To dissect the role of ISWI-mediated chromatin remodeler in controlling stem cell self-renewal, I developed a strategy to purify a large numbers of pure GSCs from the Drosophila ovary. Using this approach I generated a genome-wide transcriptome and chromatin-binding profile of ISWI on GSCs chromatin. To identify the potential regions of the genome that are bound by ISWI in GSCs, I conducted a ChIP-Seq analysis and found nearly 7000 ISWI bound coding genes. Moreover, RNA-Seq experiments conducted in ISWI mutant GSCs revealed ISWI as major regulator of about 70 % of its target genes in GSCs. Furthermore, by gene ontology analysis I identified specific gene networks under the control of ISWI. Particularly, I found that the ISWI regualtes genes playing an essential role in the maintenance of GSCs.

Our data suggest that the ATP-dependent chromatin remodeler ISWI works as a master regulator of GSCs self-renewal in the Drosophila ovary.

Reevaluating the function of a transcription factor: MBF-1 as a sea urchin chromatin organizer ?

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The Zinc-finger MBF-1 factor is involved in the expression of the early histone genes during development of the sea urchin embryo (1, 2). In spite of being a transcription activator, the DNA-binding domain of MBF-1 shares high sequence similarity with that of the chromatin organizer CTCF of vertebrates and drosophila (3). On the other hand, extensive in silico analysis failed to identify the sea urchin CTCF ortholog (4). This led us to speculate that MBF-1 somehow could have co-opted the function of CTCF during evolution of the echinoderms. Since in vertebrates CTCF binds Hox chromatin, to support our hypothesis, we first identified high-score putative binding sequences for CTCF/MBF-1 within the single sea urchin Hox gene cluster. Moreover, we observed the full evolutionary conservation of these binding sites in S. purpuratus and P. lividus species. Worth of mention, by chromatin immunoprecipitation (ChIP) assay, we detected the occupancy of MBF-1 on hox11/13-a, -b, and -c regulatory sequences at distinct stages of development. As expected from the binding of an activator, we found that the association of MBF-1 to the cis-regulatory sequences of both hox11/13-a and -b genes relates to the transcriptional status of these genes. Strikingly, we also mapped the physical binding of MBF-1 to hox11/13-c, which is instead not expressed during embryogenesis. Altogether, these observations indeed suggest the possibility that MBF-1, besides being a transcription activator, could also function as a general chromatin organizer. To further support this hypothesis, we are planning ChIP-seq experiments to identify the association of MBF-1 to the sea urchin chromatin at a genome-wide level.

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