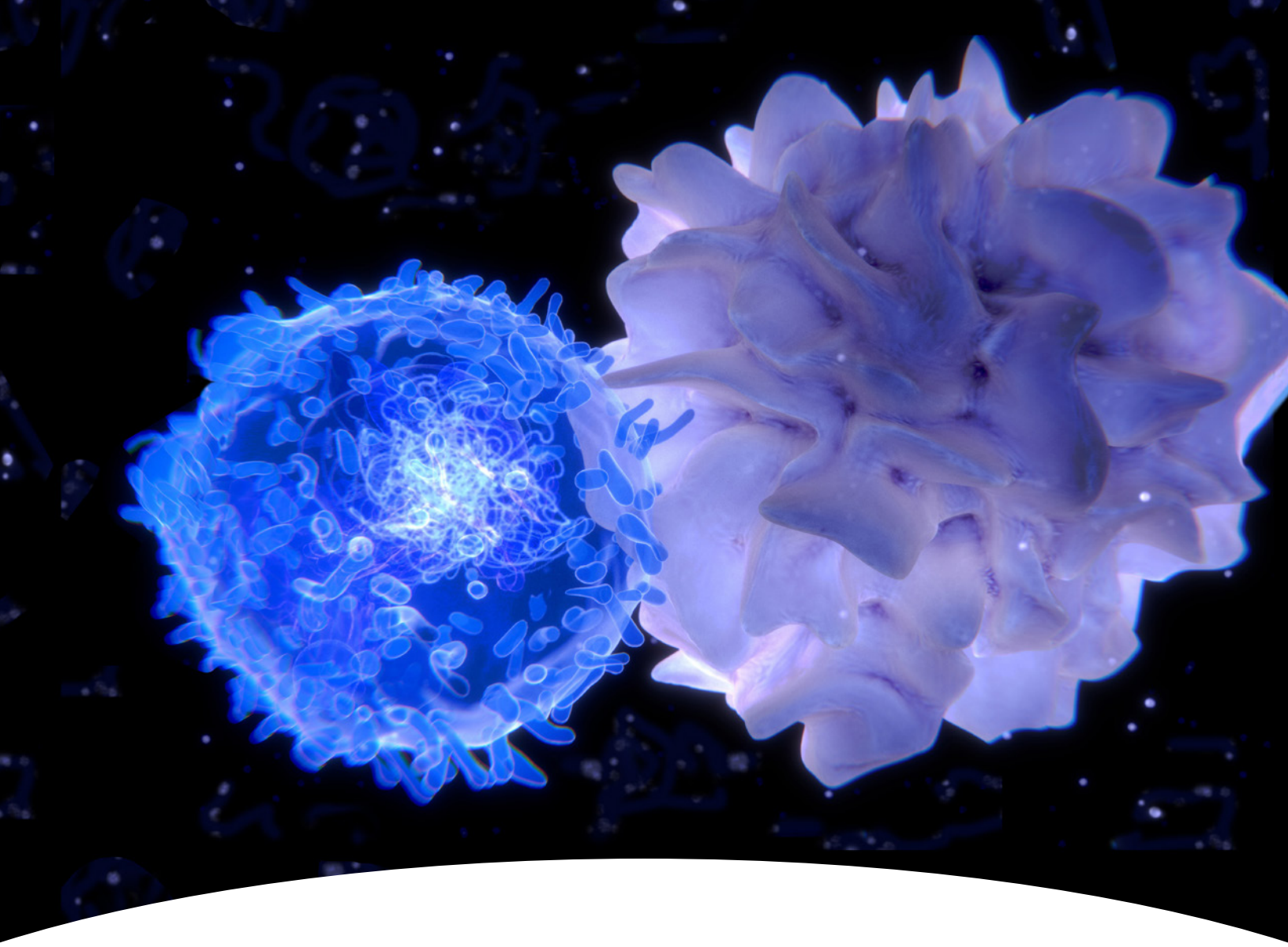

Biomarker Discovery Solutions

ACE ImmunoID Platform for Tumor Immunogenomics

Personalis®

Precision Genomics for Immuno-Oncology

Personalis®

When one biomarker doesn't tell the whole story

Understanding response to cancer immunotherapies involves examining the interaction between mechanisms of tumor escape, the tumor microenvironment, and neoantigens. Gaining these molecular insights often requires analyzing data sourced from multiple platforms and vendors. When samples are precious and limited, researchers need a way to simplify.

