Research Project Proposal
Academic year 2019-2020

Project Nº 28

Title: *Correlate tumor mutation burden with immune signatures and clonality of T cell receptors in human cancers*

Department/ Laboratory
Immunology and Immunotherapy, CIMA

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Summary

Immunotherapy is becoming increasingly noteworthy for its effectiveness in treating cancers. Nevertheless, this therapy is beneficial to only 20% of cancer patients. Tumor mutation burden (TMB) has been associated with immunotherapeutic response and better prognosis in cancer. Mutated proteins may yield neoantigens that are released by cancer cells. These neoantigens are presented by professional antigen presenting cells, which activate mutation-specific T cells. Then, T cells specific for neoantigens infiltrate tumor bed and kill tumor cells. Tumors being attack by tumor infiltrating lymphocytes exhibit a gene signature of immune response. A systematic exploration of the correlation between TMB, gene immune signature and the clonality of the repertoire of T cell receptors (TCR) of tumor-infiltrating lymphocytes is lacking. To explore this, we will choose patients form the Cancer Genome Atlas (TCGA). TMB will be assessed using whole exome sequencing data and a software pipeline set up by our lab. Gene expression analysis and the TCR repertoire will be assessed from RNAseq using DESeq2 and MiXCR, respectively. We will compare the expression levels of immune-related genes and the TCR clonality between the lower-TMB and the higher-TMB cancer types.

The questions that will be addressed in this project are: Are there any immune-related genes that are differentially expressed between the lower- and higher-TMB tumors? How do TMB, immune gene signature and TCR clonality associate with clinical outcomes in cancer?

The student will learn a spread variety of bioinformatics tools as R, Linux and different algorithms to achieve the goals.

yes	
no	**x**

Does the project include the possibility of supervised animal manipulation to complete the training for animal manipulator?