*Available on Universal Plus Panel

Distinguishing among certain Sema4 Signal hereditary cancer panels

Considerations for selecting the most appropriate panel include patient's medical and/or family history as well as provider/patient preference

Panels	Differences
• Universal • Comprehensive • High Prevalance	The Universal Panel is the largest panel Sema4 offers. Some of the genes are associated with rare conditions and/or emerging evidence to support association with increased cancer risk. The Comprehensive panel is our next largest panel that include genes strongly associated with common and rare cancer types. The High Prevalence Panel includes genes that is strongly associated with increased risk for the most frequent cancer types (such as breast, colon, ovarian, uterine etc)
Pancreatic Plus Panel ***vs*** the Pancreatic Panel	The Pancreatic Plus Panel includes genes associated with pancreatic cancer and pancreatitis. Pancreatitis is an inflammation of the pancreas. People diagnosed with chronic pancreatitis may have an increased risk of developing pancreatic cancer. A healthcare provider may choose to include the genes for pancreatitis based on the patient's medical and/or family history
Colorectal ***vs*** Lynch Syndrome Panel	The Colorectal Panel is a next-generation sequencing panel that can identify inherited risk for several hereditary colon cancer syndromes (including Lynch Syndrome). The Lynch Syndrome panel is a next-generation sequencing panel which analyzes genes for patients at high risk of Lynch syndrome **only** (previously known as hereditary non-polyposis colorectal cancer/HNPCC), all with published management guidelines, to help healthcare providers and patients make more informed decisions regarding treatment and prevention
Ashkenazi Jewish 3-site panel ***vs*** the *BRCA1* and *BRCA2* Panel	The Ashkenazi 3-site panel tests for the presence of the most common founder variants in individuals of Ashkenazi Jewish descent associated with hereditary breast and ovarian cancer. These variants account for up to 99% of identified BRCA mutations in these individuals. The *BRCA1* and *BRCA2* panel includes next generation sequencing of these two highly-penetrant genes associated with Hereditary Breast and Ovarian Cancer (HBOC)

About Sema4 Signal

Sema4 Signal is the name given for our suite of cancer solutions that enable precision oncology care across the patient journey. Our comprehensive portfolio includes somatic and germline testing, advanced informatics to structure and draw insight from clinical and genomic information, clinical trial matching, and customized services to meet your needs. With Sema4 Signal, we deliver the information needed to patients and providers to drive better care across prevention, treatment, and long-term monitoring.

Questions?

To learn more about our oncology solutions and services, please visit **sema4.com/hc-provider**, call **833-486-6260**, or email **ClientServicesOncology@sema4.com**