That's where Personalis can help. Our ACE ImmunoID Platform requires one paired tumor and normal sample, and combines whole exome and transcriptome sequencing with advanced analytics for comprehensive tumor immunogenomics to better inform your strategic decisions.

Paired Tumor/Normal Sequencing

ACE ImmunoID:
ACE Cancer Exome and ACE Cancer Transcriptome

Comprehensive Analytics

ACE ImmunoID:
Immunogenomics and Neoantigen Discovery Reports

More Informed Biomarker Strategy

Identify resistance drivers and multidimensional biomarkers

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What is ACE?

ACE is our patented Accuracy and Content Enhanced (ACE) Technology. ACE improves processes from nucleic acid extraction, to sequencing, to variant annotation, to analytics, for coverage that is both deep and more complete.

Nucleic Acid Extraction and Sequencing

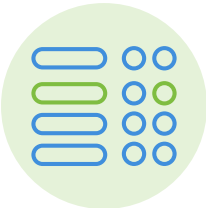
- Sample-sparing preparation
- DNA/RNA co-extraction
- Optimized protocols for diverse sample types: FFPE, FNAs, PMBCs, and whole blood
- Enhanced assays for more complete coverage

Alignment and Variant Discovery

- Improved alignment and reference sequence
- Accurate variant detection (SNVs, indels, novel fusion events) and gene expression

Variant Annotation

- Up-to-date and complete databases
- Validated and published assays[1]



Bioinformatics and Analytics

- Diversity of data format and delivery
- Focused reports on areas critical to immuno-oncology

Reference:
1. Ashley, E. *Nature Reviews Genetics.* Towards Precision Medicine. Vol 17 Sept 16 (507–522).

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ACE Cancer Exome

The ACE Cancer Exome outperforms conventional exome assays by augmenting coverage across genes poorly covered by standard approaches.

Conventional sequencing has gaps that result in possible missed variants as seen in Figure 1.

Figure 1: Coverage of STK 11 with ACE Supplementation.

