

This Week's Citation Classic

Pasteels J L. Recherches morphologiques et expérimentales sur la sécrétion de prolactine. *Arch. Biol.* 74:439-553, 1963.
[Labs. Histologie et Microscopie Électronique, Faculté de Médecine, Université Libre de Bruxelles, Belgium]

The paper demonstrates autonomous production of prolactin by rat pituitaries in tissue culture, and the existence of a hypothalamic prolactin-inhibiting factor. Similar experiments, performed on human hypophyses, were proof of the existence of a separate human prolactin, distinct from growth hormone, because addition of hypothalamic extracts to the cultures inhibited prolactin release along with stimulation of growth hormone secretion. [The SCI® indicates that this paper has been cited in over 170 publications since 1963, making it the 2nd most-cited paper ever published in this journal.]

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"I was already doing research as a student in medicine in Herlant's laboratory, when I read the elegant work of Guillemin and Rosenberg,¹

who demonstrated that the addition of hypothalamic fractions to tissue cultures of the anterior hypophysis restored their corticotropin production. For more than one year, I dreamed of performing similar experiments on prolactin. From what was known from experiments on pituitary grafts, it could be expected that the cultures would secrete prolactin autonomously, and that evidence of an inhibitory neuroendocrine control could be obtained by addition of hypothalamic extracts.

"At the end of my studies, I had the opportunity to work several months with Guillemin, when he was in the laboratory of Courrier, at the Collège de France. Guillemin was not doing tissue culture at that time, and I got somewhat involved in his LRF program. This further delayed my work on prolactin, but Guillemin, when I candidly told him in-

tentions, gave me good advice on the preparation of hypothalamic extracts.

"Back in Brussels, I benefited from the hospitality of Mulnard in his tissue culture unit, and I got the expected results on rat pituitaries in a few weeks. I then found that). Meites² and C.S. Nicoll,³

in the US, were also studying prolactin production by rat pituitaries *in vitro*. Working alone with small means, I was in no position to compete with such brilliant people. Thus, I left them to perform the obvious experimentation that could be done on prolactin physiology, and I made use of the only asset that they did not share with me, i.e., proximity of a university hospital and therefore access to human material.

"At that time, it was generally believed that there was no human prolactin, because prolactin could not be extracted from human pituitaries, and because human growth hormone (HGH) had prolactin-like activities. Working with H. and J. Brauman, who devised some precursor immunoassay of HGH, I could demonstrate that prolactin and HGH were distinct molecules, because they were submitted to reverse hypothalamic control.⁴

"Because it was a thesis, my paper had to be published as a whole and in French. Much later, as vice-dean and as dean of the University of Brussels School of Medicine, I took personal care in changing that rule. It was a long time before my work was confirmed. It was finally reported by F. Greenwood, using his well-known radioimmunoassay system. Greenwood handsomely acknowledged my paper,^{5,6}

and this came in good time, when human prolactin was finally purified (1971)⁷

"Another reason why my thesis is frequently mentioned is the discovery, by E. Flückiger, of bromocryptine, a dopamine agonist now widely used in medicine to inhibit prolactin secretion.⁸

When starting his work in this field, Flückiger gambled a lot of his career on the existence of human prolactin. He once told me that he did so because he read my thesis and was convinced. That was my best reward."

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