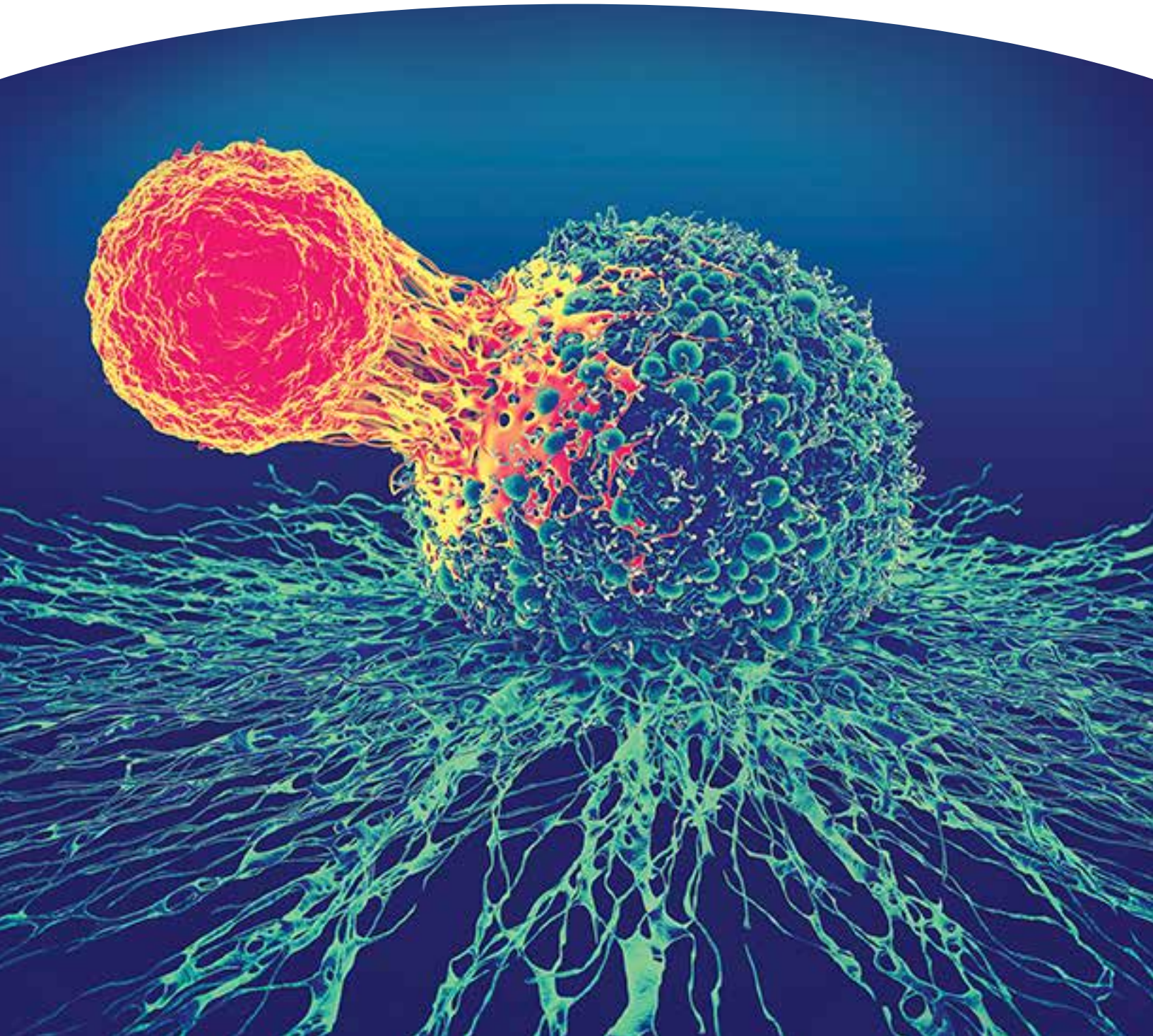
Personalis®
Precision Genomics for Immuno-Oncology

ImmunoID NeXT™

The Universal Cancer Immunogenomics Platform



Advancing Modern Precision Oncology

The Universal Cancer Immunogenomics Platform

The ImmunoID NeXT Platform is designed specifically to enable the development of more efficacious cancer immunotherapies. While the success of checkpoint blockade has been hugely promising, it's increasingly apparent that predicting response to immunotherapies and developing new ones requires a more comprehensive approach to tumor immunogenomics. By combining highly-sensitive, exome-scale DNA and RNA sequencing with advanced analytics, ImmunoID NeXT provides a multidimensional view of the tumor and the tumor microenvironment (TME) from a single sample.

For the first time, oncology translational and clinical researchers can comprehensively characterize both the tumor- and immune-related components of the TME using a single platform. The ImmunoID NeXT Platform enables customers to maximize the data generated from precious tumor samples. It also decreases the complexity of data interpretation by eliminating the need to integrate multiple assay technologies and reporting formats from several sources.

