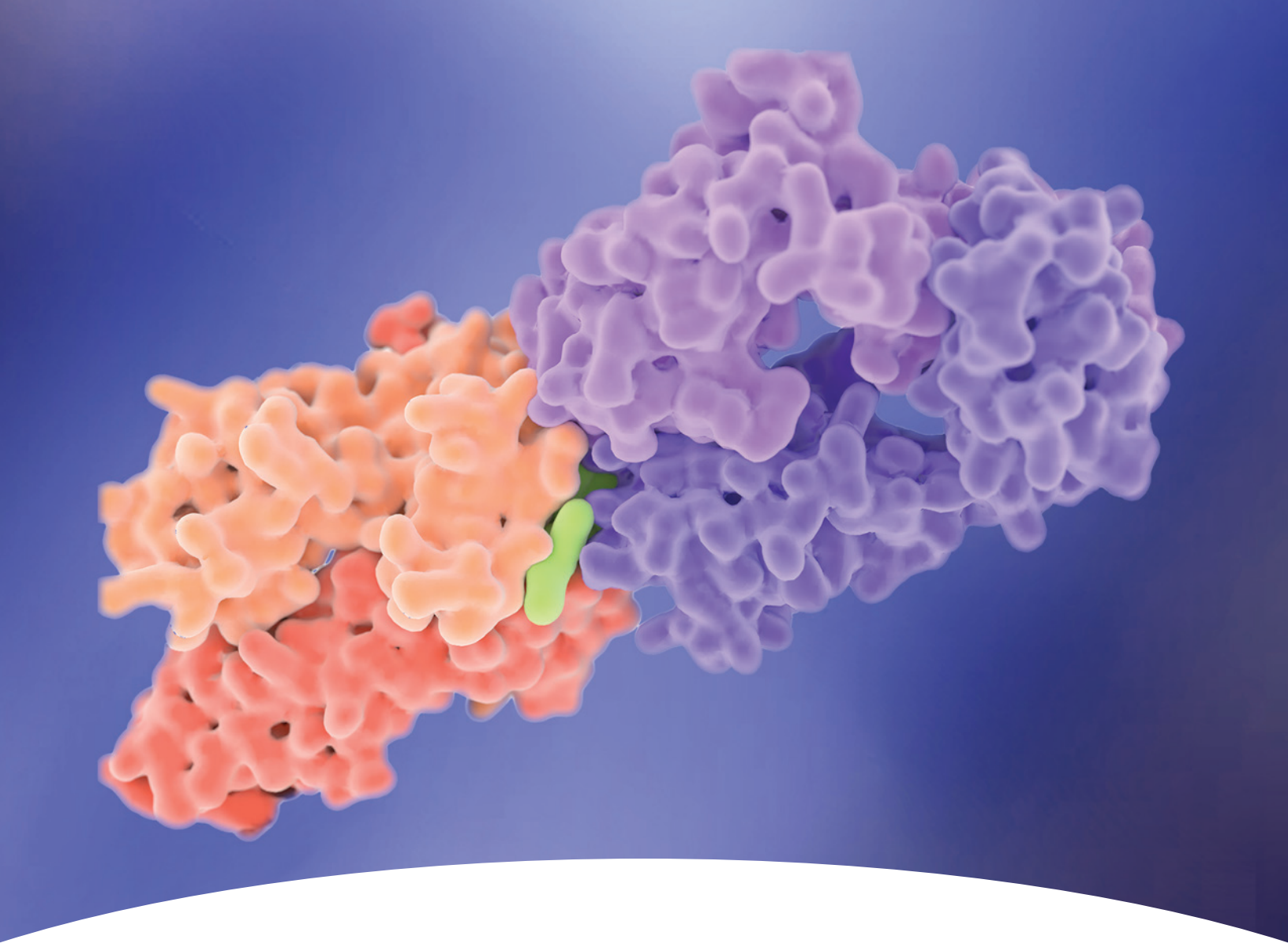


Genomics Solutions for Neoantigen Vaccines

High quality, comprehensive genomic data and analytics for personalized cancer vaccine development

Personalis®

Precision Genomics for Immuno-Oncology

Personalis, Inc.

