MEDICOVER
GENETICS

SOLID TUMOR TESTS HISTOPATHOLOGY & GENETICS

Detect&Act

Patient Information

WHAT IS SOLID TUMOR DETECT&ACT

DETECT

Solid tumors are an abnormal mass of cells that may be benign (non-cancerous) or malignant (cancerous). They represent about 90% of adult cancers and can develop in many parts of the body. Tumor samples are analyzed to diagnose the cancer and identify its stage, which tells you how advanced the cancer is.

Two types of tests are used to diagnose a tumor: histopathology and genetic testing. **Histopathology is a cellular analysis of the tumor**, which involves examining cells and tissues under a microscope. **Genetic testing is a molecular analysis of the tumor**, which involves the study of DNA sequences to identify genetic alterations that have caused tumor formation.

We offer **multiple test options combining both histopathology and genetic testing** which can provide a complete picture of the tumor and could guide management plans, predict response to a therapy and possibly select appropriate clinical trials for new therapeutic solutions in your area.

ACT

In order to create the most appropriate treatment strategy, a complete tumor profile including its cellular and molecular features is needed. Customized treatment depends on the type, stage and genetic alterations in the tumor tissue. Targeted therapy or clinical trials can improve patient care and survival.

OUR SOLUTION

HISTOPATHOLOGY

Microscopic examination of the tumor sample provides specific information about the type and the stage of the tumor, its location and size and if it has spread to other healthy parts of the body.

GENETIC TESTS

Based on the histopathological findings, genetic analysis may be recommended. Your physician can choose from individual targeted-therapy tests, gene panels or a single comprehensive gene panel.

TEST OPTIONS

HISTOPATHOLOGY

GENETIC TEST
- Targeted-Therapy Tests
- Gene Panels
- Comprehensive Panel

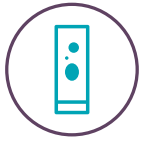
HISTOPATHOLOGY & GENETIC TEST

DIAGNOSTIC PROCESS

HISTOPATHOLOGY

Step 1: Biopsy
The tissue fragment is removed during surgery and sent to the laboratory for examination.

Step 2: Gross examination and tumor visualization
The tissue is examined macroscopically and relevant fragments are sampled. A variety of staining techniques are used to visualize cellular structure.



Step 3: Additional evaluation for breast and gastric cancers
HER2 protein levels are evaluated in breast and gastric cancers. This protein promotes cancer growth and HER2-positive cancers tend to be more aggressive, but treatments are very effective.

Step 4: Pathology report
A report is delivered to the ordering physician with a summary of pathology findings and recommendations for genetic testing, if appropriate.

SPEAK WITH YOUR DOCTOR ABOUT HEREDITARY CANCER PANELS
PREDICT&PREVENT TO TEST IF YOUR TUMOR HAS A GENETIC CAUSE

GENETIC TESTS

Step 5: Molecular analysis of the tumor tissue
Based on the pathology findings, targeted-therapy tests, gene panels or a comprehensive panel may be recommended to guide treatment and management plans or identify appropriate clinical trials.

Step 6: Final report with pathology and genetic test results
A final report is delivered to the ordering physician with a summary of all findings, treatment recommendations and relevant clinical trials.

TURNAROUND TIMES
Histopathology analysis: 7-10 working days
Genetic analysis: 7-20 working days

MEDICAL COUNSELLING
Medical counselling is an essential part of a diagnostic journey that we offer before and after testing. Our counsellors will discuss your medical history, explain the tests including risks and benefits and limitations of the diagnosis, and advise you on which tests to choose. Once results are available, they can also help with the interpretation of findings, treatment options and clinical trials. The goal of counselling is to provide you with greater knowledge of the results and the ability to make a more informed decision.

WHO COULD BENEFIT FROM THIS TEST
You may benefit from this test if you have been diagnosed with a solid tumor and require pathology and/or a genetic test analysis.

COMBINED DIAGNOSTICS
HISTOPATHOLOGY & TARGETED GENETIC TESTING

We offer the most up-to-date combination of histopathology markers and targeted genetic testing for different cancer types. Your physician will select the most suitable for you.

