Grenoble Alliance for Integrated Structural & Cell Biology

INTERNSHIP PROPOSAL

Institute and Group: BIG, équipe IMAC (Mécanismes d'Invasion en Angiogenèse et dans le Cancer)

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Research project title:

Proteomic analysis of Lysine crotonylation in kidney cancer.

5 Keywords to describe the project:

Kidney cancer, Histone Lysine modifications, gene expression regulation, proteomic analysis, exploration of large-scale genomics and proteomics datasets.

Description of the project (aims, experimental techniques, recommended background):

Gene expression is tightly regulated by several layers of chromatin modifications, including numerous histone post-translational modifications (PTMs). Aberrant histone PTMs, in particular deregulated Lysine acetylation and methylations, have been linked to cancer development. Histone Lysine crotonylation, discovered in 2011, has started attracting much interest because it constitutes a stronger mark of active gene transcription than Lysine acetylation. Moreover, Lysine crotonylation has been described to protect against acute kidney injury. In this project, we wish to decipher by proteomics which histone Lysines residues bear this PTM in cultured renal cortex cells (RPTEC) *versus* in the renal cell adenocarcinoma cell line 786-O. We also wish to explore the large-scale datasets produced by the CPTAC consortium on kidney cancer, and on colorectal, breast and ovarian cancers, to see whether histone crotonylations are variably detected between cancers and/or intra cancer between patient groups. The student will perform cell culture, histone precipitation, their comparative proteomic analysis and bioinformatic exploration of datasets published by the CPTAC. If time allows, we will also try to identify proteins interacting with crotonylated Lysines (by pull-down or ChIP followed by proteomics). The student should have a background in epigenetics.

Justification that the internship's subject fits with the general theme of GRAL:

This internship project addresses a question at the crossroad of epigenetics, cell differentiation and structural biology: we wish to study a specific histone PTM in the context of normal/cancerous kidney cells, ideally up to identifying its protein interaction partners.

Relevant publications of the team:

Combined inhibition of PI3K and Src kinases demonstrates synergistic therapeutic efficacy in clear-cell renal carcinoma. Roelants, C., S. Giacosa, C. Pillet, R. Bussat, P. Champelovier, O. Bastien, L. Guyon, V. Arnoux, **C. Cochet and O. Filhol**. Oncotarget 2018, 9(53): 30066-30078.

Systematic quantitative analysis of H2A and H2B variants by targeted proteomics. El Kennani S, Adrait A, Permiakova O, Hesse AM, Ialy-Radio C, Ferro M, Brun V, Cocquet J, Govin J*, **Pflieger D***. Epigenetics Chromatin. 2018 Jan 12;11(1):2.

Proteomic Analysis of Histone Variants and Their PTMs: Strategies and Pitfalls. El Kennani S, Crespo M, Govin J, **Pflieger D**. Proteomes. 2018 Jun 21;6(3). pii: E29.