Rita Levi-Montalcini

A Conversation with Rita Levi-Montalcini

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Watch a video of this interview online.

Key Words

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INTRODUCTION

There are very few proven theories that exist in biology. One that has stood the test of time is the neurotrophic theory. It explains why only half of the neurons produced early in development are needed to form a functional nervous system. The explanation came from the discovery of nerve growth factors (NGFs), which help nourish neurons, guide their axons to their proper connections, and prevent cell death. Rita Levi-Montalcini, who formulated this idea, celebrated her 100th birthday on April 22, 2009 in Rome. I had the opportunity to interview her at the European Brain Research Institute (EBRI) in September 2008, which forms the basis of this article. Shortly after the interview, Rita attended the International NGF meeting, held in the Upper Galilee region of Israel (Kfar Blum, Israel). Despite her age, she traveled to the meeting by flying to Tel Aviv and taking a 4-h car ride to the conference site. Remarkably, she participated in the meeting by giving a 30-min talk and sponsoring a poster (see **Figure 1**).

Rita Levi-Montalcini won the Nobel Prize in Medicine in 1986 with Stanley Cohen, decades after her groundbreaking work in Italy and the

United States. The theory she developed was quite elegant and simple. Competition of nerve cells early in development for limited amounts of growth factors produces winners and losers. The winners are nerve cells that made the correct connections with their targets, and the losers undergo death, which explains the massive amount of programmed cell death that occurs in the peripheral nervous system.

With Cohen, she identified and purified the first growth factor, NGF (1). The second growth factor isolated by Stanley Cohen, EGF, was also a landmark, as EGF receptors now form the basis of several effective cancer drugs, such as Tarceva, Erbitux, and Herceptin. The discovery of NGF was the result of an effort to understand a problem that Viktor Hamburger (1900–2001), a student of Hans Spemann, and Levi-Montalcini had followed in the 1930s and 1940s. Are inductive or diffusible substances at the target responsible for controlling nerve growth? Rita felt the answer lay in diffusible and not in inductive molecules. The discovery of NGF resulted from answering the question of how the periphery affected neuronal survival and nerve fiber growth.

As the longest-lived Nobel Prize winner ever, Rita Levi-Montalcini represents a breed of scientist rarely seen today. She not only had to endure obstacles due to gender and religion but was affected by discrimination, politics, and war. After medical school at the University of Turin, she became interested in basic research in neurology. However, with the breakout of World War II, Levi-Montalcini was not allowed to work at any Italian universities due to her Jewish heritage. During the period of 1940–1943, when heavy bombing took place in northern Italy, Levi-Montalcini carried out her research on early chick embryonic development in a makeshift laboratory in her bedroom, without any financial support, aside from that from her family. Although her parents had expected Rita to become a wife and mother, Rita never married or had children. She lived most of her life with her twin sister, Paola, who was an accomplished artist. Many of these events are described in her autobiographical book *In Praise of Imperfection* (2). When asked whether she

Figure 1

Rita Levi-Montalcini in a group picture at the 2008 International NGF meeting.

considered art as a career, Rita noted that she started her career not as a scientist but as an artist. Due to her sister's work, Rita was attracted to the beauty of the nervous system, a point she emphasized in the interview.

Rita's career decisions and contacts serve as an example of how circumstances and chance play a role in guiding a scientific career. Before exposure to research in America, she was exposed to several influential mentors and colleagues who encouraged her career. Notably, Rita was a medical school classmate of Renato Dulbecco (b. 1914) and Salvador Luria (1912–1991). These relationships spilled over to influence many prominent biologists of the past century. Luria received the Nobel Prize for his insights in bacteriophage genetics, and he was responsible for directing the Center for Cancer Research at MIT. While Luria was a professor at the University of Indiana, his first graduate student was James Watson, and at MIT, he was influential in hiring Phil Sharp, Susumu Tonegawa, and Robert Horvitz, all future Nobel laureates. Dulbecco won the Nobel Prize in 1973 with David Baltimore and Howard Temin for identifying the mechanism of tumor viruses. Rita's encounters with Luria and Dulbecco were important. Luria fled the war and went to the United States in 1940. Dulbecco also moved to the University of Indiana, where he collaborated with Luria on the study of bacteriophages. Early interactions between Levi-Montalcini, Luria, and Dulbecco presaged their future careers and decisions.

