<Further Development 18_08>

Recombination of Mammary Gland Epithelium Reveals Sex-Based Differences in its Development

Recombination experiments with mouse mammary glands have revealed remarkable sex-related differences in development. In female mice, the mammary gland completes the first part of its development in the embryo. Like the human mammary gland, it completes the second part of its development in response to estrogenic hormones made at puberty. Final development, including ductal growth and the differentiation of the milk-producing cells on the branches and tips, is accomplished during pregnancy. In male mice, however, mammary development is literally nipped in the bud. Shortly after placode epidermis has ingressed, the mesenchyme cells condense around it. The mesenchymal cells appear to stretch the epithelial rudiment and separate the male mammary epithelium from the epidermis. The epithelial portion of the male mammary gland then dies.

The condensation of the mesenchyme around the stalk of the male mammary bud is due to testosterone. The addition of testosterone to female cultured mammary rudiments likewise arrested their development. Moreover, recombination experiments with mice lacking the testosterone receptor show that testosterone acts only on the mesenchyme cells, instructing them to destroy the male mammary rudiment (Figure 1; Kratochwil and Schwartz 1976; Dürnberger et al. 1978). In humans, however, the duct in males is not severed, and male mammary development follows the female pattern until puberty. At that time, increased estrogen levels permit expanded breast development in women, while male estrogens remain at prepubertal levels. If men are exposed to estrogenic compounds (such as some endocrine disruptors), their breasts will enlarge, a condition called gynecomastia. However, since males do not secrete prolactin, gynecomastic breasts do not usually produce milk.

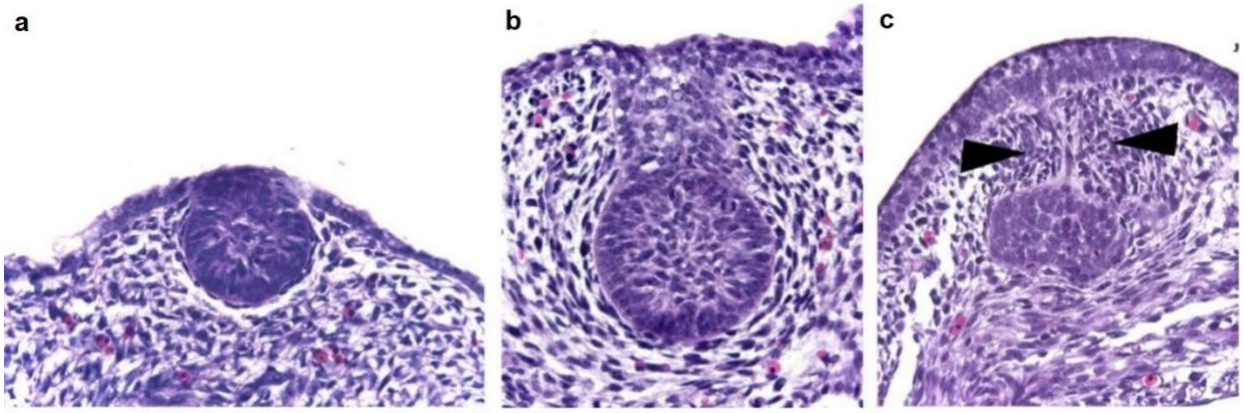

Figure 1 Embryonic mammary development. (a) Embryonic day (E)12.5. The epithelial cells have invaginated to form the initial bud, but the dense mammary mesenchyme has not yet formed. (b) Female bud at E14.5. The bud is fully formed. The epithelial cells are arrayed in a ball-on-stalk, or inverted bulb shape. The mesenchymal cells are arranged in four to five layers in a radial fashion around the epithelial cells. (c) Male bud at E14.5. Under the influence of testosterone, the mesenchymal cells condense around the stalk of the bud (arrowheads), constricting it until the connection with the surface epidermis is severed. After this occurs mammary mesenchyme cells and many epithelial cells undergo apoptosis.

Literature Cited

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