ROSALYN YALOW

NOBEL PRIZE in Physiology or Medicine 1977 "for the development of radioimmunoassays of peptide hormones"

L. Rothenberg

Dept of Medical Physics. Memorial Sloan Kettering Cancer Center 1275 YORK AVE, NEW YORK, NY 10065 UNITED STATES

I. Introduction



Rosalyn Yalow was born on July 19, 1921, and grew up in and lived almost her entire life in New York City, except for 3 and ½ years when she was a graduate student at the University of Illinois. Her mother, Clara Zipper came to the U. S. from Germany at the age of four and her father, Simon Sussman, was born on the Lower East Side of New York, a Melting Pot for immigrants from Eastern Europe. The fact that her parents came from humble backgrounds did not stop Rosalyn and her brother, Alexander, from striving for something greater. Rosalyn began to read before she began preschool. By 7th-grade Rosalyn was committed to mathematics, and then her chemistry teacher at Walton High School, a public secondary

school, aroused her interest in chemistry and science in general. When she went to Hunter College, the college for women in New York City's free college system, her interest was diverted to physics, and particularly to nuclear physics, which many considered the world's most exciting field in the late 1930's, because it seemed that every major experiment brought a Nobel Prize. Rosalyn was very excited to read the biography of Madame Marie Curie which had just been published by Eve Curie, Marie's daughter.

Rosalyn also remembered being greatly excited by having attended a lecture by Enrico Fermi in a packed lecture hall at Columbia University. Although her family thought that the best career for her would be as an elementary school teacher, she persisted in achieving a career in physics. Although she initially agreed to business school with the intent of becoming a stenographer, she was eventually offered a teaching assistantship at the University of Illinois in Champaign-Urbana. There, Rosalyn not only pursued her physics career, receiving a Ph. D. in nuclear physics under her thesis director, Maurice Goldhaber, who later became the Director of Brookhaven National Laboratories, but she also met her husband, Aaron Yalow. Eventually they both received their doctorates and settled in New York City, initially in Manhattan, but later in a house in the Riverdale section of the Bronx.

Rosalyn obtained a full-time teaching position at Hunter College but also volunteered in the laboratory of Dr. Edith Quimby at Columbia and was then introduced to the "The Chief "of medical physics at Columbia, Dr. Gino Failla. (Failla and Quimby had previously established the distinguished Department of Medical Physics at Memorial Hospital, now Memorial Sloan Kettering Cancer Center, which was to be Chaired by Dr. Yalow's fellow graduate student at Illinois, Dr. John Laughlin.)

Failla recommended and insisted that Dr. Bernard Roswit, Chief of Radiotherapy at the Bronx Veterans Administration Hospital, hire Rosalyn Yalow and that began her long career at the V. A. Hospital.

Upon transitioning from her teaching position at Hunter to a full-time role with the VA staff, Rosalyn embarked on a highly productive collaboration with Dr. Solomon Berson, who had recently completed his residency in internal medicine at the Bronx VA. Their collaborations continued from around 1950 until 1968, when Dr. Berson left their laboratory to assume the Chairmanship of the Department of Medicine at Mt. Sinai School of Medicine. Unfortunately, Dr. Berson suffered a premature death four years later. Because Dr. Yalow's work on Radioimmunoassay, described in detail below, was done with Dr. Berson, many assumed that she would never be awarded a Nobel Prize for their work – they were to be proven wrong in 1977. In addition to the Nobel Prize, Rosalyn Yalow also received many other prestigious awards: she was Distinguished Service Professor at Mt. Sinai School of Medicine, membership in the National Academy of Sciences, Albert Lasker Basic Medical Research Award, and many others.

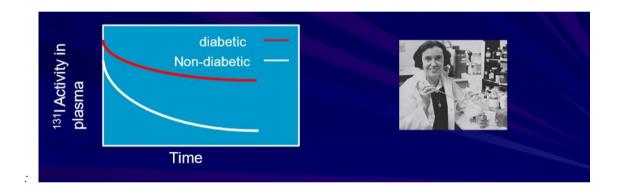
Rosalyn and Aaron Yalow had two children, Benjamin and Elanna, Benjamin became a systems programmer at the City University of New York and Elanna pursued a Doctoral degree in Educational Psychology at Stanford University. Aaron Yalow was a well-known medical physicist as well as a popular physics professor at Cooper Union university in New York City.

II. HER RESEARCH AND CONTRIBUTIONS

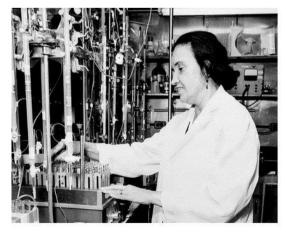
Radioimmunoassay: Fallout from a seemingly unrelated study

Dr. Arthur Mirsky had hypothesized that maturity-onset diabetes might not be due to a deficiency of insulin secretion but to abnormally rapid degradation of insulin by hepatic insulinase.

