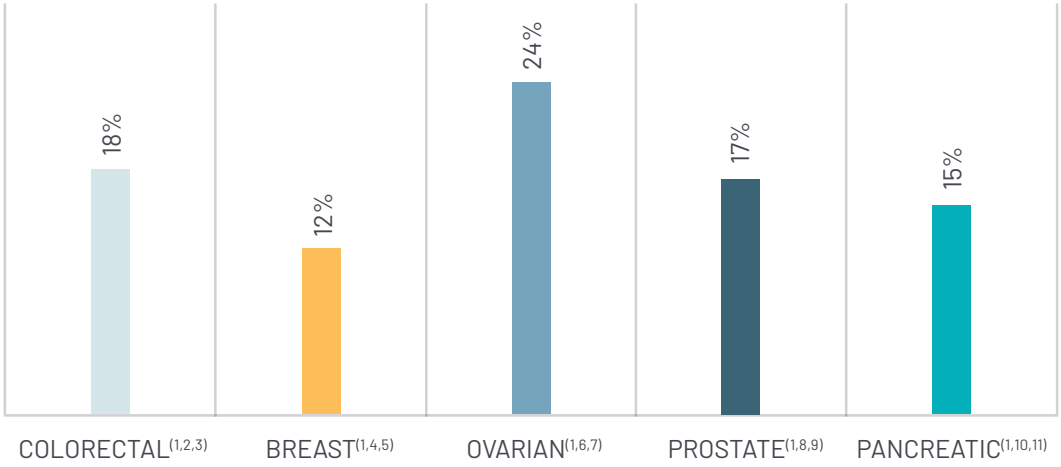
Sema4 Signal®: Personalizing cancer care with data-driven precision oncology solutions

Germline mutations play a significant role in the treatment and management of cancer

Pathogenic germline mutations are prevalent across diverse cancer types, genes, and patient ages

PERCENTAGE % OF GERMLINE MUTATIONS IN DIFFERENT TYPES OF CANCER



SEMA4 SIGNAL: COMPREHENSIVE SOMATIC AND GERMLINE OPTIONS FOR ALL CANCERS

Sema4 Signal Hereditary Cancer (HC)

Enables flexible testing options, including our 73 gene Comprehensive panel, each delivered via Sema4 Traversa™ genomic platform optimized for germline variants*

Sema4 Signal Whole Exome/Transcriptome Sequencing for all cancers (WES/WTS)

Delivers comprehensive genomic profiling, leveraging an ~18,500 exome and transcriptome platform to provide the most comprehensive molecular picture of a patient's cancer to inform the care plan today and provide insights for the future†

Sema4 Signal Solid Tumor Panel

Targets 161 of the most clinically relevant and actionable cancer genes using as little as 10-20ng of DNA for rapid turnaround time

*Cancer type-specific sub-panels available that include up to 113 total genes
†Germline actionable findings are reported; VUS are not reported

sema4

The value of Sema4 Signal Whole Exome/Transcriptome Sequencing (WES/WTS) for comprehensive genomic profiling

	Personalize clinical care **today**	Maximize clinical trial eligibility	Inform clinical care **tomorrow**
Tumor-normal advantage	• Germline variant detection • Gold standard tumor mutational burden (TMB)[12]	Germline-based clinical trial inclusion criteria	Novel germline and RNA-based biomarkers for risk stratification and treatment
Bringing RNA to the clinic	RNA sequencing increases detection of actionable fusions by >10%[13]	RNA expression to inform clinical trial inclusion	

Actionable insights based on clinical guidelines and scientific evidence[14]

165+
targeted genes mentioned in **NCCN guidelines®**[15] for cancer treatment, detection, prevention, and risk reduction

200+
genes included in **active clinical trials** in the United States

130+
genes associated with **diagnostic and prognostic relevance**

>99% Sema4 Signal Whole Exome/Transcriptome Sequencing can detect >99% of variants associated with FDA-approved therapies, standard-of-care treatments, and investigational therapies in clinical trials[16]

Sema4 Signal Whole Exome/Transcriptome Sequencing (WES/WTS) can help providers:

>> Determine diagnoses and prognoses

>> Identify and select available targeted therapies

>> Find current available clinical trials

>> Learn about certain hereditary contributions to various cancer types

Why Consider Whole Exome/Transcriptome Sequencing (WES/WTS) + Hereditary Cancer Solutions by Sema4

If your patient has	*Then Consider* Signal Whole Exome/ Transciptome Sequencing§	*Then Consider* Signal Hereditary Cancer Panel‖	*Why Consider*
A cancer with FDA-approved treatments based on germline biomarkers	✓	✓	Sema4 Signal Hereditary Cancer may identify actionable germline variants that cannot be detected with exome-based sequencing alone[17]
Met societal guidelines for hereditary cancer screening	✓	✓	
Everybody else	✓	–	Over 20% of patients with germline variants do not meet standard clinical guidelines for hereditary cancer[17]

Our unparalleled support includes:

- Genetic counseling for patients‖
- Patient education tools
- Extensive insurance network coverage & support
- Seamless workflow integration

To learn more about Sema4 Signal, please call **833-486-6260**, email **ClientServicesOncology@sema4.com**, or visit **sema4.com/oncology**

