

SPECIAL LECTURE



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Hosts: Judith Zaugg, Eftychia Kormari

“Decoding the X Factor: How X Chromosome Inactivation Shapes Immune Function and Cancer Immunity”

Abstract

Biological sex is a fundamental variable shaping immune responses, cancer susceptibility, and responses to immunotherapy. While hormonal influences have long been recognized, emerging evidence highlights the X chromosome as a key driver of immune variation between men and women. Many immune-related genes reside on the X chromosome, and a substantial subset escapes X chromosome inactivation (XCI), leading to sex-specific differences in gene dosage and immune regulation. My research explores how XCI dynamics influence T cell activation and exhaustion within the tumor microenvironment. Leveraging large-scale single-cell RNA sequencing data from non-small cell lung cancer, we uncovered pronounced sex differences in CD8⁺ T cell states, with female exhausted T cells exhibiting higher expression of canonical exhaustion markers including LAG3, and TOX. Module scoring revealed an inverse correlation between exhaustion signatures and XCI escapee gene expression, suggesting that reduced escape from XCI may drive terminal T cell exhaustion. Complementary in vitro models and CRISPR-based perturbation experiments are underway to dissect how X-linked regulatory mechanisms contribute to T cell dysfunction and to test whether modulating XCI escape can restore effector function. Together, these studies aim to uncover how chromosomal gene dosage shapes immune cell behaviour and to identify new molecular strategies to improve cancer immunotherapy in a sex-aware manner.

 **Friday, December 5th, at 11:00am**

 **Seminar room – 2nd floor, ZLF, Hebelstrasse 20,
4031 Basel**