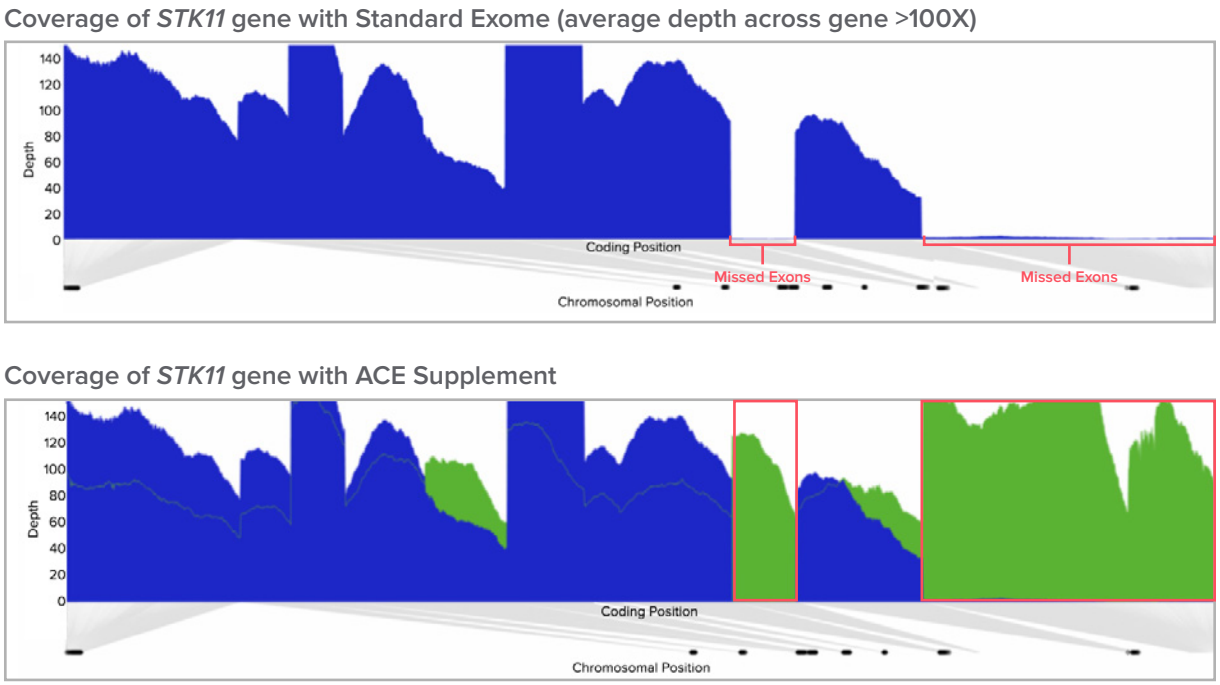


Figure 1: ACE augments these sequencing gaps (green regions), providing you with more complete coverage across the entire gene. The ACE Exome coverage includes both the blue and green regions of the gene as seen above.

Key features:

- Broad coverage across all exons (>20,000 genes) and enhanced coverage of >8,000 biomedically-important genes, including >1,400 cancer-related genes
- Augmentation and repair of coverage gaps, especially in high-GC regions
- Improved somatic variant detection of SNPs and indels

ACE Cancer Transcriptome

The same accuracy and coverage improvements are available through the ACE Cancer Transcriptome.

Many clinical studies depend on tissue archives that have been fixed using FFPE procedures. This preservation process makes it difficult to obtain a pure sample and often leads to RNA degradation. To overcome this challenge, Personalis has developed an exome-capture transcriptome protocol based on our ACE Technology that allows us to produce high-quality transcriptome sequencing results from challenging FFPE samples (Figure 2).

Key features:

- Multiple probes target each transcript, capturing transcripts even when the poly-A tail is lost due to RNA degradation, making it ideal for cancer FFPE samples
- Sequencing protocol demonstrates that >90% of the bases are mapped within the coding and untranslated regions (UTR) of the RNA
- Fusion detection and gene expression analysis

Figure 2

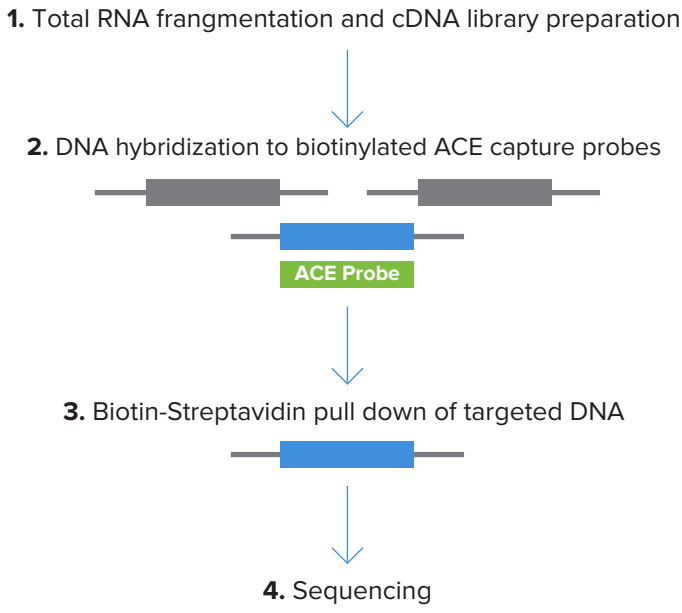
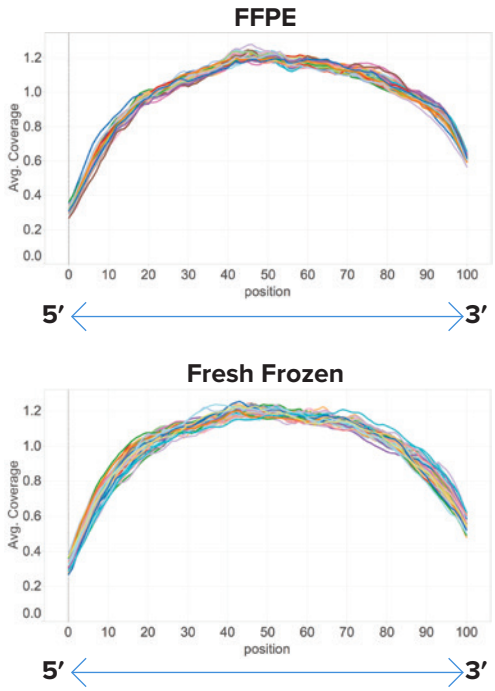


