Internship proposition
One page max
M2 0HNU 2025-26

Lab: CRCI2NA

Team: 11, Molecular Vulnerabilities of Tumor Escape in mature B cell malignancies

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Candidate: Martin BAUER

Title of the internship:

Summary of the internship proposal:

The differentiation of B lymphocytes, first in the bone marrow and then in secondary lymphoid organs during an immune response, is accompanied by major epigenetic regulation to enable the activation and repression of adapted transcriptional programs. Multiple myeloma (MM) is characterized by the abnormal proliferation of a plasma cell, a terminal cell of B differentiation, and develops in the bone marrow. MM cells are characterized by recurrent abnormalities, either odd-chromosome hyperdiploidy or translocations involving the immunoglobulin heavy chain locus. The most frequent translocation is t(11;14), which leads to overexpression of the CCND1 gene. The second most frequent translocation (around 15%) is t(4 ;14), which juxtaposes the NSD2 and FGFR3 genes downstream of the IgH promoter, leading to overexpression of NSD2. This methyltransferase deposits the H3K36me2 mark associated with transcription activation. This NSD2 alteration is over-represented in patients with a poor prognosis, and appears to play a role in tumor cell survival, proliferation and resistance. However, the molecular mechanisms involved in NSD2-mediated resistance in MM are not known.
Our preliminary data reveal the gain-of-function of NSD2 alterations by an increase in the H3K36me2 mark in MM lines that overexpress NSD2 following t(4 ;14) translocation compared with non-translocated lines. Three regions of t(4;14) translocation have been identified, depending on the patient. The breakpoint can preserve NSD2 in a complete form, or generate two more or less truncated forms, while retaining the histone methyltransferase catalytic domain. Depending on the position of the breakpoint, the patient's chances of survival are altered: the shorter NSD2 is, the lower the probability of survival.
Based on a cohort of MM lines and primary cells, the aim of the proposed internship will be to define the impact of these NSD2 alterations in MM on resistance to treatment. The arsenal of therapeutic molecules used in MM will be evaluated, as will degrader molecules specifically targeting NSD2.

Option(s) linked to the project:

X Hematology
☐ Immunology-Cancerology
X Oncology
☐ Nuclear Medicine

Option(s) linked to the profile:

☐ Clinical Research Profile
X Experimental Biology Profile
☐ Data Analyst Profile