Shiu R P C, Kelly P A & Friesen H G. Radioreceptor assay for prolactin and other lactogenic hormones. *Science* 180:968-71, 1973.
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This paper described the development of a sensitive radioreceptor assay for the measurement of biologically active prolactin and other lactogenic hormones. This assay was applied to identify and quantitate two novel placental lactogens in the pregnant rat. [The *SCI*® indicates that this paper has been cited in over 455 publications.]

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The reported work represented part of my PhD thesis project that began in the fall of 1971 when, in Henry G. Friesen's laboratory at McGill University, Peter Hwang had managed to purify human prolactin and to establish a radioimmunoassay for this hormone. It appeared advantageous to develop an alternative assay to measure the biological activity of human prolactin, since the commonly used bioassays at the time (that is, the pigeon crop sac and the mouse mammary gland organ culture assays) were laborious, expensive, and technically difficult to perform. At the time Friesen was also interested in the possible role of prolactin in human breast cancer, and we therefore chose to initiate our study using breast tumor biopsy specimens. This was our first mistake because we had no idea as to the experimental conditions under which we could detect prolactin binding. Also, it was difficult to obtain enough tumor tissues to work with. Thus, I spent most of my time during the first three months sitting in the Pathology Department, waiting for human breast tumor tissues. Only on one occasion did I manage to detect specific binding of ^{125}I-labeled prolactin. I quickly realized that I would never get my PhD if all I did was to wait for the arrival of human tumors.

It occurred to us that an animal model would be a more suitable approach to the problem. A number of groups were studying prolactin action using mouse mammary organ cultures, and we reasoned that mouse mammary gland explants must possess prolactin receptors because of their responsiveness to prolactin. This decision was our second mistake because we possessed neither the facilities nor the expertise in tissue culture. I began fumbling with organ cultures using a rudimentary facility in another building. As a result, I ended up culturing fungi and bacteria more often than mouse mammary explants. Several months went by without too much success. One afternoon during Friesen's famous "What's new?" daily visit to the laboratory, he recalled some of his experiments carried out in Edwin Astwood's laboratory in Boston, in which he could readily demonstrate prolactin induction of milk production in pseudopregnant rabbits. Since large amounts of mammary tissues can be obtained from a rabbit, this tissue might be a good source of prolactin receptors. The decision to use the rabbit mammary gland was the turning point of my study, and the rest is history.

I quickly optimized the conditions for the detection of prolactin binding, characterized biochemically the interaction between prolactin and its receptor, and developed the radioreceptor assay for prolactin capable of detecting low levels of prolactin and other known lactogenic hormones (human placental lactogen [PL] and human growth hormone). We at once realized that this assay was potentially useful to detect and quantitate novel prolactinlike hormones. Astwood and R. Greep in 1938, and later S.C. Averill and colleagues in 1950 and D.L. Matthies in 1967, had described the existence of a prolactinlike hormone produced by the rat placenta. Together with Paul A. Kelly, who was a postdoctoral fellow at the time, we decided to find out whether or not my radioreceptor assay could detect the rat placental hormone. Several pregnant rats were ordered, and very quickly we were able to measure and quantitate the circulating levels of two placental hormones (now called rat PL I and II) during pregnancy in the rat. The development of the radioreceptor assay and its application to measure rat PLs were published in *Science*.

I think this paper is cited frequently for several reasons. First, this assay quickly led to the identification and purification of PLs from a number of species[1,2] and eventually to the cloning of PL and PL-like genes.[3] Second, the techniques described in this paper have been used by many investigators to study prolactin binding in a large number of organs from a variety of species (including human breast cancer!). For example, together with Barry I. Posner, we made a survey of prolactin receptors in tissues from birds to monkeys.[4] Third, the work described in the *Science* paper established the basic techniques necessary for the subsequent purification of the prolactin receptor molecules and the generation of antireceptor antibodies.[5,6] These early studies have also influenced my current research interest in studying the molecular biology of prolactin action.

1. **Robertson M C & Friesen H G.** The purification and characterization of rat placental lactogen. *Endocrinology* 97:621-9, 1975. (Cited 45 times.)
2. **Colosi P, Marr G, Lopez J, Haro H, Ogren L & Talamantes F.** Isolation, purification, and characterization of mouse placental lactogen. *Proc. Nat. Acad. Sci. USA* 79:771-5, 1982. (Cited 30 times.)
3. **Duckworth M L, Kirk K L & Friesen H G.** Isolation and identification of a cDNA clone of rat placental lactogen II. *J. Biol. Chem.* 261:10871-8, 1986. (Cited 10 times.)
4. **Posner B I, Kelly P A, Shiu R P C & Friesen H G.** Studies of insulin, growth hormone and prolactin binding: tissue distribution, species variation and characterization. *Endocrinology* 95:521-31, 1974. (Cited 480 times.)
5. **Shiu R P C & Friesen H G.** Solubilization and purification of a prolactin receptor from the rabbit mammary gland. *J. Biol. Chem.* 249:7902-11, 1974. (Cited 230 times.)
6. **Katoh M, Djiane J & Kelly P A.** Monoclonal antibodies against rabbit mammary prolactin receptors. *J. Biol. Chem.* 260:11422-9, 1985. (Cited 10 times.)

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