The platform represents an end-to-end solution for immuno-oncology and all precision oncology applications. It combines the pioneering NeXT assay, sophisticated analytics engines, and quality support to provide researchers with the comprehensive immunogenomic data they need to drive their programs.

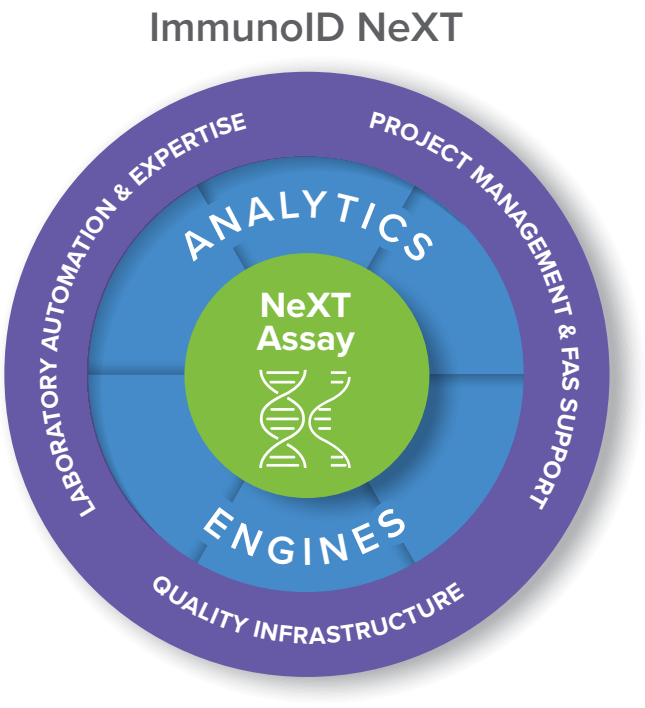


Figure 1: ImmunoID NeXT: The Universal Cancer Immunogenomics Platform.

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A Single Platform. A Single Sample. Multiple Biomarkers.

Purpose-built for precision oncology, the ImmunoID NeXT Platform can be used to investigate key areas of tumor biology; from elucidating mechanisms of tumor escape and detecting neoantigens, to identifying novel gene expression signatures and characterizing the immune repertoire. With these extensive capabilities, ImmunoID NeXT provides a complete picture of the cancer ecosystem and enables the consolidation of multiple biomarker assays into one.

Ultra-High Sensitivity. The Scale of an Exome.

Unlike other commercial genomics platforms which make trade-offs between breadth and sequencing depth, ImmunoID NeXT optimizes both footprint and limits of detection to generate accurate and comprehensive genomic data, providing ultra-sensitive detection of single nucleotide variants (SNVs), insertions/deletions (indels), copy number alterations (CNAs), and gene fusions across >20,000 genes.

ImmunoID NeXT also leverages Personalis' proprietary Accuracy and Content Enhanced (ACE) Technology to augment coverage of more complex and difficult-to-sequence regions (e.g. areas of high-GC content) across >20,000 genes that are not sufficiently covered by conventional approaches. The incorporation of ACE Technology into the design of ImmunoID NeXT, therefore, reduces the likelihood of the non-detection of potentially important somatic variants present in patients' tumor samples.

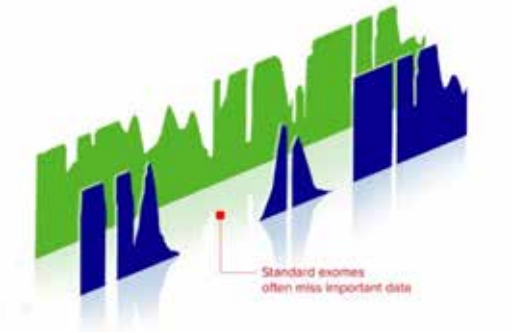

Figure 2: The sequencing coverage provided by standard exome-scale assays is shown in blue. The ACE-enabled, augmented sequencing coverage provided by ImmunoID NeXT is shown in green.

The unique, innovative design of the assay and analytical algorithms enables the delivery of critical tumor and microenvironment-related information including, but not limited to:

- T-cell receptor (TCR) repertoire composition
- Neoantigen detection and neoantigen load
- Tumor mutational burden (TMB)
- Microsatellite instability (MSI) characterization
- Human leukocyte antigens (HLA) typing, HLA and beta-2 microglobulin (B2M) somatic mutations, and HLA loss of heterozygosity (LOH)
- Tumor escape and resistance mechanisms
- Oncoviral detection

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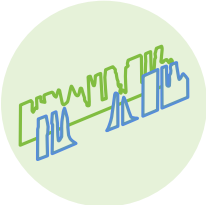
Unique Features of the ImmunoID NeXT Platform

Deep Sequencing

~300X mean coverage across the entire footprint (>20,000 genes), ultra-deep coverage of TCR/BCR gene regions, as well as clinical-grade coverage across ~250 targeted therapy cancer driver genes.