In medical school, Levi-Montalcini, Luria, and Dulbecco took histology courses taught by the same professor, Giuseppe Levi (no relation to Rita). Levi advised Rita after medical school to carry out ablation experiments in the chick limb, following approaches pioneered by the famous experimental embryologist Hamburger in the 1930s. Despite the difficulty in carrying out research in Fascist Italy without a fellowship or a grant, Rita was able to use chick embryos to study the effects of target tissue upon nerve growth. In later years, Giuseppe Levi influenced Rita's efforts to develop an in vitro system to assay for the effects of NGF. Although it was difficult to publish her experiments during World War II, her work nevertheless caught the attention of Hamburger, who read her papers. She had published two papers with Levi in 1942–1943 in Belgian journals because Jewish citizens were not allowed to publish in Italian scientific journals. Nevertheless, these papers caught the eye of Hamburger, who asked Giuseppe Levi to invite Rita to St. Louis to continue her work.

As a consequence, Rita arrived in Hamburger's lab after the War, in October 1947, and began a 30-year period of research at Washington University. Her productive research over this period with Hamburger is described by many students and colleagues (3, 4), and the subsequent controversy about the omission of Hamburger as a corecipient of the 1986 Nobel Prize in Medicine is documented in a detailed historical review by Max Cowan (4).

After arriving at Washington University in 1947, Levi-Montalcini used traditional methods of embryology and transplantation to discover that neurons undergo massive cell death in the absence of trophic substances. A key experiment was the discovery that transplanted sarcoma tumors produce a factor that allows nerve cells to grow extensively. She also developed a method to grow groups of neurons from a developing chick embryo for days in plastic dishes. For this in vitro approach, Rita traveled to Rio de Janeiro to devise a rapid and easy test to characterize humoral factors. After several attempts, she succeeded by culturing chick embryo sensory ganglia incubated in the presence of small pieces of the sarcoma tumor. Without this discovery, she knew it would not have been possible to identify NGF because it was simply too difficult to carry out each assay if one had to resort to in vivo experiments using chick embryos. Indeed, this method allowed Rita and Cohen to isolate NGF and to demonstrate its potent effects in preventing neuronal cell death (1, 5).

Ultimately, NGF was discovered from some clever deductive reasoning and brute force biochemistry. As a member of the Microbiology Department, Cohen was heavily influenced by some chance encounters with Arthur Kornberg, who suggested experiments to determine whether the factor represented a nucleic acid (6). A control experiment using snake venom phosphodiesterase to rule out RNA and DNA revealed that there was considerable NGF activity in snake venom, suggesting that submaxillary glands could be used as a rich source for NGF purification (7). Looking back at these events reminds us how chance encounters between scientists affect scientific discoveries and personal decisions. The landmark experiments were a result of a combination of expertises in different disciplines—neuroanatomy, embryology, and biochemistry—that came together at Washington University between Cohen and Rita Levi-Montalcini (see **Figure 2** for a recent photo of both scientists). Their work also resulted from keen powers of observation combined with deductive logical reasoning, qualities that both scientists shared in abundance.

Fifty years after their initial discovery, trophic factors like NGF have been shown to have an impact beyond developing neurons. In adults, nerve growth factors have the ability to convert new experience into stronger connections in the brain that mediate learning, memory, and nerve regeneration. In fact, the more active brain cells become, the more trophic molecules are produced. This principle is important because trophic factors also play a role in preventing neurodegenerative diseases, such as Alzheimer's and Huntington's diseases (8–10), and modulating pain and psychiatric disorders, such as depression and anxiety (11). There is a growing realization that cognitive activity and physical exercise lower the risk for these conditions. A major reason likely relates to the elevation of NGF and BDNF in the brain, which prevents degeneration and helps neurons to fire more efficiently.

In addition to their well-established roles in early development, neurotrophins also function in the adult nervous system, where they elicit multiple effects upon higher-order functions. Indeed, a cardinal property of neurotrophins is their ability to rapidly modulate synaptic transmission and

Figure 2

A reunion of Stanley Cohen and Rita Levi-Montalcini on the occasion of her 100th birthday in Rome (April 22, 2009).

neural plasticity (12–14). Effects upon synaptic transmission by BDNF have been observed in the hippocampus and provide long-lasting potentiation of synaptic transmission and morphological changes that result in new synaptic connections. Indeed, NGF directs rapid firing of cholinergic neurons in the basal forebrain, increases acetylcholine release (15), and is responsible for learning and retention of spatial memory (15a). Therefore, neurotrophins can influence many pre- and postsynaptic activities throughout the central nervous system. NGF and BDNF are also frequently elevated after inflammation or injury (17). This response results in greater nociceptor sensitization through rapid modulation of heat and vanilloid receptors. Therefore, blocking NGF with antagonists has been suggested to provide relief from pain. This prediction has now been borne out by a number of studies using anti-NGF antibodies and Fc-receptor fusion proteins (18–21). The absence of neurotrophins and their receptors from *Drosophila* and *Caenorhabditis elegans* indicates that they must subserve higher-order functions (16). Indeed, a clear biological function of neurotrophins is in mediating nociception (21), which was insinuated by the earlier observations of abundant amounts of NGF in snake venom.

