Identification of new proteins interacting with the LSL-1 germline factor in *Caenorhabditis elegans*

Florian Brice Michel

Master Thesis in Biology

The production of functional gametes is essential for the transmission of appropriate genetic content. In the nematode *Caenorhabditis elegans,* it has been shown that the *lsl-1* gene is required for proper meiotic progression and germ cell development. Absence of *lsl-1* results in embryonic lethality, alteration in chromosome organisation and lack of meiotic recombination. Heece-Royes and colleagues (2013) identified, using a high throughput Yeast-two-hybrid screen, the chromatin protein XND-1 as a putative binding interactor of LSL-1. XND-1 is a key regulator of germ cell development and genome stability. Both mutants share common phenotypic features and both genes are expressed in germ cells. In order to confirm this putative interaction, we performed co-Immunoprecipitation experiments followed by mass spectrometry analysis. By analysing ChIP-seq data provided by the ModERN Resource, we could highlight that LSL-1 and XND-1 share share most of their genomic binding sites, which are located mostly on autosomes. LSL-1 and XND-1 are binding in the promoter regions, at less than 1 kb away from the Transcription Start Site, suggesting that both LSL-1 and XND-1 might act as transcription factors. Gene ontology analysis also show that both proteins are functioning in the same biological process. Altogether we have also identified 1379 genes that might be common targets of LSL-1 and XND-1. Further analysis must be done in order to confirm this regulation of selected genes by LSL-1 and XND-1. Altogether, our analysis is consistent with LSL-1 and XND-1 interacting at common target gene promoters.

In order to determine if germ cells were specified normally in *lsl-1* mutants, we analysed the localisation of P granules. It results that there is an ectopic expression of P granules in the *lsl-1* mutant embryo. Defects in P granules localisation were also observed at the diplotene stage of meiosis in *lsl-1* mutant germline. Further analysis should be done in order to quantify this phenotype. In comparison with *xnd-1* mutant, it appears that both mutants exhibit mis-localization of P granules in embryo. We suggest that the defects appear during the embryogenesis and that *lsl-1* and *xnd-1* are required for proper localisation of P granules.

In conclusion, we showed that *lsl-1* and *xnd-1* mutants are sharing common phenotypic features such as mis-localization of P-granules, embryonic lethality, alteration of chromatin structure. Both proteins share common gene and chromosome distribution and biological process. We propose that *lsl-1* and *xnd-1* might act as transcriptional regulator of germline genes and might function together in the same complex to ensure production of functional gametes.

Dr. Chantal Wicky