Differential Roles of Estrogen Receptors (ERα and ERβ) in Seminiferous Epithelium: *In vivo* agonist studies in adult rats

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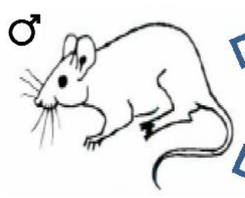
Role of Estrogen in Male Fertility

- Although the roles of gonadotropins and androgens are well established, estrogen (E2) also plays an important role in spermatogenesis
- This is evident from presence of both the estrogen receptors (ER) α and β in the testis and their absence, as in case of knockout mice models, leads to sterility
- Several reports suggest that exposure to environmental estrogens may have deleterious effects on spermatogenesis and have been associated with declining sperm counts and semen quality in men
- Exogenous estradiol treatment causes decreased sperm counts in adult rats
- However, precise steps in spermatogenesis regulated by the two ESRs cannot be understood since the ligand would bind to and signal through both the ESRs equally

Research Question



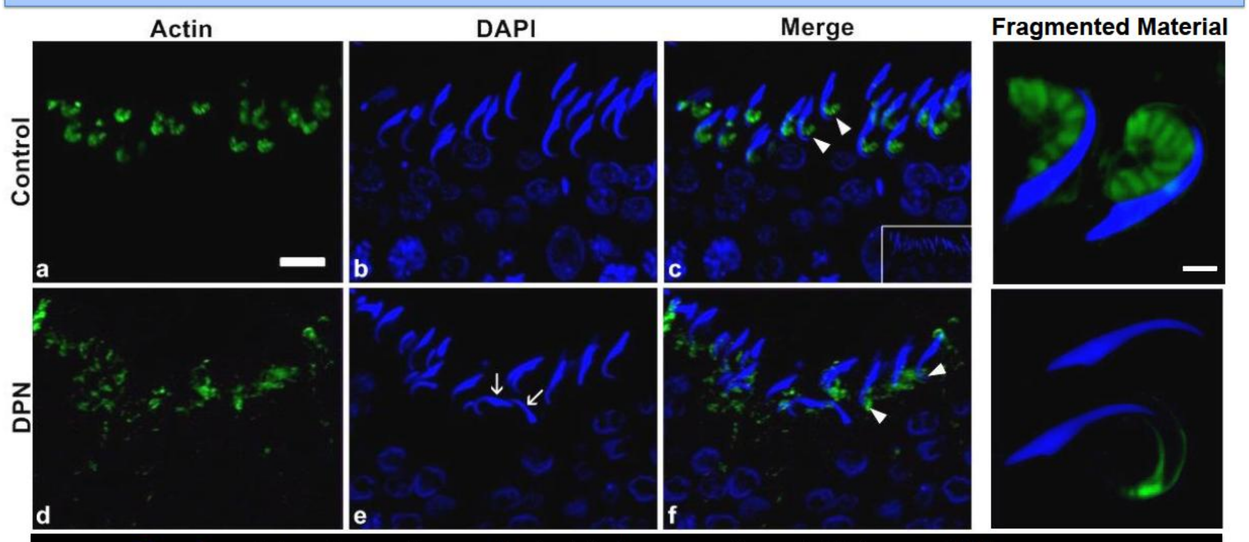
In vivo ERα agonist (PPT)

In vivo ERβ agonist (DPN)

Decrease in sperm counts ?

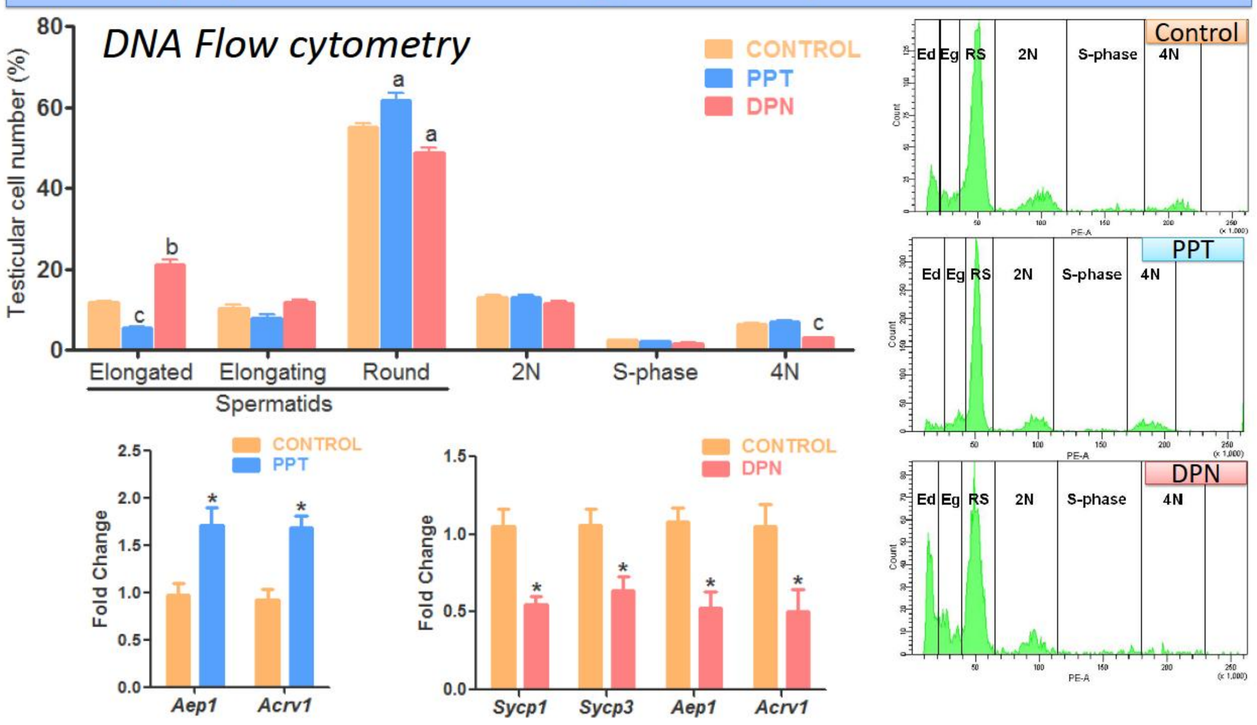
Little information on the individual roles of the two ERs and their direct contribution towards the maintenance of various processes during spermatogenesis

