

This Week's Citation Classic

Sinha Y N, Selby F W, Lewis U J & VanderLaan W P. A homologous radioimmunoassay for human prolactin. *J. Clin. Endocrinol. Metab.* 36:509-16, 1973.
[Division of Endocrinology, Scripps Clinic and Research Foundation, La Jolla, CA]

This paper described a radioimmunoassay for prolactin that was specific and sensitive enough to measure the hormone in human blood. The reagents for this assay were produced in quantities sufficient to meet the demand for distribution to investigators worldwide. The work contributed to the explosion of scientific publication on the physiology of human prolactin that followed in the 1970s. [The *SCI*² indicates that this paper has been cited over 505 times since 1973.]

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April 16, 1982

"I had joined the laboratory of Willard P. VanderLaan as a postdoctoral fellow in the fall of 1969 to work on the problem of prolactin and breast cancer. Just a year before this, U.J. Lewis in the same laboratory had devised an electrophoretic technique for the purification of mouse prolactin.¹ In view of the variety of genetically distinct models of mammary tumors available in mice, this development presented an excellent opportunity to confirm or refute the theory held by many experimental endocrinologists of the time that hypersecretion of prolactin was somehow involved in the induction of breast cancer. My goal was to develop a radioimmunoassay for mouse prolactin sensitive enough to detect it in mouse blood and then to seek a correlation between plasma levels of this hormone and the incidence of the disease. It took almost two years to develop a radioimmunoassay for mouse prolactin, but the experience gained made it possible to devise rapidly a radioimmunoassay for human prolactin once a small quantity of the human hormone was isolated.

"Our isolation of human prolactin was made possible by an extremely rare happen-

ing. Prolactin was originally discovered in animals over 50 years ago² and since then has been found to exist in a variety of species but, strangely enough, not in primates. The prevailing dogma was that in human beings growth hormone substituted for the lactogenic actions of prolactin. Not satisfied with this explanation, we and others had been examining human pituitary glands electrophoretically for some time with the objective of identifying the component that represented prolactin. Electrophoresis had proved successful in identifying mouse prolactin, but the process did not seem to work for human prolactin. Even fresh pituitary tissue obtained at surgery failed to show a distinct prolactin band. Only when we obtained a gland from a pregnant woman who had died accidentally did we find a new, previously unseen band that we identified as prolactin.³ That was the first and only time we had the opportunity to examine such a gland. However, once we learned about the electrophoretic characteristics of the protein from this experiment, we looked for the hormone in normal glands and found small amounts of it in a specific fraction.

"We injected bits of this material into two rabbits; one rabbit did not respond, but the other produced antiprolactin serum of a high titer. With this, we were able to develop a radioimmunoassay sensitive enough to detect prolactin in human plasma within a matter of a few weeks. This was a beautiful example of a quick and fruitful application to clinical medicine of experience gained in animal models.

"We shared the reagents developed by us with clinicians and investigators all over the world under the aegis of the Hormone Distribution Program of the National Institutes of Health. I believe this fact plus the fact that this paper described the details of the methodology may have contributed toward it becoming a *Citation Classic*. A review of work in this field has recently been published."⁴

1. Cheever E F, Seavey B K & Lewis U J. Prolactin of normal and dwarf mice. *Endocrinology* 85:698-703, 1969.
2. Stricker P & Grueter R. Action du lobe antérieur de l'hypophyse sur la montée laiteuse. *C. R. Soc. Biol.* 99:1978-80, 1928.
3. Lewis U J, Singh R N P, Sinha Y N & VanderLaan W P. Electrophoretic evidence for human prolactin. *J. Clin. Endocrinol. Metab.* 33:153-6, 1971.
4. Jaffe R B, ed. *Prolactin*. New York: Elsevier/North-Holland, 1981. 288 p.