Oncology Research Services

Comprehensive tumor profiling and analytics for targeted therapy
One-stop tumor profiling

A deeper understanding of cancer biology starts with comprehensive tumor characterization.

We help better inform your cancer research studies with comprehensive tumor profiling assays powered by our Accuracy and Content Enhanced (ACE) Technology.

**Assays to meet the needs of your research studies:** Whole exome and whole transcriptome sequencing available through the *ACE Cancer Exome* and *ACE Cancer Transcriptome*. Additionally, we offer broad panel assays which cover >1,400 cancer-related genes through the *ACE Cancer Panel for DNA* and the *ACE Cancer Panel for RNA*.

**Diverse sample types accepted:** Formalin-fixed-paraffin-embedded (FFPE), fine needle aspirates (FNAs), PBMCs, and whole blood are accepted for all research assays.

**Sample sparing methods:** DNA and RNA extracted simultaneously, to provide a comprehensive tumor genomic profile from a single sample.

**Flexible DNA analysis configuration:** Paired Tumor/Normal and Tumor-only configurations supported.

**Comprehensive analysis:** Reporting on somatic small variant and indel calling, CNV analysis\(^1\), fusion junction calling, and gene expression profiling, as well as germline small variant calling and annotation. We provide you with structural and functional information from numerous databases including COSMIC, Cancer Gene Census, and The Cancer Genome Atlas.

\(^1\)Available only with ACE Extended Cancer Panel and ACE Cancer Research Exome.
Personalis, Inc.

Powered by ACE technology

ACE Technology is the foundation upon which our cancer research assays are built. By optimizing each step from nucleic acid extraction through data delivery, we help to ensure you’re getting the most comprehensive tumor profile possible.

Nucleic acid extraction and sample preparation
Personalis has developed protocols to overcome the challenges of working with difficult samples, including FFPE. Additionally, we simultaneously extract both DNA and RNA from the same sample in a sparing manner.

Sequencing
Gaps or inconsistent coverage can result in missed content. Personalis ACE Technology augments sequencing gaps for more complete coverage.

Alignment and variant discovery
Our state-of-the-art bioinformatics pipelines are optimized for accuracy and performance, resulting in superior sequence alignments and variant calls, including improved SNV and indel detection.

Variant annotation
We’ve implemented comprehensive annotation to overcome both mapping/nomenclature issues, and to overcome errors and inconsistencies in database curation.

Data deliverables
Data is available both as raw data files (e.g. FASTQ, BAM files) as well as reporting on cancer-relevant genes, and is delivered with QC and statistical summary reports.
ACE Cancer Research Exome

Using our patented ACE Technology, the ACE Cancer Exome outperforms conventional exome assays by augmenting coverage across intronic and difficult-to-sequence (high-GC content) regions, ensuring the capture of variants that would be otherwise missed (Figure 1).

Our proprietary ACE Technology allows us to provide improved coverage as well as increased sensitivity to detect known and novel cancer-associated variation as part of a biomarker discovery study, and improved resolution in studies of tumor stratification, metastatic evolution, and therapeutic response.

**Figure 1**

**At-a-Glance**

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<tbody>
<tr>
<td>Genes Covered</td>
<td>&gt;20,000</td>
</tr>
<tr>
<td>Genes Augmented</td>
<td>&gt;8,000 biomedically-important genes, of which &gt;1,400 are cancer-relevant</td>
</tr>
<tr>
<td>Sequencing Depth</td>
<td>≥100x (tumor)/≥65x (normal)</td>
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<tr>
<td>Analysis Configuration</td>
<td>Tumor only or paired tumor and normal</td>
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<tr>
<td>Reporting</td>
<td>Somatic variant detection of SNVs, indels, and CNVs</td>
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**Figure 1:** Example exon coverage and depth for cancer genes using the ACE Exome vs. standard exome sequencing. The blue regions show coverage and depth across the length of each gene from a standard, commercially available assay. The green regions illustrate ACE augmentation of regions of the gene which are poorly covered by the standard offering. Personalis returns both the green and blue regions.
ACE Cancer Research Transcriptome

Transcriptome sequencing provides complementarity information for your cancer studies, including data on gene expression levels, fusion transcripts, variants in expressed genes, and allelic expression. Our process allows RNA to be extracted from the same tissue sample used for exome sequencing, maximizing the data generated from limited samples.

Optimized for FFPE

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.

Our enrichment protocol directly selects for transcripts using the optimized ACE capture probes, eliminating background noise and focusing the sequencing on regions of interest. Sequencing using the ACE Transcriptome protocol demonstrated that >90% of the bases mapped within the coding and UTR regions of the RNA (Figure 2). Thus, the ACE approach results in high quality data and low off-target reads.