Augmented Coverage

ImmunoID NeXT utilizes our proprietary ACE Technology to provide augmented coverage of difficult-to-sequence gene regions across the entire >20,000-gene footprint.

Specific Targeting

Enhanced targeting of HLA genes, MSI-related loci, as well as oncoviral genes to enable the accurate characterization of investigational and predictive precision oncology biomarkers.

Ultra-High Sensitivity

Accurate detection of somatic SNVs, indels, CNAs, and gene fusions, including low-abundance mutations, which is critical for the analysis of samples with low tumor content.

Optimized Algorithms

The Personalis framework of analytical pipelines integrates both proprietary and advanced, publicly-available *in silico* tools to generate the most informative and usable insights from the comprehensive raw DNA and RNA data.

Mastering Challenging Samples

Personalis' protocols optimize nucleic acid extraction from difficult formalin-fixed paraffin-embedded (FFPE) samples. This approach enables dual extraction of both DNA and RNA from the same, precious tumor sample.

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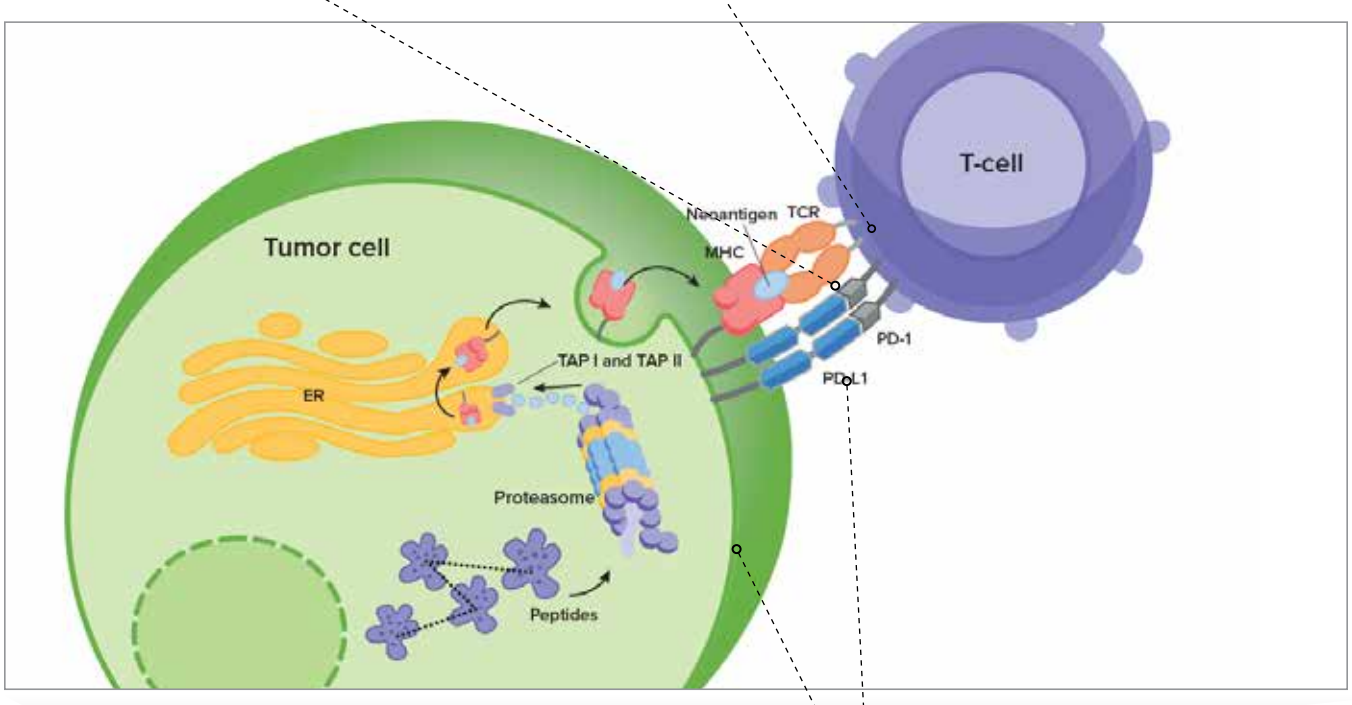
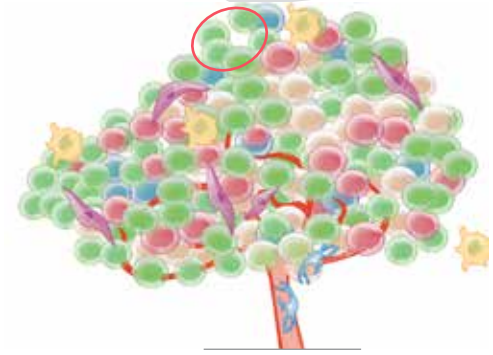
Evaluate the Entire Cancer Ecosystem

ImmunoID NeXT analytics leverage the accurate, raw data to evaluate the status of the most relevant oncology biomarkers, as have been identified and investigated in the literature. **Figure 3** below illustrates how the analytics modules elucidate the complex interplay between tumor cells and the immune cells of the TME.

