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Topaz1 suppression disrupts the expression of testicular long non-coding RNAs during murine spermatogenesis

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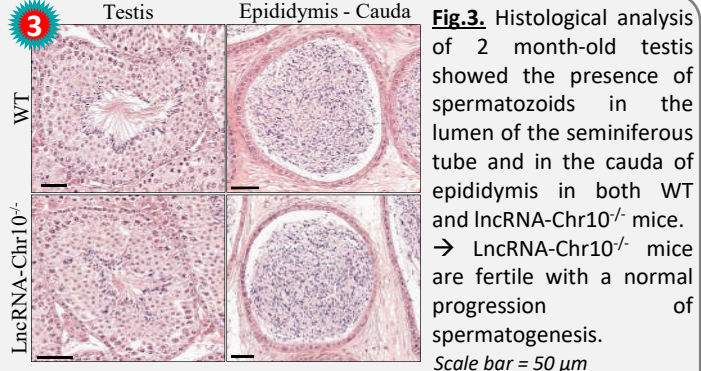
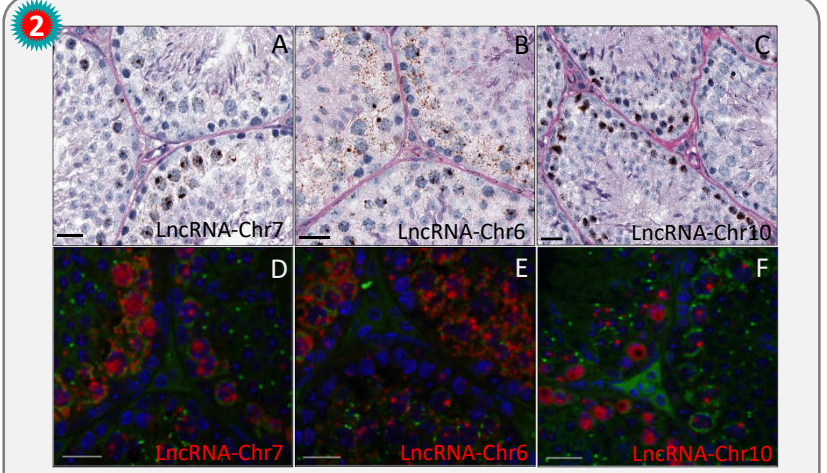
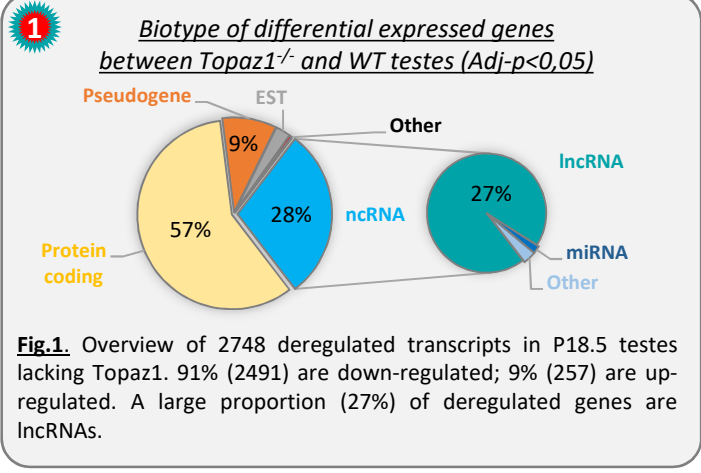


Background of Topaz1: Topaz1, for Testis and Ovary specific PAZ domain gene 1, has been characterized in our lab as a new germ cell specific gene highly conserved in vertebrates with a role during gametogenesis of mammals¹. To study the role of this gene, a line of Topaz1-depleted mice has been generated. Thus, whereas female mice are fertile, homozygous male mutants are infertile². Abnormal meiosis occurs in testes Topaz1^{-/-} mice causing cell death and an absence of spermatozoa. Previous transcriptional study of Topaz1^{-/-} mice by microarray comparative analysis highlighted the significant proportion of deregulated long non-coding RNA (lncRNA) in mutant testis.

