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Brief summary of the research work submitted for Sun Pharma Science Scholar Awards by **Ms. Sanketa Raut:**

Research Summary:

A normal, unperturbed system of germ cells and Sertoli cells from adult rat testis was used to study androgen and estrogen responsive genes using genome-wide sequencing. Germ cells and Sertoli cells were successfully enriched from adult rat testis. ChIP for ER α and ER β in germ cells and ER β and AR in Sertoli cells was carried out and genome-wide ChIP-sequencing was done using Illumina NextGen Sequencing. Lists of differentially enriched genes regulated by estrogen and androgen were obtained which was then subjected to pathway analysis by KEGG and DAVID database. A number of different pathways like metabolic pathways, pathways in cancer, PI3K-Akt signaling were enriched. In germ cells, pathways whose role in spermatogenesis is unexplored were picked for validation, namely, prolactin, GnRH, and Oxytocin signaling pathway. In Sertoli cells, since metabolism plays a crucial role in spermatogenesis and Sertoli cells are responsible for providing energy substrates to germ cells, lipid metabolism genes were studied. A total of 20 genes in germ cells and 14 genes in Sertoli cells, all showing presence of EREs and AREs were validated by ChIP-qPCR and *in vitro* culture. The results obtained by ChIP-qPCR showed significant enrichment by ER and AR ChIP, thereby confirming the binding of the receptors to these genes. For germ cells, seminiferous tubule cultures were treated with estrogen receptor specific agonist and antagonist, and the results obtained showed a significant alteration in the relative expression of the genes, thereby confirming the role of estrogen in regulation of these genes. Since seminiferous tubule culture comprises mostly of germ cells, adult Sertoli cells culture was performed for genes obtained in Sertoli cells ChIP-Seq. All the selected genes involved in lipid metabolism showed alteration in the expression after treatment with receptor agonist. In summary, our study gives a genome-wide map of androgen and estrogen regulated gene. The knowledge of ER and AR binding sites in germ cells and Sertoli cells of the seminiferous epithelium will help us in understanding the role these steroid hormones during normal spermatogenesis and its implications in male fertility.

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