

19

 SEPT
2024

Thursday

LECTURE

11.00am - 12.00pm

MEET & EAT *

Light lunch provided

12.30pm - 2pm



Immunometabolism in Immunotherapy and Inflammation

ABSTRACT

T cells in tumors and other inflamed tissues accumulate signs of stress and mitochondrial damage that affect cell metabolism but remain poorly understood. The metabolism of T cells and other immune cells is dynamically regulated and influences biosynthesis, signaling, and cell fate. We have shown that CD4 T cell subsets are metabolically distinct and that each requires a specific metabolic program for their function. Temperature is a microenvironmental variable that changes with body location, fever, and inflammation. While heat is well-known to influence activities of enzymes and complex structures, the impact of fever or locally increased temperatures on T cell metabolism and function are uncertain. We tested the effects of elevated temperatures found that T cells become more pro-inflammatory but begin to experience stress that may shape immunity. Effector CD4 T cells of all subsets tested had increased proliferation and cytokine secretion. While Treg also had increased proliferation, they had reduced ability to suppress. Interestingly, Th1 cells selectively showed mitochondrial stress, with many cells experiencing mitochondrial dysfunction, reactive oxygen species, and DNA damage that Th17 and Treg did not experience. This ultimately led to p53 and STING activation to enhance both inflammation and apoptosis. Mechanistically, our data point to mitochondrial electron transport complex 1 (ETC1) as sensitive to elevated temperatures and Th1 as selectively dependent on this complex. Together, these data show that physiologic heat is pro-inflammatory and that Th1 cells selectively develop mitochondrial stress with ETC1 as a potential thermosensitive modulator of mitochondrial metabolism. This heat sensitive ETC1 mitochondrial stress pathway may have broad implications in fever and inflamed tissues.



SPEAKER

Prof. Jeffrey Rathmell

Cornelius Vanderbilt Professor of Immunobiology,
Vanderbilt University Medical Center

HOST:

Department of Infection and Immunity (LIH)

RESPONSIBLE SCIENTIST:

Dirk Brenner (dirk.brenner@lih.lu)

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

Locations:

Lecture:

House of BioHealth
Conference Room
(ground floor 0)
29, rue Henri Koch,
L-4354 Esch-sur-Alzette

Meet & eat:

House of BioHealth
Salle Françoise Barré Sinoussi
Registration mandatory