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Contribution ID: **30** Type: **TALK**

Sex-Bias Immune Aging and its Interplay with X-Inactivation Escape Genes at Single-Cell Level

The world is aging, and improving the health of the elderly is crucial. Elderly individuals are particularly susceptible to immune system failure, leading to increased vulnerability to infectious diseases. Immune responses exhibit sex-specific patterns due to a combination of hormonal and genetic factors, including the number of X chromosomes and the expression of genes escaping X-inactivation in females. However, which genes escape X-inactivation throughout life and their impact on immune cell functions remain unclear.
Using single-cell multiomics methodologies, we assess whether age-related changes in cellular composition, chromatin accessibility, and transcription are sex-specific in mice. Our findings reveal a similar aging-specific remodeling of the T-cell compartment in both sexes and a pronounced sex influence on the B-cell transcriptome. Moreover, we describe a cell-type-specific landscape of X-inactivation, with escape genes contributing to female-biased expression. Notably, a subset of aged T-cells, which play a key role in aging and cancer progression, demonstrates increased transcriptional activity from the inactive X chromosome, accompanied by heightened chromatin accessibility. Our work sheds new light on the intricate interplay between sex and age, highlighting cell-type-specific escape dynamics in shaping sex-specific immunological trajectories and advantages.

Research type

Basic research

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Session Classification: Short talks #2