Figure 2: ACE Cancer Transcriptome Enrichment Workflow

For RNA-Seq, looking at the uniformity in sequencing coverage across the transcript can provide insight into the data quality. Transcript coverage plots to the right show representative ACE Cancer Transcriptome performance. Each colored line denotes a different sample in the study. As shown, RNA-Seq sequencing coverage performance is very uniform across the transcripts from the 5' to 3' ends using the ACE enrichment protocol. Whether we started with a fixed sample (top panel) or a frozen specimen (bottom panel), coverage is uniform (Figure 3).

Figure 3: Uniform ACE Cancer Transcriptome Coverage



Bioinformatics deliverables

ACE ImmunoID includes raw data and variant annotation deliverables through our validated somatic variant analysis pipeline.

DNA Analysis

- Raw data files: FASTQ, BAM files
- Somatic variant (SNVs, indels) analysis and report: VCF file
- Somatic variant annotation: VAR file
- Filtering and annotation of variants by cancer relevance and frequency
- Quality Control Report and Statistical Summary Report

RNA Analysis

- Raw data files: FASTQ, BAM files
- Variant (SNVs, indels) analysis: VCF file
- Gene-associated variant analysis with additional filtering by cancer relevance
- Fusion gene analysis and report
- Gene-based expression results
- Quality Control Report and Statistical Summary Report

Advanced analytics to power your biomarker strategy

Immunogenomics Report

Developed for use with ACE ImmunoID, the Immunogenomics Report guides the investigation of critical immuno-oncology genes. This report interrogates exome and transcriptome data to allow you to go beyond gene expression, with information including variant effect impact, DNA/RNA allelic fractions and population metrics (COSMIC, dbSNP). This additional information can be used to evaluate a variant's potential influence on the tumor's biology.

Our gene lists are curated from recent thought leader publications and provide an overview of pathways and genes that have been implicated in immuno-oncology. The report allows for the rapid evaluation of the tumor biology of a sample in key areas including:

- **Antigen Presentation:** Translational research empowers a better understanding of the pathways that tumor cells use to evade immune surveillance. Detecting critical mutations in genes such as B2M are important to comprehend the mechanisms of acquired resistance to immunotherapies. B2M deficiency has been shown in Adoptive Cell therapies (Restifo et al., 1996), Checkpoint Inhibitors (Zaretsky et al., 2016) and Neoantigen Vaccine strategies (Sahin et al., 2017)
- **Repair and Replication:** Microsatellite Instability High (MSI-H) or DNA mismatch repair deficiency tumors are thought to be an important biomarker for patient response. Recently, the FDA approved the use of pembrolizumab based upon the tumor's MSI status.
- **Checkpoint Modulators:** The activation of T-cells is regulated by both stimulatory and inhibitory signals. Understanding the tumors checkpoint ligand expression is key to understand the likely mechanisms of tumor escape.

