

Folliculo-stellate Cells of the Human Pituitary: A Type of Adult Stem Cell?

Eva Horvath, PhD
Kalman Kovacs, MD, PhD

Department of Laboratory Medicine and Pathobiology,
St. Michael's Hospital, University of Toronto,
Toronto, Canada

Ultrastructural and immunocytochemical observations of pituitary folliculo-stellate cells (FSC) in a large series of adenomatous and nontumorous human pituitaries led to the following conclusions: (1) The endocrine cells of both the nontumorous and the adenomatous pituitary are capable of transforming into FSC while changing from endocrine to nonendocrine phenotype. (2) As shown on consecutive sections in prolactin cell adenomas with FSC-rich areas including microcyst formation, S-100 protein and glial fibrillary acidic protein (GFAP) immunoreactivities are strongest in the smallest newly formed follicles. The 2 immunoreactivities do not overlap. The epithelium of older microcysts is immunonegative, implying that expression of the 2 markers is restricted to the early phase of FSC formation. (3) Transformation of endocrine cells into FSC may signify retrodifferentiation into their Rathke's pouch derived precursors as suggested by occasional presence of ciliated and/or mucin producing cells in the lining of microcysts. (4) In lymphocytic hypophysitis a marked activation as well as increase of number and size of FSC are evident in areas of ongoing immune destruction supporting their immune role. (5) Considering the multifaceted nature of FSC, it is suggested that they represent a type of pluripotent adult stem cell.

Keywords adenohypophysis, folliculo-stellate cells, immunocytochemistry, pituitary adenoma, ultrastructure

The folliculo-stellate cells (FSC) of the pituitary were first described at the dawn of electron microscopy by Farquhar [1]. Since then many aspects of FSC have been investigated, yet the deceptively simple cells have eluded precise definition so far. This article provides a short account of the morphologic aspects of FSC in the nontumorous and adenomatous human pituitary. The data presented herein are based on our extensive experience over the last 30 years, gained in the course of routine ultrastructural examination of more than 8,500 pituitary biopsies [2-4]. The overwhelming majority of these represented adenomas, but nontumorous adenohypophysial tissue was present in at least 1,500 biopsies.

The usually central follicle is an essential part of every acinus in the human pituitary. They consist of FSC [5-7] joined at their apical surfaces by terminal bars, which may be incomplete. They extend slender processes among the hormone-producing cells. Desmosomal attachments are present along their lateral cell borders and between FSC and glandular cells as well. If they have no content, the human follicles may be inconspicuous. The nuclei of FSC vary in shape determined by the spaces left for them by the much larger glandular cells. The small cytoplasm contains scanty RER, small Golgi complex, and few mitochondria. Lysosomal bodies, vimentin-type filaments, and, rarely, glycogen particles may be present. In 1974 [8] we reported that necrosis of hormone-producing cells initiated by rupture of plasmalemma triggers transformation of adjacent glandular cells into FSC. Presumably, the first step of the process is the formation of junctional complexes (terminal bars) between the affected cell(s) and the adjacent glandular cells or already existing FSC, accompanied or followed by rapid reorganization of cytoplasm from endocrine to nonendocrine phenotype (Figure 1). Fully granular FSC are encountered only occasionally (Figure 2). In the early phase of transformation secretory granules may still be detectable and accumulation of lysosomes may occur as well. The cell debris, at first containing

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Address correspondence to Eva Horvath, PhD, Associate Professor of Pathology, St. Michael's Hospital, Department of Pathology, 30 Bond Street, Toronto, Ontario M5B 1W8, Canada