Role of ERβ in Spermiation

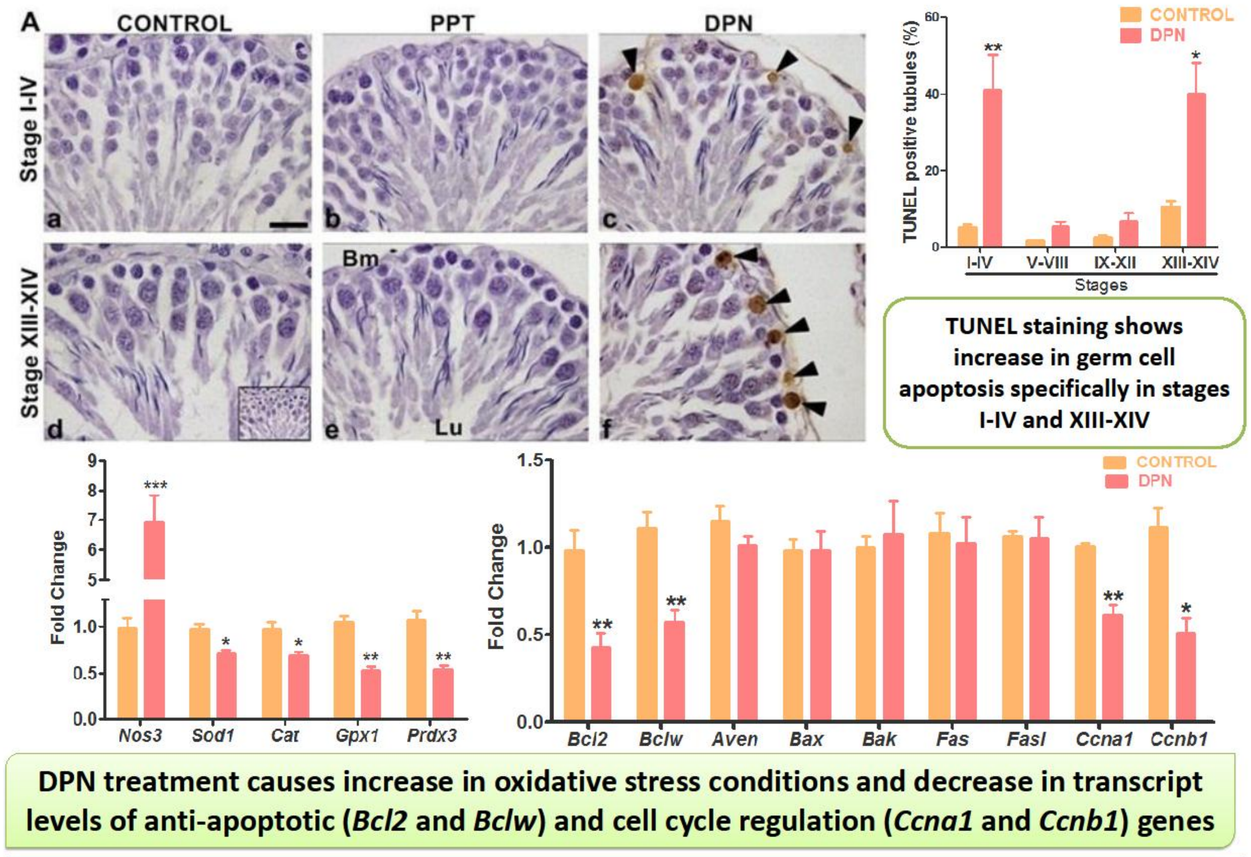


DPN treatment causes spermiation failure due to disrupted TBC formation and altered spermatid polarity; mainly because of down-regulation of ERβ-regulated genes involved in spermiation like *Arpc1b*, *Evl* and *Picalm*

