Universitat Pompeu Fabra Barcelona

Master in Bioinformatics for Health Sciences

Master project 2021-2022

Personal Information

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Project

Computational genomics

Project Title:

Identification of novel classes of neoantigens in cancer

Keywords:

Transcriptomics; cancer; small ORFs; neoantigens; immunotherapy.

Summary:

Mutations affecting proteins expressed in cancer cells can generate neoantigens, which are small peptides presented by MHC receptors. These peptides can be recognized by T cells and lead to the destruction of cancer cells. The identification of neoantigens expressed by cancer cells is thus crucial to develop anti-cancer vaccines and predict the response to immunotherapy. Neoantigens derived from single mutations in coding sequences can be predicted using whole exome sequencing (WES), which has become a widely employed technique for the molecular characterization of cancer samples. There is one important class of neoantigens, however, that cannot be detected by WES. This class is made of peptides that are cancer-specific – absent from normal tissues - and that are usually not annotated in the databases. These neoantigens are predicted to be highly immunogenic and thus could improve the development of new treatments for cancer. They include peptides originated from the translation of ORFs in cancer-specific transcripts or peptides derived from frameshift mutations that escape nonsense mediated decay. This type of neoantigens can only be identified using RNA sequencing data (RNA-Seq) of cancer samples. The aim of the project is to identify different classes of neoantigens using available WES and RNA-Seq data from diverse cohorts of cancer patients that have been treated with immunotherapy (Litchfield et al., 2021). We will measure the prevalence of neoantigens carrying single mutations and of neoantigens that are cancer-specific, and investigate how their abundance correlates with the response to immunotherapy. In the group we have previously employed massive transcriptomics data to identify recently originated transcripts in human and mouse and predict novel peptides (Ruiz-Orera et al., 2015; Ruiz-Orera et al., 2018). Here we will use similar techniques to identify cancer-specific transcripts and neoantigens.

References:

Litchfield, K., Reading, J.L., Puttick, C., .., Quezada, S.A., McGranahan N., Swanton, C. (2021). Meta-analysis of tumor- and T cell-intrinsic mechanisms of sensitization to checkpoint inhibition. Cell, 184: 1–19. Ruiz-Orera, J., Grau-Verdaguer, P., Villanueva-Cañas, J-L., Messeguer, X., Albà, M.M. (2018). Translation of neutrally evolving peptides provides a basis for de novo gene evolution. Nature Ecology and Evolution, 2:890–896. Ruiz-Orera, J., Hernandez-Rodriguez, J., Chiva, C., Sabidó, E., Kondova, I., Bontrop, R., Marqués-Bonet, T., Albà, M.M (2015) Origins of de novo genes in human and chimpanzee. Plos Genetics, 11 (12), pp. e1005721.

Expected skills::

Interest in computational genomics and transcriptomics; basic knowledge of a programming language; basic knowledge of R; good command of English.

Possibility of funding::

Yes

Possible continuity with PhD: :

Yes
