Sema4 Signal™ Hereditary Cancer

Delivered on our Traversa™
Comprehensive Genomic Platform

sema4

Genetic testing can provide actionable insight into a patient's risk for cancer

Hereditary cancer genetic testing can help determine if a patient carries an inherited genetic change that increases their risk for certain cancers.

Both positive and negative genetic test results may meaningfully impact a patient's medical management. The risks associated with certain cancer predisposition genes may warrant increased cancer screening beginning at an earlier age, preventative surgery, or medications. As genetic changes can be inherited results may also have implications for a patient's family members.

Who may benefit from hereditary cancer testing

Your patient may benefit from hereditary cancer testing if there is a personal or family history of:

- Early onset of common cancers, such as the diagnosis of breast, colon, or uterine cancer before the age of 50
- Multiple cancers, including ≥2 primary tumors or ≥10 colorectal polyps in the same person or cancer in ≥2 close relatives on the same side of the family
- Rare cancers diagnosed at any age, such as ovarian, pancreatic, male breast, metastatic prostate, or triple negative breast cancer
- Ashkenazi Jewish ancestry*

Please note, genetic testing may also be appropriate for individuals who have personal and family history that is not listed above. The Sema4 Family History Questionaire, found at sema4.com/hc-patient can help identify appropriate patients for testing. Patients may also be referred to a genetic counselor for a comprehensive risk assessment.

Genetic testing-informed treatment approach for patients with cancer

For patients diagnosed with cancer, genetic testing can help identify underlying hereditary causes. Sometimes, this information can help determine the best treatment approach, including eligibility for new therapies like PARP inhibitors, and identification of strategies to reduce the risk of developing other cancers.

Integrating hereditary cancer testing with our Sema4 Signal precision oncology offerings creates a holistic approach that can help inform better clinical decisions for personalized cancer care.

Finding an underlying hereditary cause for a patient's cancer can also provide important information for the patient's family members.

*Pre- and post-genetic counseling recommended if testing not performed within a research study

Sema4 Signal Hereditary Cancer

Sema4 Signal Hereditary Cancer offers a menu of panels to help you and your patients understand their individual risk for developing cancer or to inform treatment decisions. These tests are enabled through a set of digital tools and services to support easy identification, ordering, resulting, counseling, and access to testing.

Our hereditary cancer panels:

- 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)

Customizable panels and single gene testing available to fit your needs

Accelerate clinical care with Sema4 Signal Hereditary Cancer

Workflow Efficiency

- 14-21 days for all panels
- Ability to re-requisition panels within 120 days of initial receipt at no additional cost (please see website for details)
- Reflex option to add further tests available

Physician Support

- Patient identification tools to understand for whom genetic testing may be appropriate
- Panels customizable according to your patient's needs
- Easy-to-use test results, medical management recommendations when appropriate, and patient-friendly explanation
- Turnkey integration with your EMR or Sema4 Provider Portal

Patient Care

- Pre- and post-test educational materials accessible via Sema4 Patient Portal
- Post-test genetic counseling for patients at no additional charge‡
- Patient financial programs and support
- Resources to support cascade (variant) testing and family education‡
- VUS Family Studies Program available for eligible family members

‡Depending on result type ‡Applies for first and second-degree relatives only

Advanced Testing Technology with Sema4 Signal

- Multiple methods of analysis ensure one of the highest detection rates, delivered via our Sema4 Traversa™ comprehensive genomic platform with biobanking to support future clinical testing
- High-throughput, next-generation sequencing (NGS)
    - Full exon NGS with custom bioinformatics algorithm for copy number variant (CNV) detection
    - Targeted gene regions have an average depth of coverage ~200X, with >99.9% of regions covered at greater than 20X
- Long-range polymerase chain reaction is used to capture the functional gene for accurate analysis of the *PMS2* gene, which has a known pseudogene
- Multiplex ligation-dependent probe amplification (MLPA) is used to detect copy number changes for the *BRCA* and Lynch syndrome genes, along with the common *MSH2* inversion. MLPA and/or qPCR are performed to confirm CNVs
- Sanger sequencing is used to sequence exons not meeting a minimum of >20X read depth and/or to confirm sequence variants
- Confirmatory testing utilizing MLPA, qPCR, ddPCR and/or Sanger sequencing, depending on the specific variant

Sema4: Your partner in scientific and clinical excellence

Sema4 is a patient-centered health intelligence company dedicated to advancing the diagnosis, treatment, and prevention of disease through data-driven insights:

- Made up of an interdisciplinary team of scientists, data engineers, and clinicians from premier research and academic organizations with 150+ PhDs, MDs, and CGCs along with 175+ trained and certified lab technicians
- As one of the leading clinical genomics labs in the world, Sema4 has run >500,000 large NGS panels
- World-class leaders in data science, artificial intelligence and networking modeling with over 150 peer-reviewed publications

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 tumor profiling 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 patient and providers to drive better care across prevention, treatment, and long-term monitoring.

Seamless workflow with Sema4 Signal

Ordering hereditary cancer testing through Sema4 is simple. We accept blood and saliva samples, and provide specimen collection kits and requisition forms designed specifically for hereditary cancer testing

Upon ordering genetic testing for hereditary cancer

- Provide pre-test education so that the patient can understand the benefits and limitations of genetic testing. Certain insurers, including Cigna, may require pre-test genetic counseling
- Obtain a signed consent form from the patient
- Collect a blood or saliva sample from the patient
- Ship the specimen, completed test requisition form, and insurance information to Sema4. To arrange for specimen pick up through a local courier service, please call 833-486-6260
- Upon specimen receipt, Sema4 will initiate a benefits investigation to estimate patient out-of-pocket costs
- After testing is complete, you will receive a comprehensive results report via EMR, portal, or fax. Genetic counseling is also available depending on results

Billing and insurance information

Sema4 is committed to simplifying the payment process for both providers and patients

- We are contracted with the majority of payors covering >200m lives
- We verifiy eligibility, obtain precertification or pre-authorization for testing, and determine estimated potential out-of-pocket (OOP) expenses
- We contact patients if there are any OOP expenses
- We offer financial assistance and payment plans when eligible

Genetic counseling

At Sema4, we believe that genetic counseling plays an important role in supporting and educating patients throughout the testing process. Depending on the results, we offer tele-genetic counseling through experienced, board-certified genetic counselors. Counseling sessions include documenting a three-generation pedigree, review of results, identification of family members at risk, and recommendations for specialist referrals. If your patient goes through genetic counseling, you will receive detailed consultation notes via EMR, portal, or fax, that summarize the session.

Specimen requirements

Whole blood samples:

- Two EDTA (lavender top) tubes
- 5-10 mL of blood are required from the patient

Saliva samples:

- Saliva samples should be collected in Oragene DNA (OG-500) kits by DNA Genotek

Shipping requirements

- Sample should be kept and shipped refrigerated or at room temperature
- Do not freeze

Turnaround time

- ~2-3 weeks from receipt of specimen

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

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