WHAT IS IMMUNOSELECT-R™?

Neoantigens are a class of immunogens based on the personal, exquisitely tumor-specific mutations found uniquely in each patient’s tumor. Combining PGDx’s highly accurate cancer exome analyses (CancerXome™) with in silico neoantigen prediction, ImmunoSelect-R™ identifies and prioritizes the most relevant mutation-derived neoantigens to enable adoptive T-cell transfer, cancer vaccine development, and prediction of clinical utility of checkpoint inhibitors.

IMMUNOSELECT-R™ DELIVERABLES

- Unparalleled cancer exome sequencing accuracy to ensure identification of true somatic mutations — 95% sensitivity and 97% PPV down to 10% mutant allele frequency at 150x coverage
- Accurate HLA typing using whole exome sequencing
- Prediction and prioritization of the most relevant neoantigens from exome-based mutations and novel open-reading-frames

IMMUNOSELECT-R™ PIPELINE

WT/Somatic Peptides (Mutation, neoORF) → Expression (mRNA or Protein) → Similarity to Known Ag → Generate Fasta of WT/Som Peptide Pairs (B-Fla)

HLA-information → * .fastq → In Silico HLA-typing → HLA-A01: 01 HLA-A26: 01 → HLA-A01: 01 HLA-A26: 01 → HLA-A01: 01 HLA-A26: 01

Candidate Neo-Ag (MHC-peptide IC50< 500nM) → Self-Similarity → Mutant Allele Frequency → Antigen Processing → MHC Binding Affinity → Priming and activation (APCs & T cells) → Trafficking of T cells to tumors (CTLs)

IMMUNOSELECT-R™ ID:

Patient ID | HLA Type | Gene Name | Peptide ID | MUT Peptide | MUT MHC Affinity | MUT CTL Class | Mean Exp in Tumors | Priority
---|---|---|---|---|---|---|---|---
Patient 1 | HLA-A’02:01 | GAS7 | 1_p09490_10 | SLADEAEYVL | 14.4 | E | 236 | High
Patient 1 | HLA-B’04:03 | CSNK1A1 | 59_p06000_8 | GLFGDLYL | 5.72 | E | 4633 | High
Patient 1 | HLA-A’24:02 | KIAA031 | 124_p11981_11 | KLLQQLNWYMM | 25.3 | E | 2063 | High
Patient 1 | HLA-A’02:01 | RRPIB | 197_p19240_11 | FLKPPLFFRA | 16.63 | E | 1111 | High


LONG-TERM OUTCOMES

- Improved cancer outcomes
- Enhanced immune response
- Increased patient safety and efficacy
ONLY CANCERXOME™ DELIVERS THE SENSITIVITY AND SPECIFICITY REQUIRED TO PREVENT FALSE POSITIVE MUTATIONS FROM CONFOUNDING NEOANTIGEN IDENTIFICATION

NUMBER OF DNA BASE PAIRS VALIDATED WITH AN INDEPENDENT METHOD USED FOR PIPELINE OPTIMIZATION
Using 100 to 1,000 times more independently validated data points to optimize the bioinformatics pipeline ensures unmatched accuracy of PGDx exome sequencing.

IMPACT OF INCREASED SPECIFICITY ON EXOME SEQUENCING PPV
Pipelines that have not been validated against whole exome Sanger sequencing using matched normal controls will be less than 99.99999% specific.

IMPUNOSELECT-R™ VALIDATION

- Identified 18 out of 19 experimentally validated neoantigens as being strong neoantigen candidates, suggesting an assay sensitivity of greater than 90%
  SOURCE OF DATA: cancerimmunity.org/peptide/mutations/

- Reproduced the tetra-peptide signature predictive of clinical benefit of CTLA-4 blockade in melanoma
  SOURCE OF DATA: “Genetic Basis for Clinical Response to CTLA-4 Blockade in Melanoma” New England Journal of Medicine, 04 December 2014

IMMUNOSELECT-R™ CONSISTENTLY RANKED EXPERIMENTALLY VALIDATED NEOANTIGENS WITHIN TOP 20% OF ALL NEOANTIGEN CANDIDATES DERIVED FROM WHOLE EXOME SEQUENCING

IMMUNOSELECT-R™ KEY PERFORMANCE ATTRIBUTES

- Unparalleled cancer exome sequencing accuracy to ensure research is focused on true somatic mutations for neoantigen prediction
  — 95% sensitivity and 97% positive predictive value down to 10% mutant allele frequency at 150x coverage
  — Works on FFPE or frozen tissue
  — Matched patient normal (germline DNA) is required for optimal results
  — Accurate inference of HLA typing from whole-exome sequencing

- Neoantigen analysis can be offered alone or in combination with CancerXome™ and completed within 48 hours of tumor mutation analysis completion
  — Effective in silico pipeline to discover and prioritize candidate neoantigens by incorporating the following:
    — Comprehensive identification of tumor-specific mutated peptides and neo-ORF
    — State-of-the-art prediction of HLA-types, antigen processing and MHC-peptide binding
    — Proprietary strategy to select most-relevant candidate neoantigens for experimental validation

IMMUNOSELECT-R™ IS FOR RESEARCH USE ONLY, NOT FOR DIAGNOSTIC PURPOSES.