Contribution ID: **12** Type: **Poster**

Molecular coupling of Xist regulation to the formative pluripotency network

Wednesday, September 18, 2024 6:40 PM (20 minutes)

Xist, the master regulator of X-chromosome inactivation (XCI) in mammals, is upregulated in the epiblast during the formative phase of pluripotency, specifically in females. In the past, its regulation has been tightly linked to repression during naive pluripotency. However the identity of activators at the onset of XCI remains unknown. To fill this gap, we perform a comprehensive CRISPR screen targeting transcription factors during the early differentiation of female mouse embryonic stem cells. We identify a large set of activators, which is transiently expressed during the formative pluripotent stage. Subsequently, we use a series of CRISPR screens targeting individual reporter constructs in order to functionally connect trans-regulators to the cis-regulatory landscape of Xist. We detect a group of factors, including the X-linked TF ZIC3, which activate promoter-proximal elements in a X-dosage sensitive manner. Furthermore, we find a group of factors, including the master regulator of the epiblast OTX2, which interact with distal enhancer elements to control transcript levels following basal Xist activation. With this study, we provide a systems level view of the trans- and cis-regulatory network that links Xist activation to formative pluripotency and ensures female-specificity.

Primary author: SCHWÄMMLE, Till (Schulz Lab, MPI for Molecular Genetics)

Co-author: SCHULZ, Edda (Schulz Lab, MPI for Molecular Genetics)

Presenter: SCHWÄMMLE, Till (Schulz Lab, MPI for Molecular Genetics)

Session Classification: Poster Session I (Wed)