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Automated analysis pipeline for identifying immunogenic neo-antigens from next generation sequencing data from patients

Recent advances in cancer immunotherapy and sequencing technologies have created promising opportunities for precision cancer medicine. The biology underlying ohow endogenous T cells recognize and destroy the cancer cells is complex and under active investigation, but one fundamental step involves T-cell recognition of peptide epitopes that are presented on major histocompatibility complexes (MHCs) on the surface of tumor cells but not in normal cells. Somatic mutations in cancer genomes produce amino acid alterations that can generate new immunogenic peptides, frequently called neoantigens. Tumor mutation burden, and, even more specifically, neoantigen load have been correlated with strength of T-cell reactivity, response to immunotherapy, and prognosis. Most often these mutations are unique to individual patients, and, thus, point to a personalized, precision medicine approach for using immunotherapy. This requires investigating and predicting the interactions between T cells and mutation-derived tumor neoantigens. Next generation sequencing technologies such as whole exome sequencing allow us to identify nonsynonymous mutations in the protein-coding portions of genes in cancer patients and predict potential neoantigens. The ideal neoantigen derived from genomics data has the following properties: i) nonsynonymous somatic mutation, ii) expressed in transcriptome data, iii) translated neopetide with strong binding affinity to patient's own MHC molecules, and iv) belong to larger/diverse subpopulation. Once found and validated, neoantigens can be used to help predict and potentially enhance checkpoint therapy response as well as to identify targets for the development of adoptive T cell therapies and therapeutic tumor vaccines. We developed an automatic pipeline with consensus approach to identify immunogenic neo-antigens based on genomic data. This software identifies and characterizes

neoantigens as needed. While other technological pipelines are emerging, there is high variability in the methods used and studies on large human data sets are still lacking. Therefore, our system has been validated using quality control data sets. Overall, this software enables one to evaluate neoantigens from any individual tumor and consider the role of immunotherapy approaches using these results.

Applications

- Our pipeline can identify/prioritize the immunogenic neo-antigens for any cancer patients with DNA sequencing and RNA-Seq (milllions of sequence reads) using the generated results.

Advantages

- Development of a fully integrated bioinformatics pipeline that includes all the necessary steps needed for neoantigen development. This can be run as a single command that implements all steps. Identification of whether a specific neoantigen is represented among quantitative fraction of tumors cells from a given patient.

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