To test this hypothesis, Drs Berson and Yalow studied the metabolism of ¹³¹I-insulin in diabetic patients on insulin and in non-diabetic subjects. Their hypothesis was that the retarded rate of insulin disappearance was due to the binding of labelled insulin to antibodies, produced in response to the administration of exogenous insulin.

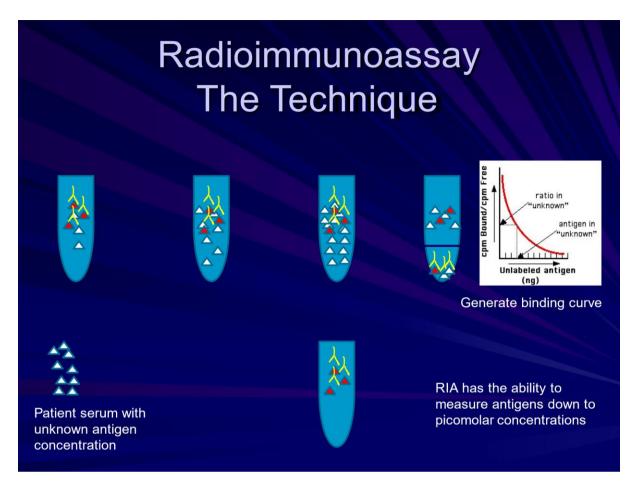


Using a variety of techniques, Berson and Yalow were able to demonstrate the ubiquitous presence of insulin binding antibodies in insulin treated diabetic subjects.





Yalow and Berson



This concept was so foreign to immunologists of the time that Dr. Yalow's paper was rejected by Science.

It was then sent to the Journal of Clinical Investigation where it was initially rejected there as well. The Journal editor Stanley Bradley said amongst other comments "The second major criticism relates to the dogmatic conclusions set forth which are not warranted by the data". Finally, the journal accepted this landmark study provided that the authors would remove the use of the word insulin antibody from both the paper title and the Conclusions.

The Legacy

The blood concentrations of many substances have been measured by radioimmunoassay including insulin, thyroxin, thyroid stimulating hormone, estrogens, testosterone, human chorionic gonadotropin, and gastrin.

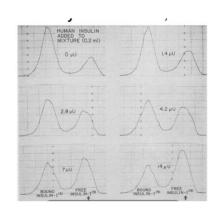
"The radioimmunoassay principle is not limited to immune systems. The specific antibody can be replaced by any specific binding protein in plasma, a specific enzyme or tissue receptor site."

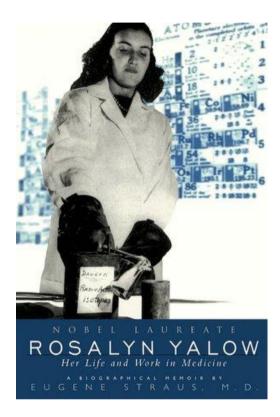
This is a truly universal vision and shows the importance and enormity of Berson and Yalow's discovery.

IMMUNOASSAY OF ENDOGENOUS PLASMA INSULIN IN MAN
By ROSALYN S. YALOW AND SOLOMON A. BERSON
(From the Radiciatops Service, Veteran Administration Haspital, New York, N. Y.)
(Salmitted for publication March 7, 1969; accepted March 22, 1969)

Eer years inventionable hour sought an agent

for insulin which would combine virtually absolute specificity with a high degree of sensitivity, sufficiently exquisite for measurement of the minute insulin concentrations usually present in the circulation. Methods in use recently depend on the ability of insulin to exert an effect on the metabolism of glucose in vivo or in excised muscle or adipose tissue. Thus, the insulin concentration in plasma has been estimated: a) from the degree of hypoglycenia produced in hypophysectomized, asternalectomized, altoran-diabetic rats by by isolated rat hemidisplaymag (2); or c) from the increased existing of glucose-1-C¹⁰ by the rat epidelymal fat pad (3). Since there have been reports indicating the presence, in plasma, of insulin action (4) and of non-insulin substances capable of inducing an insulinifice effect (5), these procedures, while yielding interesting information regarding the effects of various plasmas on glucose metabolism in tissues, are of doubtful specificity for the measurement of insulin per se (3).





III. PROMOTION OF WOMEN IN SCIENCE

Concerns about Discrimination of Women in Science:

Throughout her years of undergraduate and graduate education, Rosalyn Yalow always felt that she had to far exceed the efforts of her male fellow students in order to be recognized. Also, since obtaining funded positions in graduate education was extremely difficult at the time when she was a student, she never stopped campaigning for women in science. She herself was greatly inspired by the work of Marie Curie. At every opportunity Dr. Yalow pushed for greater opportunities and greater recognition for women in science, never having forgotten that, when she graduated from her undergraduate studies, it appeared that the only opportunities would be in either in elementary school teaching or stenographic work.

