CeGaT

Research &
Pharma Solutions

Liquid Biopsy Exploratory

Bioinformatic Note

Liquid Biopsy Exploratory

The blood-based analysis of circulating tumor cells or tumor-derived nucleic acids is referred to as liquid biopsy. The main target of this analysis is cell-free DNA (cfDNA), which is released into the bloodstream by necrotic and apoptotic cells. Elevated levels of cfDNA are found in patients with cancer and other types of diseases. Since only a small fraction of the circulating DNA is derived from the tumor (circulating tumor DNA = ctDNA), highly sensitive detection methods are required.

Liquid biopsy applications are manifold, with several striking advantages over conventional tissue analysis. Most importantly, the analysis of liquid biopsies is based on a simple blood draw and, thus, easily repeatable.

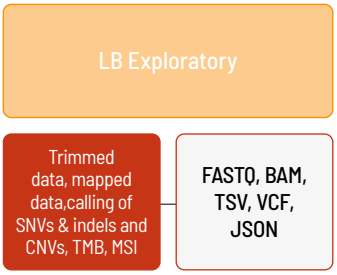
Application areas of liquid biopsies:

- Monitoring of tumor disease
- Monitoring of treatment response
- Patient stratification and treatment selection
- Detection of minimal residual disease
- Early detection and profiling of resistance to therapy

We offer three different liquid biopsy products:

- LB Target
- LB Focus
- LB Exploratory

In the following, we will focus on the bioinformatic analysis of the LB Exploratory (TSO500) product:



Only one level of bioinformatic analysis is available for the LB Exploratory (TSO500) product.

Bioinformatic Analysis

LB Exploratory uses the Illumina TruSight Oncology 500 (TSO500) ctDNA assay. The assay comprises the enrichment and the analysis with their own bioinformatics pipeline. The quality of FASTQ files is analyzed. Subsequently, the sequencing data are processed.

The project report generated at the end of each project provides information for every sample about the laboratory protocol, including data about quality control of the starting material, library preparation, sequencing parameters, and the Q30 value of the sequencing. The number of sequenced fragments and bases, the sequence length and quality of the reads, and the averaged GC content over all samples is reported.

The raw data, such as FASTQ and BAM files, and the analysis results are delivered. For every sample, various files are generated, which are explained briefly.

One TSV file contains the combined variant output. In this file, variants and biomarkers, such as small variants (SNVs and indels), gene amplifications, TMB, MSI, fusions, and splice variants are included. Besides the variants and biomarkers, this file contains analysis and sequencing run details. As TSO500 can be used with DNA and/or RNA, some of the columns might be empty, depending on the used input material. The TMB and MSI evaluation can be performed without the need for both a tumor and a normal sample.

A metrics output in TSV format describes all relevant quality control metrices for all samples.

A VCF file with SNVs and small indel calls is provided for DNA samples. This file contains a genotype call for every genomic position that is analyzed, including all positions where the sample does not differ from the reference sequence. In addition to the VCF file, the merged small variants annotated file provides variant annotation information in JSON format. It includes data from ClinVar, COSMIC, dbSNP, gnomAD, MITOMAP, 1000 genomes, TOPMed, ClinGen, DGV, ExAC, OMIM, and phyloP.

The TMB trace TSV file describes all relevant variants for the TMB estimation. A VCF file includes all copy number variants.

A raw fusion calls file in CSV format is provided for RNA samples. This file includes all called fusions. Additionally, a raw splice variant calls VCF file is delivered.

For your convenience, the values for TMB, MSI, and the number of CNVs are provided in the project report for every sample.

Please note that TSO500 is also offered for tissue samples or already isolated DNA.

In contrast to the other LB products, LB Exploratory does not require any previous knowledge of, e.g., the tumor or variants of interest. The application areas range from patient stratification to detection and characterization of therapy resistances to the detection of minimal residual disease after an operation.

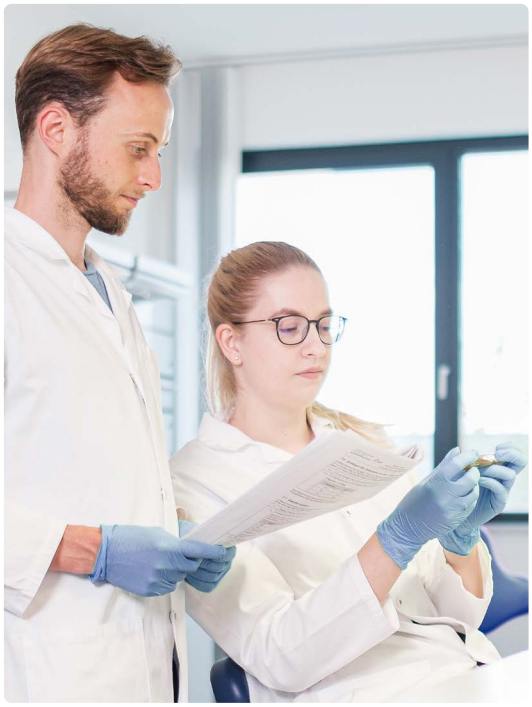
About Us

CeGaT was founded in 2009 in Tübingen, Germany. Our scientists are specialized in next-generation sequencing (NGS) for genetic diagnostics, and we also provide a variety of sequencing services for research purposes and pharma solutions. Our sequencing service portfolio is complemented by analyses suited for microbiome, immunology, and translational oncology studies.

Our dedicated project management team of scientists and bio-informaticians works closely with you to develop the best strategy to realize your project. Depending on its scope, we select the most suitable library preparation and conditions on our sequencing platforms.

We would be pleased to provide you with our excellent service.
Contact us today to start planning your next project.

For more details please visit
www.cegat.com/rps



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