

FGF9 – Nodal signaling negatively control meiotic entry of postnatal male germ cells

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Fibroblast growth factor 9 (FGF9) produced by the somatic cells of the testis acts directly on germ cells to inhibit meiosis by upregulating levels of the RNA binding protein Nanos2, both in fetal and postnatal gonad [1]. Several studies have recently demonstrated that the anti-meiotic effect of FGF9 in the fetal testis is mediated by Nodal, a member of the TGF-Beta morphogen family. In fetal male germ cells FGF9 upregulates Cripto, which is a Nodal co-receptor, making these cells unable to enter meiosis [2]. However it is currently unknown how FGF9 acts postnatally to inhibit entry into meiosis of male mitotic germ cells. We first investigated which was the signal transduction pathway activated by FGF9 on postnatal mouse spermatogonia. We found that FGF9 signaling is dependent on ERK but not on AKT activation, which is instead triggered by Kit ligand (an inducer of meiotic entry that cooperates with retinoic acid). By qRT-PCR we found that Nodal and Cripto are expressed in postnatal spermatogonia and that FGF9 (but not Kit ligand) treatment promotes their upregulation. By western blot we found that phospho-Smad2, an indicator of active Nodal signaling, is increased in spermatogonia upon FGF9 treatment, suggesting that Nodal mediates FGF9 action also in postnatal male germ cells.

References

- [1] Barrios F. et al (2010) Opposing effects of retinoic acid and FGF9 on Nanos2 expression and meiotic entry of mouse germ cells. *J Cell Sci* 123(Pt 6): 871-80.
- [2] Spiller C.M. et al (2012) Endogenous Nodal signaling regulates germ cell potency during mammalian testis development. *Development* 139(22): 4123-32.

Key words

Fibroblast growth factor 9, Nodal, Kit ligand, Signal transduction, Meiosis, Spermatogonia, Spermatogenesis.