Getting neoantigen vaccines right

The first step of developing personalized cancer vaccines is the identification of patient-specific neoantigens. These peptides can arise from anywhere in the genome, and methods for predicting which of these peptides will result in an efficacious vaccine are in early stages. That's where we can help.

At Personalis, we've developed solutions to overcome the complexity of selecting neoantigens for cancer vaccines. We provide whole exome and transcriptome sequencing, performed within timelines which make sense for vaccine development, as well as analytics to better inform your decisions:

Paired Tumor/Normal Sequencing

ACE ImmunoID™: ACE Cancer Exome and ACE Cancer Transcriptome

Reliable Delivery

Project oversight and genomics information management

Comprehensive Analytics

ACE ImmunoID: Neoantigen Discovery and Immunogenomics Engines (RUO)

Personalis®

Broad genomics platform for neoantigen identification

ACE ImmunoID is an all-in-one immunogenomics platform. It combines our analytically-validated ACE (Accuracy and Content Enhanced) Cancer Exome and ACE Cancer Transcriptome assays, in a tumor/normal configuration, to provide robust genomic data. Additionally, through our Neoantigen Discovery Engine, ACE ImmunoID provides analytics to elucidate the tumor's neoantigen landscape.

ACE ImmunoID uses our patented ACE Technology, which improves processes from nucleic acid extraction, through sequencing, to analytics. ACE ImmunoID stands apart by:

- Performing dual DNA/RNA extraction from FFPE samples: Maximizing the use of precious patient samples
- Providing augmented coverage to enhance neoantigen detection: Missed mutations lead to downstream inaccuracies in neoantigen predictions
- Identifying neoantigens not only from SNVs, but also fusions and indels: Fusions and indels are a rich source of potential immunogenic peptides (Turajlic et al., 2017)
- Reporting HLA Class I and Class II typing: Validated *in silico* prediction from exome data to save time and sample
- Listing putative peptides which bind to the sample's MHC Class I and Class II: Both are important in eliciting a sustained T-cell response as has been recently shown in first-human neoantigen-based vaccine trials (Sahin et al., 2017, Ott et al., 2017)

ACE Cancer Exome

The ACE Cancer Exome assay provides high-coverage, high-accuracy sequencing of >20,000 genes, with improved coverage of >1,400 cancer related genes, for superior neoantigen identification.

Gene-wide analysis of SYN1 (Figure 1, Panel B) shows the sequencing coverage provided by the standard exome (blue regions) as well as the ACE-augmented coverage (green regions). ACE Cancer Exome coverage encompasses both the standard blue and the augmented green regions.

Positional analysis of peptide mutations and binding potential across the SYN1 genes (Figure 1, Panel A, highlighted region) indicates the number of predicted binding peptides that are captured in the augmented green region only (ACE supplementation) — these peptides would have been missed by the standard offering.

