MEDICOVER
GENETICS

SOLID TUMOR TESTS HISTOPATHOLOGY & GENETICS

Detect&Act

Physician Information

WHAT IS SOLID TUMOR DETECT&ACT

DETECT

Close to 20 million new cancer cases and 10 million deaths have occurred annually in recent years. Solid tumors represent ~90% of adult cancers and millions of histopathology slides are analyzed annually revealing information crucial for cancer diagnosis and staging. In up to 40% of patients, complex genomic alterations are identified which can serve as biomarkers to predict response to a specific therapy and/or prognosis.

Histopathological examination and genetic testing can determine the tumor profile and suggest appropriate management or treatment plans, when available.

We offer both histopathology and molecular genetic analyses for solid tumors.

ACT

Characterizing the cellular and molecular changes in a solid tumor is critical for treatment strategy. Customized treatment depends on the type, severity (stage) and the specific genetic alterations in the tumor tissue. Genotype-directed therapy or genotype-matched 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

CANCER TYPES COVERED BY OUR PANELS

BLADDER CANCER

BREAST CANCER

COLORECTAL CANCER

GASTRIC CANCER

GASTROINTESTINAL STROMAL TUMOR

GLIOBLASTOMA

LIVER CANCER

LUNG CANCER

MELANOMA

OVARIAN CANCER

PANCREATIC CANCER

PROSTATE CANCER

SALIVARY GLAND SARCOMA

SOFT TISSUE SARCOMA

THYROID CANCER

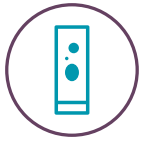
DIAGNOSTIC PROCESS

HISTOPATHOLOGY

Step 1: Biopsy
The tissue fragment is removed from the patient during surgery and sent to the laboratory for microscopic examination to determine the diagnosis.

Step 2: Gross examination
The tissue is examined macroscopically and relevant fragments are sampled.

Step 3: Conventional and complementary stainings
- **Hematoxylin and eosin (H&E) staining:** to visualize overall cellular structure
- **Special stains:** to visualize cell morphology, detect and localize subcellular components
- **Immunohistochemistry:** to detect specific protein markers that support tumor classification, assessment of prognostic and predictive factors, and identification of biomarkers for targeted therapy



Step 4: HER2 evaluation for breast and gastric cancers
HER2 levels are evaluated using silver *in situ* hybridization (SISH).

Step 5: Pathology report
A report is delerived to the ordering physician with a summary of pathology findings and recommendations for sequencing, if appropriate.

SEQUENCING

CONSIDER ADDITIONAL HEREDITARY CANCER PANEL TESTING

Step 6: Molecular diagnostic analysis of the tumor tissue
Based on the pathology findings, specific sequencing analysis may be recommended.

Step 7: Final report with pathology and sequencing results
A final report is delivered to the ordering physician with a summary of all findings, treatment recommendations and relevant clinical trials.

TISSUE REQUIREMENTS
Tissue fragments from a biopsy:
- Stored in 10% formalin (stable for 24-72 hrs)
- Embedded in paraffin blocks (stored in dry and dark conditions)

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

MEDICAL COUNSELLING
We can provide expert medical interpretation of the results for the specialist physician and the patient, where needed. This includes advice on which tests to choose, interpretation of findings, treatment options and relevant clinical trials.

WHO COULD BENEFIT FROM THIS TEST
Patients who are diagnosed with a solid tumor and require a pathology and/or genetic test analysis.

COMBINED DIAGNOSTICS
HISTOPATHOLOGY & TARGETED GENETIC TESTING

Specific tumor classification using IHC

The standard markers are listed for each cancer type. Additionally, the pathologist may decide to use extra markers for thorough assessment of a tumor in some cases.