Neoantigen Discovery Report

The Neoantigen Discovery Engine complements the Immunogenomics Engine by providing a deep dive into the neoantigen landscape:

- Identifies neoantigens resulting from SNVs, indels, and fusions
- Tumor mutational burden and neoantigen load
- Allelic fraction and gene expression of variants
- Phasing for allele-specific expression determination
- MHC Class I and MHC Class II peptide binding affinities (based on the sample's HLA alleles)

Figure 4: Multidimensional Biomarker Analysis

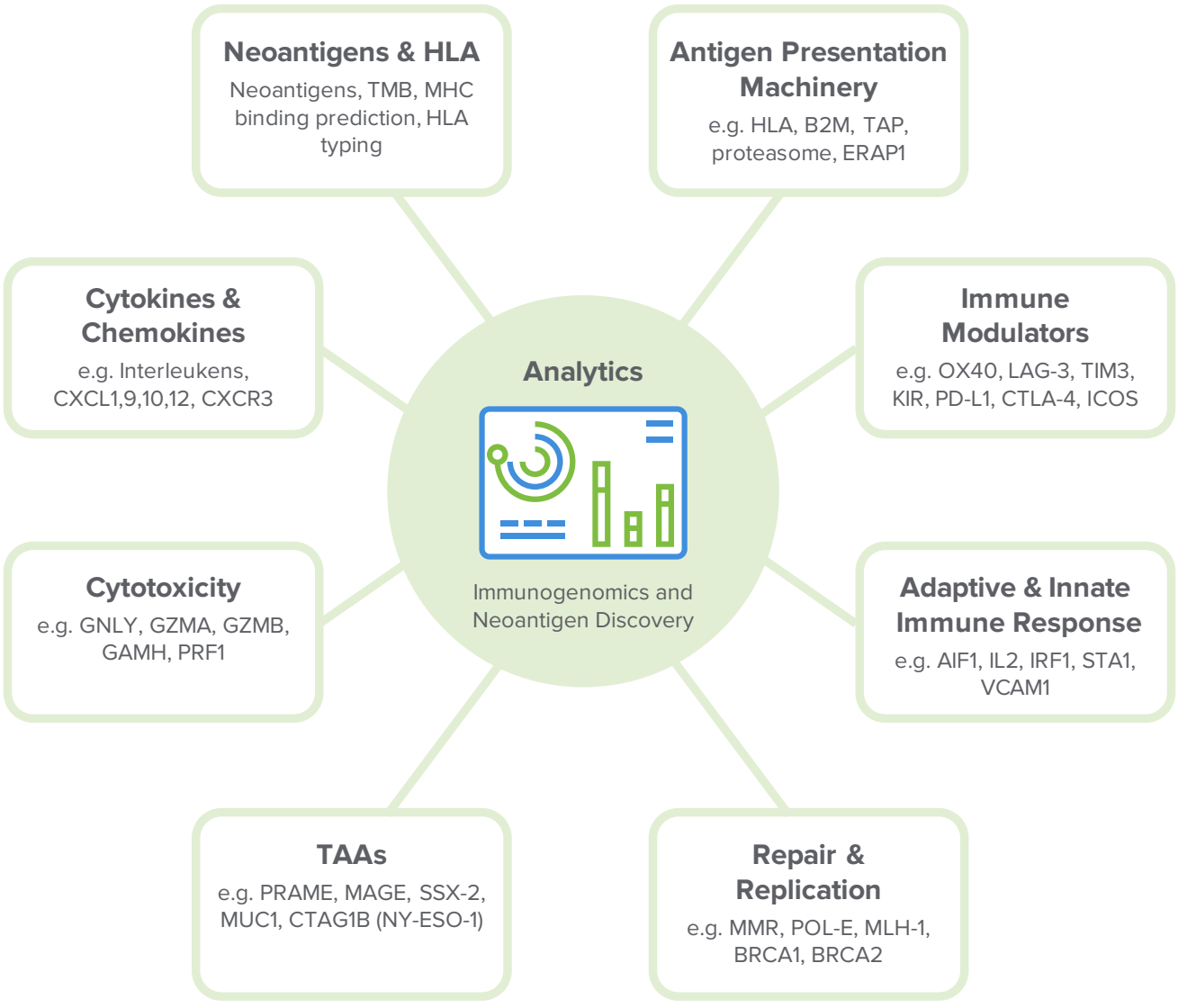


Figure 4: Immunogenomics and Neoantigen Discovery Engines allowing multidimensional biomarker analysis.

