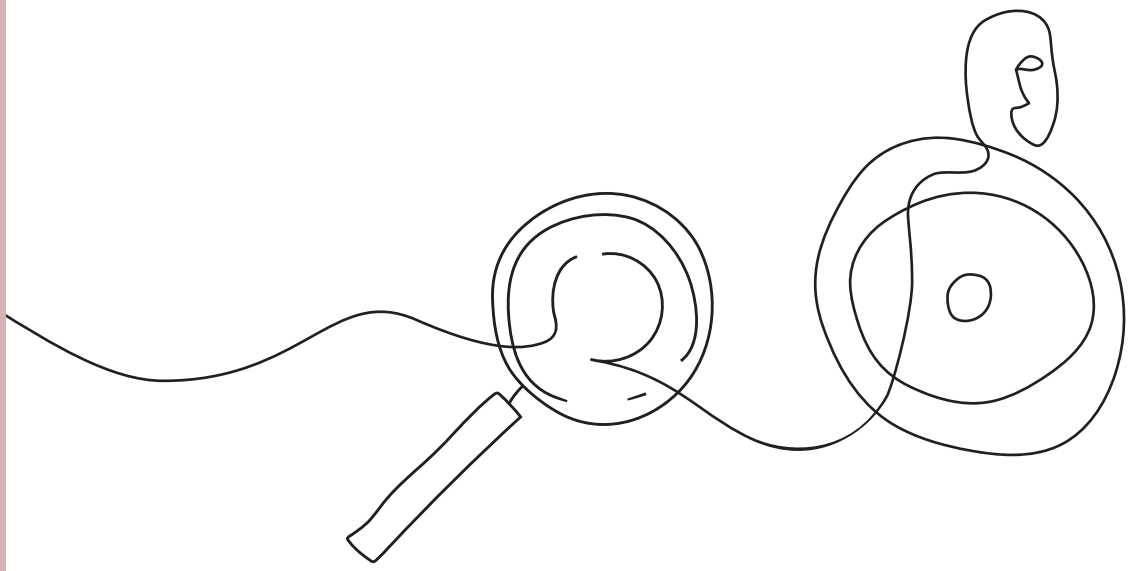
prime DX

PRECISION INDIVIDUALIZED MEDICINE



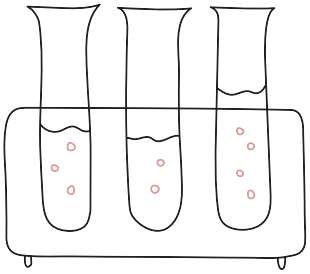
Genekor

Committed to Biotechnological Innovation

The prime DX new technology for tumor molecular profiling is compatible with FFPE, as well as PLASMA.

Prime DX is designed to give the physician a comprehensive outlook on treatment options related to

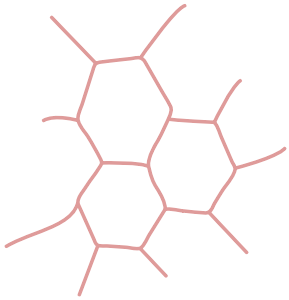
» Targeted therapy
» Immunotherapy
» Chemotherapy



Clinical Application	Type of Drugs	Indicator	Indicator Dimension
1. Prediction for **Targeted Treatmets**	**171 different treatments**	Target point mutation (Tissue/blood) (eg: EGFR L858R, EGFR exon 19 Del, etc.)	Somatic variation ---------- Germline variation (liquid)
2. Prediction for **Immunotherapy**	**11 different treatments**	TMB/MSI/PD-L1 amplification/PBRM1 negative mutation	Somatic variation
3. Prediction for **Chemotherapy**	**23 different treatments**	Pharmacogenomics site (eg: rs8175347 of UGT1A1 relating to Irinotecan)	Germline variation

The new **prime DX** assay is a **1021-gene NGS Panel** that also analyzes immunotherapy biomarkers MSI, TMB and PD-L1. In addition, it includes Loss of Heterozygosity (LOH) analysis, which can be used as biomarker for PARP inhibitor treatment. It is one of the most detailed, sensitive and specific tests for tumor biology configuration, enabling physicians to **plan an efficient treatment strategy for the patient, including immunotherapy, chemotherapy, PARP inhibitors and clinical trial participation compatibility.**

Prime DX test is recommended in the following cases:



» Tumors with no standard treatment available
» Patients with advanced solid tumors
» Second-line or post-line treatment
» Rare Tumors
» Tumors of unknown primary origin
» Tumors with many available treatment options, where the physician must clarify the most effective one based on the individual tumor profile of each patient.

Also,

» For the identification of immune response biomarkers, in order to predict if an immunotherapy plan would be a suitable plan or/and in order to create an efficient immunotherapy plan.

