ASHBi SEMINAR

Investigating the function of the non-canonical SMC protein SMCHD1 in regulating X chromosome inactivation

Lecturer: **Dr. Marnie Blewitt**

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Date **Friday, 27 August 2021**

Time **2:00pm – 3:00pm**

Venue **Zoom Online Meeting***

***Register via the right QR code**

Abstract

SMCHD1 is a large chromosomal ATPase critical for gene silencing in normal development. Heterozygous mutations in SMCHD1 are associated with four distinct diseases. Therefore, we have been interested to understand how SMCHD1 contributes to epigenetic silencing at the molecular level so that we can understand its roles in normal development and consider how its function might be targeted to treat disease.

Using the inactive X chromosome as a model of epigenetic silencing, we have found that SMCHD1 is first recruited to chromatin dependent on polycomb repressive complex 1-mediated H2AK119, but independent on polycomb repressive complex 2-mediated H3K27me3. Once at the chromatin SMCHD1 mediates long range interactions, without SMCHD1 H3K27me3 spreads to cover more of the inactive X than is normally the case. These data suggest SMCHD1 plays a role in insulating the inactive X from other epigenetic regulators, potentially via the steric constraints of the long range interactions. With these data in mind, I will discuss our recent unpublished work on a neomorphic allele of SMCHD1, which are able to refine our model of SMCHD1 silencing. We are now extending our studies to how SMCHD1 functions at its autosomal targets including the Hox clusters, imprinted genes and other clustered gene families.

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