Eukaryotes employ an elaborate protein machinery, the spliceosome, for the precise removal of introns to generate a mature mRNA necessary for correct translation. The spliceosome consists of a myriad of proteins and several small nuclear RNAs. Due to its complex composition and function mistakes occur and cause many human diseases. Even though most splicing factors are ubiquitously expressed, those also have been reported to have tissue, stage and even transcript specific functions in multi-cellular organisms. However, knowledge about these specific functions is still sparse.

Here I characterize the function of two splicing factors, the novel candidate Ecdysoneless (Ecd) and its interaction partner, the core component of the spliceosome Prp8, *in vivo* using *Drosophila melanogaster* as a model system.

The steroid-deficient ecd^1 strain of *Drosophila* has long served to assess the impact of ecdysone on gene regulation, morphogenesis, and reproduction. However, it still remains unknown why ecd^1 mutants lack ecdysone. Here I demonstrate that in *Drosophila* cells, Ecd directly interacts with core components of the U5 snRNP spliceosomal complex, including the conserved splicing factor Prp8. In agreement with a role in pre-mRNA splicing, Ecd and Prp8 are cell-autonomously required for survival of proliferating cells within the larval imaginal discs. In the steroidogenic prothoracic gland (PG), loss of Ecd compromises pre-mRNA processing of a critical ecdysone-biosynthetic factor *Cyp307A2/spookier*, eliminating its protein product and explaining the hormone deficiency of ecd^1 mutants. Strikingly, transgenic overexpression of the human Ecd ortholog in the PG substitutes for its fly counterpart. It reestablishes splicing of *spok*, resulting in its protein expression, and restores ecdysone levels and development.

Strikingly, mutations in Ecd's interaction partner Prp8 have been implicated to cause the disease retinitis pigmentosa (RP), which is characterized by the gradual loss of vision due to progressive photoreceptor degeneration. While the homozygous loss of Prp8 function is lethal across species, it remains perplexing that its heterozygous mutations invariably induce photoreceptor cell death and retinal degeneration. To shed light on tissue specific effects and molecular mechanisms underlying Prp8-RP-based pathology seven RP-causing mutations were introduced into *Drosophila* Prp8. Their expression was targeted to the PG as it is highly sensitive to the loss of Prp8 and Ecd. I demonstrate that overexpression of epitope-tagged Prp8-RP mutants in the PG results in a developmental arrest, delays pupation or has no phenotype depending on

the specific mutation. The observed phenotypes are associated with aberrant processing of *spookier* pre-mRNA. Importantly, the severity of the phenotypes in *Drosophila* correlates with the severity of reported phenotypes in patients.

To summarize, this work characterizes the function of Ecd and Prp8 in a multi-cellular organism. It identifies Ecd as a novel pre-mRNA splicing factor and demonstrates that Ecd and Prp8 are important for the splicing of the PG specific transcript *spookier* and for cell survival of proliferative cells. Furthermore, it shows that the PG is sensitive to overexpression of Prp8-RP mutants and thereby highlights the suitability of the *Drosophila* model for functional studies of genes and mechanisms related to RP pathology.