The selection basis of the 1021 gene list is based on:

✓ NCCN guidelines + FDA + EMA
✓ Authoritative international public database

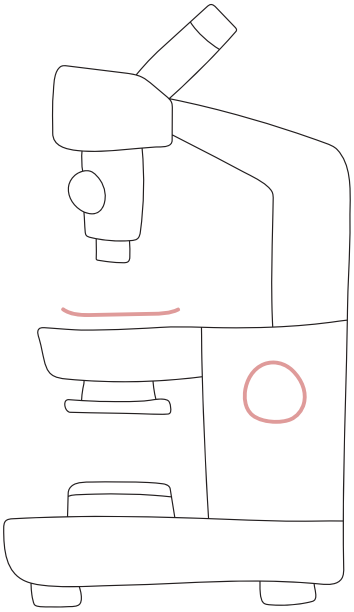
- No. of genes: **1021 genes**
- Target size: **1.6 Mb**
- Target regions:

✓ **Whole exons**
- 4847 exons of **312 genes**

✓ **The region of introns, promoters and fusion breakpoints**
- **38 genes:** 54 intronic regions of 26 genes + breakpoint regions of 12 genes

✓ **Promoter region or other non-coding region**
- TERT, PMS2, BCL2L11

✓ **Coding regions**
- 1778 coding regions of **709 genes**



prime DX Liquid
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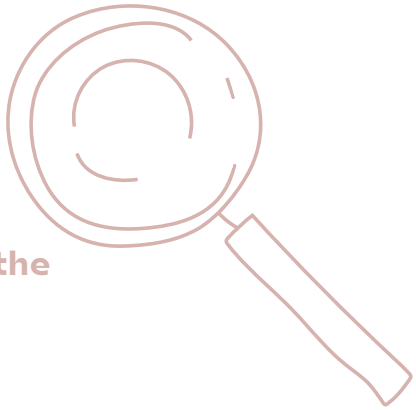
Molecular Profiling of the tumor using liquid biopsy

Having the option of performing prime DX on liquid biopsy samples, provides a more rapid and clinically actionable tool to the treating physician to assess the tumors' molecular profile and to identify the most effective treatment.

The new **prime DX Liquid** assay is also a **1021- Gene panel** that analyzes the two immunotherapy biomarkers MSI and TMB, enabling physicians **to plan an efficient treatment strategy for the patient, including immunotherapy, chemotherapy, PARP inhibitors and clinical trial participation compatibility.**

Germline Gene Analysis

prime DX Liquid, also, analyzes genes involved in the genetic predisposition to cancer, giving information to the physician about the probability of a hereditary cancer syndrome.



Prime DX Liquid is recommended in the following cases:

- When there is not enough FFPE tissue or recent biopsy
- When the quality of the tissue is poor (ex. bone biopsy)
- When there is a metastatic and / or multifocal disease
- To evaluate patient's response / resistance to treatment
- When the patient relapses and there is a need to analyze the molecular profile with no recent biopsy available

The Technology

The new prime DX assay is based on advanced molecular technology using hybridization capture NGS with UMIs. The test utilizes the Oncology Multi-Gene Variant Assay (GenePlus) which is a qualitative *in vitro* diagnostic test (CE-IVD) that detects variants in 1021 tumor-related genes and gene rearrangements / fusions in 38 genes.

It analyzes biomarkers for immunotherapy response, including detection of HLA and biomarkers for chemotherapy response.

MGI-DNBSEQ-G400 is a CE-IVD platform which allows the simultaneous processing of multiple samples with high sensitivity and specificity thus producing faster, reliable results at a lower cost.

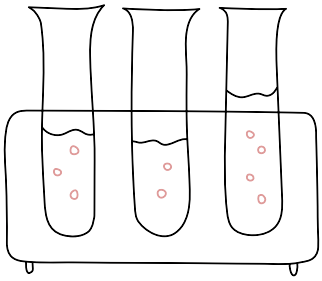
Clinical value	Biomarker	1021 Panel	Level of Evidence	Source of evidence
Targeted therapies	"EGFR, ROS1 , MET, ALK , RAS, BRCA1/2 , FGFR2/3 , RET, NTRK1/2/3, IDH1 , ERBB2, BRAF, KIT, PDGFRA, PIK3CA, HRR gene"	YES	Strong	FDA / NCCN
	LOH *FFPE samples only	"YES , Results include loss of heterozygosity (LOH) for ovarian cancer patients"		
Chemotherapy drugs	19 polymorphism variants related to chemotherapy drugs	YES	Moderate	"J Clin Oncol. 2020 Feb 20;38 (6): 548-557"
Immunotherapy	TMB / MSI (Pan - cancer)	YES	Strong	FDA / NCCN
	HLA type (Pan - cancer)	YES	Moderate	"Science. 2018 Feb 2;359 (6375): 582-587"
	Biomarkers affecting the immunotherapy treatment response (reporting on positive & negative correlations).	46 genes with positive and negative correlation	Moderate	"Ferdinandos Skoulidis 2019 ASCO Abstract 102, ESMO 2017 Abstract # 1138"

