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Abstract

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“DHEA is an anabolic steroid like testosterone and THG”

We have recently taken advantage of the unique sensitivity of DNA microarrays to compare the genomic expression profile of tetrahydrogestrinone (THG) with that of dihydrotestosterone (DHT), the most potent natural androgen, thus clearly demonstrating that THG is an anabolic steroid. We use the same DNA microarray technique in the present study to demonstrate that DHEA exerts an effect similar to DHT and THG on a large series of genes, thus demonstrating that DHEA is, without any doubt, an anabolic steroid like the other natural androgens and a series of synthetic compounds already included in the list of the Anabolic Steroid Control Act of 2004. Recently, this Act has amended the Controlled Substances Act to include androstenedione (4-dione) as an anabolic steroid. Despite the well recognized steroidogenic pathway showing that DHEA is a precursor of both 4-dione and androst-ene-3 α , 17 β diol (5-diol), two steroids directly transformed into testosterone, DHEA has been excluded from the list along with estrogens, progestins and corticosteroids, three classes of steroids well known to have no androgenic activity (except for some progestins).

In fact, DHEA is an obligatory intermediate in the synthesis of testosterone and DHT in peripheral tissues in both men and women. C57BL6 mice were gonadectomized and treated for 24 hours or 4 weeks with daily subcutaneous injections of 0.1 mg DHT or 3 mg DHEA. Treatment for one month with either DHT or DHEA increased ventral prostate, dorsal prostate, seminal vesicle weight ($p < 0.01$ for all tissues). Twenty four hours after single injection of DHT or DHEA, 228 genes were differentially expressed in the ventral prostate by both DHT and DHEA. In the seminal vesicles, gastrocnemius muscle and preputial glands, the number of probe sets commonly modulated by DHT and DHEA were 389, 30 and 135, respectively. After 1 month of treatment, on the other hand, 519 and 849 genes were commonly modulated by DHEA and DHT in the ventral prostate and seminal vesicles, respectively.

The power of gene expression profiling has been well demonstrated in clinical medicine, especially in acute myeloid leukemia, diffuse large B-cell lymphoma, medulloblastoma, lung carcinoma and breast carcinoma, thus giving a molecular classification of diseases which permits specific treatments and more accurate prognosis. In analogy with THG, the present microarray data provide an extremely precise and unquestionable genomic signature and proof of the androgenic anabolic activity of DHEA. Such an approach is applicable to all potential androgenic or anabolic compounds.

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