High intratumoral dihydrotestosterone is associated with antiandrogen resistance in VCaP prostate cancer xenografts in castrated mice

pjoshea13•

1 day ago•6 Replies

A new Finnish-Swedish paper (with no mention of NATO) [1]

Dr. Myers has said that the purpose of ADT is to deny PCa access to dihydrotestosterone [DHT]. A minority of men produce DHT via the alternative pathway that does not involve testosterone [T]. Myers was one of the few doctors who checked DHT levels. (Most doctors assume that castrate T = castrate DHT.)

However, when PCa is on the road to CRPC, cells may discover the alternative pathway. A blood test will not detect DHT in those cells. So, some men cover that possibility by taking the 5alpha-reductase inhibitor Dutasteride [Avodart].

"Using xenografts of VCaP cells we showed that growth of antiandrogen resistant CRPC tumors were characterized by a higher intratumor dihydrotestosterone (DHT) concentration than that of treatment responsive tumors."

The mice had been castrated, so the presumed origin of the hormones leading to DHT was the adrenal glands [2].

"... the slow tumor growth after adrenalectomy was associated with a low intratumor DHT concentration."

"... intratumor DHT concentration and expression of several androgen-dependent genes in CRPC lesions is an indication of enzalutamide treatment resistance and an indication of the need for further androgen blockade."

Abiraterone is a CYP17A1 inhibitor. The CYP17A1 enzyme acts upon pregnenolone and progesterone to produce downstream hormones that include androgens.

"The presence of an androgen synthesis, independent of CYP17A1 activity, has been shown to exist in prostate cancer cells, and thus, novel androgen synthesis inhibitors are needed for the treatment of enzalutamide-resistant CRPC tumors that do not respond to abiraterone."

However, from what I know, Avodart will inhibit the final step that results in DHT.

How often is Enzalutamide [Xtandi] resistance due to intratumor DHT? I don't know, but Avodart is an inexpensive safety play. imo

-Patrick

[1] pubmed.ncbi.nlm.nih.gov/355...

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High intratumoral dihydrotestosterone is associated with antiandrogen resistance in VCaP prostate cancer xenografts in castrated mice

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Abstract

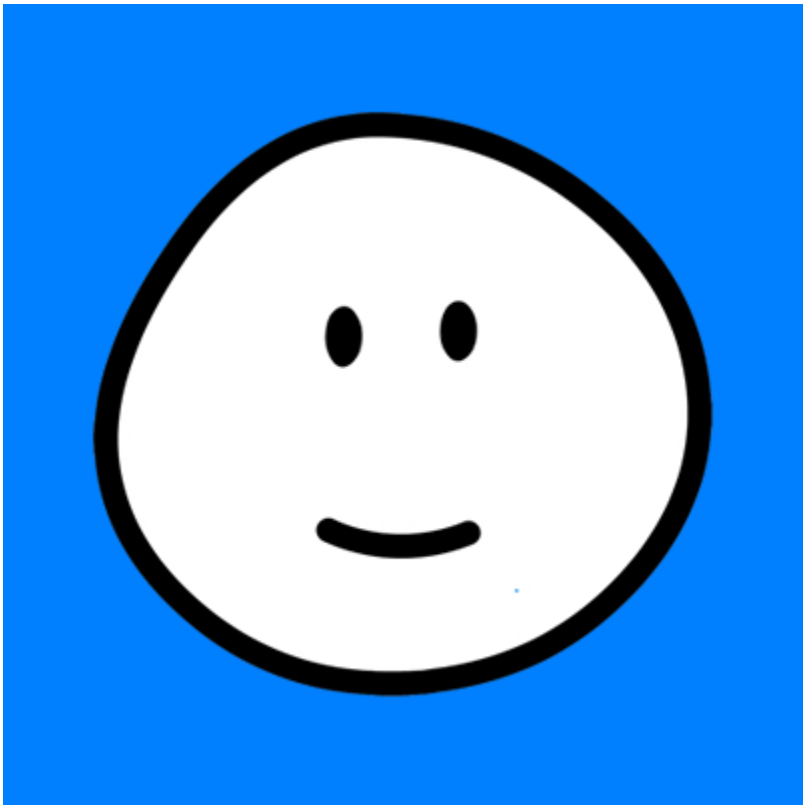
Antiandrogen treatment resistance is a major clinical concern in castration-resistant prostate cancer (CRPC) treatment. Using xenografts of VCaP cells we showed that growth of antiandrogen resistant CRPC tumors were characterized by a higher intratumor dihydrotestosterone (DHT) concentration than that of treatment responsive tumors. Furthermore, the slow tumor growth after adrenalectomy was associated with a low intratumor DHT concentration. Reactivation of androgen signaling in enzalutamide-resistant tumors was further shown by the expression of several androgen-dependent genes. The data indicate

that intratumor DHT concentration and expression of several androgen-dependent genes in CRPC lesions is an indication of enzalutamide treatment resistance and an indication of the need for further androgen blockade. The presence of an androgen synthesis, independent of CYP17A1 activity, has been shown to exist in prostate cancer cells, and thus, novel androgen synthesis inhibitors are needed for the treatment of enzalutamide-resistant CRPC tumors that do not respond to abiraterone.

Keywords: Cancer; Endocrinology.

[2] en.wikipedia.org/wiki/Adren...

Written by



pjoshea13

United States

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Reply to pjoshea13

6 Replies

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RSH1 1 day ago

I don't think that this picture has been posted before.

DHT pathways

LearnAll in reply to RSH1 1 day ago

Thanks. That's a nice picture and explains a lot. Blocking DHT by Finasteride/Dutasteride can certainly help many men. And so is reducing lipids by Statins. Not to forget Metformin/Berberin.

Last edited by LearnAll

RSH1 in reply to LearnAll 1 day ago

Zytiga inhibits CYP17. But then there is the backdoor pathway that Patrick discusses.

Kuanyin 1 day ago

High Patrick. I think we should also mention foods that help block 5-Alphas Reductive--Edamame

--Green Tea

--Coconut (Lauric Acid)

--Onions

--Flax (seeds, not oil which is too volatile)

Supplements

--Quercitin

--Calcium d-Glutarate and others

RSH1 in reply to Kuanyin19 hours ago

Does anyone have any experimental data for these? Baseline DHT, supplements/foods, subsequent DHT?

I have data but only for dutasteride/finasteride and there are plenty of studies that show the reduction amount so my data is rather moot (good for me personally of course).

Last edited by RSH1

EdBar6 hours ago

Yep, I continue to take dutasteride daily per Dr. Myers while on ADT. I've been taking it for about 8 years now, my PSA continues to be <0.1. Myers was so far ahead of his time on many "outside the box" treatments he prescribed.

Ed