MBG FOCUS TALK

hosted by Erik Østergaard Jensen

MBG Focus Talks in Molecular Biology

Tuesday June 19 at 9:15 - 10:00 am

iNano, Auditorium (1593-012)

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Regulation of pluripotency and differentiation programs by RNAi factors

The subjects of our laboratory are focused on the importance of stem cells in future medical applications and the need to understand the fundamental molecular mechanisms regulating stemness and differentiation. We are interested in gene expression patterns and cell fate specification, which take place during embryogenesis in mammals.
Complex systems of gene regulation are instrumental to ensure the maintenance of cellular identity during early development. Eukaryotic small RNAs have emerged as critical players in RNA interference (RNAi) by mediating gene silencing. Most of RNAi mutant mice are lethal at the implantation stage, which is a difficult in vivo stage to be addressed experimentally. Moreover, these proteins are essential for proliferation and differentiation into the three germ layers of mouse embryonic stem cells (mESCs). It was assumed that this lethality and the stem cells phenotypes were due to an impairment of the microRNA pathway. Nonetheless, microprocessor mutant mice have a different phenotype than the Dicer mutant mice. In addition, new functions of a subset of RNAi proteins, independent of their roles in RNAi pathways, have been demonstrated. Finally, new concepts in Stem cell biology emerged. Therefore, we re-evaluated the RNAi mutant phenotypes focusing on noncanonical functions that may contribute to the molecular mechanisms governing mESC commitment. This work allowed us to discover a novel noncanonical function of one RNAi protein in the control of the exit from pluripotency of mESCs and a novel role for AGO2 in the differentiation of mESCs toward extra-embryonic endoderm cells. We also demonstrated the importance of the DICER protein in the regulation of transposable elements. Moreover, we are developing computational approaches to integrate several genome-wide datasets. Our goal is to construct a system level understanding of cell fate specification and maintenance, which is key to better apprehend healthy and disease contexts.