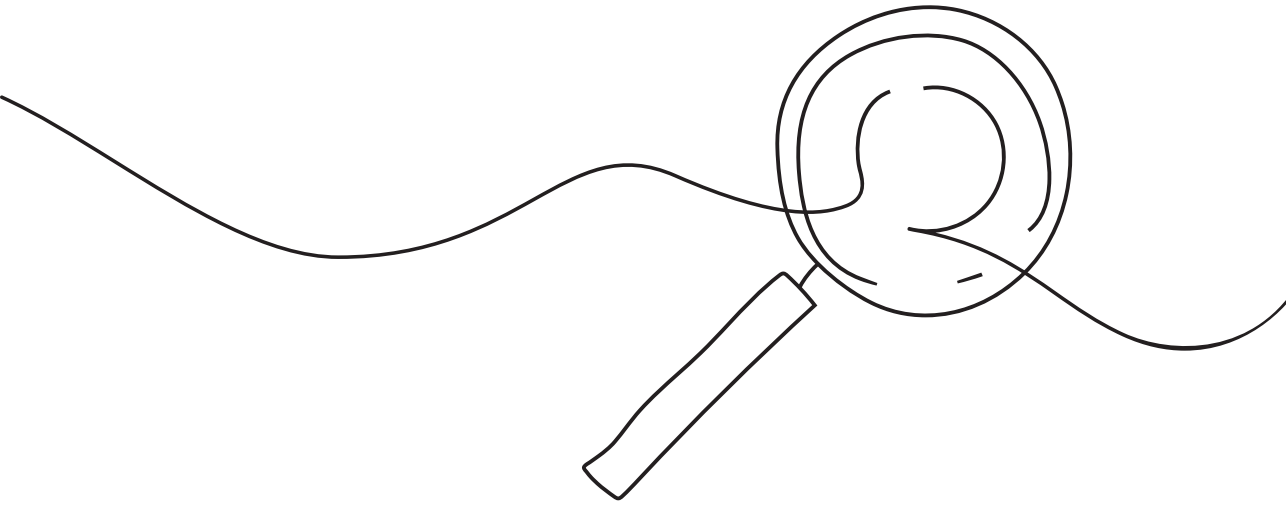
primeDX Gene Panel

Why is the NGS analysis of multiple genes necessary?

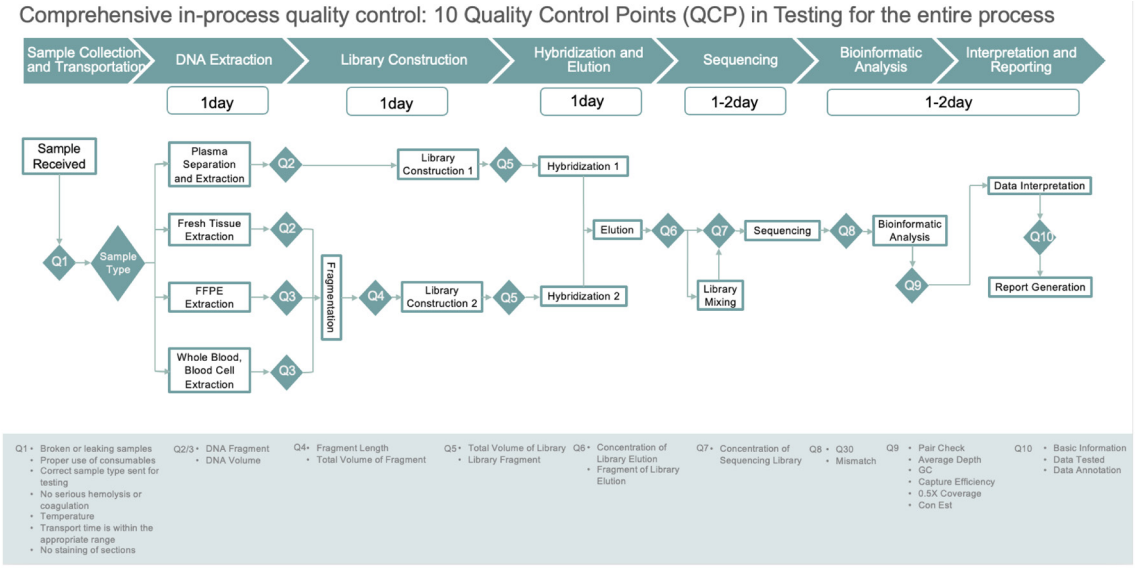
- Quantity and quality of information
- Reduced time
- Reduced cost

A multi-gene panel results in the production of a large volume of multilevel information useful for individualized treatment of patients. Thus, it increases the likelihood of finding a therapeutic target for a patient with on-label treatment, off-label treatment and/or participation in clinical trials, using minimum amount of tissue or a liquid biopsy sample and analyzing several genes simultaneously, faster and at lower cost.



