

# This Week's Citation Classic

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**Braunstein G D, Vaitukaitis J L, Carbone P P & Ross G T.** Ectopic production of human chorionic gonadotrophin by neoplasms. *Ann. Intern. Med.* 78:39-45, 1973.  
[Reproduction Research Branch, Natl. Inst. Child Health and Human Development, and Clinical Oncology Area, Natl. Cancer Inst., Natl. Insts. Health, Bethesda, MD]

Using a sensitive and specific radioimmunoassay to measure serum concentrations of human chorionic gonadotrophin (hCG), 59 percent of patients with testicular tumors and over seven percent of patients with a wide variety of non-testicular cancers were found to have immunoreactive hCG in their sera. [The *SCI*<sup>®</sup> indicates that this paper has been cited in over 330 publications since 1973.]

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"In 1970, I had the good fortune of joining Griff Ross in his laboratory at the National Institutes of Health. Griff had received highly purified preparations of human chorionic gonadotrophin (hCG) and its alpha and beta subunits prepared by Robert Canfield at Columbia University College of Physicians & Surgeons. Griff and Judy Vaitukaitis immunized a number of rabbits with these materials in order to develop antisera that would be useful in defining the immunologic characteristics of hCG and the other glycoprotein hormones. It was known that the intact hCG molecule shared some structural characteristics with human thyroid stimulating hormone, follicle stimulating hormone, and especially luteinizing hormone (hLH). Indeed, the biologic and immunologic activity of native hCG and hLH were so similar that only elaborate chromatographic or electrophoretic methods were capable of separating these two hormones.

"Griff had predicted that antibodies generated against the purified subunits of hCG might have a greater affinity for intact hCG than hLH, and therefore would allow the development of a radioimmunoassay that could be used to distinguish serum levels of hCG from circulating hLH. His prediction

was proved correct when we found that the antibodies raised against the beta subunit of hCG had relatively little cross-reactivity with hLH. We immediately recognized the potential clinical application of a radioimmunoassay using these antibodies for diagnosis of early pregnancy and for monitoring the therapy of gestational trophoblastic disease. Our paper describing this radioimmunoassay (beta hCG RIA) has recently been featured as a *Citation Classic*.<sup>1,2</sup>

"In initiating our clinical studies of hCG measurements with this assay, we found that we had numerous blood samples from women with gestational trophoblastic disease, but relatively few samples from men with trophoblastic testicular tumors. We learned that Paul Carbone of the National Cancer Institute had established a tumor serum bank which contained blood samples obtained from patients with testicular tumors. The serum bank contained hundreds of samples from patients with a wide variety of malignancies as well as some samples from patients with non-neoplastic disorders. We measured the immunoreactive hCG in the sera from 918 patients with cancer and 443 control patients and found that 59 percent of the patients with testicular tumors and 7.2 percent of the patients with non-trophoblastic neoplasms had immunoreactive hCG in their circulation while only 0.7 percent of the control patients had detectable hCG. Patients with carcinomas of the stomach, liver, pancreas, and breast, and with myeloma and melanoma had the highest frequency of positive responses. This was a higher frequency of hCG production by non-trophoblastic cancers than had been previously recognized.

"I feel that this study became a *Citation Classic* because it was one of the first systematic investigations of ectopic production of a hormone by tumors. The unexpectedly high frequency of hCG production by non-trophoblastic cancers stimulated a number of laboratories to study the ectopic production of hCG and other hormones by tumors.<sup>3</sup> Furthermore, our study suggested that hormones may be useful as objective markers for the diagnosis of cancer and for monitoring the effects of therapy."

1. Vaitukaitis J L, Braunstein G D & Ross G T. A radioimmunoassay which specifically measures human chorionic gonadotropin in the presence of human luteinizing hormone. *Amer. J. Obstet. Gynecol.* 113:751-8, 1972.
2. Vaitukaitis J L. Citation Classic. Commentary on *Amer. J. Obstet. Gynecol.* 113:751-8, 1972. *Current Contents/Clinical Practice* 11(10):24, 7 March 1983.
3. Braunstein G D. hCG expression in trophoblastic and non-trophoblastic tumors. (Fishman W H, ed.) *Oncodevelopmental markers: biologic, diabetic and monitoring aspects, volume II.* New York: Academic Press. In press, 1983.