Transitions in the RNA polymerase II machinery during oocyte growth and zygotic genome activation

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Résumé

Folliculogenesis and the initiation of embryonic development require precise regulation of gene expression, particularly at the level of transcription initiation by RNA polymerase II (RNA Pol II), which transcribes all protein-coding genes. In somatic cells, the initiation of transcription by RNA Pol II results from the sequential assembly of the pre-initiation complex (PIC) at a basal promoter. The PIC comprises six general transcription factors (GTFs) and RNA Pol II. The first GTF to be recruited is TFIID, composed of the TATA-binding protein (TBP) and thirteen TBP-associated factors (TAFs).
During oocyte growth, an intense transcriptional activity is required for the establishment of the maternal transcriptome. This process relies on a change in the RNA Pol II transcription initiation machinery. The TBP-TFIID complex is replaced by the specific TBPL2-TFIIA complex, which allows the accumulation of maternal reserves essential from oocyte maturation through the onset of embryonic development, a period during which transcription is inactive. At the onset of development, the maternal-to-zygotic transition (MZT) occurs, during which the maternal transcriptome is progressively replaced by the zygotic transcriptome, notably through zygotic genome activation (ZGA).

At this stage, a new mechanism for RNA Pol II transcription initiation is established. Although its composition remains largely unknown, TBP has been shown to be re-expressed, while TBPL2 disappears suggesting that the TBP–TFIID complex is required for ZGA. However, although zygotic deletion of *Tbp* is lethal in mice, it does not result in a defect in RNA polymerase II activity, indicating that the mechanism of transcription initiation during ZGA remains to be elucidated.
Thus, my thesis project aims to identify the protein complexes that govern Pol II transcription initiation during these transitions. The central question of my project is therefore: what is the composition of the RNA polymerase II transcription initiation machinery during oocyte growth and early embryonic development?

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