

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

Manon Chadourne, Elodie Pומרol, Bruno Passet, Luc Jouneau, Eric Pailhoux, Béatrice Mandon-Pepin

► **To cite this version:**

Manon Chadourne, Elodie Pומרol, Bruno Passet, Luc Jouneau, Eric Pailhoux, et al.. Topaz1 suppression disrupts the expression of testicular long non-coding RNAs during murine spermatogenesis. 21st European Testis Workshop, May 2021, Virtual edition, Spain. hal-03298411

HAL Id: hal-03298411

<https://hal.inrae.fr/hal-03298411>

Submitted on 23 Jul 2021

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.



Chadourne Manon, Pomerol Elodie, Passet Bruno*, Jouneau Luc, Pailhoux Eric and Mandon-Pépin Béatrice

Université Paris-Saclay, UVSQ, INRAE, BREED, 78352, Jouy-en-Josas, France.

*Université Paris-Saclay, INRAE, AgroParisTech, GABI, 78350, Jouy-en-Josas, France.

manon.chadourne@inrae.fr / beatrice.mandon-pepin@inrae.fr

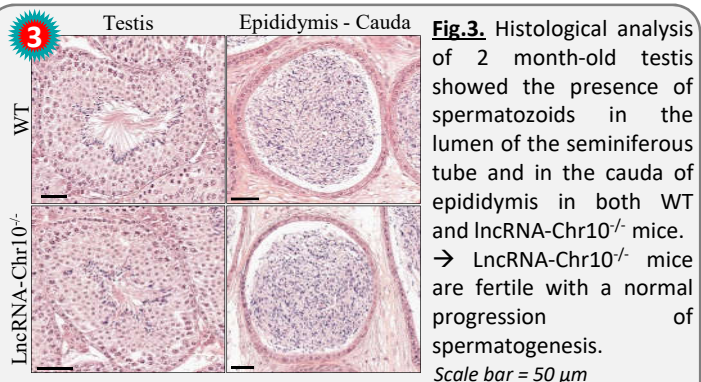
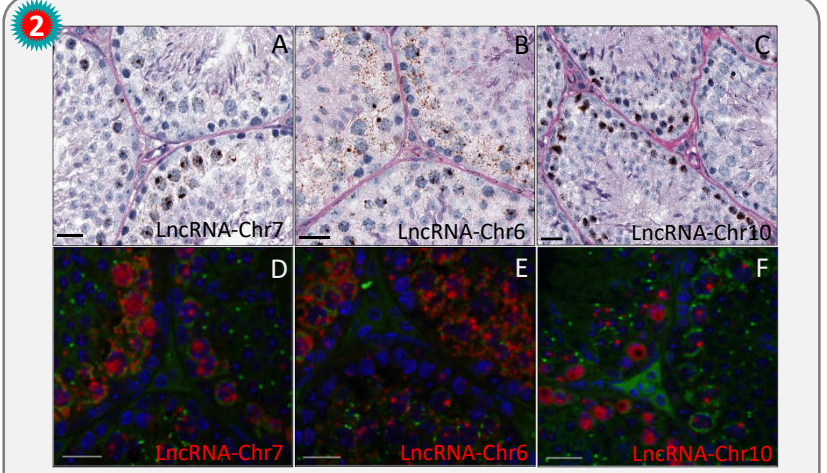
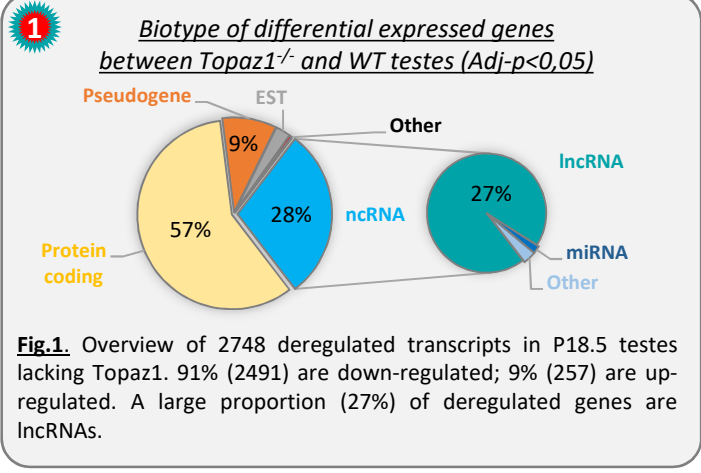


Background of Topaz1: Topaz1, for Testis and Ovary specific PAZ domain gene 1, has been characterized in our lab as a new germ cell specific gene highly conserved in vertebrates with a role during gametogenesis of mammals¹. To study the role of this gene, a line of Topaz1-depleted mice has been generated. 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.

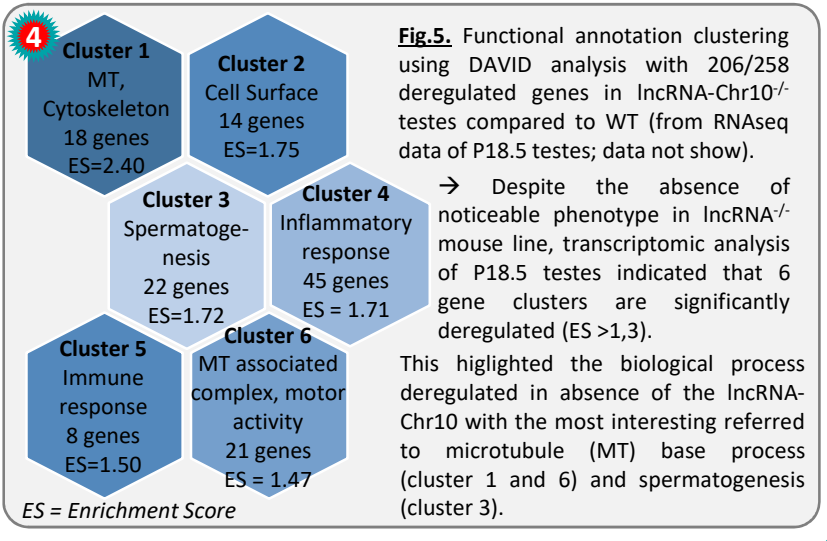
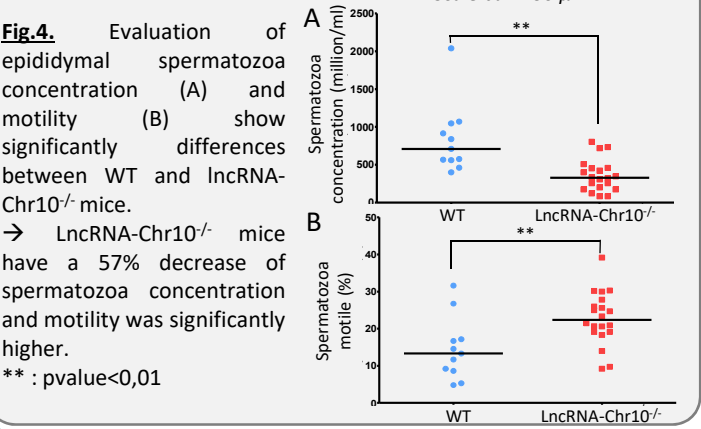
The aim of this work is to study (1) the whole transcriptome of Topaz1^{-/-} mouse testes and (2) the involvement of lncRNA in murine spermatogenesis.

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.

References : (1) Baillet A, et al. PLoS One. 2011;6(11):e26950; (2) Luangpraseuth-Prosper A, et al. Dev Biol 2015;406:158-171.