This review discusses the use of placental proteins and their subunits as markers to help monitor the response of certain tumors to therapy. [The SC® indicates that this paper has been cited in over 215 publications.]

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The work began in 1962 when Frank Fusco, then a resident at the Washington, DC, Veterans Administration Hospital (VAH) and now a pulmonologist in Vienna, Virginia, diagnosed lung carcinoma in a chronic smoker with gynecomastia and referred him to the Clinical Center for endocrine studies. During the following two years, Fusco referred three additional cases of lung carcinoma to us, and beginning with that first patient, we began gathering evidence that these carcinomas produced ectopic gonadotropin.1

Soon after, Bruce Weintraub came to my laboratory as a clinical associate: he is now a branch chief of the Division of Oncology at New York University and chief of the Chemotherapy Service at the Finsen Institutet in Copenhagen, who furnished sera from their extensive lung-cancer population.

Meanwhile, back at the NIH, Judith Vaitukaitis, then in the National Institute of Child Health and Human Development (NICHHD) and now chief of endocrinology at Boston University, had developed a novel radioimmunoassay that discriminated between chorionic gonadotropin (CG) and luteinizing hormone and allowed the easy assay of multiple sera. She, Glenn Braunstein, and their colleagues in NICHHD assayed more than 1,000 cancer sera and found evidence in 12 percent for the ectopic production of CG. The subunit nature of CG was then being recognized, and Weintraub and I found cases of unbalanced and even isolated production of one or the other CG subunit. Moreover, Alan Rabson, then senior investigator at the NCI and now director of its Division of Cancer Biology, succeeded in establishing a cell line in vitro that mirrored the unbalanced ectopic production of CG and its subunits in the patient from which it was derived. [To commemorate this blessed event, Weintraub and I gave Rabson a poster showing the long-distance capture of a fly by a frog with an enormous tongue. The caption read: "When you're hot, you're hot!"]

In California, Jerome Hirshman, then and now chief of endocrinology at the Wadsworth VAH, had been studying what appeared to be placental thyrotropins (but that we now realize were probably will-o'-the-wisps related to thyrotropic activity inherent in massive amounts of CG). The time seemed ripe for pulling together this disparate material, and the Combined Clinical Staff Conference of the NIH Clinical Center, an institution still going strong, seemed a nice locus.

I suspect the review has been highly cited because it summarizes in one place the work with a new group of proteins perceived as potentially useful tumor markers. CG is still widely used to monitor non-germ-cell testis cancers, and PAP is beginning to be used in testicular germ-cell cancers; the other placental proteins, however, have been disappointing as tumor markers. Nonetheless, the questions of why the placenta produces them and what is the mechanism of their biosynthesis and regulation are still much studied.