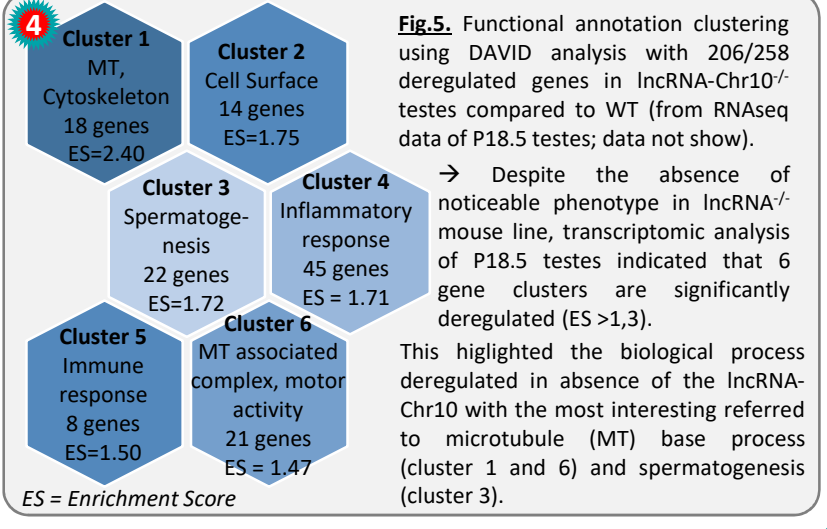
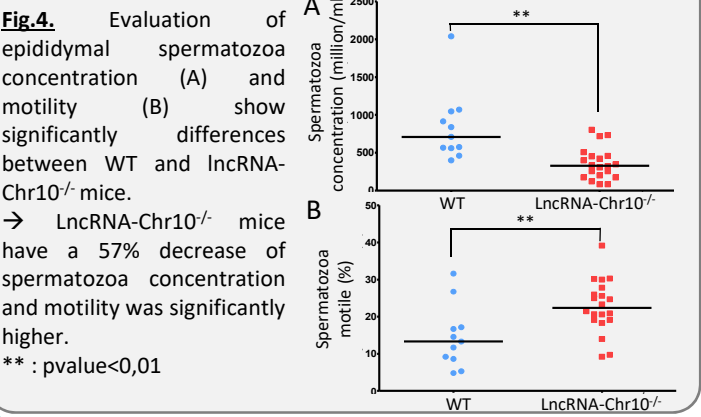
The aim of this work is to study (1) the whole transcriptome of Topaz1^{-/-} mouse testes and (2) the involvement of lncRNA in murine spermatogenesis.

Methodologies :

- RNA sequencing (RNA Seq) to identify all deregulated genes in Topaz1^{-/-} testis whose lncRNA.
- Localization by *In Situ* hybridization (ISH) of some deregulated lncRNA.
- Generation of a new line of knockout mice (Crispr/Cas9 technology) without one of these lncRNA → Studies of the phenotype.



→ lncRNAs are expressed in different spermatocytes depending on the stage of the seminiferous epithelium: lncRNA-Chr10 seems nuclear whereas lncRNA-Ch6 cytoplasmic. lncRNA-Chr7 looks as if located in both cytoplasm and nuclei. Scale bar = 20μm



Conclusion :

Number of lncRNA expressed in the testes is significant. In Topaz1 null mice, with male meiotic arrest, a large number of testicular lncRNA are significantly deregulated (Fig1). Three of them were observed by ISH showing different localisations into spermatocyte cells, suggesting distinct roles during spermatogenesis (Fig2). To determine a potential spermatogenetic role, a new mouse line deleted of one of them (LncRNA-Chr10, expressed in nuclear germ cells) has been created. These mice are fertile in both sexes (Table 1) and spermatogenesis of mutant takes place normally (Fig3). However, they have a decrease of epididymal spermatozoa concentration and an increase of spermatozoa motility (Fig5). Moreover, transcriptomic analysis of P18.5 lncRNA-Chr10^{-/-} testes (by RNAseq) shows more than 250 deregulated genes involved particularly in cytoskeleton and spermatogenesis (Fig5). → Thus, although lncRNA-Chr10, expressed exclusively in the testes with an expression linked with Topaz1 expression, its depletion does not appear crucial for fertility in mice. The lncRNA-Chr10 seems to play role in spermatozoa motility and concentration. This lncRNA may regulate protein coding gene expression especially genes in relation to the cytoskeleton.