IX. Androgen-Binding Protein (ABP)

A. Introduction

A protein that binds androgenic steroids with high affinity is produced in the Sertoli cells of the testis, is secreted into the lumen of the seminiferous tubules, and transported to the epididymis (Hansson et al. 1975a; Means et al. 1976). This protein, known as ABP, has been found in the rat, rabbit, ram, goat, bull, and man. It has been purified from several species and characterized; recent reviews are available (Tindall and Means 1980; Bardin et al. 1981; Lobl 1981; Musto et al. 1982; DePhilip et al. 1982).

In the late sixties and early seventies, the thinking about steroid-binding proteins in reproductive tissues, as opposed to blood plasma, was dominated by the concept of steroid hormone receptors (King and Mainwaring 1974). Ritzen et al. (1971) demonstrated in the cytosol of the rat epididymis a specific protein with a high affinity for DHT which showed a single peak of 4S in sucrose gradient centrifugation and thus differed from the 3.5S and 8S receptor peaks present in prostate cytosol. Further characterization by Hansson (1972) gave a \( S_{20,w} \) of 4.6, a MW of approximately 90,000, and a \( K_a (4^\circ) \) for DHT of about \( 2 \times 10^8 \text{ M}^{-1} \) with limited capacity. It became clear that the binding protein is produced in the testis and secreted into the epididymis, suggesting the function of a local transport protein for testosterone from the testis to the epididymis. The properties, including stability and concentration, differed from those of the DHT receptors in the rat ventral prostate (Baulieu et al. 1971); a certain similarity with SBP was recognized.

French and Ritzen (1973a) examined the relationship of ABP in the 105,000 \( \times g \) supernatants of testis homogenates with that in the supernatants of epididymis homogenates. Blocking of the exocrine secretion of the testis by ligation of the efferent ducts resulted in increased ABP concentration in the testis, in proportion to the retention of testicular fluid, while at the same time ABP disappeared from epididymis supernatant. The authors concluded identity of the testicular and epididymal binding proteins. The ABP in efferent duct fluid of the rat testis was also found identical with that in the epididymis (French and Ritzen 1973b).

Identity of the testicular and epididymal rat ABP was also reported by Hansson et al. (1973a). Chromatographic behavior, sedimentation rate, mobility in PAGE, steroid binding specificity (DHT > T > \( E_2 > \) progesterone > estradiol-17\( \alpha \)) as well as pH- and heat-stability were indistinguishable.

In contrast, the intracellular DHT receptor in the epididymis of the adult rat had different properties, comparable to those of the rat ventral prostate receptor: both were destroyed by exposure to 50° for 30 min, treatment with p-chloromercuriphenyl sulfonate, and charcoal adsorption (Hansson et al. 1973b).
The androgen receptor of the rat testis (Hansson et al. 1974a; Smith et al. 1975) was also different from ABP and resembled the epididymal receptor. The androgen receptor in Sertoli cell-enriched rat testis could be separated from ABP by quantitative precipitation with 40% ammonium sulfate, whereas ABP precipitated at 50% and albumin between 60 and 80% (Tindall et al. 1977).

Tindall et al. (1975b) have investigated the relationship of the entry of ABP into the caput epididymidis and the development of a blood-testis barrier and formation of a continuous lumen from testis to epididymis. ABP is found in normal testis as early as 14 days postnatally before the blood-testis barrier is established. ABP is not detectable in the epididymis until 18–20 days of age at which time blood-testis barrier formation and lumen development are complete. ABP is also involved in the intratesticular transport of androgens providing protection from enzymatic attack (Purvis et al. 1977b).

Binding specificity and some physicochemical properties of ABP have a similarity with those of SBP (Vigersky et al. 1976b; Hsu and Troen 1978). This is one reason why most studies on ABP have been performed with the rat which does not contain SBP in measurable amounts so that a distortion of the results by the presence of SBP in a possible blood contamination is excluded.

B. ABP in the Rat

1. Synthesis and Regulation

The ABP concentration in the caput epididymidis increases from 1.2 pmol (bound DHT) per mg cytosol protein at 5 weeks of age to a maximal value of 6 pmol/mg at 8 weeks, and decreases to 2–3 pmol in adult rats of 16–32 weeks (Hansson et al. 1973c). The level of ABP in the cauda of the epididymis is much lower. Most of the ABP is destroyed during passage through the epididymis (French and Ritzén 1973a). Purvis and Hansson (1978) measured the segmental distribution of ABP in the epididymis (40 ng/g tissue in caput and 10 ng/g in cauda). There was a high correlation between ABP level and DHT concentration; ABP is the primary factor to determine the DHT level in the epididymis.

When the pure ABP became available later, it was possible to raise monospecific antibodies and use them in immunocytochemical techniques to investigate the localization of ABP in the reproductive tract (Pelliniemi et al. 1981). ABP was thus demonstrated in the apical portion of the epithelium in the seminiferous tubules, apparently in spermatids and/or Sertoli cells. The protein was also localized in granules in the apical cytoplasm of the principal epithelial cells of the proximal part of the caput epididymidis and in the epithelial cells of the ductuli efferentes. ABP was not contained in the distal part of the caput or in the corpus or cauda of the epididymis. Numerous coated vesicles were present in the supranuclear cytoplasm of the epididymal epithelium where ABP is taken up. The results indicate that ABP is absorbed from the lumen by epithelial cells of the ductuli efferentes and the proximal part of the caput epididymidis.

Feldman et al. (1981) by similar techniques localized ABP in the seminiferous tubules of the rat testis and in secretory granules of cultured Sertoli cells.