Bladder

CD44, CK20, CK7, GATA3, Ki67, p53

FGFR2, *FGFR3*

Breast

E-CD, ER, GATA3, HER2, Ki67, PR

BRCA1, *BRCA2*, *PIK3CA*, fusion genes, MSI

Colon

CDX-2, CK20, MLH1, MSH2, MSH6, PMS6, villin

BRAF, *KRAS*, *NRAS*, fusion genes, MSI

Gastrointestinal

CD34, c-KIT (CD117), desmin, DOG1, Ki67, S100

BRAF, *KIT*, *NF1*, *PDGFRA*, *SDHA*, fusion genes

Gastric

CDX-2, CG-A, CK20, CK7, HER-2, Ki67, SYN

fusion genes, MSI

Melanoma

HMB45, Ki67, Melan-A, p16, S100, SOX10

BRAF, *KIT*, *NRAS*, fusion genes

NSCLC

ALK, CG-A, EGFR, p40, PD-L1, ROS, SYN, TFF1

BRAF, *EGFR*, *ERBB2*, *KRAS*, *MET*, fusion genes

Ovarian

AFP, calretinin, EMA, ER, hCG, inhibin, napsin A, OCT3/4, p16, p53, PAX8, PR, SALL4, WT1

BRCA1, *BRCA2*, fusion genes, MSI

Pancreatic

CK19, CK20, CK7, MUC5AC

BRAF, *BRCA1*, *BRCA2*, *KRAS*, *PALB2*, *SMAD4*, fusion genes, MSI

Prostate

BCC-AMACR, CK34BE12, CK5/6, NKX3.1, p63, PSA, PSAP

ATM, *BRCA1*, *BRCA2*, *CDK12*, *CHEK2*, *FANCA*, *PALB2*, *PTEN*, *RAD51*, MSI

List of markers used to assess the tumor tissue using a technique called immunohistochemistry and visualized using a microscope.

List of genes analyzed for mutations, as well as fusion genes (gene made by joining parts of two different genes) and MSI (condition describing a predisposition to mutations).

Fusion genes: ALK, NTRK, RET, ROS; NSCLC, non-small cell lung carcinoma

GENETIC TESTS

	Your physician can choose from the following three options:	TARGETED-THERAPY TESTS	GENE PANELS	COMPREHENSIVE PANEL
	Number of genes	Up to 9 genes	Up to 29 genes	>500 genes
	Turnaround time	7-10 days	20 days	20 days
Actionability	**Approved treatments**	√	√	√
Actionability	**Available therapies**		√	√
Actionability	**Referral to clinical trial**		√	√
Markers analyzed	**Full-gene sequencing**	√*	√	√
Markers analyzed	**Fusion genes** the abnormal joining of parts of two different genes	√*	√	√
Markers analyzed	**MSI** microsatellite instability, an analysis of mutation frequency within microsatellites (short, repeated sequences of DNA)	√*	√	√
Markers analyzed	**SNV** single nucleotide variants, a DNA sequence variation that occurs when a single nucleotide in the genome sequence is altered (mutated)	√	√	√
Markers analyzed	**Other biomarkers** biological molecule that is a sign of a normal or abnormal process, or of a disease		√	√
Markers analyzed	**CNV** copy number variants, altered number of copies of a gene present in the genome			√
Markers analyzed	**TMB** tumor mutational burden, total number of mutations found in the DNA of cancer cells			√

