Radium, Telomeres, and Ribosomes: Glass Ceilings Break in Stockholm

Marie Curie (1867–1934), Prix Nobel 1903, 1911. Image courtesy National Library of Medicine, NIH.

Carol Greider, (1961–), Prix Nobel 2009. Image courtesy Johns Hopkins University.

Elizabeth Blackburn (1948–), Prix Nobel 2009. Image courtesy University of California, San Francisco.

All my colleagues have told me that it is preferable you not come here on December 10. I therefore beg you to remain in France [and] hope that you will telegraph the Secretary of the Academy or even me that it is impossible to come.

Svante Arrhenius to Marie Curie, 1911 (1)

Summers offered three possible explanations, in declining order of importance, for the small number of women in high-level positions in science and engineering. The first was the reluctance or inability of women who have children to work 80-hour weeks. Summers [also] said that women do not have the same "innate ability" or "natural ability" as men in some fields.

The Boston Globe, January 2005 (2)

That was the case two weeks ago, when Greider was up, as usual, before 5. With time to spare before going to spin class, she was folding laundry [when] the call came. Several days later, when she heard that President Obama had won the Nobel Peace Prize, she thought to herself: "I bet he wasn't folding laundry."

The Washington Post, October 2009 (3)

Interviewer: *I just wanted to ask you [why] telomerase and telomere research is a field which has, happily, a large number of women working in it?*
Elizabeth Blackburn: I'll turn your comment around and say it's fairly close to the biological ratio of men and women. It's all the other fields that are aberrant.

Nobel Interview, October 2009 (4)

THE STIMULUS OF FAME

Last month in Stockholm, aberrancy ran into equality. Three of the six new Nobel laureates in fields related to experimental biology were women: Elizabeth Blackburn of the University of California San Francisco and Carol Greider of Johns Hopkins University in physiology or medicine and Ada E. Yonath of the Weizmann Institute of Science in chemistry. Adding the female laureates in literature and the Nobel Memorial Prize in Economics, the Nobel committee was proud to note that five of the 13 new laureates were women, the largest number ever to mount the podium in Stockholm. Blackburn and Greider have the distinction of breaking another glass ceiling: It

0892-6638/10/0024-0001 © FASEB

was the first time that any Nobel Prize in the sciences has been awarded to more than one woman (5).

The awards were no surprise; Blackburn, Greider, and Jack Szostak, their fellow laureate, had received honors galore. In 1982, Blackburn and Szostak had shown that telomere DNA from Tetrahymena could protect chromosome shortening in yeast (6), and on Christmas Day of 1984, Greider got the first inkling of telomerase, a reverse transcriptase that adds DNA to telomeres by means of an RNA template (7). Telomerase solved the "end replication problem" by explaining how DNA could be added to one of the two strands of DNA as the polymerase comes to the ends of chromosomes during cell division (8).

Ada Yonath became only the fourth woman ever to have won the Nobel Prize in chemistry for her X-ray diffraction solution of ribosomal structure. She describes the results succinctly: *"The ribosome is a machine that gets instructions from the genetic code and operates chemically in order to produce the product. . . . The product is a protein and if you think about the kangaroo in a pocket, the product goes first into a pocket which is actually in the ribosomal tunnel."* (9) The marsupial analogy is correct and resulted from Yonath's application to crystals of bacterial ribosomes of the Bragg equation, $n\lambda = 2d\sin\theta$ (William and Lawrence Bragg, father and son, Prix Nobel, 1915). Protein crystallization is as much art as science, and crystallizing large molecules is the greatest art of all. It took 20 years, and once the art was accomplished, new science could begin. Sure enough, it turns out that the 3-D structure permitted Yonath and her colleagues to determine that many potent antibiotics work by preventing newborn proteins from leaving the kangaroo's pouch, the ribosomal tunnel (10).

Yonath describes her admiration for Dorothy Crowfoot Hodgkin, also a crystallographer. Hodgkin, a mentor for other female crystallographers, such as Rosalind Franklin, was the third woman to win a Nobel Prize in chemistry (1964). She had worked out the 3-D structure of penicillin and vitamin B_{12}. *"There was Marie Curie (1911) and her daughter (Irene Joliot-Curie, 1935)* and *. . . Dorothy Hodgkin and now it's me,"* said Yonath (9). It's been a long time coming.

