

## Letter to the Editor

### To the Editor:

In their recent review on the hormonal regulation of spermatogenesis, McLachlan et al (2002) point out the fact that mammalian spermatogenesis requires an intratesticular testosterone concentration many times higher than normal serum levels. In the rat, 20 ng/mL (~70 nM) of intratesticular testosterone is required for the quantitative maintenance of spermatogenesis, compared to the approximately 2 ng/mL (~7 nM) found in serum (for a review, see Roberts and Zirkin, 1991). The reasons for the high testosterone requirement of spermatogenesis have not been established. The authors suggest that there may be specific interactions between testosterone and its receptor in the testis, potentially involving other cofactors, that create this high testosterone requirement. However, a simpler possibility, and one that the authors did not comment on, is that the presence of testicular androgen-binding protein (ABP) is responsible, at least in part, for creating this high androgen requirement.

Given that ABP binds testosterone with high affinity ( $k_d = 2.4$  nM), it is possible that this protein binds a portion of the intratesticular testosterone and sequesters it away from the androgen receptor. We have demonstrated that recombinant ABP can reduce the effective concentration of testosterone in an in vitro androgen-dependent transcription assay (Roberts and Zirkin, 1993). We further showed that the concentration of ABP in the testis (20 nM) is sufficient to create the high testosterone requirement of spermatogenesis in the rat. In the regressed testis of rats contracepted with testosterone-containing implants, the concentration of ABP rose to almost 40 nM in the seminiferous tubule fluid, while the concentration of testosterone dropped to 30 nM. With ABP in molar excess of testosterone, a suppressive effect on androgen-dependent function of the testis would be expected. (Unfortunately, our manuscript describing these experiments was published in the *Endocrine Journal*, which has subsequently changed names and cannot be found with electronic search engines, such as Pubmed.) Our results are consistent with an earlier study

demonstrating that sex hormone-binding globulin, a homolog of ABP produced in the liver, can bind androgens and prevent the androgen-stimulated growth of a line of human prostatic cancer cells (LNCaP) in culture (Damassa et al, 1991).

These studies support the hypothesis that testicular ABP may be responsible for the high intratesticular testosterone requirement for spermatogenesis, although this hypothesis awaits experimental verification in vivo. If proven true, the concentration of ABP or similar binding proteins in the testis will be an important parameter in the design of androgen deprivation-based contraceptives.

Respectfully,  
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McLachlan RI, O'Donnell L, Meachem SJ, Stanton PG, De Kretser DM, Pratis K, Robertson DM. Hormonal regulation of spermatogenesis in primates and man: insights for development of the male hormonal contraceptive. *J Androl.* 2002;23:149–162.

### References

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- Damassa DA, Lin T-M, Sonnenschein C, Soto AM. Biological effects of sex hormone-binding globulin on androgen-induced proliferation and androgen metabolism in LNCaP prostate cells. *Endocrinology.* 1991; 129:75–84.