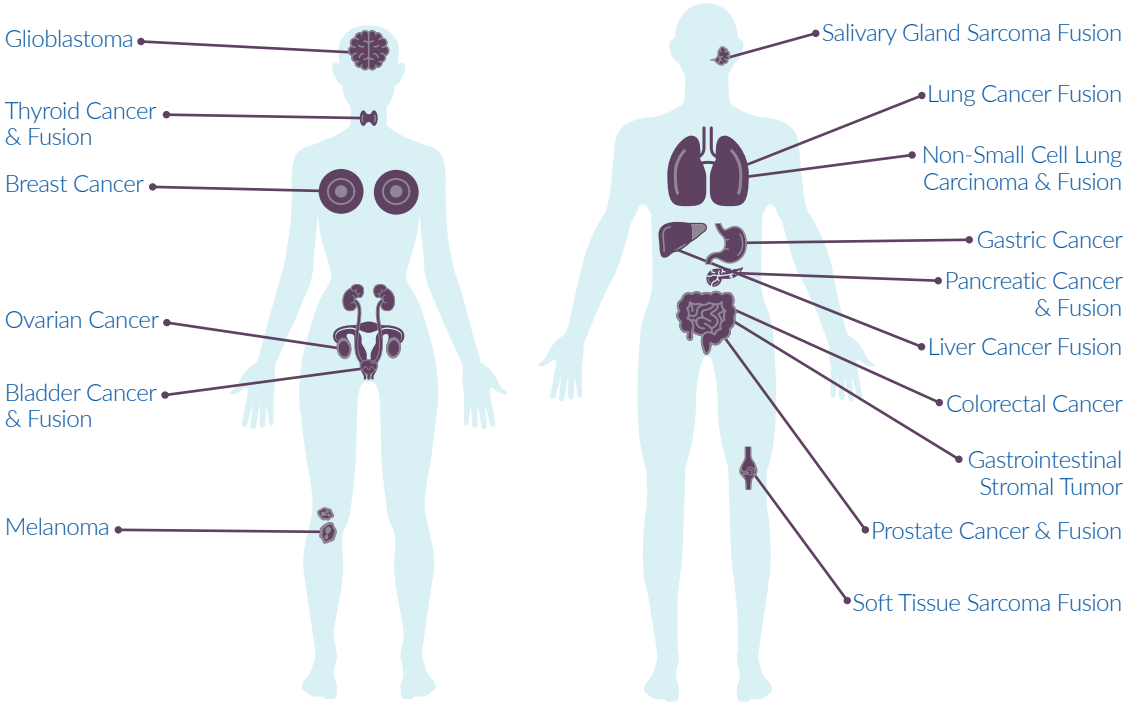
**In special cases only*

COMPREHENSIVE SOLID TUMOR PANEL

By analyzing >500 genes, this panel provides a complete molecular profile of the tumor by investigating genomic mechanisms involved in tumor formation, including microsatellite instability and tumor mutation burden analysis. This panel is recommended for patients with cancer of unknown primary origin and other rare cancers. The analysis also includes:

- 523 genes — Single nucleotide variants
- 59 genes — Copy number variants
- 54 genes — Fusion genes

SOLID TUMOR GENE PANELS & FUSION GENE PANELS



Speak with your doctor about Hereditary Cancer Panels Predict&Prevent to test if your tumor has a genetic cause

For the most up-to-date information about our tests, including technical information and gene lists, please visit:

www.medicover-genetics.com

WHAT ARE THE POSSIBLE OUTCOMES OF THE TEST

A diagnostic report outlining the results of the histopathology and/or the sequencing results from genetic testing is provided to help your doctor with diagnosis and treatment.

Histopathology report includes macroscopic and microscopic descriptions of the tumor sample, results of all tests conducted, and conclusions based on the final histopathological diagnosis. Conclusions include details about the tumor's features, and potential recommendations, with the suggestion to perform genetic analyses included if necessary.

Genetic test report includes changes in DNA sequence alterations including single nucleotide variants, copy number variants (only for comprehensive panel) and fusion genes, as well as tumor mutational burden and microsatellite instability, as well as the effect on carcinogenesis (process by which normal cells are transformed into cancer cells). Possible therapy options and clinical trials relevant to your location will be listed.

Targeted-therapy analysis, solid tumor panels and the comprehensive tumor panel are covered as part of the genetic test report where applicable.

- **Targeted-therapy analysis** identifies specific genomic changes that are relevant to therapy with approved therapeutic products (targeted therapies).
- **Solid tumor panels and comprehensive tumor panel** may identify additional genomic findings that are not prescriptive or conclusive for use of any targeted therapies. Use of these panels does not guarantee you will be matched to a treatment. A negative result does not rule out the presence of an alteration.

WHY US

- A network of +100 histopathologists and medical institutions **makes us a leader in pathology and genetic testing** in >10 countries with foundations dating back to 1998
- Home to digital scanners, allowing a **faster and more accurate diagnosis**
- A clinical team comprised of scientists, physicians and medical geneticists, several with **>20 years of experience** in genetic testing, assuring meaningful and comprehensive genetic tests
- **Up-to-date diagnostic algorithms** and gene panels based on current scientific literature and international guidelines
- Expertise in gene variant analysis ensuring **"no variant left behind"**
- Cutting-edge technology in sequencing and laboratory methods allows for **short turnaround times**
- **Quality** assessed by several certifying bodies, including EFI, DIN EN ISO 15189 accreditation for medical laboratories, DIN EN ISO/IEC 17025 accreditation for testing and calibration laboratories and a generally valid GMP (Good Medical Practice) certificate
- **Data privacy** is your right and our priority

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