Rita Levi-Montalcini

(1909–2012)

Nobel prizewinning neurobiologist and eminent advocate for science.

It is unusual to dominate a field so extensively as to be synonymous with it. Such was the stature of Rita Levi-Montalcini, who shared a Nobel prize for her discovery of nerve growth factor. Had her extraordinary life been scripted by Hollywood, it would have been rejected as too improbable.

Levi-Montalcini died on 30 December 2012, aged 103. She was born in 1909 to a well-to-do Italian Jewish family in pre-Fascist Turin. Rita Levi (she added her mother's family name as an adult) began her medical studies at the University of Turin in 1930, after convincing her autocratic father that this was an appropriate choice for a young woman. Her first mentor, Giuseppe Levi, kindled her interest in the nervous system and remained a colleague for many years.

In 1938, Levi-Montalcini was forced out of the university by Fascist race laws. This began a period of hardship, despair and perseverance. She carried out research on embryological neurodevelopment in her home 'laboratory', first in Turin, and later in Florence after her family was forced to flee. She did experiments using crude, hand-made dissection tools and fertilized chicken eggs, later eaten for dinner.

During this period, she read an article by Viktor Hamburger, an embryologist at Washington University in St. Louis, Missouri. He wrote that when the growing limbs of chick embryos were cut off, the resultant atrophy in the neuronal cell clusters intended to innervate them was due to a loss of an 'inductive factor' from the absent limbs. Hamburger suggested that this factor was necessary for the growth and differentiation of the neural precursor cells.

Levi-Montalcini repeated this experiment with Levi, using the silver-staining technique he had taught her. At first, the neurons continued to grow, dying only when they could not reach their surgically eliminated target. Levi-Montalcini concluded that the neuronal death resulted from the absence of a growth-promoting substance — rather than an inductive factor — released by the target of the growing neurons. After the war, Hamburger invited her to his laboratory in the United States to resolve their differing views.

As with most great discoveries, the identification of nerve growth factor (NGF) depended on serendipity. First, a student of Hamburger's, Elmer Bueker, observed that a fast-growing sarcoma became highly innervated when transplanted into a chick

embryo — providing a testable source of NGF. Then Stanley Cohen, in the same lab, discovered that snake venom and the submandibular glands of adult male mice were even richer sources (Cohen joined Levi-Montalcini in the biochemical characterization of NGF).

In 1952, in Rio de Janeiro, Brazil, Levi-Montalcini captured the first image of the production of nerve fibres growing under the influence of NGF from chick-embryo neurons that had been excised and placed in culture in the laboratory of Hertha Meyer, a friend from student days and an expert in the required techniques. With the aid of two tumour-bearing mice, smuggled into Brazil in Levi-Montalcini's handbag, the women developed the first 'halo' assay of NGF. This dramatic bit of scientific art confirmed the existence of the target-derived growth-promoting substance she had predicted; it was one of her favourites.

The discovery revolutionized neurobiology and endocrinology, and set the stage for cell-signalling research. But, at first, NGF was not universally accepted as significant. Levi-Montalcini had to deal with many a naysayer until the early 1970s, when evidence for the importance of NGF (and many similar factors) became overwhelming. She was also not a biochemist, and when Cohen left St Louis in 1959, she had to leave the molecular characterization of NGF to others. She prided herself on her intuition, but rebelled against the idea that NGF was a hormone-like substance and

that it was representative of a larger group of growth factors with broad specificities. That said, she, with colleagues in Rome, did subsequently contribute important observations about its expanded role, particularly in the immune system and in ophthalmology.

Levi-Montalcini remained on the faculty of Washington University for 30 years. Missing her twin sister, Paola, she began a gradual return to Italy during the 1960s. In 1969, she became the director of the new Italian Research Council's Laboratory of Cell Biology in Rome, which grew to be one of the largest research centres in the country.

In 1986, with Cohen, she was awarded the Nobel Prize in Physiology or Medicine — becoming the first Italian woman so honoured. This launched her as the omnipresent advocate for Italian science. Over the next quarter of a century, she participated in television debates, wrote popular-science books and provided advice to the government and other agencies. In 2001, she became a senator for life in the Italian government, influencing key policy questions.

In 1992, she established the Rita Levi-Montalcini Foundation, which supports women from developing countries — particularly Africa — in finding careers in science. She also founded the European Brain Research Institute in Rome in 2002.

Rita has been described as ambitious, autocratic, generous, possessive, aristocratic, demanding, persevering, insightful and totally dedicated to her work. All are accurate. She had disagreements with many scientists who worked on NGF. However, as the importance of her discoveries became increasingly appreciated, she mellowed in her outlook (if not her drive) and seemed to accept the mantle of matriarch that was truly her due.

In April 1986, I co-organized the first meeting on NGF, in Monterey, California, to coincide with her 77th birthday (complete with cake and candles). Six months later, when she and Cohen were awarded the Nobel prize, I sent congratulations. She replied that while it was a wonderful recognition of her life's work, she enjoyed her party more. This diminutive woman was a giant in science. ■

Ralph A. Bradshaw is professor emeritus in the Department of Physiology and Biophysics at the University of California, Irvine. He collaborated with Levi-Montalcini on the characterization of NGF.
e-mail: rablab@uci.edu

HERB WEITMAN/BECKER MEDICAL LIBR., WUSTL