Figure 2

Figure 2: ACE Cancer Transcriptome focuses on regions of high interest.
Accurate gene expression data

Using paired FFPE and matched adjacent Fresh Frozen tissues, we found high correlation of normalized (TPM) gene expression (Figure 3) across various tumor types. This data demonstrates the Personalis ACE Cancer Research Transcriptome for gene expression is an accurate, reliable method for characterizing expression in even challenging materials such as FFPE.

Figure 3: Correlation plots of log₂ transcripts per million (TPM) between matched FF (x-axis) and FFPE (y-axis) pairs in A-D) colon, E) lung, and F) rectum tumor samples.

At-a-Glance

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<tr>
<td>Reporting</td>
<td>SNVs, indels, fusion detection, gene expression analysis</td>
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ACE Extended Cancer Panel for DNA

Covering more than 1,400 cancer genes, the ACE Extended Cancer Panel for DNA includes a core set of clinically actionable\(^2\) genes, all genes in the Cancer Gene Census, genes from TCGA reports, and those within canonical cancer pathways proposed by Vogelstein et al., (Science, Mar 29 2013) and other leading academic groups.

The accuracy of our ACE Cancer Panel has also been enhanced over standard NGS panel approaches by augmenting and repairing coverage gaps, especially in targeted regions with high-GC content. This is accomplished by performing separate targeted capture under optimized sample prep conditions and combining data from these separate targeted preps into a single high-quality sequencing dataset. This results in genes with more complete coverage.

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<tr>
<td>Depth of sequencing</td>
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<tr>
<td>Assay Sensitivity</td>
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<tr>
<td>Assay Specificity</td>
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<tr>
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ACE Extended Cancer Panel for RNA

The ACE Extended Cancer Panel for RNA provides unparalleled detection of unique variant types that are not identifiable by DNA sequencing analysis alone. The assay identifies gene expression levels, gene fusions, SNVs and indels in over 1,400 cancer-associated genes. This panel enables extensive gene fusion discovery of both clinically actionable\(^3\) fusions involving critical genes such as ALK, ROS1, RET, and novel fusions involving other targeted genes that might be missed with DNA analysis alone.

Personalis’ targeted approach to RNA sequencing provides researchers with higher quality RNA results compared to those achieved by conventional transcriptome sequencing practices. We accomplish this by focusing only on genes related to cancer biology (by excluding intronic RNA from unspliced transcripts) and by using a capture method that can isolate degraded RNA better than other methods. This results in higher quality RNA reads with minimized background.

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\(^{2,3}\)Genes referred to here as being clinically actionable reflects the fact that the efficacy of cancer drugs, FDA approved or in clinical trials, are thought to be modulated by variants in these genes. This does not imply that this panel is for clinical use — it is a Research Use Only service.
ACE Cancer Analysis and Annotation Pipeline

**DNA Analysis**
The Personalis DNA Analysis Pipeline for Cancer performs high accuracy alignment and variant calling for both germline and somatic variants. Somatic variants can be identified in either Tumor/Normal, or from Tumor-only data sets. Somatic variant types including single nucleotide variants (SNVs), small insertions and deletions (indels), and copy number variants (CNVs) are reported. All of these variants are annotated against databases of known variants and cancer information and collated into reports. In addition, filtered and refined reports are generated for ease of use. Finally, QC reports delineating sequencing metrics as well as somatic analysis summary statistics are included in html format.

**RNA Analysis**
The Personalis RNA Analysis Pipeline for Cancer performs a high accuracy gapped alignment and variant calling. The Personalis pipeline is capable of detecting a wide variety of important cancer related events from RNA sequencing data, including SNVs, indels, and gene fusion events. Comparison of variants identified in RNA vs DNA, from the same sample, makes it clear which DNA variants are actually expressed, and at what level, in the tumor. RNA read depths can also be used to digitally quantify relative gene expression. To further empower researchers, our pipeline thoroughly annotates variants using a wide variety of sources, including information covering many important cancer features. As with the DNA analysis, detailed reports are provided for each variant class, easing accessibility.

*Fusions referred to here as being clinically actionable reflects the fact that the efficacy of cancer drugs, FDA approved or in clinical trials, are thought to be modulated by occurrence of these fusions. This does not imply that this panel is for clinical use — It is a Research Use Only service.*
## Bioinformatics deliverables

### DNA Analysis
- Raw data files — FASTQ, BAM
- Somatic variant (SNVs, indels) analysis and report: VCF file
- Somatic CNV reports and plots
- LOH reports and plots (exome only)
- 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
- 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

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## Supporting precision medicine innovation

Our cancer research products are designed to provide you with the most complete and accurate genomic data possible for your research studies. To learn more about how we can partner together to advance targeted therapies, contact us at info@personalis.com.