Figure 1

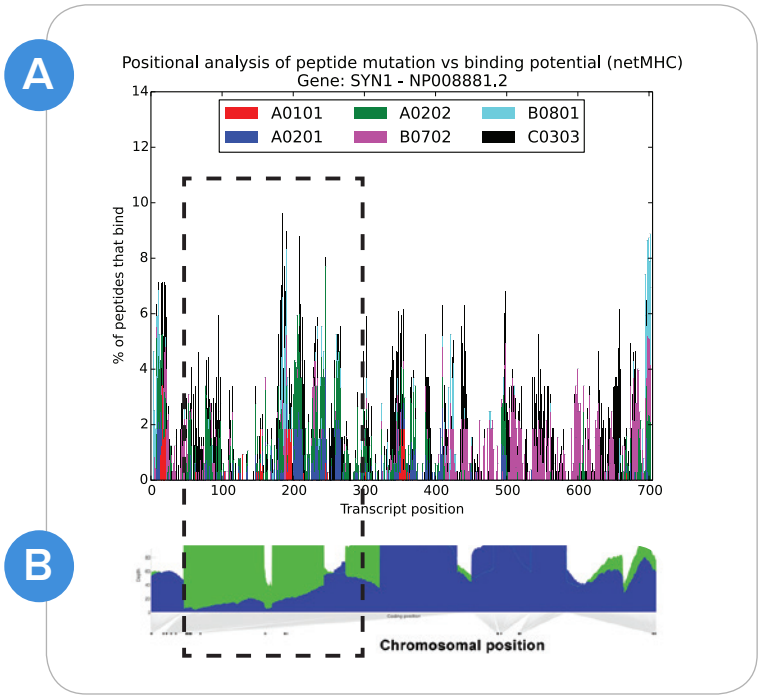


Figure 1: Superior coverage provided by the ACE Cancer Exome results in the identification of neoantigens that would have otherwise been missed by the standard exome.

ACE Cancer Transcriptome

The same accuracy and coverage are delivered with our ACE Cancer Transcriptome enrichment protocol.

When compared to a standard exome enrichment protocol, the ACE Cancer Transcriptome shows more uniform and deeper coverage across the entire gene (see Figure 2). In addition, because we use the most current gene definitions, the ACE Cancer Transcriptome covers exons that are missing in the standard annotation and other exon capture methods (Figure 3).

Figure 2

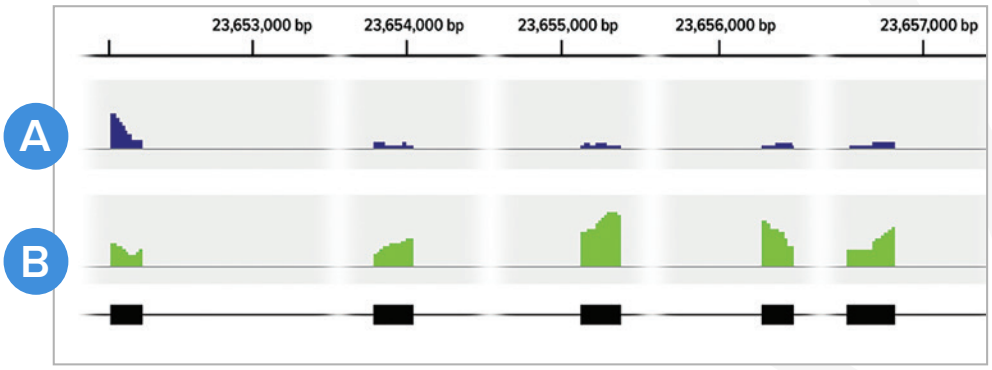


Figure 2: Deeper, more even coverage. Samples were prepared with both a standard exome capture method (A) and the ACE Cancer Transcriptome protocol (B). Five exons of the BCR gene are shown. The ACE Cancer Transcriptome protocol shows deeper and more even coverage across all five exon regions.

