

### Stages d'été

Centre de recherche Azrieli du CHU Sainte-Justine



## Un été ensoleillé avec prévision de science

# 01 – Targeting the metabolism of T-cell leukemia

Accepted Academic Levels (in progress):
□ College ⊠ Bachelor's □ First-cycle PhD □ Master's
Research Team
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#### **Research Project Description**

T-cell acute lymphoblastic leukemia (T-ALL) is an aggressive hematologic malignancy, accounting for 10–15% of pediatric and 25% of adult ALL cases. Although survival rates have improved with intensified treatment protocols, about 25% of children with T-ALL relapse due to refractory disease. This highlights the need to develop more targeted and effective therapies for the treatment of T-ALL.

Lipids are a major component of the cell membrane. The lipid composition of the membrane can determine which signaling pathways are activated within the cell. This is particularly true in cancer cells, where survival pathways are essential for proliferation. We found that T-ALLs exhibit highly active lipid biosynthetic pathways, accompanied by elevated levels of phospholipids. Moreover, we observed that cell lines and patient-derived xenografts from T-ALL are sensitive to the inhibition of CHKA, the rate-limiting enzyme of the phosphatidylcholine (PC) biosynthesis pathway.



#### Role of the candidate during the internship

We performed untargeted lipidomics and RNA sequencing (RNA-seq) to determine how pharmacological inhibition of CHKA alters lipid abundance and species distribution. The trainee will validate these results using flow cytometry and Western blot assays, and will characterize the molecular mechanisms disrupted by genetic deletion of CHKA using CRISPR technology. The results obtained here will pave the way for new combinatorial treatment options for T-ALL.

#### **Academic Programs**

Students enrolled in one of the following academic programs, or in a related field, are invited to apply:

Biomedical science, biochemistry, microbiology and immunology

#### Required Skills and Expertise

 Cell culture, molecular biology techniques (cloning, PCR, Western blot), flow cytometry

#### **Internship Details**

Schedule		<b>Duration</b> (approximative)	
	s/week)		4 months
□ Part-time		$\boxtimes$	3 months
			2 months
			1 months

#### **Funding**

Funding will vary depending on the type of internship:

- Internship recognized by the academic institution: A minimum stipend of CAD
  \$550 per week (based on a 35-hour schedule) will be provided from the supervisor's research funds or in combination with other funding sources.
- Internship outside the academic curriculum: An hourly wage ranging from CAD
  \$16.10 to \$18.72 will be provided from the supervisor's research funds.

#### **Keywords**

Cancer, leukemia, molecular biology, metabolism, therapeutics

#### Address

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