

both rat and human prostate.

To determine whether the nuclear receptor is essential for the expression of hormonal sensitivity, we compared the amount of nuclear androgen-binding and the activities of acid phosphatase and plasminogen activator in the transplantable prostatic adenocarcinoma of Nb rats. Androgen-stimulated tumours were found to have more nuclear receptor and less acid phosphatase activity than autonomous tumours. Also the plasminogen activator activity was 7-fold lower in the androgen stimulated tumours than in the latter. These observations are consistent with the view that a diminished concentration of nuclear androgen receptor in prostatic carcinoma is associated with an increasing grade of malignancy.

13. Comparison between the contents of cytosolic steroid hormone receptors in the Dunning R-3327 prostatic adenocarcinoma of the rat and in human prostatic carcinoma. E. DAHLBERG, M. SNOCHOWSKI and J.-Å. GUSTAFSSON, Departments of Chemistry and Medical Nutrition, Karolinska Institutet, Fack, S-104 01 Stockholm, Sweden

The R-3327 transplantable rat prostatic adenocarcinoma was investigated with regard to receptors for hormonal steroids. It was found that glucocorticoid (dexamethasone) receptors, and progestin (R 5020) receptors were non-detectable in all tumors analyzed, i.e. 7 and 4 tumors, respectively. Estrogen (R 2858) receptors, and androgen (R 1881) receptors were detected in 5 of 6, and 8 of 9 tumors, respectively. The analyses were carried out using a dextran-coated charcoal technique, and the binding parameters were calculated according to Scatchard. The apparent dissociation constants ( $K_d$ ) for estrogen and androgen receptors in the Dunning tumor were similar, and ranged from 0.57 to 1.85, and 0.73 to 1.85, respectively. The maximum number of binding sites ( $B_{max}$ ) for the estrogen receptors ranged between 638 and 5,810 fmol/g tissue (8.31 - 90.2 fmol/mg protein; 304 - 1,260 fmol/mg DNA), and those for the androgen receptor ranged between 1,490 and 25,100 fmol/g tissue (19.4 - 363 fmol/mg protein; 710 - 5,450 fmol/mg DNA). In all cases containing both androgen and estrogen receptors, the former were more abundant.

Since several authors have suggested that this rat tumor may serve as a model for cancer of the human prostate, we compared our steroid receptor analyses of the Dunning tumor to those obtained with the same technique in primary and metastatic cancer of the human prostate. In a series of 25 biopsies from primary human prostatic carcinoma, methyltrienolone receptors were detected in 20 cases. In our series of 5 metastases from human cancer of the prostate, we found methyltrienolone (R 1881) receptors in 4 cases ( $B_{max}$  110 - 28,500 fmol/g tissue), glucocorticoid receptors in 3 cases ( $B_{max}$  4,730 - 13,600 fmol/g tissue), and progestin receptors in 2 cases ( $B_{max}$  424 - 1,410 fmol/g tissue), but none of the metastases contained detectable estrogen receptors.

Hence, it may be concluded that although the Dunning tumor and the human cancer of the prostate are both androgen-dependant, and contain androgen receptors in most cases, the rat model seems to differ from metastatic prostate cancer with regard to steroid receptor content. On the other hand, it is possible that it is a suitable model for primary cancer of the human prostate. It would thus be of interest to compare this, and other animal tumors with primary cancer of the human prostate in order to find the most optimal model system for studies of the hormonal control of human prostatic cancer.

14. Distribution of dihydrotestosterone and of nuclear androgen receptors between stroma and epithelium of human benign hyperplastic prostatic tissue (BPH), D.A.N. SIRETT, S.K. COWAN, A.E. JANECKZO and J.K. GRANT, University Department of Steroid Biochemistry, Royal Infirmary, Glasgow G4 0SF, Scotland, U.K.

Previous work in our laboratory has indicated that 1) testosterone 5 $\alpha$ -reductase activity is located predominantly in BPH stroma rather than in the epithelium, and 2) BPH androgen receptors are found predominantly in the nuclear fraction of whole tissue samples. To further examine stromal-epithelial relationships in BPH tissue, we have measured the concentrations of endogenous dihydrotestosterone (DHT) and of nuclear androgen receptors in separated epithelium and stroma. Endogenous androgens were ether-extracted from tissue homogenates, and DHT separated by Lipidex column chromatography and quantitated by RIA. Crude nuclei were extracted with buffer containing 0.5 M KCl, and the receptor concentration was determined by exchange with [ $^3$ H]DHT. Similar concentrations of DHT were found in stroma and epithelium, when results were expressed in terms of the DNA content of the separated tissue (stroma:  $5.0 \pm 1.2$  ng/mg DNA; epithelium:  $6.2 \pm 2.6$  ng/mg DNA,  $n = 6$ ). All results mean  $\pm$  S.E.M.). Epithelial enrichment of DHT was evident in terms of tissue protein (stroma:  $93 \pm 15$  pg/mg protein; epithelium:  $468 \pm 98$  pg/mg protein,  $n = 6$ ). Receptor concentrations, expressed on a DNA basis, were similar in nuclear extracts from both components (stroma:  $556 \pm 76$  fmol/mg DNA; epithelium:  $697 \pm 182$  fmol/mg DNA,  $n = 8$ ). These results suggest 1) low testosterone 5 $\alpha$ -reductase activity in BPH epithelium does not prevent the accumulation of large amounts of DHT by this component, and 2) both epithelium and stroma from BPH tissue contain nuclear androgen receptors and so are probably androgen-sensitive.

