PGDx | IMMUNOSELECT™

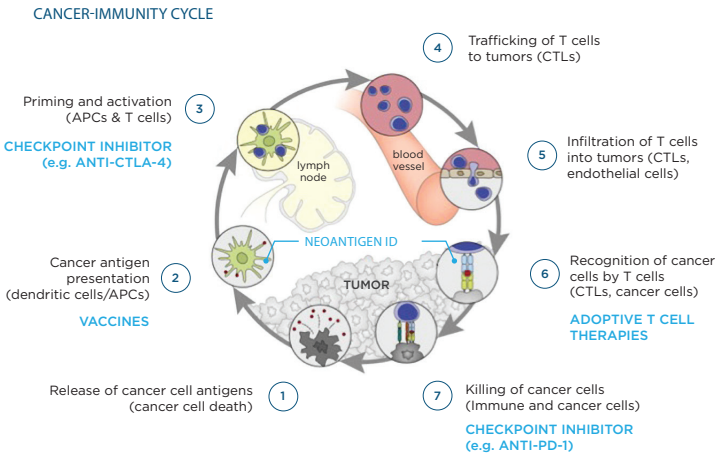
# IDENTIFY AND PRIORITIZE CANDIDATE NEOANTIGENS FROM CANCER EXOME SEQUENCING RESULTS WITH UNMATCHED ACCURACY

## WHAT IS IMMUNOSELECT™?

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 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.

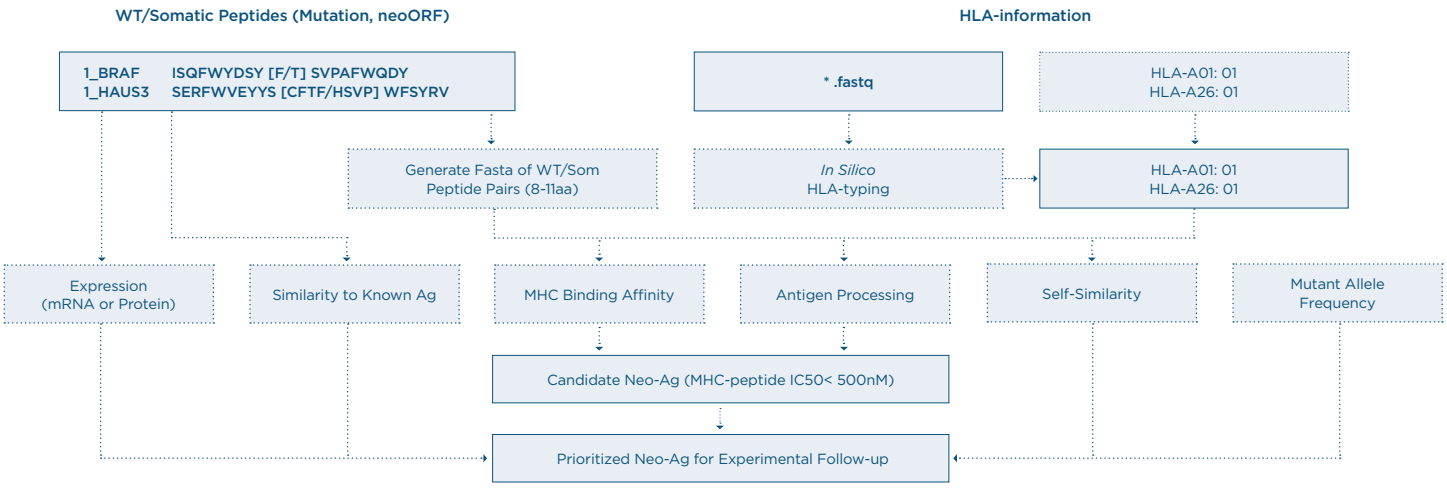
## IMMUNOSELECT DELIVERABLES

- Unparalleled cancer exome sequencing accuracy to ensure identification of true somatic mutations with >95% sensitivity and 97% PPV (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




SOURCE: "Oncology meets immunology: the cancer-immunity cycle", *Immunity*, 25 July 2013

## IMMUNOSELECT PIPELINE




## EXAMPLE REPORT OUTPUT

| 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 | SLADEAEVYL | 14.4 | E | 236 | High |
| Patient 1 | HLA-B*44:03 | CSNK1A1 | 59_p06000_8 | GLFGDIYL | 5.72 | E | 4633 | High |
| Patient 1 | HLA-A*24:02 | KIAA031 | 124_p11981_11 | KLLQQLNGWYM | 25.3 | E | 2063 | High |
| Patient 1 | HLA-A*02:01 | RRP1B | 197_p19240_11 | FLPKPLFFFRA | 16.63 | E | 1111 | High |

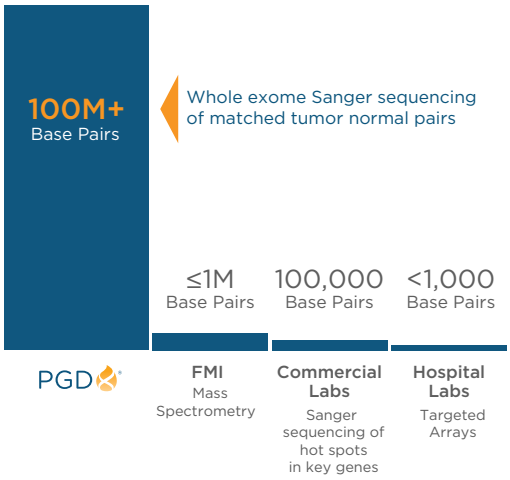
**PERSONAL GENOME DIAGNOSTICS** | 2809 BOSTON STREET, SUITE 503 | BALTIMORE, MARYLAND 21224 | TEL (888) 571-2163

## 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.

### Mutation-Calling Pipeline Optimization




### IMMUNOSELECT™ 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: Retrieved from http://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 CONSISTENTLY RANKED EXPERIMENTALLY VALIDATED NEOANTIGENS WITHIN TOP 20% OF ALL NEOANTIGEN CANDIDATES DERIVED FROM WHOLE EXOME SEQUENCING

| Sample | #Mutations | #Neo-Ag (IC50<500nM) | #Neo-Ag Post Prioritization | Rank of Validated Neo-Ag |
|---|---|---|---|---|
| Patient 1 | 504 | 128 | 55 | 1, 14, 15, 16 |
| Patient 2 | 257 | 277 | 30 | 1, 2, 3, 4, 15, 16 |
| Patient 3 | 58 | 97 | 30 | 9, 10, 14, 15, 16 |

SOURCE OF DATA: "Mining exomic sequencing data to identify mutated antigens recognized by adoptively transferred tumor-reactive T cells." *Nature Medicine*. 05 May 2013.

### IMMUNOSELECT 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 (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™**
- **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 IS FOR RESEARCH USE ONLY, NOT FOR DIAGNOSTIC PURPOSES.