Dehydroepiandrosterone administration or G(alpha)q overexpression induces (beta)-catenin/T-cell factor signaling and growth via increasing association of estrogen receptor-(beta)/Dishevelled2 in androgen-independent prostate cancer cells.


Endocrine Section, Laboratory of Clinical Investigation, National Center for Complementary and Alternative Medicine, National Institutes of Health, Bethesda, Maryland 20892, USA. xunxianl@mail.nih.gov

beta-Catenin/T-cell factor signaling (beta-CTS) plays multiple critical roles in carcinogenesis and is blocked by androgens in androgen receptor (AR)-responsive prostate cancer (PrCa) cells, primarily via AR sequestration of beta-catenin from T-cell factor. Dehydroepiandrosterone (DHEA), often used as an over-the-counter nutritional supplement, is metabolized to androgens and estrogens in humans. The efficacy and safety of unregulated use of DHEA are unclear. We now report that DHEA induces beta-CTS via increasing association of estrogen receptor (ER)-beta with Dishevelled2 (Dvl2) in AR nonresponsive human PrCa DU145 cells, a line of androgen-independent PrCa (AIPC) cells. The induction is temporal, as assessed by measuring kinetics of the association of ERbeta/Dvl2, small interfering RNA administration depleting ERbeta, or AR overexpression arresting ERbeta. These data suggest that novel pathways activating beta-CTS play roles in the progression of AIPC. Although DHEA may enhance PrCa cell growth via androgenic or estrogenic pathways, the effects of DHEA administration on clinical prostate function remain to be determined.

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DHEA metabolism in prostate: For better or worse?

Arnold JT.

ICF-Endocrine Section, National Center for Complementary and Alternative Medicine (NCCAM), National Institutes of Health (NIH), Building 10, 2847 MSC 1547, 9000 Rockville Pike, Bethesda, MD 20892-1547, USA. jarnold@mail.nih.gov

Dehydroepiandrosterone (DHEA) is commonly used in the USA as a nutritional supplement for antiaging, metabolic support or other uses. Investigations into understanding the effects of DHEA on human prostate cancer progression have posed more questions than answers and highlight the importance of communications between stromal and epithelial tuftiuotu elements within the prostate that contribute to the regulation of DHEA metabolism. Intracrine metabolism of DHEA to androgens (A) and/or estrogens (E) may occur in one cell compartment (stromal) which may release paracrine hormones or growth/inhibitory factors to the epithelial cells. Alternatively, androgen or estrogenic pathways, the effects of DHEA administration on clinical prostate function remain to be determined.

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Comparative effects of DHEA vs. testosterone, dihydrotestosterone, and estradiol on proliferation and gene expression in human LNCaP prostate cancer cells.

Arnold JT, Le H, McCann KK, Blackman MR.

Endocrine Section, Laboratory of Clinical Investigation, Division of Intramural Research, NCCAM, NIH, 9 Memorial Dr, Rm 1N105, Bethesda, MD 20892-0933, USA. jarnold@mail.nih.gov

Serum levels of the adrenal androgen dehydroepiandrosterone (DHEA) peak in men and women in the third decade of life and decrease progressively with age. Increasing numbers of middle-aged and older individuals consume over-the-counter preparations of DHEA, hoping it will retard aging by increasing muscle and bone mass and strength, decreasing fat, and improving immunologic and neurobehavioral functions. Because DHEA can serve as a precursor to more potent androgens and estrogens, like testosterone (T), dihydrotestosterone (DHT), and 17beta-estradiol (E2), supplemental DHEA use may pose a cancer risk in patients with nascent or occult prostate cancer. The steroid-responsive human LNCaP prostate cancer cells, containing a functional but mutated androgen receptor (AR), were used to compare effects of DHEA with those of T, DHT, and E2 on cell proliferation and protein and/or gene expression of AR, prostate-specific antigen (PSA), IGF-I, IGF-I receptor (IGF-IR), IGF-II, IGF-binding proteins-2, -3, and -5, (IGFBPs-2, -3, and -5), and estrogen receptor-beta (ERbeta). Cell proliferation assays revealed significant stimulation by all four steroids. DHEA- and E2-induced responses were similar but delayed and reduced compared with that of T and DHT. All four hormones increased gene and/or protein expression of PSA, IGF-IR, IGF-I, and IGFBP-2 and decreased that of AR, ERbeta, IGF-II, and IGFBP-3. There were no significant effects of hormone treatment on IGFBP-5 mRNA. DHEA and E2 responses were similar, and distinct from those of DHT and T, in time- and dose-dependent studies. Further studies of the mechanisms of DHEA effects on prostate cancer epithelial cells of varying AR status, as well as on prostate stromal cells, will be required to discern the implications of DHEA supplementation on prostatic health.