Figure 3

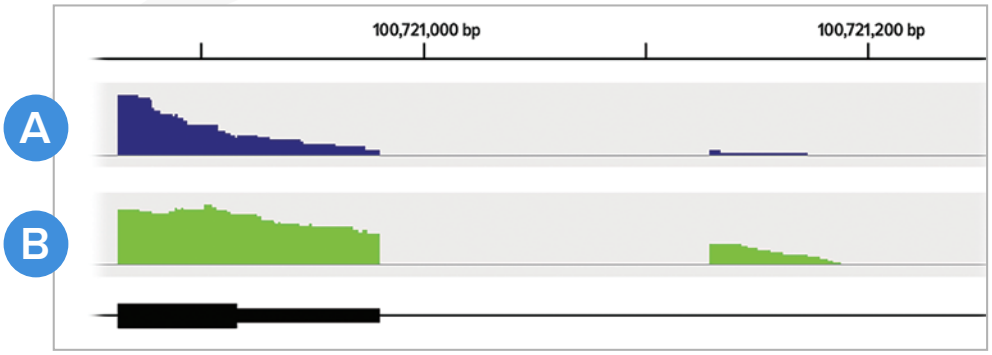


Figure 3: Missing annotation. Samples were prepared with both a standard exome capture method (A) and the ACE Cancer Transcriptome protocol (B). Two exons of the AFF3 gene are shown. The standard exome capture method misses the second exon while the ACE Cancer Transcriptome protocol shows deeper and more even coverage of both.

Bioinformatics Deliverables

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

For 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

For 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 research

Detecting tumor-specific neoantigens and predicting those that will be presented is a complex problem. The scientists at Personalis developed the Neoantigen Discovery Engine (RUO) to inform your translational research programs by consolidating molecular information known to be critical to neoantigen prediction. The analytics engine provides an optional output from ACE ImmunoID, delivering comprehensive data for the evaluation of candidate neoantigens:

- 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)

We provide additional insights for your research programs through our Immunogenomics Engine. The Immunogenomics Engine guides the investigation of critical immuno-oncology genes with information including expression, variant effect impact, and DNA/RNA allelic fractions, allowing you to rapidly evaluate the tumor biology of a sample in critical areas including:

- Antigen Presentation Machinery
- Checkpoint Modulators
- Adaptive and Innate Immune Response
- Repair and Replication
- Cytokines and Chemokines

Reliable project and data delivery

Processes and systems to ensure your project is delivered within the agreed upon timelines:

One Point of Contact

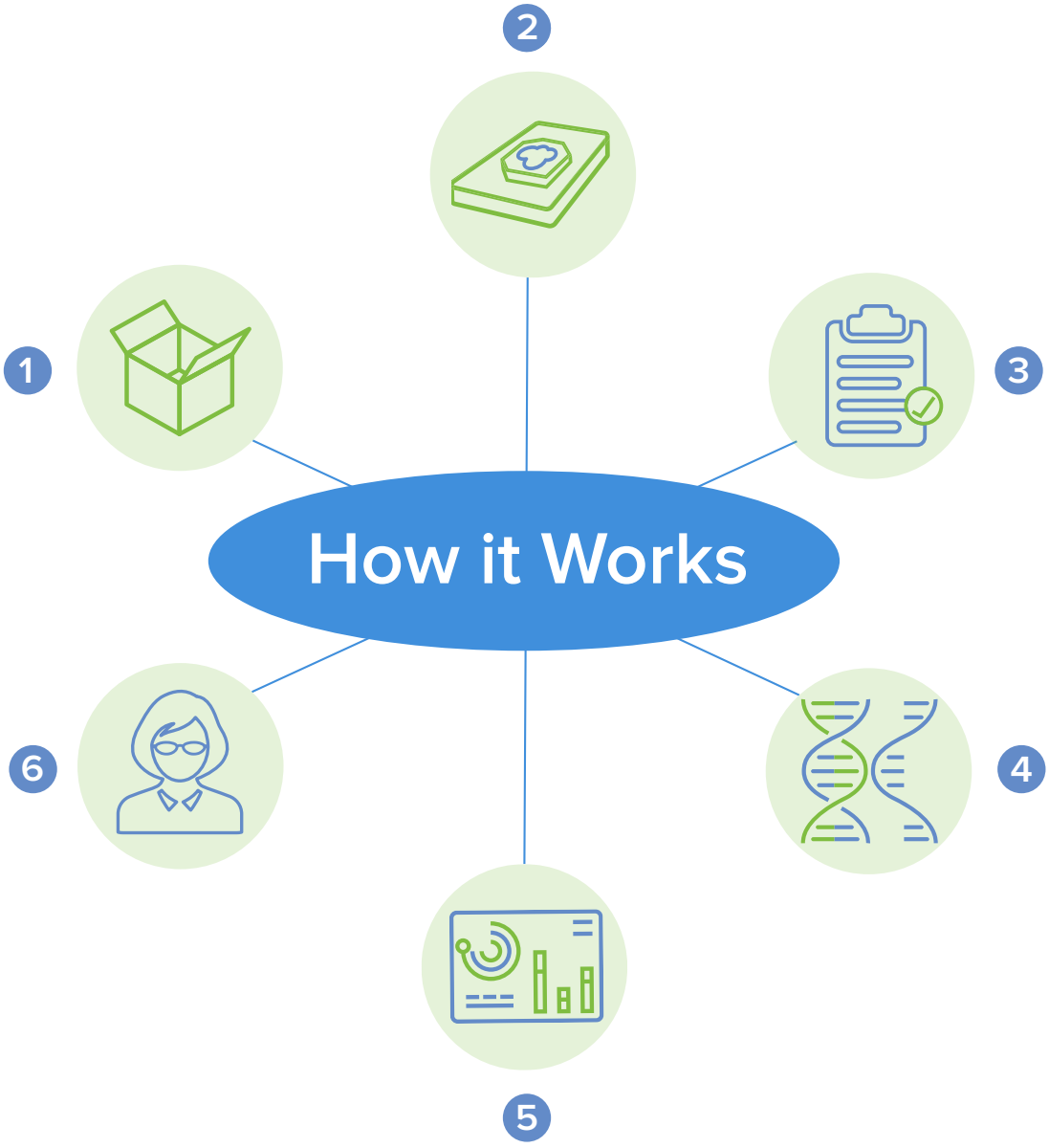
- Your project manager (PM) is your one point of contact for status updates and communication to Personalis
- PMs are PhD-level scientists with deep scientific and laboratory experience