ER agonists treatment affects different germ cell populations leading to low sperm counts



Role of ERβ in germ cell apoptosis



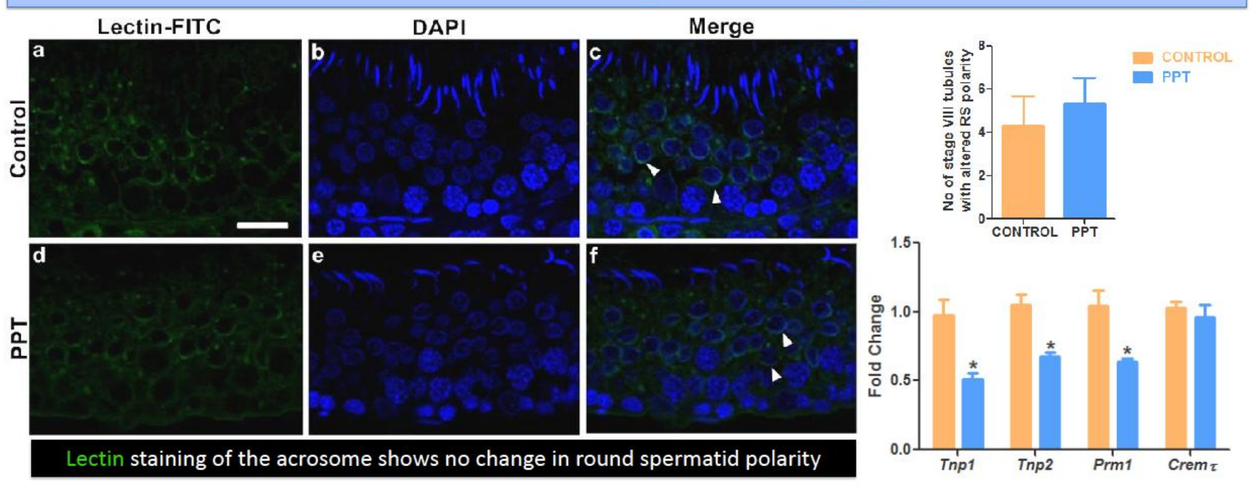
TUNEL staining shows increase in germ cell apoptosis specifically in stages I-IV and XIII-XIV

DPN treatment causes increase in oxidative stress conditions and decrease in transcript levels of anti-apoptotic (*Bcl2* and *Bclw*) and cell cycle regulation (*Ccna1* and *Ccnb1*) genes

PPT → Increase in round spermatid population → Decrease in testicular sperm population → Decrease in caudal sperm counts

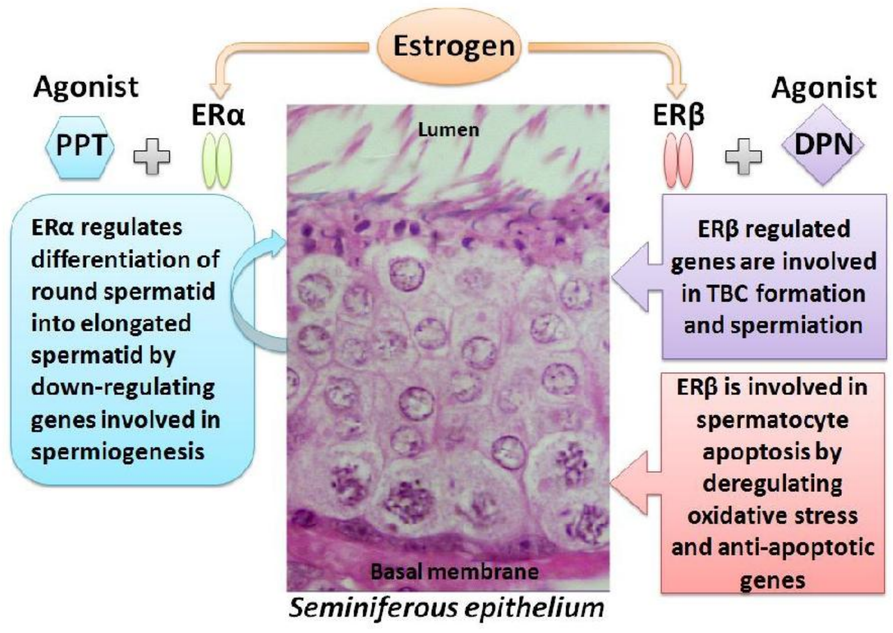
DPN → Decrease in 4N and round spermatid population → Increase in testicular sperm population → Decrease in caudal sperm counts

Role of ERα in spermiogenesis



PPT treatment affects the genes involved in spermiogenesis (*Tnp1*, *Tnp2* and *Prm1*) without affecting polarity of round spermatids

To Summarise



Since many environmental estrogens can bind and affect the ERs differently, these observations can be used to predict their putative effects on spermatogenesis

Acknowledgements

The study had been funded from NIRRH core budget. The authors acknowledge ICMR for SRF.