LECTURE SERIES 2024
CANCER RESEARCH

LUXEMBOURG INSTITUTE OF HEALTH | UNIVERSITÉ DU LUXEMBOURG

25 OCT 2024
Friday
LECTURE*

11.00am - 12.00pm

Epitranscriptomic regulation of meiosis and the preimplantation embryo

ABSTRACT

The epitranscriptome define the collection of post-translational chemical modifications of RNA in a cell. The dynamic nature of some of these epitrancriptomic modifications, the first identified being 6-methyladenine (m6A) in mRNA, was identified very recently. Early studies on m6A modifications in mRNA of various model organisms have identified crucial roles of this modification in meiosis. We showed that the demethylation of m6A to the canonical Adenine (A) in mice is required for meiosis and fertility and depends on the ALKBH5 gene (Zheng et al., Mol Cell. 2013 49:18-29). The reversible nature of this modification points towards important regulatory roles. In a collaborative study headed by Alexey Ruzov (University of Nottingham) we recently showed that m6A modification on RNA on the RNA/DNA hybrids (so-called R-loops) are associated with genome instability and in future studies we will study the role of the dynamic m6A modification for genome stability (Abakir et al., Nat Genet 2020 52:48-55).

Our work today focuses on the role of m6A on RNAs in meiosis. We (and others) have shown that the m6A modification is highly dynamic during meiosis and preimplantation embryogenesis. We also show that m6A is enriched at retrotransposon derived RNAs, again pointing towards a role in genome stability (Wang et al., Nat Struct Mol Biol. 2023 30:703-709). Mice lacking the m6A demethylase ALKBH5 appear normal but are characterized with chromosome breakage and meiotic failures of metaphase I oocytes (unpublished).

An overarching goal of our research is to understand the role of epigenetic and epitranscriptomic information in the passing of life from one generation to the next, including their functions in genome stability, chromosome segregation and retrotransposon activity.

SPEAKER

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Supported by the Luxembourg National Research Fund

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