§Tumor-normal sequencing may reveal hereditary cancer predisposition as well as non-cancer genes, as per ACMG guidelines
‖ Genetic counseling available for germline findings

sema4

References:

1.Samadder NJ, Riegert-Johnson D, Boardman L, et al. Comparison of universal genetic testing vs guideline-directed targeted testing for patients with hereditary cancer syndrome. JAMA Oncol. 2021 Feb 1;7(2):230-237. doi:10.1001/jamaoncol.2020.6252

2.Nielsen SM, Dalton J, Hatchell KE, et al. Clinical impact of medical policy supporting universal germline testing for patients with colorectal cancer. Journal of Clinical Oncology. 2021 39:15_suppl, 10514-10514

3.Muller C, Nielsen SM, Hatchell KE, et al. Underdiagnosis of Hereditary Colorectal Cancers Among Medicare Patients: Genetic Testing Criteria for Lynch Syndrome Miss the Mark. JCO Precis Oncol. 2021;5:PO.21.00132. doi:10.1200/PO.21.00132

4.Beitsch PD, Whitworth PW, Hughes K, et al. Underdiagnosis of Hereditary Breast Cancer: Are Genetic Testing Guidelines a Tool or an Obstacle?. J Clin Oncol. 2019;37(6):453-460. doi:10.1200/JCO.18.01631

5.Yang S, Axilbund JE, O'Leary E, et al. Underdiagnosis of Hereditary Breast and Ovarian Cancer in Medicare Patients: Genetic Testing Criteria Miss the Mark. Ann Surg Oncol. 2018;25(10):2925-2931. doi:10.1245/s10434-018-6621-4

6.Walsh T, Casadei S, Lee MK, et al. Mutations in 12 genes for inherited ovarian, fallopian tube, and peritoneal carcinoma identified by massively parallel sequencing. Proc Natl Acad Sci U S A. 2011;108(44):18032-18037. doi:10.1073/pnas.1115052108

7.Norquist BM, Harrell MI, Brady MF, et al. Inherited Mutations in Women With Ovarian Carcinoma. JAMA Oncol. 2016;2(4):482-490. doi:10.1001/jamaoncol.2015.5495

8.Nicolosi P, Ledet E, Yang S, et al. Prevalence of Germline Variants in Prostate Cancer and Implications for Current Genetic Testing Guidelines. JAMA Oncol. 2019;5(4):523-528. doi:10.1001/jamaoncol.2018.6760

9.Pritchard CC, Mateo J, Walsh MF, et al. Inherited DNA-Repair Gene Mutations in Men with Metastatic Prostate Cancer. N Engl J Med. 2016;375(5):443-453. doi:10.1056/NEJMoa1603144

10.Esplin ED, Truty R, Yang S, et al. Effect of access to germline genetic testing on pancreatic cancer precision treatment across disease stage and ethnicity. J Clin Oncol. 2020;38(15_suppl):e16783-e16783

11.Salo-Mullen EE, O'Reilly EM, Kelsen DP, et al. Identification of germline genetic mutations in patients with pancreatic cancer. Cancer. 2015;121(24):4382-4388. doi:10.1002/cncr.29664

12.Büttner R, Longshore JW, López-Ríos F, et al. Implementing TMB measurement in clinical practice: considerations on assay requirements. ESMO Open. 2019;4(1):e000442. Published 2019 Jan 24. doi:10.1136/esmoopen-2018-000442

13.Solomon JP, Linkov I, Rosado A, et al. NTRK fusion detection across multiple assays and 33,997 cases: diagnostic implications and pitfalls. Mod Pathol. 2020;33(1):38-46. doi:10.1038/s41379-019-0324-7

14.Figures updated March 2022

15.NCCN Clinical Practice Guidelines In Oncology (NCCN Guidelines®) Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines) for Guideline Name V.X.2019. © National Comprehensive Cancer Network, Inc. 2020. All rights reserved. Accessed January 10, 2020. To view the most recent and complete version of the guideline, go online to NCCN.org. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility of their application or use in any way.

16.Chakravarty D, Gao J, Phillips SM, et al. OncoKB: A Precision Oncology Knowledge Base. JCO Precis Oncol. 2017;2017:PO.17.00011. doi:10.1200/PO.17.00011

17.Lincoln SE, Nussbaum RL, Kurian AW, et al. Yield and Utility of Germline Testing Following Tumor Sequencing in Patients With Cancer [published correction appears in JAMA Netw Open. 2021 Jul 1;4(7):e2123147]. JAMA Netw Open. 2020;3(10):e2019452. Published 2020 Oct 1. doi:10.1001/jamanetworkopen.2020.19452

About Sema4:

Sema4 is a patient-centered health intelligence company dedicated to advancing healthcare through data-driven insights. Sema4 is transforming healthcare by applying AI and machine learning to multidimensional, longitudinal clinical and genomic data to build dynamic models of human health and defining optimal, individualized health trajectories. Centrellis®, our innovative health intelligence platform, is enabling us to generate a more complete understanding of disease and wellness and to provide science-driven solutions to the most pressing medical needs. Sema4 believes that patients should be treated as partners, and that data should be shared for the benefit of all.

sema4