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:

Disruption of p53 dependent DNA repair axis accelerates tumour maintenance by impairing chromosomal instability

Keywords:

cancer, p53, CNVs

Summary:

The tumour suppressor gene p53 is the most frequently mutated gene in human cancers. In Janic laboratory we are interested in what are the most important p53 activities needed for tumour suppression. Our hypothesis is that the p53-mediated tumour suppression relies on collective and cooperative activation of the p53 target gene network. To answer this important question, we have conducted functional genomic shRNA and sgRNA screens in vivo to identify p53 target genes whose deficiency can promote tumour development. The E3-ubiquitin ligase RNF, was the most potent hit from our screens. Understanding the mechanisms, by which RNF act in healthy and cancer cells, and how they mediate their tumour suppressive function is the major focus of this project. Our preliminary data shows that RNF deficient cells are aneuploid and have increased DNA damage signalling. In this project we will test if aneuploidy is due to chromosomal instability and genomic alternations using genetically stable RNF deficient cell lines. Karyotype abnormalities observed by an analysis of chromosome spreads will be confirmed by performing low-coverage (shallow) whole genome sequencing to identify copy number alterations and total mutational burden in RNF deficient cells. To achieve better understanding of how large chromosomal changes evolve in our mutants we will isolate genomic DNA for WGS at two timepoints for comparison: the timepoint 0 (T0), on the day when cells will be orthotopically injected into the recipient mice, and at the humane endpoint when mice develop tumours (T1). Shallow sequencing and data analysis will be performed within in-house genomics facility, and data analysis and interpretation of the results by a master student under the co-supervision of Dr Fran Supek (IRB Barcelona) that has extensive expertise cancer genomics. In this master project combining cell and computational biology methods we aim to discover how RNF as DNA repair regulator contributes to genomic stability.

References:

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Expected skills:

Programing

Possibility of funding:

Yes

Possible continuity with PhD:

To be discussed

Comments:

remote/hybrid work model,