

CPH Seminar in Precision Medicine

“Alternative Splicing Links Histone Modifications to Embryonic Stem Cell Fate Decision through Cell Cycle-dependent Mechanisms”

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Alternative splicing (AS) is one of the most important pre-mRNA processing for normal development and human diseases. Its regulation has long been thought to involve genetic elements, but recently was extended with multi-level epigenetic properties, such as histone modifications (HMs), to exhibit an increasingly complex regulation model. Inspired by emerging regulations of AS from HMs and their both critical roles in in embryonic stem cells (ESCs) maintenance and differentiations, it is highly desirable to decipher an extended splicing code incorporating both the genetic and epigenetic mechanisms across diverse human cell/tissue types and developmental stages. In this presentation, I will talk about our recent studies on how to link the histone modifications to stem cell fate decision and on deciphering the splicing (epi)genetic code. We employed both the deep learning neural network and integrative transcriptomics and epigenomics analyses, followed by experimental validations. We showed that epigenetic features are more important in decoding the AS and revealed two possible mechanisms that convey the HM dynamics into cell fate decision through the AS regulation of cell cycle related genes and pathway. Our studies demonstrated the involvement of HMs in cell fate decision via determining the transcript structure, rather than only the expression abundance.

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