PhD Research Proposal Form
China Scholarship Council (CSC)

A remplir en français ou en anglais en fonction de la langue qui sera utilisée pour la thèse

FIELD

Biology / Immunology

Thesis subject title: **Sphingosine-1 phosphate receptors in T and NK cell homeostasis**

Name of the French doctoral school/Ecole doctorale: BMIC

Name of the Research team/Equipe de recherche: Lab T Walzer “lymphocyte activation and signaling”
Website: http://ciri.inserm.fr/en/team/all-teams/differentiation-and-migration-of-cytotoxic-lymphocytes/general-interests/

Name of the Supervisor/Directeur de thèse: Thierry Walzer
Email: Thierry.walzer@inserm.fr

Lab Language/ Langue de travail: English

Research Proposal Abstract/Présentation du sujet:

Sphingosine-1 phosphate (S1P) is a lipid vehicled by albumin in the blood and in the lymph. It regulates the physiology of several systems, including the immune system. In particular, it can regulate lymphocyte survival and trafficking. S1P can bind to five related G-protein coupled receptors (GPCR) called S1PR1-5. Our lab discovered in 2007 that S1PR5 was essential for Natural Killer (NK) cell homeostasis. NK cells develop in the bone marrow and circulate in the blood when they are mature. We found that S1PR5 acted as a chemotactic receptor for S1P, promoting NK cell exit from the bone marrow to the blood. Moreover, other labs established that S1PR1 was the major S1P receptor promoting T cell exit from the thymus to the periphery. However, many points remain to be clarified in this research field:

- the role of S1PR2 and S1PR4 are poorly understood and our lab suggested that they may act as natural antagonists of other S1P receptors.
- all lymphocytes express variable combinations of S1P receptors, and the importance of such combinations is currently unknown.
- the coordination between S1PR and chemokine receptors is also not well known. In particular our lab showed that CXCR4 desensitization is required for NK cell exit, but how this is linked to S1PR5 engagement is unknown
- the precise pattern of S1PR expression is difficult to assess because antibodies allowing FACS measurements are lacking.
To address these different questions, the PhD student will use unique unpublished tools generated in the lab (new mouse or cellular models with modified or deficient S1PR and CCR), new S1PR antibodies, and various in vitro and in vivo assays of cellular migration, survival, and signal transduction. The student will be integrated in the multi-disciplinary TW team with expertise on NK cells, B cells, mouse and human immunology.

References:


PLEASE SEND THE DOCUMENT TO
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