For centuries before Lawrence Summers' gaffe, women were considered intellectually inferior to men, especially in the "hard" sciences. Summers and his ilk had failed to ask a question posed by Wendell Philips in 1851 at the Second National Woman's Rights Convention in Worcester:

> *When woman has enjoyed for as many centuries as we have the aid of books, the discipline of life, and the stimulus of fame, it will be time to begin the discussion of these questions: 'What is the intellect of woman?' 'Is it equal to that of man?'* (11)

In 2010, the answer is to be found in every lab, on every lecture podium, and on every editorial masthead; equality is beating out aberrancy (Elizabeth Blackburn's term). The "stimulus of fame" has played no small part; Irene Joliot-Curie might testify to that. Indeed, the worldwide enthusiasm with which the 2009 awards have been greeted should assure us that many more Elizabeths, Carols, Adas, and Irenes will mount the podium in Stockholm.

IT IS NOT GOOD THAT MAN SHOULD BE ALONE

It wasn't all open arms and worldwide celebration each time Marie Curie learned that she had been awarded a Nobel Prize. Her first (physics, 1903) had been with husband Pierre and with Henri Becquerel. In fact, her name had been added almost as an afterthought only after Pierre had intervened with the committee, writing that her inclusion would be *"plus joli d'un point de vue artistique"* (more attractive from an esthetic point of view). The condescending note continued to the prize ceremony itself, when on December 10, 1903, Dr. H. R. Törnebladh, president of the Royal Swedish Academy of Sciences, quoted Genesis:

> *The great success of Professor and Madame Curie is the best illustration of the old proverb, coninucta valent, in union here is strength. This makes us look at God's word in an entirely new light: 'It is not good that the man should be alone; I will make him an helpmeet for him.'*

The helpmeet motif was the tune of the day, as newspaper and magazine images of the two winners always depicted the figure of a passive, seated lady receiving a dangerous object from an erect French male (see *Le Petit Parisien* below).

By 1911, when Marie Curie was nominated for her second Nobel Prize, fortune had turned against her. Pierre had died suddenly and tragically, she had lost a bitter election fight to the *l'Académie des Sciences*, and worse yet, she was involved in a duel-enlivened love triangle with Paul Langevin, a physicist colleague of Pierre's. Indeed, Marie Curie was in imminent danger of being involved in a trial for alienation of affection, scheduled for—of all days—December 10th of 1911. Her detractors had argued in the press that she was "an alien, a Polish woman, a researcher supported by our French scientists," who had "come and stolen an honest French woman's husband" (12).

The trial and attendant publicity prompted that letter from Arrhenius asking her not to attend the ceremonies (1). Maria Salomea Sklodowska Curie replied to the committee that she had been given the prize for her discovery of radium and polonium and that she "*could not accept the principle that appreciation of the value of scientific work should be influenced by slander concerning a researcher's private life"* (12). In the event, the litigation was settled in the first days of December, and she traveled to Stockholm. At the ceremony, Dr. E. W. Dahlgren, president of the Royal Swedish Academy of Sciences, again stressed the male contribution to the discovery of radium and polonium:


Huit pages : CINQ centimes

Le Petit Parisien

SUPPLÉMENT LITTÉRAIRE ILLUSTRÉ

DIRECTION: 18, rue d'Enghien (10e), PARIS

UNE NOUVELLE DÉCOUVERTE. — LE RADIUM

M. ET Mme CURIE DANS LEUR LABORATOIRE

Marie Curie (1867–1934) and Pierre Curie (1859–1906), in Their Laboratory. Prix Nobels 1903. Image courtesy National Library of Medicine, NIH.

Ada E. Yonath (1939–), Prix Nobel 2009. Image courtesy Corbis.

> *We know that radium claims its most promising results especially in the treatment of cancerous growths and of lupus. . . . the Royal Academy of Sciences considers itself well justified in awarding the Nobel Prize for Chemistry to the sole survivor of the two scientists to whom we owe this discovery, to Mme. Marie Sklodowska Curie.* (13)

Marie Curie's reply was implicit in her lucid, self-confident acceptance speech. She spoke of "All the elements emitting such radiation *I have termed radioactive* [editor's italics], and the new property of matter revealed in this emission has thus received the name radioactivity" and "*I was struck by the fact* [editor's italics] that the activity of uranium and thorium compounds appears to be an atomic property of the elements. . . ." She clearly distinguished her own contribution from those made by both Curies working together (14). It was a stimulus to fame that has outlived her detractors.

THE SOLE SURVIVOR

On April 19, 1906, the 47-year-old Pierre Curie was run over by an oversized, horse-drawn wagon filled with bales of army uniforms. He was negotiating that tricky Parisian intersection where traffic from the Rue Dauphine, the Quai Conti, the Quai des Grand Augustins, and the Pont Neuf has created Gallic havoc for over a century. Curie had just quit a meeting of reform-minded university professors, where he argued for legislation to improve the lot of junior faculty and to prevent laboratory accidents. He had planned to stop at his publisher's office on the Quai, but the office was shut because of a strike by equally reform-minded trade unionists. Absent-minded and somewhat radium-sick, he turned away in the spring rain and was on his way to the library of the *Institut* when that six-ton wagon rumbled down the bridge from the Ile de la Cité to crush his skull (15).

