OncoPept™: An integrated platform to generate novel cancer immunotherapeutics

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Cancer immunotherapeutics engage the body's immune system to fight cancer. Two recently approved checkpoint control antibodies Ipilimumab and Nivolumab target the PD-1 receptor on T-cells blocking negative signaling that attenuates T-cell activation maintaining them in their activated state. Activated $CD8^+$ cytolytic T-cells (CTLs) recognize and eliminate tumor cells by recognizing peptides derived from mutated cellular proteins. Identifying T-cell-activating cancer mutations will lead to the development of novel therapeutics including peptide vaccines and engineered T-cell receptors. OncoPept is an integrated platform that combines powerful analytics to analyze exome and RNA-seq data with multistep prioritization to select cancer vaccine candidates as therapeutics. The platform generates neo-antigens from different types of genetic alterations such as SNVs, indels and fusion genes to generate a library of peptides that are automatically interrogated through the multiple prioritization steps. The optimized process has been validated on published datasets. Additionally, OncoPept translates the RNA-seq data to quantitate the epithelial, stromal and immune cell infiltrate producing a holistic view of the tumor microenvironment. The T-cell neo-epitope burden and the tumor immune microenvironment are significant predictors of response to cancer immunotherapy drugs.

OncoTope™: A database of T-cell neo-epitopes from 540 cancer-causing genes mutated and/or overexpressed in 28 different cancer types

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Recent studies have demonstrated that the T-cell reactivity against tumor-specific neo-antigens determines efficacy of cancer immunotherapy drugs. The response can be accentuated further by including peptide vaccines derived from patient-specific neo-antigens. Cataloging T-cell-activating neo-antigens derived from patient's mutations is an important area of investigation. OncoTope™ is a database of neo-antigens derived from genetic alterations in 540 cancer-causing genes across 28 different cancer types. The database captures $CD4^+/CD8^+$ T-cell neo-epitopes from 563,936 neo-antigens based on their binding affinity to 12-different HLA types and selected based on their expression in cancer cells. Mutated genes are rank ordered according their T-cell neo-epitope burden. The

analysis provides an explanation as to why T-cell neo-epitopes are largely private and not shared between samples.