Role of splicing dynamics in specification of the *Caenorhabditis elegans* germline

The germ cells generate gametes (eggs and sperm) and are vital in the transmission of genetic information from one generation to the next. Hence, the maintenance of a healthy germline is critical for successful reproduction. This is achieved through the action of stem cells which, on one hand, divide symmetrically to self-renew and, on the other, give rise to a pool of differentiating cells that eventually develop into mature gametes. An imbalance between self-renewal and gamete specification leads to tumors and infertility. Germline functions are governed by the establishment of specific gene expression patterns. One of the critical regulators of this patterning is pre-mRNA splicing and alternative splicing regulation. Splicing is a process in which precursor messenger RNA (pre-mRNA) is processed to remove non-coding portions (introns) and join coding parts (exons) to produce a mature mRNA particle. Alternative splicing allows for the generation of multiple proteins from a single gene by selecting different exons. Several studies have established that defects in splicing may lead to germline dysfunctions. **However, the exact role of splicing in maintaining germ cell balance and homeostasis remains unclear.**

The human germline is challenging to study due to ethical reasons and methodological constraints; thus, scientists turn to model organisms like the nematode *Caenorhabditis elegans*, a microscopic worm with ~1000 somatic cells and ~2000 germ cells in hermaphrodites. As a hermaphrodite, *C. elegans* can produce both eggs and sperm, enabling the study of both male and female germ cells in a single organism. Moreover, the worm germline is localized in linear gonads, which enables streamlined and efficient cytological analysis. **In this project, we aim to understand the involvement of splicing factors and alternative splicing events in the regulation of *C. elegans* germline biology.**

The project comprises three primary objectives. **First,** we will use cutting-edge methodology to analyze the dynamics of splicing factors and alternative splicing events across different parts of the germline. This will allow us to identify specific splicing events that are critical for the proper regulation of the germline. **Second,** we will study how splicing factors function to regulate germ cell developmental fates. To this end, we will employ genome or proteome editing techniques to create worms with misbalanced control of splicing factor levels and determine the resulting phenotypes. **Finally,** we will analyze the relevance of alternative splicing for physiology and identify genes that undergo alternative splicing during germline specification.

By studying the relatively simple germline of *C. elegans*, we will gain insights into the fundamental mechanisms governing germ stem cell development and differentiation. In the future, these findings might contribute to the development of improved treatments for reproductive disorders and germ cell-originating cancers.