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Dissertation: Identification and characterization of structural elements of the Ty1 retrotransposon genomic RNA and its interactions with the Gag protein crucial for dimerization and packaging of the genome into virus-like particles.

ABSTRACT

Transposable elements occur in most, if not all, characterized eukaryotic genomes and significantly influence their organization, evolution, and function. Many of them are LTR retrotransposons, which display similarity in structure and replication cycle to retroviruses but are not infectious. During retrotransposition, they form virus-like particles (VLPs), resembling retroviral virions. VLPs are composed of numerous Gag proteins, contain the retroelement genomic RNA (gRNA) in dimeric form, and the specific enzymes required for reverse transcription and later integration of cDNA into a host genome. gRNA packaging into VLPs is one of the key steps in retroelement replication. This process has been extensively studied for retroviruses, and the available literature data indicate that gRNA packaging is coupled with its dimerization, and both processes are regulated by the Gag protein. In contrast to retroviruses, the process of gRNA dimerization and packaging is poorly understood for LTR retrotransposons.

The main goal of my dissertation was to investigate the processes of retrotransposon gRNA dimerization and packaging into VLPs. My model system was Ty1 LTR-retrotransposon, naturally occurring in the genome of *Saccharomyces cerevisiae*. In the publications constituting my dissertation (Gumna et al. *RNA Biology*, 2019; Gumna et al. *IJMS*, 2021; Gumna et al. *PLoS One*, 2020), I indicated that the mechanism of Ty1 gRNA dimerization is similar to the analogous process in retroviruses and regulated by the Ty1 Gag protein. To elucidate the role of Ty1 Gag in the selection and packaging of retrotransposon gRNA into VLPs, I analyzed the properties of the Ty1 Gag interactions with RNA and defined structural motifs in Ty1 RNA relevant for these interactions. I used my experience in RNA secondary structure mapping to develop, in collaboration with the Department of Structural Bioinformatics IBCH PAS, a computational tool – RNAthor. This tool serves for fully automated normalization, visualization, and statistical analysis of data obtained in RNA structural probing experiments and resolved by capillary electrophoresis.