2-Year postdoctoral position
Turing Centre for Living Systems

Ref offer: PD2018-08

Deciphering the role of PTEN in leukemic T-cell development using systems biology approaches

Project abstract – T-cell acute lymphoblastic leukemias (T-ALL) are malignant proliferations of immature T-cell progenitors resulting from various combinations of genomic alterations. Among them, *PTEN* loss-of-function is one of the most potent and is frequently associated with TCRαβ+ TALL. Recently, we revealed a cross-talk between PTEN and TCR signaling networks which can lead to opposite cell fate: leukemogenesis or apoptosis. Our main objective is, thus, to decipher mechanisms determining TCRαβ+ thymocytes fate toward leukemia or cell death. First, we will define the molecular mechanisms allowing PTEN loss to interfere with thymocytes selection processes and notably the mechanism that, by inducing apoptosis, impedes leukemia development. Then, our ultimate goal will be to uncover strategies to activate this apoptotic program in tumoral cells. To achieve our objectives, we will combine *in silico* and wet-lab approaches: discrete mathematical modeling (Gene regulatory network inference from single cell expression data, logical network parametrization and dynamical analysis), mouse genetics, and cutting-edge experiments in molecular biology (scRNAseq, CyTOF). We expect to acquire a global view of molecular circuitry in the different cell states (pretumoral and tumoral), and thus to obtain a comprehensive understanding of tumoral development of PTEN-deficient TCRαβ+ thymocytes. *In fine*, this project might uncover some actionable pathways that can be therapeutically targeted.

Expected profile – Preferentially, the applicant should have skills in either Mathematics, Computer sciences or Bioinformatics. Training in the specific fields of immunology and oncology will be provided by D. Payet (CIML); thus skills in these fields are not required to apply. However, the applicant should have a strong interest in biology and in interdisciplinary approaches to decipher biological processes. He/she will be in charge of constructing/analyzing the mathematical model (under the supervision of E. Remy (I2M)) and to analyze single-cell data using bioinformatic tools. Thus prior knowledge in mathematical modelling, in programming/scripting and/or bioinformatics (omics data processing) would be a plus.

Supervisors

Dominique Payet Bornet - CIML, UMR 7280 - Laboratory of genomic instability and human hemopathies
Elisabeth Remy - I2M, UMR 7373 - Mathématiques et algorithmes pour la biologie des systèmes

Deadline for application: 28th February