



Internship proposition  
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M2 I3/OHNU 2024-25



Lab: CRCI2NA

team: 12 – Manipulation of lymphocytes

Name and position of the supervisor: Christelle Harly, CR CNRS

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Candidate: open to any candidate interested in development, normal or pathological, and *in vivo* studies.

Title of the internship:

**Generation and characterization of mouse models for chronic neutrophilic leukemia**

Summary of the internship proposal:

Chronic neutrophilic leukemia (CNL) is a rare cancer (1 new case per million per year) affecting hematopoietic precursors. The cause of this cancer is unknown, and its diagnosis is extremely difficult. As a result, patients are diagnosed late (average age 65) and have a poor prognosis (average survival 2 years). The only curative treatment currently available is bone marrow transplantation, which is associated with high mortality. The scarcity of patients and the lack of animal models recapitulating the disease hinders diagnostic and therapeutic advances in CNL.

By studying hematopoiesis, we identified a transcription factor whose loss in mice causes the development of characteristic symptoms of patients with CNL. In this project, we propose to manipulate the expression and function of this transcription factor to set up several mouse models for studying CNL, *in vivo* and *in vitro* (hematopoietic stem cell manipulation by retroviral transduction, transplantation for the generation of chimeric mice). We will then characterize in detail the development of the pathology in these models (flow cytometry, cell culture).

The results obtained will enable us to initiate a research program aimed at understanding the mechanisms causing CNL. Ultimately, our study should identify early symptoms of CNL, enabling early diagnosis and better patient management. It could also identify clinically useful control points in the CNL developmental process. Our preliminary results indicate that CNL is triggered earlier than thought, in young adults.

Option(s) linked to the project:

Experimental Biology Profile