Rosalyn Yalow stands out as a model for all young women contemplating a career in scientific endeavor.

IV. Activities in Medical Physics Organizations

RAMPS:

The Radiological and Medical Physics Society of New York (RAMPS) was founded by a group of medical physicists in the New York City area. During the mid-1940's, physicists associated with medical institutions in the metropolitan New York City region commenced meetings to compare instrumentation and their measurements of the quantity of radioactivity in solutions in medical use. This was necessary for uniformity, and also for accuracy since the national standard available appeared to be inconsistent. This was just prior to the availability of megavoltage x rays and electrons, and the primary concern of the physicists was associated with the uses of radioactive nuclides. The clinical uses of iodine-131 and other radionuclides (phosphorus 32, yttrium-90, etc.) were being actively explored and agreement on the amount of activity being administered was essential. Such measurements led to the "New York Millicurie," which served a vital purpose. By 1948the meetings of these medical physicists were on a scheduled basis with elected officers and records. Those initially active in RAMPS included Mones Berman, Hanson Blatz, Carl Braestrup, Giacchino Failla, Sergei Feitelberg, Elizabeth Focht, Hiram Hart, Lillian Jacobson, Robert Loevinger, Leo Marinelli, Eleanor Oshry, Edith Quimby, Edward Siegel, Aaron Yalow, Rosalyn Yalow, and others. This group established the measurement procedure for the "New York Millicurie,' and their meetings served both scientific and professional functions. A constitution was written in 1954 by R. Yalow and J. Laughlin, and revised in 1957 by them. RAMPS has continued to grow from its modest beginning to its current membership of about 150 and conducts monthly meetings which are well attended. Their meetings usually include scientific presentations by a member or guest on physical aspects of treatment, diagnosis, nuclear medicine, or protection. Also, a symposium on a pertinent scientific topic is held annually. RAMPS welcomed the initiation of the AAPM and became a chapter in it.

When Rosalyn Yalow returned from Sweden in 1977 after receiving the Nobel Prize, she mesmerized the attendees at a RAMPS Meeting by describing many aspects of her trip to receive the award including meeting the Swedish Royal Family, considerations in choosing the appropriate formal fashion items for herself and Aaron, and a description of all of the events that took place in Stockholm.

AAPM:

The United State national organization of medical physics was established as the American Association of Physicists in Medicine (AAPM) in 1958. Both Rosalyn and Aaron Yalow were Charter Members.

V. LEGACY

Rosalyn Yalow died on May 30, 2011. She will always remain a hero to medical professionals in general for her outstanding work on radioimmunoassay and other scientific efforts, and to women in science for her tireless efforts to recognize the contributions of women and to ease the pathway for young women who wish to enter the many fields of scientific endeavor.



VI. FIGURES AND ILLUSTRATIONS

VII. REFERENCES

- 1. Yalow, RS, Berson, SA.(1960) Immunoassay of endogenous plasma insulin in man. J. Clin. Invest. 39:1157-1175.
- 2. Rothenberg, L, St. Germain, J, Marshall, C. (2011). Obituary-Rosalyn Sussman Yalow, 1921-2011. Med. Phys. 38: v-vi.

VIII. BIBLOGRAPHY

The Nobel Prize in Physiology or Medicine 1977, Rosalyn Yalow Autobiography, Novelprize.org
The Nobel Prize in Physiology or Medicine 1977, Rosalyn Yalow Banquet Speech, Nobelprize.org
J. L. Humm. Rosalyn Yalow: Contributions and Legacy. Presented at AAPM Annual Meeting, Charlotte, NC,
July 30, 2012 (Invited Speaker Handout 68-19777-236349-90003.pdf)
S. J. Goldsmith. Rosalyn S. Yalow, Ph.D., A Personal & Scientific Memoir, Presented at AAPM Annual Meeting,
Charlotte, NC, July 30, 2012. (Invited Speaker Handout 68-19762-236349-90004.pdf)

APPENDIX

Author Information



Lawrence N. Rothenberg, Ph.D. is Attending Physicist Emeritus in the Department of Medical Physics at Memorial Sloan Kettering Cancer where he is Director of the Medical Imaging Physics residency program. His main areas of interest in diagnostic radiology have included mammography, computed tomography, and education of radiology residents, medical physics students, and technologists. He is Past President of AAPM, Quimby Lifetime Achievement Awardee, Fellow of AAPM, ACR, ACMP, and HPS, and Distinguished Emeritus Member of NCRP.

Contacts of the corresponding author:

Author: Lawrence N. Rothenberg, Ph.D.

Institute: Department of Medical Physics, Memorial Sloan Kettering

Cancer Center Street: 1275 York Ave City: New York, NY

Country: USA

Email: rothenbl@mskcc.org