Stem cells protection from and by transposable elements

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Abstract

The maintenance of mammalian tissue architecture relies on the constant renewal of differentiated cells by division of stem cells. Thus, if most differentiated cells can be considered expendable, because replaceable, stem cells need to be specifically shielded from insults. For example, stem cells are under pressure to fine-tune the expression of transposable elements (TEs). Published work, as well as our preliminary data, indicate that RNA interference (RNAi) mediated by a specialized Dicer protein or its antiviral isoform aviD, transcriptionally regulates certain TE subfamilies in stem cells. This project aims at **deciphering the role of RNAi in controlling transposable elements in stem cells**.

To tackle this question, we first aim to unravel the molecular mechanism(s) of TE control in stem cells. We generated mouse embryonic stem cells (mESC) lines encoding for degron-tagged versions of Dicer or aviD, allowing auxin-inducible loss of RNAi. Our preliminary data suggest that certain TE subfamilies are de-repressed upon depletion of Dicer and aviD. We now aim to determine the identity of RNAi-controlled TEs, as well as understand the molecular mechanism of control. Published work indicate that certain protein-coding TEs can hinder viral infection, suggesting that TE expression can, in specific contexts, be beneficial for stem cells. We are exploring this question in the context of neural stem cells infected with herpes simplex virus 1 (HSV-1). Our preliminary data suggest that evolutionary young TEs documented to counteract HSV infection may be upregulated during infection in a RNAi-dependent manner.

Overall, we aim at unraveling the means of RNAi-driven TE control in stem cells and understanding the putative role of such mechanism during viral infection.

Keywords: Stem cells, transposable elements, RNA interference, innate antiviral immunity

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