Real-time Project and Sample Status

- Symphony Genomics Management System links LIMS, pipelines, databases, and other systems for real-time project status and sample-level tracking, this allows your PM to keep your project on track

Lock Down Assays and Pipeline Versions

- Symphony also down assays and analysis pipeline versions for the life of your study
- Symphony can globally accommodate re-analysis on updated pipelines, even after a study has closed



1. Arrival

ACE ImmunoID requires paired tumor/normal analysis. The moment samples arrive at our CAP-accredited, CLIA-certified laboratory, the samples are given a unique sample ID and are tracked in LIMS and Symphony.

2. Sample Sparing Preparation

Our laboratory staff bring a wealth of operational expertise, allowing us to implement our superior sample-sparing method.

3. Quality Review

Prior to sequencing, samples undergo robust QC assessment.

4. Sequencing

The ACE ImmunoID ACE Cancer Exome and ACE Cancer Transcriptome assays run simultaneously to streamline processes and save time.

5. Analysis

Data is then run on our somatic variant pipeline for standard data deliverables. Additional analytics provided through our Neoantigen Discovery and Immunogenomics Engines can be included based on your research and project needs.

6. FAS Support

Upon data delivery, your Field Application Scientist is available to walk through the data with you, to answer any questions, and follow up with our scientific team as needed.

Personalis, Inc.

Working together for more effective neoantigen vaccines

When you work with Personalis for neoantigen identification, you get a team of scientific and operational experts who are focused on your success.

Unlike other genomics providers that require multiple specimens, or the shipping of specimens to additional partner labs, ACE ImmunoID requires only one tumor sample and one normal sample—simplifying operations and decreasing risks.

ACE ImmunoID provides enhanced coverage of all coding genes to help you identify neoantigens that would otherwise be missed by standard exome assays. While we provide you with variant calls and raw data and we've also developed analytics for deeper insights into tumor biology.

Through our broad platform, advanced analytics, and project management we reliably deliver high quality molecular data to better inform your clinical and translational studies.

Get in touch.

To learn more about how we can help with your neoantigen identification needs, contact us at info@personalis.com.

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