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Getting over testosterone: postulating a fresh start for etiologic studies of prostate cancer.

Carpenter WR, Robinson WR, Godley HA.


Ory Heti.


[Significance of dehydroepiandrosterone and dehydroepiandrosterone sulfate in different diseases]

[Article in Hungarian]


Semmelweis Egyetem, Alkádás Orvostudományi Kar, 1. Belgyógyászati Klinika, Budapest. bacsö@bell.sote.hu

http://www.medicinacomplementar.com.br/convertido/ca-0656.htm
Dehydroepiandrosterone and dehydroepiandrosterone-sulfate are precursors of androgens and estrogens, support the gonadal sexual steroid production. The levels of dehydroepiandrosterone and dehydroepiandrosterone-sulfate are maximal between the ages of 20 and 30 years, then start a decline of 2% per year, leaving a residual of 10-20% of the peak production by the eight decade of life. The age-associated decrease may lead to osteoporosis, deterioration of lipid-metabolism, cardiovascular diseases and second type of diabetes mellitus. Decreased levels were found in autoimmune diseases and in sexual dysfunction, too. Intracrinology describes the formation of active hormones which exert their action in the same cells where synthesis took place without release into the pericellular compartment. The high local androgen and estrogen concentration may be important in the pathomechanism of hirsutism, acne, seborrhea, breast and prostate cancer. Administration of dehydroepiandrosterone resulted in a reduction of postmenopausal osteoporosis, also the decreased symptoms in systemic lupus erythematosis, psychiatric diseases and sexual dysfunction. The authors summarize the metabolism of dehydroepiandrosterone and dehydroepiandrosterone-sulfate and their role in different diseases.

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Beneficial effects and side effects of DHEA: true anti-aging and age-promoting effects, as well as anti-cancer and cancer-promoting effects of DHEA evaluated from the effects on the normal and cancer cell telomeres and other parameters.

Heart Disease Research Foundation.
The author evaluated the effects of DHEA (Dehydroepiandrosterone) on the amount of telomeres of normal cells and cancer cells and found the following: Contrary to the literature, which often recommended 25-50 mg of DHEA daily for the average adult human being, the author found that, depending on the individual, the maximum increase of normal cell telomere was obtained by a single optimal dose of 1.25-12.5 mg. This was examined in 50 people, both males and females, between the ages of 20-80 years old. When one optimal dose was given to each individual, the average telomere amount in normal tissues, measured in Bi-Digital O-Ring Test units, often increased from anywhere between 25-300 ng to between 500-530 ng. Cancer cell telomere reduced from higher than 1100 ng to less than 1 yg (=10^{-24} g) with equally significant normalization of abnormal cancer parameters (such as Integrin alpha5beta1, Oncogen C-fosAb2, Acetylcholine, etc.). Circulatory improvement and an increase in grasping force of up to 25% were also detected, along with the changing of a few white hairs to black hairs. The beneficial effects of one optimal dose of DHEA generally lasted between 1 to 4 months, though in some individuals it lasted for a much shorter period of time due to a number of negative factors such as excessive stress/work, excessive exposure to low temperatures and toxic substances, or use of common pain medicines. On the other hand, if a patient took an excessive dose of DHEA, the amount of normal cell telomere decreased, while there was an increase in cancer cell telomere. It was found that those who took an overdose of 25-50 mg daily for more than 3 months had a high incidence of cancer of the prostate gland, breast, colon, lung, and stomach. Also, when the average normal cell telomere levels were less than 110 ng, compared with a normal value of 120-130 ng, and when DHEA in different parts of the body was also extremely low (less than 1-2 ng), one could suspect the possible presence of a malignant tumor somewhere in the body. When normal cell telomere was less than 110 ng, most individuals felt very weary with marked tiredness in the eyes, and grasping force was often reduced.

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