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

Special stains used for broad tumor identification:

Gram, Ziehl Nielsen, Giemsa, PAS, Masson's Trichome, Silver, GMS II, Alcian Blue ph 2.5, Amylase, Perls, Weigert Van Gieson, Congo Red

Fusion genes: ALK, NTRK, RET, ROS; IHC, immunohistochemistry; MSI, microsatellite instability; NSCLC, non-small cell lung carcinoma

GENETIC TESTING 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			√

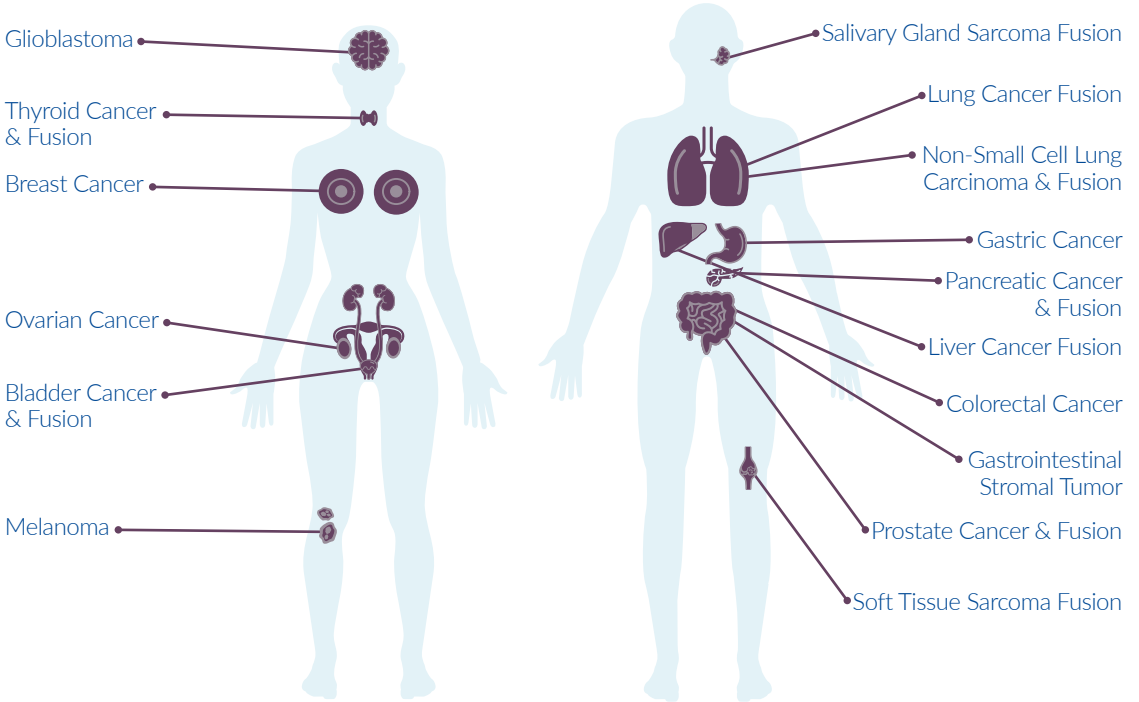
**In special cases only*

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



Consider Hereditary Cancer Panels Predict&Prevent if your patient's 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.

Pathology report includes macroscopic and microscopic descriptions of the provided sample, results of all tests conducted, and conclusions based on the final histopathological diagnosis. Conclusions include classification of lesions, WHO disease code, and recommendations, with the suggestion to perform sequencing analyses included if necessary.

Sequencing report includes changes in DNA sequence (variants) 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. Possible therapy options and clinical trials relevant to the patient's location will be listed.

Targeted-therapy analysis, solid tumor panels and the comprehensive tumor panel are covered as part of the sequencing 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 a patient will be matched to a treatment. A negative result does not rule out the presence of an alteration.

CHOOSING THE RIGHT TEST FOR YOUR PATIENT

We can discuss specific cases to help you select the most appropriate test for your patient and allow you to differentiate between our tests. We provide guidance during the entire diagnostic journey.

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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