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GONOCYTE TRANSFORMATION INTO SPERMATOGONIAL STEM CELLS: THE KEY TO UNDERSTAND INFERTILITY AND MALIGNANCY OF CRYPTORCHIDISM

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Undescended testis (UDT) is a major health problem, affecting over 2% of new-born boys with increased infertility (30-60%) and testicular cancer (5-10 fold higher than normal males) later in life. Author have studied animal models in conjunction with human biopsies of UDT in order to understand the process of gonocyte transformation into spermatogonial stem cells (SSC) to elucidate how to prevent infertility and testicular cancer in cryptorchidism. We used testes from OG2 (Oct4-promoter-driving GFP transgenic mice), androgen knockout (ARKO), Bax knockout (BaxKO) and hypogonadal (hpg) mice and human biopsies for gene expression with real-time PCR and immunohistochemistry with antibody labelling followed by confocal imaging analysis. Serum and testes were collected from C57Bl/6 male mice for hormone analysis to examine mouse minipuberty. We have found that mouse gonocyte (Oct4+/C-Kit-) transformed into SSC (Oct4+/C-Kit+) between postnatal 2-6 days. There was transient testosterone surge at postnatal day 1-3 and gene expression of both FSH receptor and Oct4 peaked at postnatal day 3-6 in mouse. There were no difference for number of gonocytes transformed into SSC/tubule between ARKO mice and wild type littermates. Germ cells/tubule was significantly less in hpg mice comparing with wild-type littermates. Persisting gonocytes exist in BaxKO mouse testis and human testicular biopsies of UDT beyond six months old and germ cells/tubule significantly decreased whereas number of empty tubules without germ cells significantly increased with increasing age of orchidopexy. In conclusion, they found that minipuberty does exist in mouse which coincides with the gonocyte transformation into SSC like human. Gonocyte transformation in mouse is independent from androgen and disruption of apoptosis derange; the process causing persistent gonocytes which could be the source of malignancy. Orchidopexy at older age showed significant germ cell depletion and persisting gonocytes. The results suggest that FSH or/and non-androgenic factors may play an important role in gonocyte transformation into SSC.