Endogenous retrotransposon activity in the Drosophila intestine - towards the mechanisms of action of selfish DNA in the soma

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Abstract

A growing body of research uncovers the importance of selfish DNA in somatic lineages throughout development and adult life. Endogenous retrotransposons, transposable elements that propagate via copy-and-paste mechanisms involving an RNA intermediate, occupy large portions of all eukaryotic genomes. A great majority of their multiple copies remains silenced in somatic cells, nevertheless, some are transcribed, and a small fraction retains its ability to mobilize, often in a tissue specific manner. Because of the highly repetitive nature of retrotransposons, identification of the precise active copies is often challenging. Consequently, the mechanisms that drive their somatic activity are not well understood.

In our previous work (Siudeja, van den Beek et al, 2021) we provided sequencing-based evidence of somatic retrotransposon mobility in the intestinal tissue of *Drosophila melanogaster*, which can lead to tumor suppressor inactivation and formation of gut neoplasia in aged midguts. Here, I will present our ongoing efforts towards revealing the mechanisms of action of these selfish elements. Using short- and long-read DNA and RNA sequencing, we identified the first fly "hot" donor locus of an endogenous retroviral element *rover*, highly active in the gut tissue. We then dissected the transcriptional landscape and local sequence and chromatin environment of all fixed *rover* copies present in the genome. This analysis offered insights into how locus-specific features allow active retrotransposon loci to escape repression, produce functional transcripts and mobilize in a somatic lineage.

Using this model system, my newly established team aims to further dissect the modes of retrotransposon regulation in the soma and the interplay between selfish genetic elements and tissue homeostasis *in vivo*.

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Keywords: somatic transposition, Drosophila, LTR retrotransposons, endogenous retroviruses, ERVs, intestin, stem cells, aging