Marie Curie later recollected that on the Rue Dauphine, "I lost my beloved Pierre, and with him all hope and all support for the rest of my life." She was right; although Curie was to survive her husband until 1934, her contributions to science after 1911 were less focused on day-to-day laboratory work. She turned her tough mind to the application of her discoveries, to teaching young scientists, and to construction of the Radium Institute, which she turned into a world center of physical science.

Curie's generous 1911 Nobel lecture spells out the

details of an incredible run the two Curies had together. In the course of six short years, they had laid the foundations for the next century of physics and set the clock of our atomic age. Pierre had already become famous for his work with Jacques Curie on piezoelectricity (some crystals, e.g., ceramic or bone, generate an electric current when compressed). He had earned his doctorate for studies with Paul Langevin on paramagnetic resonance (the moment of an atom or electron varies inversely with the temperature). It was the same year (1895) that Wilhelm Roentgen took the first picture of the bones of his wife's hand by means of his novel rays.

By 1897, Henri Becquerel had found that uranium also produced rays—"emanations"—that left Roentgen-like shadows on photographic plates kept in the dark. Almost simultaneously, William Thomson, Lord Kelvin, discovered that the "ionizing" emanations from uranium imparted an electric charge to the air. In December of that year, Pierre and Marie set out to quantify the Becquerel emanations—ionizing radiation—of a great variety of natural substances. For this purpose, they used the piezoelectric quartz balance, an instrument that Pierre had designed, and by February, had found that the residue of pitchblende, from which uranium had been extracted, gave far greater signals than uranium itself. They deduced correctly that there was an ionizing substance far more active than uranium lurking in the sticky brew. It was the same year that Émile Zola wrote *J'accuse*, and France split forever into the supporters of the falsely accused Dreyfus, the *Dreyfusards*, and their right-wing opponents.

By the end of 1898, the Curies had postulated that the new element, which she had dubbed "radium," decayed into another, which Marie called "polonium," after the country of her birth. "Radioactivity" was the new name for emanations from these elements (14, 16). In 1902, by means of heroic preparative procedures, Marie Curie, at last, isolated radium in pure form. Later that year, Pierre calculated that 1 g radium emitted 3.7×10^{10} disintegrations per second; we call this amount of radioactivity one Curie. Shortly thereafter, Pierre made the heuristic discovery that 1 g radium could heat 1 g water from 0^{o} to 100^{o}; we call this sort of transformation "atomic energy," and nowadays, it powers more than half of France. By 1903, the year that Pierre and Marie won the Nobel Prize, they had also come down with the first signs of radium sickness.

For six unmatched years of discovery in the setting of the Third Republic, axes were drawn between right and left, church and state, theory and application, and risk and benefit of a new science in a new century. It's a grand story, and although the Curies are on the spoor of the new, with the Dreyfus case breaking about them, it's an exemplary tale of science in service to reason. However, after Pierre's death on the Rue Dauphine, the story of Marie Curie becomes less of a life in science, as the outrageous attacks on her by the anti-Dreyfusard press turned her attention from science to the broader social scene (17). Her public efforts proved to be as successful as her work in the lab. It was in recognition of the many mobile X-ray units she organized during the First World War that a grateful France forgave her for the Langevin affair by permitting her to establish the Radium Institute.

THE REPUBLIC DOES NOT NEED SCIENTISTS

No published material explores what must have been the remarkable relationship between Madame Curie, a pale, intense widow in a plain black dress who lived on the fashionable Quai de Béthune, and her daughter, a physicist at her mother's institute, who married a brilliant young co-worker. Playing out the story of *Marie et Pierre Redux*, Irene and Frederic Joliot-Curie not only shared the Nobel Prize in chemistry for induced radioactivity in 1935—five prizes in one family—but also an abiding attachment to the Communist party. As the Dreyfus case had been the cause that engaged Pierre and Marie, the Popular Front of the 1930s enlisted Irene and Frederic. The story of the Curies reached from the Quai de Béthune to the ranks of the Comintern. Both generations encountered enmity of the most virulent sort from nativists and anti-intellectuals (18).