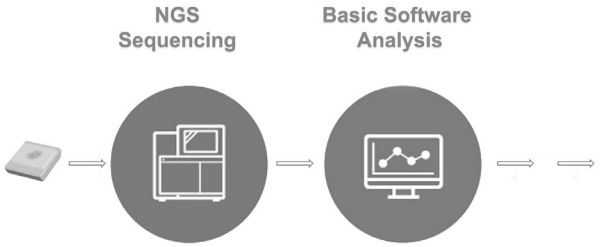


Workflow and Quality Control Points



LAB vs LAB

Other Labs



VS

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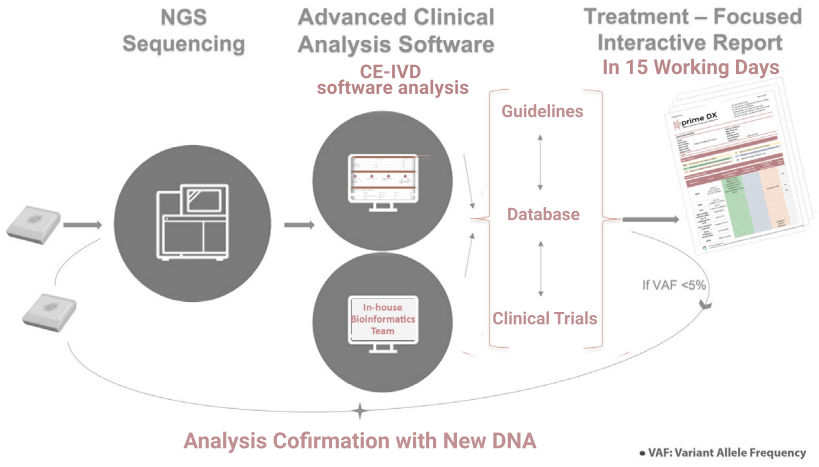


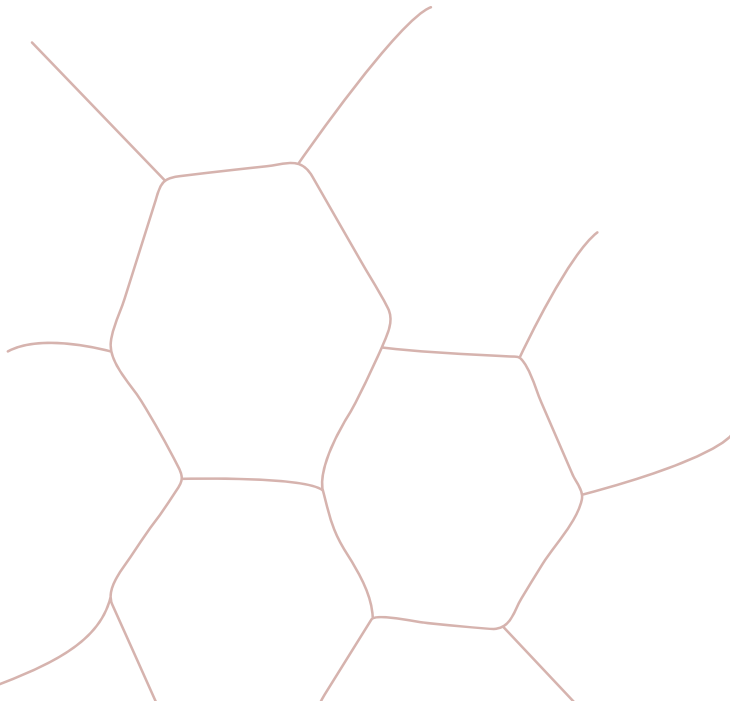
Besides the state-of-the-art technology, the scientific team of the lab plays a very important role, since it is responsible for producing thorough, fast and reliable results.

Genekor's team consists of very experienced scientists, that are dedicated in finding dependable solutions for physicians and their cancer patients, have multiyear experience in the cancer field and have participated in numerous international publications.

During the analysis there are a few very important aspects of the process that differentiate Genekor lab from the others:

- Comprehensive data analysis and management platform, with integrated high-performance hardware using CE-IVD software.
- All positive results with VAF < 5% are validated by an alternative method analysis.
- The in-house bioinformatics team enhances the analysis process by providing computational pipelines for comprehensive reporting with high clinical value
- The generated report is interactive, allowing the physician to go through all the necessary information related to gene alterations, on-label and off-label treatment options and ongoing clinical trials.

Finally, Genekor offers scientific support and genetic counselling before, throughout and after the examination process.



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