University of Fribourg / Faculty of Science and Medicine / Department of Biology

The transcription factor LSL-1 is a major regulator of the germline transcriptional program in *C. elegans*

Thesis No: 5462

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Tight regulation of gene transcription programs is critical to coordinate cell proliferation and differentiation throughout the eukaryotic development. This gene activity is mainly controlled by the concerted action of transcription factors and chromatin-associated proteins. *Caenorhabditis elegans* has become a reference model system to study chromatin function during development, and in this context the mechanisms that silence inappropriate transcriptional programs at the level of chromatin in germ and somatic cells have been thoroughly investigated in *C. elegans*. However, the mechanisms that trigger the tissue-specific activation of the appropriate sets of genes, such as germline-specific genes, are less well understood. For instance, chromatin factors such as the remodeler LET-418/Mi2 or the heterochromatin protein HPL-2/HP1 have been identified as crucial repressors of the germline transcriptional program in the soma, leading to ectopic P-granule assembly around somatic nuclei in the absence of LET-418 or HPL-2 activity. By studying the function of LET-418/Mi2 in more details our research group identified a gene, named *lsl-1*, as a putative zinc-finger transcriptional regulator of germline genes in *C. elegans*.

In this dissertation we report the functional characterization of LSL-1. LSL-1 is first detected in the P4 germline blastomere, when zygotic transcription is initiated, and remains present in all stages of germline development, from primordial germ cell proliferation to the end of meiotic prophase. *lsl-1* mutants exhibit chromosome pairing defects, high levels of germline apoptosis and produce almost no functional gametes. Transcriptomic and ChIP-seq data indicate that LSL-1 acts as a direct transcriptional activator of a large set of germline genes involved in processes ranging from germ cell fate maintenance to meiotic prophase progression and genome stability. In addition, genetic interaction studies show that LSL-1 functions by antagonizing HPL-2 and LET-418 to ensure the production of viable progeny. Overall, this thesis proposes that LSL-1 is a major regulator of the germline transcriptional program required for germ cell development and fate maintenance, and contributes to gain new insight into the gene regulation of cell proliferation and differentiation, mainly during the germ cell development into gametes.

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