47

BINDING OF THE NON STEROIDAL ANANDRON (FU 23908) TO STEROID BINDING PROTEINS IN THE RAT PROSTATE. M. MOGUILEWSKY, Centre de Recherches Roussel Uclaf, 93230 Romainville FRANCE

Anandron is a pure non steroidal antiandrogen which inhibits the binding of androgens to their cytosol androgen receptor (AR) in the castrated (CX) rat prostate in vitro and in vivo. Since its structure is very different from that of natural hormones, we investigated whether the inhibition of binding of androgens to AR is due to direct competition of anandron at the androgen binding sites or to binding to a distinct site or protein interacting with AR. After incubation with the cytosol of CX rat prostate, (^{3}H)anandron bound to at least 2 proteins : 1) a protein (PBP) present in high concentrations and whose characteristics (sedimentation coefficient, resistance to charcoal adsorption in spite of a low affinity, tissular and hormonal specificity, precipitation by ammonium sulfate at 50-70% saturation, resistance to heating, decrease by castration ...) were similar to those of the "prostatic steroid binding protein", known to inhibit the binding of AR to chromatin 2) AR, which was only detected after prior separation from PBP. The relative binding affinity (RBA) of anandron for AR was influenced by the presence of PBP : it was higher in the seminal vesicles (s.v.) or epididymis cytosol, where PBP is in low concentration or absent, than in the prostate cytosol. When preheated prostate cytosol or the 70% ammonium sulfate precipitated prostatic fraction (containing PBP) was added to v.s. cytosol, the RBA of anandron for v.s. AR was shifted to weaker values. Therefore, the binding of anandron to PBP might modulate its antiandrogen activity.

48

HORMONAL CLASSIFICATION OF RESPONSE TO FLUTAMIDE THERAPY IN ADVANCED PROSTATE CANCER
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In a Phase II Trial of flutamide in advanced prostate cancer, 25 patients were assessable for clinical response. Sixteen (16) of them have had serial assays of the following pituitary and steroidal hormones; luteinising hormone (LH), IU/L; follicle stimulating hormone (FSH), IU/L; testosterone (T), nmol/L; androstenedione (A'dione), nmol/L; estradiol, (E) pmol/L and 17 α-hydroxyprogesterone (17OHP), nmol/L. A consistent elevation of T & E was found in responders but was absent in non-responders. When results are expressed as the mean maximum change ± SEM from commencement of flutamide therapy the following values were found.

	T	E_2	A'dione	17OHP	LH	FSH
Responders (n=7)	16.2 ± 4.6	167.6 ± 37.5	-0.2 ± 1.4	-0.2 ± 1.6	14.3 ± 3.2	13.1 ± 3.2
Non-responders (n=9)	2.0 ± 0	23.4 ± 22.1	1.0 ± 0.9	0.6 ± 0.8	17.9 ± 5.4	17.7 ± 6.4
p	<0.0005	<0.0005	0.5	0.6	0.5	0.6

In this study patients who responded to flutamide showed a significant increase in the serum T & E levels with no significant alteration in other steroids or in the pituitary hormones. These findings suggest that T & E may predict response to flutamide therapy in advanced prostate cancer.