

Homologue chromosome pairing dynamic and chromatin dynamic in the meiotic mutant *lsl-1* in the nematode *Caenorhabditis elegans*

Magali Marguerite-Marie Nanchen

Master thesis in Biology

The process of meiosis is essential for the production of haploid germ cells, consisting in sperms and oocytes. It ensures the perpetuation of the species that reproduce sexually. This process comprises a DNA replication step and a long prophase during which the chromosomes are highly rearranged to be paired and recombined, followed by two cell divisions (meiosis I and II) allowing segregation of the chromosomes. Failure to complete this process can lead to the formation of aneuploid gametes which can cause developmental defects such as the Down Syndrome, miscarriage and sterility.

In *C. elegans*, the zinc finger transcription factor LSL-1 is involved in the production of functional gametes. Phenotypic analysis of two *lsl-1* loss-of-function mutants shows that this protein is required to maintain genome integrity in this nematode, and plays an important role for proper meiotic prophase progression. The aims of this project are to investigate the course of homologue chromosome pairing in *lsl-1* mutants, and to understand how germline genes become downregulated in these mutants.

lsl-1 mutant germlines present features indicative of defects in the pairing process: they show an extended zone in which chromosomes stay clustered in one part of the nucleus, associated with morphological defects in the chromatin. Using immunostaining of pairing components and chromosome FISH, I could show that X chromosomes present a precocious pairing and chromosomes V a partial reduction of pairing, in these mutants. Altogether, these observations point towards a lack of coordination during the pairing process.

In *lsl-1* mutants, transcriptomic analysis revealed that a large number of genes involved in pairing and genome stability are downregulated, raising the question of whether repressive chromatin could be forming at these gene loci. Using a genetic approach, I could demonstrate that *lsl-1* defects are dependent on the chromatin-binding protein HPL-2.

In summary, I found that homologue chromosome pairing is impaired in *lsl-1* mutants and that this may be due to a problem in the loading of the synaptonemal complex between the homologues. Furthermore, I propose that LSL-1 is antagonizing the action of the repressive chromatin-associated protein HPL-2 at promoter of genes involved in pairing and genome stability processes.

Supervisor : Dr. Chantal Wicky