



Letter to the Editor

Reply to A. Edward Friedman's Letter to the Editor re: Abraham Morgentaler, Abdulkhaled M. Traish. Shifting the Paradigm of Testosterone and Prostate Cancer: The Saturation Model and the Limits of Androgen-Dependent Growth. Eur Urol 2009;55:310-21

We are grateful to Dr. Friedman [1] for raising discussion of the Saturation Model [2], which we believe offers new and exciting lines of inquiry regarding androgens and prostate cancer. Dr. Friedman writes, "For any biological model, however, to be an accurate representation of reality, it must be consistent with all known experimental results." We heartily agree with this comment. Yet it is important to recognize that most cancers are heterogeneous, and different experimental models, especially *in vitro* systems such as cell culture systems, may produce variable responses to hormones and growth factors.

Dr. Friedman appears to be generally in agreement with the Saturation Model. The model posits an exquisite sensitivity of prostate cancer to changes in androgen concentrations at very low levels but indifference to such changes at higher concentrations. Dr. Friedman, however, suggests that a study by Eggener et al [3] provides results that are inconsistent with the Saturation Model.

We disagree. The model used by Eggener et al [3] exposed nude mice implanted with LnCaP tumors to intermittent androgen ablation, a treatment known to cause prostate tumors to escape normal androgenic regulation. Moreover, the study authors themselves recognized a major irregularity in their results, since prostate-specific antigen concentrations failed to decline with androgen deprivation, as is usually seen with LnCaP tumors. This result indicates that this experimental system did not respond normally to androgenic stimuli. For this reason, we

do not believe the study by Eggener et al has relevance to the Saturation Model.

Dr. Friedman's comments regarding androgen membrane receptor activity are interesting, but we believe this process is unrelated to the Saturation Model.

Conflicts of interest: The authors have nothing to disclose.

References

- [1] Friedman, AE. Re: Abraham Morgentaler, Abdulkhaled M. Traish. Shifting the paradigm of testosterone and prostate cancer: the Saturation Model and the limits of androgen-dependent growth. *Eur Urol* 2009;55:310-21. *Eur Urol* 2009;56:e4.
- [2] Morgentaler A, Traish AM. Shifting the paradigm of testosterone and prostate cancer: the Saturation Model and the limits of androgen-dependent growth. *Eur Urol* 2009;55:310-21.
- [3] Eggener SE, Stern JA, Jain PM, et al. Enhancement of intermittent androgen ablation by "off-cycle" maintenance with finasteride in LnCaP prostate cancer xenograft model. *Prostate* 2006;66:495-502.

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