The normal morphogenesis and cytodifferentiation of rodent prostatic epithelium is strongly dependent on the continuous association with mesenchymal cells of proper (i.e. urogenital) origin (1,2). The inductive capacity of urogenital stroma has been tested on different epithelia, and it was found that, in the presence of androgens, integumental epithelium was transformed by urogenital stroma into a glandular epithelium characteristic of the source of the stroma (1,3). Moreover, adult bladder epithelium could be induced to form prostate-like acini by embryonic stroma of urogenital origin (3). From these observations McNeal (4) hypothesized that the formation of prostatic acini during the development of benign prostatic hyperplasia may be the result of a re-expression of embryonic inductive capacity. Cunha et al. (5) summarized the pre-requisites for prostatic development to be i) the presence of androgens; ii) the presence of "inductive" stroma and iii) the ability of the epithelium to respond to the inductive influences.

According to the generally accepted mechanism of steroid hormone action, androgens exert their effect(s) on target tissues through specific receptors present in the cytoplasm, which translocate to the nucleus after binding the androgen. In the nucleus, mRNA and protein synthesis are stimulated, leading ultimately to the observed hormonal effects (6). Prior to receptor binding, testosterone is reduced to 5α-dihydrotestosterone (7), which has a higher affinity for the androgen receptor. Androgen receptors (8-11) and 5α-reductase (11-14) are indeed present in human prostatic tissue.
CELL SEPARATION

For the study of possible biochemical interactions between stroma and epithelium from human prostatic tissue, the availability of a method to separate the two tissue compartments is essential. Mechanical (15,16) and enzymatic (17,18) methods have been used for the separation of human prostatic epithelium and stroma. Generally, however, the yield was low and the cells obtained lacked viability. In our laboratory a method was developed for the isolation of human prostatic epithelial cells, which is based on squeezing of finely minced tissue and purification of the epithelium by a series of sedimentation steps at unit gravity (19). Although 95% of the cells excluded trypan blue and about 45% of the cells incorporated uridine, it has not yet been possible to maintain the cells in culture. As an alternative to separation of cells, selective cultivation of fibroblasts, which are assumed to represent the stroma and epithelium (20,21) have been used to obtain separated cell types. A possible disadvantage of these methods is that the cells obtained may not properly reflect the cells present in the original prostatic tissue sample.

MARKERS

The prostate is known to be rich in acid phosphatase and ornithine decarboxylase (22). Acid phosphatase is generally accepted to be a marker for prostatic epithelial cells (23-25) and its activity was found to be 25 times higher in epithelial cells than in the remaining stroma (19). Although the activity of prostatic acid phosphatase in the serum of patients with advanced prostatic carcinoma decreases after castration, the dependency of the enzyme activity on hormones has not yet been established unequivocally. Using the prostatic cell line MA 160, Ban et al. (26) showed that both androgens and oestrogens decreased acid phosphatase activity. There are, however, serious doubts whether this cell line is still to be considered as being prostatic (for review, see 27).

In 25% of patients with prostatic cancer and 8% of patients with benign prostatic hyperplasia elevated serum levels of spermidine have been detected (28). Because of the abundance of ornithine decarboxylase in the prostate, this enzyme, which catalyses the first step in polyamine biosynthesis, may be useful for the study of androgen dependency of prostatic tumours. Carcinoembryonic antigen secretion has also been used as a marker for prostatic epithelial cells in culture (29). In the same study, the polyamine concentration of the culture medium was found to be of no value as a marker for prostatic epithelial cells.