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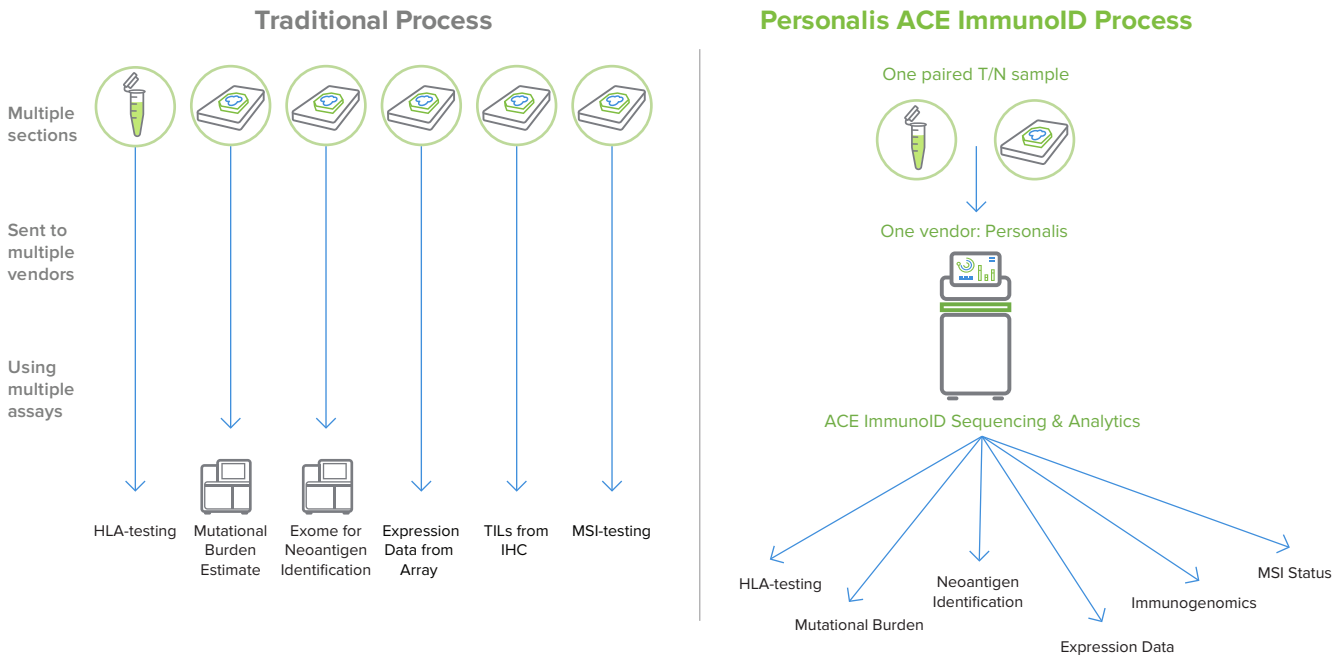
Do more with less sample

Obtaining research samples can be challenging. Evaluating data across diverse biomarkers typically involves sending multiple sections to several different vendors. This not only increases complexity, but can waste your precious samples.

ACE ImmunoID simplifies this situation by requiring only one paired tumor and normal sample, allowing you to do more with less sample.



Get in Touch

To learn more about how we can help with your immuno-oncology research, contact us at **info@personalis.com**.

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