LECTURE SERIES 2022
INFECTION & IMMUNITY

LUXEMBOURG INSTITUTE OF HEALTH

16 Nov 2022
Wednesday

LECTURE
11.00 - 12.15 pm

MEET & EAT*
Light lunch provided
12.45 - 2 pm

7 8 9 10 11 12 1 2

Atypical chemokine receptors ACKR3 and ACKR5

ABSTRACT

Atypical chemokine receptors (ACKRs) scavenge chemokines contributing to gradient formation by binding, internalizing and delivering chemokines for lysosomal degradation. Unlike canonical chemokine receptors, they do not couple to G-proteins and fail to induce typical signaling. ACKRs are thought to act as sinks that can eliminate chemokines from the nearby extracellular environment.
Chemotaxis is an essential physiological process, often harnessed by tumors for metastasis. CXCR4, its ligand CXCL12 and the atypical receptor ACKR3 are overexpressed in many human cancers. Interfering with this axis by ACKR3 deletion impairs lymphoma cell migration towards CXCL12. We propose a model of how ACKR3 controls the migration of the diffused large B-cell lymphoma cells in vitro and in vivo in response to CXCL12 and show that LTB4 acts synergistically with CXCL12 in stimulating the migration of VAL cells.

The closest relative of ACKR3, GPR182, has been partially deorphanized as a potential novel ACKR. We generated a comprehensive map of ACKR3, ACKR4, and GPR182 expression in mouse tissue using transgenic reported mice and specific fluorescent chimeric chemokines. We found areas of both unique and common expression of either receptor in organs including generative and secondary lymphoid organs, intestine and colon, liver and kidney.
We confirm the "atypical" nature of the receptor, wherein canonical intracellular signaling is not activated following ligand stimulation, and that β-arrestins are required for chemokine uptake and ligand-independent internalization. In vivo, we observe elevated chemokine levels in the serum but also in SLO interstitium. In lymphocytes the atypical chemokine receptor 3 (ACKR3) defines two phenotypically, transcriptionally and functionally distinct, equal-sized populations of mouse MZ B cells. By contrast a phenotype was found in ACKR5-KO mice with a reduced marginal zone (MZ), both in size and in cellularity. These mice produced a lower antibody response to the T-independent antigen TNP-Ficoll.

SPEAKER

Prof Dr Marcus Thelen

Institute for Research in Biomedicine,
Università della Svizzera italiana

HOST:

Department of Infection and Immunity (LIH)

RESPONSIBLE SCIENTIST:

Andy Chevigne / (andy.chevigne@lih.lu)

***Please note that registration is mandatory by sending an email to carole.weis@lih.lu or michelle.roderes@lih.lu**

Locations:

Lecture:
Lycée Guillaume Kroll
d'Esch/Alzette
Room: Salle de Projection*

Meet & eat:
House of BioHealth
Salle Françoise Barré Sinoussi
29, rue Henri Koch,
L-4354 Esch-sur-Alzette
Registration mandatory

**Opposite Luxembourg Institute of Health, House of BioHealth, 29, rue Henri Koch, L-4354 Esch-sur-Alzette*

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