LUXEMBOURG INSTITUTE OF HEALTH

LECTURE

Martina Seiffert

02.12.2026

HoBH, ground floor lecture room (lecture)
Room FBS (meet & greet lunch)

11:00 - 12:00

12:00 - 14:00 meet & greet lunch*

Decoding Cancer Immune Escape: From Microenvironmental Mechanisms to Novel Immunotherapies

Effective anti-tumor immunity requires not only the presence of immune cells within tumors, but also their ability to recognize and eliminate cancer cells in a sustained manner. Tumors evade immune control by shaping an immunosuppressive microenvironment and driving T-cell dysfunction. Understanding the mechanisms that support effective anti-tumor responses is therefore essential for developing durable immunotherapies.

In the first part of this talk, we investigate the immune landscape of breast cancer brain metastases. We identify T-cell-infiltrated immune ecotypes, tertiary lymphoid structures (TLS), and TLS-associated gene signatures linked to improved survival. Within tumor islands, we identify clonally expanded, tissue-resident memory-like $CD8^+$ T cells that retain cytotoxic activity despite expressing exhaustion-associated markers. These cells recognize and kill autologous tumor cells and respond to immune checkpoint blockade, highlighting their therapeutic potential.

In the second part, we explore strategies to sustain T-cell function using chronic lymphocytic leukemia (CLL) as a model. We show that IL-10 receptor signaling in $CD8^+$ T cells supports their function during disease progression. Therapeutic IL-10-Fc limits CLL development in a CLL mouse model by reducing T-cell exhaustion and suppressive monocyte accumulation, and improving immune control. Combined with T-cell-engaging bispecific antibodies, IL-10-Fc enhances anti-tumor efficacy in B-cell lymphoma patient-derived 3D cultures and mouse models of CLL, while promoting immune memory.

Together, these findings demonstrate that durable tumor control requires both tumor-reactive T cells and the maintenance of their functional capacity. Identifying effective T-cell populations and developing strategies to sustain their activity may help overcome immune escape and advance more durable cancer immunotherapies.



SPEAKER:

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HOSTS:
Ulf Nehrbass, Frank Glod

* Please register for the meet & greet by sending an email to: **Carole.Weis@lih.lu / Michelle.Roderes@lih.lu**