

TUMOR-DIAGNOSTICS

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SUMMARY

- Molecular profiling of 551 cancer-relevant genes
- Complete sample-to-diagnosis pipeline
- Reliable detection of variants down to 20% tumor content
- Only 100 ng of starting material required
- Medical report with clinical interpretation as treatment decision support
- Valuable data for clinical studies

BACKGROUND

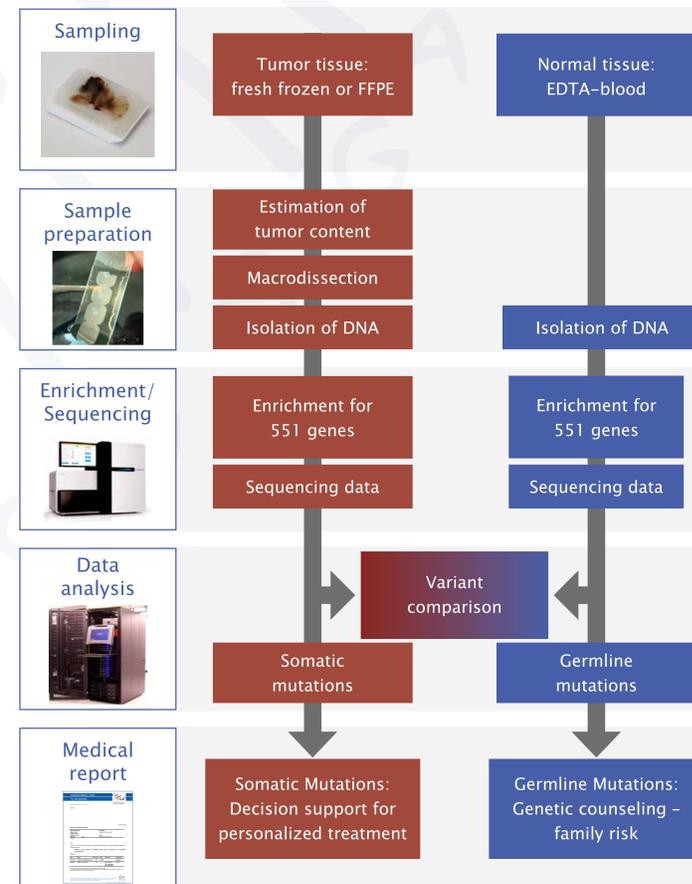
An increasing number of targeted anti-cancer drugs are becoming available, raising the requirement for comprehensive molecular profiling of tumors.

Next-generation high-throughput sequencing (NGS) offers the opportunity to analyze a huge number of genes from a small quantity of starting material.

We have developed a complete clinical diagnostic pipeline for the analysis of 551 cancer-relevant genes using next-generation sequencing.

Comprehensive molecular profiling using panel-based next-generation sequencing can identify therapeutic targets in tumor patients.

WORKFLOW



We use fresh frozen as well as FFPE tumor tissue. The clinician may send whole paraffin blocks or unstained slides. We also accept extracted DNA of sufficient quality. Usually, DNA from blood is used as normal tissue.

Tumor tissue is cut, stained and reviewed by an experienced pathologist. After estimating the tumor content, the tumor is macrodissected to achieve a high tumor content (must be > 20 %) in the DNA sample.

Enrichment for 551 cancer relevant genes using a custom Agilent SureSelect Kit. Sequencing on Illumina HiSeq 2500 using 2x100 bp paired end reads. Mean coverage depends on the estimated tumor content and is usually 500x to 1500x.

Variants are called and annotated using a custom bioinformatic pipeline. Datasets from normal and tumor tissue are compared to find somatic mutations even in samples with down to 20 % content or multiple subclones. The normal tissue dataset can also be analysed for pathogenic germline mutations.

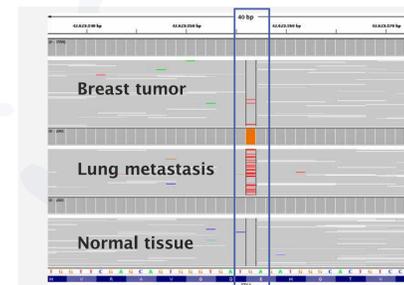
Reports are written by our team of expert scientists and physicians. All somatic mutations are reported, actionable mutations are emphasized and annotated with additional information for the treating oncologist. Germline mutations are reported separately and should be communicated by a geneticist or a genetic counselor.

SAMPLE CASE

- 46 year old patient with locally recurrent breast cancer and lung metastasis histologically defined as adenocarcinoma of unknown primary (possibly stomach).
- Panel-based sequencing of a lung biopsy and a local breast cancer metastasis.



Somatic activating mutation E17K in AKT1. The mutation is present in the tumor, but not in the normal tissue (blood).



A nonsense mutation in STK4 is present in a small (but detectable) subclone of the breast tumor (Allele frequency 3 %). The same mutation is more frequent in the lung metastasis (Allele frequency 29 %).

RESULTS

- Lung metastasis is clonally related to the recurrent breast cancer (same origin).
- Activating AKT1 mutation conferring resistance to tamoxifen
- TP53 mutation, studies show lower benefit from anthracycline-based therapies