Universitat Pompeu Fabra Barcelona | Master in Bioinformatics for Health Sciences

Master project 2024-2025

Personal Information

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Project

Computational genomics

Project Title:

Bioinformatics analysis of antitumor immunotherapy

Keywords:

genomics, cancer immunotherapy, biomarkers

Summary:

The project proposed here will be executed by a multidisciplinary team that will capitalize on the synergies in expertise of the team members. All teams have currently active, funded projects in which they are using the specific methodologies necessary for this proposal. The synergy of the methodologies (mouse cancer models, single cell immunology and genomics) will allow us to reconstruct the antitumor immunotherapy response in vivo using cancer mouse models and to efficiently test new immunomodulatory therapies for the treatment of cancer. We will combine current in vivo immunotherapy approaches with modulation of tumor DNA repair mechanisms to study their effectiveness in the control of tumor cell progression in a physiologically relevant setting. Specifically, to confirm mismatch repair mutations (MMR deficient, MMRd) and investigate the degree of mutational burden in our cancer models before and after checkpoint immunotherapy treatment, we will microdissect the tumors, isolate their genomic DNA, prepare Illumina sequencing libraries using a PCR-free method to reduce the possibility of artefacts, and perform whole exome sequencing (WES). Reads will be aligned to mm10 assembly using Borrows-Wheeler Aligner (BWA), and somatic mutations called with Mutect2 and Strelka2 pipelines used in the Pasquali laboratory. A WES of a healthy tissue sample will be used for germline variant removal during somatic mutation calling. Mutational burden and mutational spectra of MMRd tumors will be characterized using Integrative Onco Genomics (IntOGene). Moreover, to further validate and refine immunotherapy approaches, genetic features of the tumor will be searched for, by drawing on the genomes of untreated versus treated tumors, obtained from our controlled experiments in MMRd tumor mice. Therefore, this project will facilitate the discovery of novel genetic tumor markers that might anticipate tumor progression or its response to immunotherapy. The collective expertise of our teams will be instrumental for the development of this master project: 1. Ana Janic: in vitro and in vivo experiments to generate MMRd cancer models. 2. Cristina López-Rodríguez and Jose Aramburu: in vivo MMRd tumour immuno-therapy treatments, monitor outcomes and collect samples to define key immune cell populations. 3. Lorenzo Pasquali: computational analysis to address the role of mutational instability in immune checkpoint therapy in MMRd cancer models.

Expected skills:

Programming, R

Possibility of funding:

To be discussed

Possible continuity with PhD:

To be discussed

Comments:

PRBB, hybrid work model