NeoantigenID informs candidate neoantigen selection through MHC-binding prediction, and other key data including HLA typing, similarity-to-self, similarity-to-known antigens, and immunogenicity.

RepertoireID enables the analysis of the clonality/ diversification of the repertoire of TCRs present in the TME.





Tumor Microenvironment

ImmunogenomicsID provides an overview of the TME and critical areas of tumor and immune biology such as the adaptive and innate immune response, immune checkpoint modulation, antigen processing machinery (APM), tumor associated antigens (TAAs), DNA repair and replication, MSI characterization, oncoviruses, among others.

Figure 3: ImmunoID NeXT analytics modules provide insights into the complex and dynamic interactions between the tumor cells and immune cells of the microenvironment.

Analytics Modules

RepertoireID

RepertoireID enables the analysis of TCRα and TCRβ clonotypes in patients' tumor FFPE (as well as fresh frozen) samples. The ultra-deep, TCR-specific RNA sequencing data derived from the NeXT assay is processed by our TCR Analytics Engine, and a report is generated providing key metrics relating to both the TCRα and TCRβ chains such as clonality; CDR3 nucleotide and amino acid sequences; clonotype quantitation, distribution, and frequency; V, D (for TCRβ only), and J gene segments usage and overlap; and CDR3 nucleotide sequence length.

ImmunoID NeXT is the first commercial platform that enables the comprehensive characterization of the immune repertoire using data derived from an augmented, exome-scale platform, designed specifically to explore multidimensional oncology biomarkers.

ImmunogenomicsID

ImmunogenomicsID provides an overview of the TME and critical genes that are involved in, or highly impact key oncology functional groups including antigen processing machinery (APM), DNA repair and replication, immune checkpoint modulation, tumor associated antigens (TAAs), adaptive and innate immune response, cytokines and chemokines, and cytotoxicity. Analytics captured include tumor mutational burden (TMB), gene-level expression (transcripts per million or TPM), variant type, variant expression, DNA/RNA allelic fraction (>5%), and variant effect impact.

A key component of ImmunogenomicsID is the ability to identify somatic mutations occurring in the HLA and B2M genes, as well as the detection of HLA LOH; events which have emerged as potential mechanisms utilized by tumors to resist immunotherapy and combination treatment regimens.

Utilizing an advanced algorithm, this analytics module also provides a characterization of MSI within a tumor sample, highlighting the stability status of five canonical loci, as well as the exome-wide analysis of the proportion of all microsatellite loci that are found to be unstable.

Additionally, ImmunogenomicsID — via the specific targeting of viral genomes in both DNA and RNA — reports out on the presence (or absence) of viruses that are known to contribute to oncogenesis in a broad variety of cancer types. These oncoviruses include HPV, HBV, HCV, EBV, KSHV, MCV, and HTLV, and their associated genotypes and subtypes.

NeoantigenID

Neoantigens are non-self (or foreign) peptide fragments that can arise as a result of somatic alterations present anywhere across the genome. Therefore, deep and uniform coverage (of both DNA and RNA) is critical for both comprehensive neoantigen identification and the accurate assessment of neoantigen load. ImmunoID NeXT ensures highly-sensitive variant detection via both the depth of sequencing (~300X mean coverage) and the augmented coverage of difficult-to-sequence regions across the entire >20,000 gene footprint. Combined, these features reduce the chances of neoantigen-producing variants (SNVs, indels, and/or fusions) going undetected.

NeoantigenID utilizes the tumor and matched normal ImmunoID NeXT configuration to accurately differentiate between somatic and germline mutations and to generate analytics for the identification of potentially immunogenic neoantigens, incorporating information such as HLA typing, MHC-binding prediction (for Class I and Class II), similarity-to-self, similarity-to-known antigens, and immunogenicity.

Performance for the Present. Foundations for the Future.

Integrating a broad, exome-scale approach into your clinical and translational research will prove beneficial in the long run. ImmunoID NeXT provides comprehensive, accurate, and practically applicable genomic data at the forefront of today's immuno-oncology field, while also enabling the discovery of yet-to-be-identified biomarker signatures.

A Single Platform. A Single Sample. Multiple Biomarkers.

Ready to streamline your precision oncology translational and clinical programs? Contact us at info@personalis.com.

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