In her losing battle for election to *l'Académie des Sciences* in 1911, Marie had found staunch allies in her fellow *Dreyfusards* of the Sorbonne. Mathematicians, physicists, and chemists, such as Paul Appel, Gabriel Lippmann, and Henri Poincaré, became the targets of the proto-fascist ranks of *La France profonde*. Léon Daudet also led the right-wing attack on Marie Curie's nomination for the 1911 Nobel Prize. Attacking the God-less Sorbonne professors in *l'Action francaise*, he accused Curie's champions of no longer "hiding behind the Lives of the Saints but behind algebra, physics and chemistry treatises" (19). He reverted to Antoine Quentin Fouquier-Tinville's notorious cry that had sent Lavoisier to the guillotine: "The Republic does not need any scientists" (12). Certainly, the Republic of Daudet did not need any women scientists. Daudet's mother, Julia, had cast a traditional curse at the likes of Marie and Irene Curie:

> *Science is useless to women, unless they are the exceptions who are inclined to a masculine career, and that is always too bad . . . this excessive independence of ideas, quest for liberal ideas, usurpation and intrusion in the role of lawyer or of intern in the hospitals . . . all that seems to me the fantasies and ambitions of those with dormant hearts, women without children or households. . . .* (20)

On December 10, 2009, five of 13 women Nobel laureates, distinguished for their independence of ideas and their quest for liberal rather than nativist values, received the plaudits of that distinguised assembly in Stockholm. Elizabeth Blackburn representing a generation of scientists, who are also wives and mothers, had an answer for Mme. Daudet and her ilk: "Our

lives were work and family and that was it ... that wasn't a sacrifice; we love both our family and our work (21)." One could hear a glass ceiling crack. FJ

Gerald Weissmann
Editor-in-Chief
doi: 10.1096/fj.10-0101ufm

REFERENCES

1. Quinn, S. (1995) *Marie Curie A Life*, New York, NY, USA, Simon & Schuster, 327.
2. Bombardieri, M. (Jan. 17, 2005) "Summers' remarks on women draw fire," Boston, MA, USA, *The Boston Globe*.
3. Mundy, L. (Oct. 20, 2009) "Success is in her DNA: Greider wins the Nobel Prize in a field in which relatively few women thrive," Washington, DC, USA, *The Washington Post*.
4. Smith, A., interviewer (Oct. 5, 2009) "Elizabeth H. Blackburn: the Nobel Prize in physiology or medicine 2009," Nobelprize.org, http://nobelprize.org/nobel_prizes/medicine/laureates/2009/blackburn-telephone.html.
5. Nobelprize.org. Meet the Nobel laureates! http://nobelprize.org.
6. Szostak, J. W., Blackburn, E. H. (1982) Cloning yeast telomeres on linear plasmid vectors. *Cell* 29, 245–255.
7. Greider, C. W., Blackburn, E. H. (1985) Identification of a specific telomere terminal transferase activity in Tetrahymena extracts. *Cell* 43, 405–413.
8. Greider, C. W., Blackburn, E. H. (1989) A telomeric sequence in the RNA of Tetrahymena telomerase required for telomere repeat synthesis. *Nature* 337, 331–337.
9. Smith, A., interviewer (Oct. 7, 2009) Ada E. Yonath: the Nobel Prize in chemistry 2009, Nobelprize.org, http://nobelprize.org/nobel_prizes/chemistry/laureates/2009/yonath-telephone.html.
10. Bartels, H., Gluehmann, M., Hansen, H., Auerbach, T., Franceschi, F., Yonath, A. (2001) High-resolution structures of ribosomal subunits: initiation, inhibition, and conformational variability. *Cold Spring Harb. Symp. Quant. Biol.* 66, 43–56.
11. Philips, W. (1968; orig. 1884) Woman's rights. In *Speeches, Lectures and Letters*, New York, NY, USA, Negro Universities Press, 16.
12. Fröman, N. (Dec. 1, 1996) Marie and Pierre Curie and the discovery of polonium and radium, Nobelprize.org, http://nobelprize.org/nobel_prizes/physics/articles/curie/index.html.
13. Nobelprize.org. The Nobel Prize in chemistry 1911. Presentation speech, http://nobelprize.org/nobel_prizes/chemistry/laureates/1911/press.html.
14. Nobelprize.org. Marie Curie. The Nobel Prize in chemistry 1911, http://nobelprize.org/nobel_prizes/chemistry/laureates/1911/marie-curie-lecture.html.
15. Quinn, 231.
16. Quinn, 154.
17. Quinn, 295.
18. Quinn, 316.
19. Quinn, 290.
20. Quinn, 280.
21. Lowen, L. Work life balance-Nobel Winner Elizabeth Blackburn's work life balance story. http://womensissues.about.com/od/intheworkplace/a/WorkLifeBalanceElizabethBlackburn.htm.