Rosalyn Sussman Yalow (1921–2011)

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Rosalyn S. Yalow, a member of the National Academy of Sciences and the second woman to win a Nobel Prize in Physiology or Medicine, died on May 30, 2011, at the age of 89, having suffered recurrent strokes and a prolonged period of decline. She was awarded the Nobel Prize in 1977 for creation of the radioimmunoassay (RIA), a discovery that revolutionized almost every field of medicine by providing precise and specific measurements of the concentration of peptide hormones and many other biologically relevant substances in blood and other body fluids (1) (Fig. 1).

Born and raised in New York City's borough of the Bronx, she was a top graduate of Hunter College, the legendary all-female, tuition-free sister school to City College of New York (an excellent biography is in ref. 2). Her mother hoped that she would become a teacher, but Yalow was determined to have a career in physics. Despite her outstanding record in physics and other studies and despite the World War II shortage of male applicants, no graduate programs in physics to which she applied granted her admission, at least in part because she was female and Jewish. Finally, as a favor to one of her Hunter College professors, the University of Illinois at Urbana–Champaign accepted her (their first female) into the PhD program in nuclear physics with the condition that they bear no responsibility for placing her in a job after graduation.

An outstanding student who finished her doctorate in 4 years, Yalow again encountered closed doors. Eventually, she was hired for 1 year as an assistant engineer at a Federal Telecommunications Laboratory. For another year, she worked as a teacher at Hunter College. In 1947, she accepted an offer to become head of a newly formed Radioisotope Unit at the Bronx Veterans Administration Hospital and a researcher in that field, pursuits that occupied her for the rest of her professional life. Here, she was tasked with finding new uses for radioisotopes in medicine. Recognizing the sparseness of her training in biology, Yalow decided to hire a physician. In what turned out to be one of the most important decisions of her life, Yalow selected Solomon Berson, an internist with no research training. However, even after a short conversation, Yalow concluded that he was "the most brilliant person she had ever met" (3). Over the next several decades, this creative and driven pair solved one of the greatest challenges of the time: how to measure accurately the tiny amounts of hormones and other biologically relevant substances found in the blood and other body fluids.

Fig. 2. Rosalyn Yalow at a Veterans Administration Center meeting in California in December of 1978. Photo courtesy of William A. Bauman and Ben Yalow.

As with many discoveries, their key insight came while doing an experiment to test another hypothesis, namely that diabetes might be caused by overly rapid degradation of insulin in the blood. What Yalow and Berson found, however, was that, when radioactive insulin was injected into an insulin-taking diabetic patient, it disappeared more slowly, not more rapidly, than in patients never treated with insulin. They showed that the retarded disappearance of insulin in the insulin-treated patients was because of reversible sequestration by insulin-binding antibodies, which slowed the clearance of the hormone (4). This work was rejected initially by *The Journal of Clinical*

Fig. 1. Rosalyn Yalow with King Carl XVI Gustaf of Sweden at dinner on the occasion of her Nobel Prize in Physiology or Medicine on December 10, 1977. Photo courtesy of William A. Bauman and Ben Yalow.

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Investigation, because the reviewers were skeptical that humans make antibodies to small molecules like insulin. For years after winning the Nobel Prize, Yalow proudly showed this rejection letter in her public presentations.

Within a few years after that seminal paper, Yalow and Berson, using antiinsulin antibodies, created a sensitive and quantitative assay for insulin. A series of tubes were prepared that contained fixed amounts of antibody and radiolabeled insulin and increasing known amounts of unlabeled insulin; the unlabeled insulin progressively competed with the labeled insulin for antibody binding. By measuring how much of the labeled insulin was antibody-bound vs. free in solution, one could calculate the exact concentration of insulin in the sample being tested. The paper describing the insulin RIA, published in 1960, became a highly cited paper and was used widely to create new RIAs for other molecules (5). Over the next decade, their group developed RIAs for growth hormone, adrenocorticotropic hormone, parathyroid hormone, and gastrin. In each case, these new assays led to important new insights into the role of these hormones in normal physiology and how the role was altered in disease states.

Berson and Yalow were extraordinarily generous with their new discoveries. They not only chose not to patent the technique, but visiting scientists from all around the world were welcomed to learn about the technique and often left bearing gifts of one of their precious antibodies. When Berson died suddenly in 1972 at the age of 53, Yalow was devastated but carried the work forward, naming the laboratory in Berson's honor and continuing to publish important papers in several new areas of research. In 1977, she was awarded a Nobel Prize in Physiology or Medicine, and in her acceptance speech, she praised the partnership with Berson that led to this award (1).

At a personal level, Yalow had extraordinary drive and a legendary capacity for work. Despite her commitment to her research, she strove to balance her career with family. She would frequently run home to prepare meals for her husband Aaron and their two children, Ben and Elanna, before returning to the laboratory. She shunned feminist organizations but was a forceful advocate for equal opportunities in science, and she was known to encourage high school girls to pursue scientific careers. Ultimately, she was a pioneering scientist and great intellect who without formal training in biology, helped unravel many mysteries of physiology and medicine.

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