Testis plays an important role in the development of male reproductive system, providing the hormones for sexual maturation as well as the site of spermatogenesis. Sertoli cells (Sc), present in the seminiferous tubular compartment of the testis, play a key role in Germ cell (Gc) development. Critical location and morphology of Sc renders them vital for spermatogenesis. Germ cell development occurs under the structural support and milieu exclusively provided by the Sc. Receptors for both FSH and T are present only in Sc. Interaction of these hormones with Sc has a crucial role in the initiation and maintenance of spermatogenesis. The endocrine activity of the hypothalamic-pituitary-testicular axis, as reflected by the circulating levels of LH, FSH and T (androgen), in infant rats and monkeys is similar to that found in adults. In spite of adult-like concentrations of LH, FSH and T in infant male monkeys and rats, development and differentiation of spermatogonia is restricted. Lack of initiation of spermatogenesis in the face of adequate hormones in infants is a situation similar to that found in certain categories of idiopathic male infertility and demands a physiological justification. In response to FSH and T the Sc in adults create a favorable environment inside the seminiferous tubule and produce factors necessary for the development and differentiation of Gc into spermatozoa. Hence, a comparative evaluation of the functionality of FSH and T signal transduction pathways in Sc from adult testis (containing advanced Gc) and infant testis (containing only spermatogonia) may unfold developmental deficits, if any, in FSH and androgen signaling ability of infant Sc.

In the present study, 9 days old rats and 3-4 months old monkeys, who display azoospermia despite normal to high circulating levels of gonadotropins, were proposed as surrogates for the infertile males. For comparison, 40 days old rats and GnRH-driven juvenile monkeys (pseudoadult), exhibiting active spermatogenesis in the testis, were used as the donors of mature Sc. Although FSHR expression was detected in the 9 as well as 40 days old rats, the deficit in the infant Sc was found at two levels of the FSH signaling pathway, a) low cAMP response due to FSH treatment and b) defective post-cAMP signaling cascade which might prevent the further transduction of hormonal signal. This low cAMP response in these cells could not be augmented by treatment with cholera toxin (an irreversible stimulator of the Gs subunit coupled to the FSHR), indicating a defect in either the Gs subunit or the adenyl cyclase. Relative expression of AR was less in the Sc from the 9 days old rat and a deficit in the ability of AR to bind its ligand in the Sc from the 9 days old rat confirmed inferiority of 9 days old rat Sc to propagate T signal.
Real time PCR studies revealed the low expression of FSHR in the Sc from the infant monkey and, like the infant rat, a low cAMP response due to FSH treatment is observed in these Sc. However, this low cAMP response could be augmented by treatment with cholera toxin, demonstrating the activity of the intracellular signaling molecules of this pathway at least up to the level of cAMP production. Similar to the infant rat, the AR activity in the infant monkey was significantly compromised although AR expression by RT PCR and real time PCR was found to be same in the infant and pseudoadult monkeys.

Studies of the expression of inhibinβB, transferrin, steroid acute regulatory protein (StAR) and ornithine decarboxylase (ODC) by RT PCR suggested inactivity of AR and FSHR in the 9 days old rats and infant monkeys, confirming our preliminary observations. This study reported several findings for the first time, especially in the primates.

The findings indicated the primary deficits in the FSH and T mediated signaling in the infant Sc. It provides evidence of cross talk between the FSH and T signaling pathways. The study also emphasizes the necessity of a short-term hormone exposure to study the hormone effects in vitro to efficiently mimic the in vivo conditions.

Thus, the limited activity of the AR and FSHR, hampering signal transduction by hormones, in the infant Sc seems to be the primary cause underlying the spermatogenic quiescence of the infant testis in spite of adult-like hormonal milieu. Transfection of normal AR and FSHR genes in the Sc of infant testis, in vivo, or their seminiferous tubules, in vitro, may thus result into the induction of Gc development and differentiation. Such an attempt, if successful, might pave the way for the treatment of certain forms of male idiopathic infertility (of which the infant Sc was a surrogate in our study), occurring due to primary testicular failure.