15. Prostatic cancer - diagnostic and prognostic methods, F.H. SCHRÖDER, Erasmus Universiteit Rotterdam, Department of Urology, Rotterdam, The Netherlands

About 9% of all malignant tumors diagnosed clinically are prostatic carcinomas. This amounts to about 50 new cases per 100,000 males per year and makes prostatic cancer

second to third most frequent malignancy in males.

A peculiar problem associated with this tumor is the fact that the incidence of prostatic carcinoma in autopsy studies is very much higher and has been found to vary between 28.9% and 100% for the age groups 50 - 90 years. The incidence depends on age and on the numbers of stepsections taken from prostatic specimens. This finding indicates that many more men live with their prostatic carcinoma than die from it.

Unfortunately there is still no reliable method of determining beforehand which particular tumor is going to kill and which one will remain stationary. To solve this problem is the key issue in the field of diagnosis of prostatic cancer.

Rectal examination is the most important single step in the diagnosis of this tumor. Changes of consistency of prostatic tissue turn out to be due to carcinomatous growth in about 50% after histological or cytological examination has been carried out on a biopsy specimen.

At the present time there is no other reliable screening parameter for prostatic cancer although immunological and immunochemical determinations of prostatic acid phosphatase and the use of ultrasound may prove to be valuable in this respect.

A number of other markers are presently being explored, they include alkaline phosphatase, LDH isoenzymes, urinary cholesterol, urinary ketosteroids, CEA, spermine and spermidine and others.

For the diagnosis of metastases bone X-rays, bone scanning, lymphangiography, lymph-node biopsy, serum acid phosphatase and bone biopsies are commonly used parameters.

Local extension of the primary, the grade of malignancy, the elevation of serum acid phosphatase and other evidence for metastatic disease are the most important prognostic factors.

16. Purification and characterization of prostatic secretion protein (PSP), a major androgen-dependent protein in male accessory sexual glands in rat and man, Å. POUSETTE<sup>1</sup>, P. BJÖRK<sup>3</sup>, K. CARLSTRÖM<sup>2</sup>, B. FORSGREN<sup>3</sup>, J.-Å. GUSTAFSSON<sup>1</sup> and B. HÖGBERG<sup>3</sup>, <sup>1</sup>Department of Chemistry and Department of Medical Nutrition, Karolinska Institutet, S-104 01 Stockholm 60, <sup>2</sup>the Hormone Laboratory, Sabbatsberg Hospital, S-113 24 Stockholm, and <sup>3</sup>AB Leo Research Laboratories, Pack, S-251 00 Helsingborg, Sweden

The prostatic secretion protein (PSP) was discovered when investigating the mechanism of action of estramustine phosphate (Estracyt®), a drug used in the treatment of prostatic carcinoma. The dephosphorylated drug was shown to bind to the protein with a  $K_d$  of about  $10^{-8}$  M, and the binding was shown to be relatively specific with regard to the ligand-binding site. The formed estramustine-PSP complex had an  $M_r$  of 46,000, as estimated by gel filtration, and an isoelectric point of about 5. The protein was purified

to homogeneity using chromatography on DEAE-cellulose, Sephadex G-100 Superfine, Octyl-Sepharose CL-4B and polyacrylamide gel electrophoresis. Antibodies against the protein were raised in rabbits, and a radioimmunoassay was developed to quantitate the protein. Using this method, it was shown that PSP was predominantly found in the accessory sexual glands of the male rat. It was estimated that PSP constituted about 18% of the total protein in rat ventral prostate. PSP was also present in the dorsal and lateral lobes of the prostate and in the seminal vesicles, coagulating glands, epididymis and preputial glands of the male rat. An immunologically similar protein is also present in the human prostate, seminal vesicles and epididymis. As this protein is almost exclusively found in the male accessory sexual glands and is secreted into the reproductive tract, it may be of great importance for maintaining normal male fertility. Furthermore, it may be suggested that this protein could be used as a probe for androgen action. Quantitation of PSP in biopsies from human prostatic carcinoma may aid in predicting the individual response to treatment with Estracyt®.

17. Radioimmunoassay of human prostate-specific acid phosphatase in the diagnosis and follow-up of therapy of prostatic cancer, P. VIHKO, Departments of Anatomy and Clinical Chemistry, University of Oulu, SF-90220 Oulu 22, Finland

Prostate-specific acid phosphatase (PAP) in serum was determined by radioimmunoassay (RIA) (1), before and during various forms of endocrine therapy. The results of PAP-RIA were compared with those obtained by measurement of the catalytic activity of acid phosphatase. Serum concentrations of immunoreactive acid phosphatase for healthy men ranged from <1 to 10 µg/l and for patients with advanced prostatic carcinoma from 100 to 500 µg/l. The concentrations of the enzyme in the sera of patients with benign prostatic hyperplasia were similar to those in the sera of the reference group. The survival of the immunologic activity of the enzyme at room temperature was over 48 h, and repeated freezing and thawing (three times) had no effect on the immunologic activity of the enzyme. The percentage changes in radioimmunoassayable PAP were much larger and appeared earlier than those obtained by the measurement of the catalytic activity. They also preceded changes later found by X-ray or isotopic techniques. The results suggest that the RIA of PAP is a reliable and sensitive method for the diagnosis and follow-up of therapy of human prostatic carcinoma.

#### Reference

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