

## ***This Week's Citation Classic***

**Bruchovsky N & Wilson J D.** The conversion of testosterone to 5 $\alpha$ -androstane-17 $\beta$ -  
3-one by rat prostate *in vivo* and *in vitro*. *J. Biol. Chem.* **243**:2012-21, 1968.  
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**Nuclear association of testosterone 5 $\alpha$ -  
reductase, intranuclear abundance of  
dihydrotestosterone, and retention of  
dihydrotestosterone exclusively by target  
tissues for testosterone were reported here.  
On this evidence it was suggested that  
dihydrotestosterone is the active form of  
testosterone in peripheral tissues. [The SC<sup>®</sup>  
indicates that this paper has been cited over  
640 times since 1968.]**

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"Recalling this past experience is doubly pleasurable since the effort not only brings to mind a stimulating and productive time in the United States, but also affords an occasion to read 56 letters written to my then future wife. My surprise upon her welcome revelation that the letters were still in existence was possibly exceeded by the satisfaction of being able to sharpen my memory concerning the following events.

"After completing MD and PhD programs at the University of Toronto in 1966, I had hoped to continue with residency training in internal medicine at the Southwestern Medical School in Dallas. Since all positions were filled, I accepted an alternative appointment of postdoctoral fellow and non-remunerative resident. The latter assured me of free meals in the Parkland Hospital cafeteria, conceivably an important benefit, in return for modest clinical duties.

"The objective of the research project, started with J.D. Wilson in October, was to determine whether a testosterone binding protein could be isolated from prostatic nuclei. After an abortive attempt to purify nuclear phosphoprotein, I tried a less

specific approach. Animals were injected with tritiated testosterone and binding of radioactivity to nuclear components was then successfully shown by the relatively new procedure of gelexclusion chromatography. The need to ascertain the identity of the nuclear radioactivity was obvious, but unexpectedly little of this material was recoverable in the form of testosterone when analysed by thin-layer chromatography.

"In February and March of 1967 the careful examination of chromatograms in discrete sections revealed that the majority of radioactivity co-migrated with a potent metabolite of testosterone, dihydrotestosterone. At first this observation was viewed with skepticism, and Wilson and I found ourselves debating the merits of different follow-up experiments. On one occasion the discussion became so lively that I thought my postdoctoral position would soon have to be vacated. For a few evenings I attended to my anxiety by the frequent playing of Chopin's Prelude No. 20 for piano, which I discovered by chance to be a good musical sedative.

"Doubts about dihydrotestosterone were dispelled in the next two months as it became clear that the prostate contained enzymes very active in converting testosterone to dihydrotestosterone, and the latter to androstanediol. With help and much work, enough data were available by August for us to consider writing a report. The third draft of a paper was finished by the end of October and distributed locally for comment. On the suggestion of M.D. Siperstein, more emphasis was given in the final version to the possible role of dihydrotestosterone as the active androgen. Only minor changes were necessitated by subsequent editorial review."

"This paper is cited because it was the first to attach biological significance to the formation of dihydrotestosterone within target cells for testosterone."