

**Supervisor and location:**

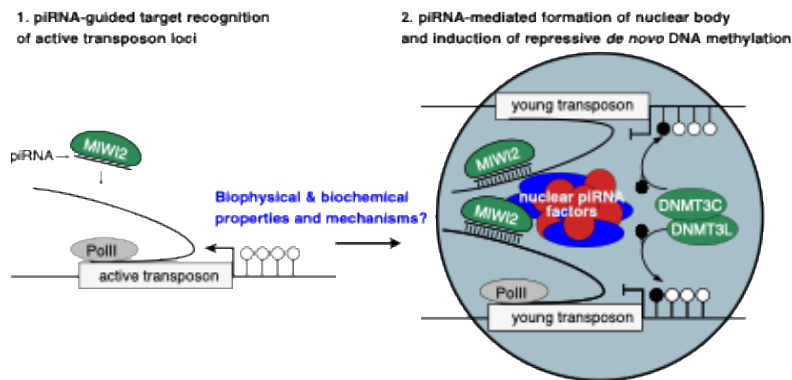
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**Understanding chromatin remodelling at piRNA-targeted transposons**

We study how the mammalian germline defends genome integrity against jumping genes called transposons. The germline, the cell lineage that will eventually make sperm and egg cells, passes on our genetic information to the next generation. Maintaining the integrity of the germline genome is thus paramount to the continuation of life. Transposon activity threatens genome integrity through mutagenic transposition and deregulation of chromatin. The piRNA pathway identifies active transposon loci and targets them for epigenetic silencing by *de novo* DNA methylation. We recently discovered that piRNA-guided silencing leads to the formation of nuclear bodies containing piRNA factors. Their formation depends on a small, disordered protein that is prone to aggregation. We thus hypothesise that the nuclear piRNA bodies represent a phase-separated aggregation of repressive factors and target loci that ensures precise epigenetic silencing of transposon loci while avoiding off-target epimutations.

In this project we will investigate the biophysical properties and composition of these bodies to identify if these are indeed phase-separated entities and shed light on the mechanisms of their formation and molecular functions. This project will focus on studying the aggregation and phase-separation behaviour of recombinantly expressed nuclear piRNA factors using biochemical and biophysical analysis methods. Insights gained will then inform the design of cell-based reporter assays and mouse models to study the relevance of aggregation for the piRNA-guided silencing process.