

ARMI EXTERNAL SEMINAR SERIES 2023



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The epigenetic dynamics of X-chromosome inactivation in development and disease

Professor Edith Heard – EMBL Director General - Germany

Abstract

X-chromosome inactivation (XCI) during early female development is an essential epigenetic process that is required to achieve appropriate dosage between the sexes for X-linked gene products. We are interested in understanding how the differential treatment of the two X chromosomes in the same nucleus is set up during development and how this differential expression is then maintained, or reversed in certain circumstances, either normally or in a disease context such as cancer. The establishment of XCI involves the non-coding Xist RNA that triggers chromosome-wide chromatin re-organisation and gene silencing. Our lab is studying the role of these epigenetic changes as well as the mechanisms of differential gene silencing along the X chromosome.

In particular we have studied the role of the Xist-recruited SPEN protein, that triggers gene silencing and dampens expression of genes that escape XCI (Dossin et al, 2020). We have also recently investigated the role of PRC1 and PRC2 Polycomb complexes in vivo and uncovered essential and independent roles for each complex in maintaining the silent state of the inactive X in extraembryonic tissues.

Finally, our studies using chromosome conformation capture techniques have revealed that the loss of topologically associating domains (TADs) is an early event during XCI and genes that escape XCI form TAD-like structures (Giorgetti et al, 2016; Collombet et al, 2020). We are exploring whether these domains are a cause or a consequence of gene reactivation on the Xi. Our recent insights into the relationship between chromatin states, 3D chromosome organisation and escape from XCI will be presented, considering the implications of increased X-linked gene dosage due to escape for normal female physiology, as well as in cancer.

Bio

Professor Edith Heard is Director General of the EMBL. She studied Natural Sciences specialising in Genetics at Cambridge University and then obtained her PhD from the Imperial Cancer Research Fund in London. After a postdoc at the Institut Pasteur in Paris, she set up her group in 2001 at the Institut Curie where she became Director of the Genetics and Developmental Biology Unit in 2010.

She was appointed as Professor of the Collège de France in 2012 to the Chair of Epigenetics and Cellular Memory, and in 2019 she became Director General of EMBL. Edith's laboratory studies epigenetics, focusing on the process of X-chromosome inactivation (XCI) whereby one of the two X chromosomes is silenced during female development. Her group has revealed the remarkable dynamics of epigenetic processes in development and disease.

This has been recognised by many prizes, most recently the L'Oréal-UNESCO For Women in Science International Award, the Hansen Family Award, the Karl Bonhoeffer Award, Inserm Grand Prix, the European Society for Human Genetics Award and the Prix René et Andrée Duquesne of la Ligue contre le cancer. Edith has participated in numerous scientific boards and is currently a member of the Scientific Advisory Board of the CNRS (France), the BRIC (Copenhagen, Denmark), the IMBB (Crete, Greece), the Crick Institute (London, UK) and the WHO Science Council.



EVENT DETAILS

DATE:

Tuesday February 7th 2023

TIME:

5:00pm AEDT

VENUE:

Zoom details to be circulated via email at midday of Tuesday February 7th

HOST:

A.Prof. Edwina McGlinn



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The Australian Regenerative Medicine Institute (ARMI) acknowledges the generous support of Monash University and the Victorian State Government.