SORS: Uncovering the missing X factors and their function to understand sex bias in disease

Abstract

Cardiovascular disease (CVD) manifests and progresses differently in men and women, a phenomenon known as sex bias. Understanding the mechanisms underlying this sex bias is critical to the development of sex-specific treatments. Hormonal differences have been suggested to account for the sex bias by the observation that younger women are routinely protected from CVD until postmenopause. However, hormone replacement therapies have not provided broad cardioprotection, suggesting that other biological factors contribute to the sex bias. One likely contributor is the set of genes that escape X-chromosome inactivation in females, resulting in higher gene dosage compared to males. Here, we characterized the escape landscape in major organs of the mouse to elucidate the functions of escape genes and the extent of organ- and lineage-specific escape. In addition, we captured gene escape in mouse models of cardiac disease at the cell-type resolution and characterized the function of selected candidate genes. The overall goal is to identify novel sex-specific regulatory disease mechanisms with the perspective of developing RNA-based therapies for sex-specific treatment.

Short Bio

Daniel Andergassen received his Diploma degree in Molecular Biology from the University of Vienna in 2012. He then had the privilege to do his Ph.D. at **CeMM** under the supervision of **Denise Barlow**, a driving force of epigenetics, genomic imprinting, and lncRNA biology (2016). In her lab, he generated the most comprehensive map of allele-specific expression in the mouse, including identifying all the imprinted genes and X chromosome inactivation (XCI) escapers. To accomplish this, he developed a bioinformatics pipeline to detect allele-specific expression from high-throughput sequencing data. To learn more about lncRNA biology and epigenetic regulation, he joined the lab of **John Rinn** and **Alexander Meissner** as a postdoctoral researcher at **Harvard**, where he focused his research on X-linked lncRNA loci with sex-specific features that have been linked to the structure of the inactive X chromosome. In another project, he used CRISPR-Cas9 to target epigenetic key pathways in vivo, which revealed the imprinting mechanism genomewide. Furthermore, this approach demonstrated, for the first time, that the inactive X chromosome could be reactivated in vivo. Since 2020, he has been leading an **independent junior research group** at the **TUM**, aiming to understand the impact of the non-coding genome in heart disease and elucidate the contribution of sex chromosomes to sex differences in cardiovascular disease. To achieve these goals, the Andergassen lab combines allele-specific (Epi-) Genomics with the pharmacological translational expertise of the host institute, with the overall objective of developing RNA-based therapies for sex-specific treatments.

Speakers

Speaker: Daniel Andergassen. Independent Junior Group Leader Technische Universität München (TUM).
Host: Marta Melé. Leading researcher, Transcriptomics and Functional Genomics Lab, Life Sciences

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