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Stem cells, due to their unique abilities, have been the subject of research since the 1980's and have received increasing attention by scientists and the general public. With each cell division stem cells have to choose to either self-renew and regenerate their pool or differentiate into specified cell types. Despite major scientific efforts many of the molecular mechanisms determining how this decision is made remain unclear.

In eukaryotes post-transcriptional regulation of gene expression plays a key role in almost all cellular processes including stem cell differentiation. This regulation is achieved by RNA-binding proteins (RBPs) which guide messenger RNA (mRNA) at various steps of gene expression. To read information encoded in mRNA transcripts they have to be decoded during the translation process, which leads to the production of proteins. Protein groups (called protein complexes) are macromolecular effectors that perform most of the cellular functions in living organisms (e.g. repair DNA after exposure to UV radiation). Understanding how proteins function requires a detailed knowledge about their three-dimensional architecture and interactions within the complexes. The project focuses on structural characterization of a novel protein complex (SXL-RC) involved in regulation of stem cells differentiation during fly oogenesis. I have chosen structural biology to study the basis of fundamental translational control in embryonic stem cells to understand how mRNA transcripts and associated proteins influence important cell fate decisions.

Sex Lethal (Sxl) protein together with three others proteins, namely Bam, Bgcn and Mei-P26, have been suggested to form a sex lethal repressive complex (SXL-RC) on a specific RNA, namely the *nanos* mRNA. The SXL-RC interaction with mRNA transcript leads to the repression of a stem-cell renewal factor, namely the Nanos protein, which initiates differentiation of stem cells. Failure to repress translation of self-renewal factors results in continued proliferation of stem cells, tumorous overgrowth and fly sterility.

The aim of this project is to obtain structural information about the SXL-RC complex. First, individual protein fragments (domains) engaged in protein-protein and protein-RNA interaction will be designed and purified to test their interaction with predicted partner domain(s) by so called *in vitro* interaction assays. This approach will allow us to reconstitute minimal sub-complexes for subsequent structural analyses by x-ray crystallography. Finally, to understand the molecular mechanisms of the SXL-RC formation we aim to identify RNA motifs binding to the SXL-RC. The strength of the proposed project lies in the fact, that all findings can be immediately functionally validated in flies by our collaborating partner laboratory.

Interestingly, homologues of the involved components are also specifically expressed in human stem and germ cells. Hence, unravelling structural details of the SXL-RC will provide deeper understanding of molecular mechanisms involved in embryonic development and carcinogenesis.

In summary, these studies will not only provide significant understanding of how protein translation is regulated by mRNPs formation, but may also lead to discovery of potential diagnostic markers aimed to design personalized therapeutic strategies for several severe human diseases