So from answering a basic question of how the nervous system develops, Rita Levi-Montalcini has made a lasting contribution to biology and human disease. Her work produced one of the first molecules relevant to the nervous system and foresaw the start of the field of molecular neurobiology, well before the advent of DNA cloning and sequencing. From her early upbringing in Turin, she was motivated to study and to help those who suffer. Her early decision to study the nervous system was based upon her fascination with its beauty and complexity. The discovery of how and why cells in the nervous system grow and regenerate forms the basis of solving many neurological and psychiatric diseases in this century.

In later years, Rita became a staunch supporter of women in science. Influenced by the work of Albert Schweitzer in Africa, Rita has established a foundation to assist young African girls with scholarships to further their education. Rita has stated she has no plans to retire and regularly attends scientific meetings, where she is often delighted to interact with younger scientists (see **Figure 3**).

Levi-Montalcini has continued to be involved with research as Head of the EBRI and is a senator for life in the Italian Senate. As she enters her second century of life, she is still active in promoting scientific research and the role of women in underprivileged countries.

The following interview took place at Rita Levi-Montalcini's office at the EBRI, which is located an hour outside of Rome (**Figure 4**). Rita visits the office and laboratories several times each week. During the interview, she was extremely gracious and grateful for the opportunity to talk about her life in science. She was refreshingly candid about career choices and opportunities for young scientists. At times, she was forceful and opinionated, particularly on issues dealing with women in science, politics, and discrimination. Unexpectedly, in an answer to a question about what she would do now as a scientist, she confided that she would become a molecular biologist. She was talkative and engaged and displayed a remarkably clear memory of events that took place more than 70 years ago.

Although quite healthy and sharp in her mind and thinking, Rita did have some difficulty with her hearing and vision. During the interview, she would often lean toward me to listen better but was extremely active, animated, and energetic. She was accompanied by her scientific colleague, Pietro Calissano, who assisted in the question-and-answer session. Although much has been written about her life and scientific career, she revealed a number of unanticipated responses and perspectives about her life and the difficulties and challenges of performing science and attracting young people to biomedical research. As a neuroscientist, politician, leader, and prolific writer who is still producing books at the age of 100, Rita has an unabating influence that is now extending into a second century.

Figure 3

A group of graduate students and postdoctoral fellows interacts with Rita Levi-Montalcini.

Figure 4

Moses Chao interviews Rita Levi-Montalcini at her office at the EBRI (September 2, 2008).

INTERVIEW AT THE EUROPEAN BRAIN RESEARCH INSTITUTE (SEPTEMBER 2, 2008)

Chao: Dr. Levi-Montalcini, it is such an honor to be here and to visit the EBRI Foundation. I am very honored to be here.

Levi-Montalcini: Thank you so much, thank you Moses. To me it's a great honor. I have such admiration for your work. I am very, very happy. Thank you so much, Moses.

Chao: The Annual Reviews of Physiology and Biochemistry have a series where they would like to ask a senior neuroscientist to talk about their life in science. This article will be directed to young scientists as well as older scientists who would like to know about the history of neuroscience.[1]

Levi-Montalcini: Thank you so much Moses. I am delighted. No person would be better than you, Moses, for my admiration for all the work you have done.

Chao: Thank you.

Levi-Montalcini: I still do work in spite of my age.

Chao: So, yesterday you said you were motivated to be a scientist because you found beauty in the nervous system.

Levi-Montalcini: Perfect, correct!

Chao: What did you find beautiful about the nervous system?

Levi-Montalcini: Well, you know, every cell, I mean, nerve cells, particularly in the brain, is such a marvelous object to study. I was a neuroscientist, you know, so I was delighted particularly when it was discovered, the in vitro system, and Giuseppe Levi did not discover, but brought it in Italy. So I had all the reasons to want to work in this way, not as a scientist, but to see beauty. This is true.

Chao: So the in vitro system was discovered in the mid-1950s? 1950?

Levi-Montalcini: Discovered by me. I knew very well tissue culture. It was not known in Italy. I was a student of Giuseppe Levi, who brought the in vitro system to Italy. So, I decided, because it was very difficult to find the initial chemical nature of the factor because, you know, the in vitro is the best way. So I went to Rio de Janeiro, applied all that I knew, and I discovered the effect not of NGF, but pro-NGF. So without this discovery nobody would have ever found the initial of the nerve growth factor in the chicken embryo. It was too difficult. It was necessary—a system which was the in vitro system to bring the possibility to a biochemist, Stanley Cohen, to identify the factor.

Chao: So, earlier in 1940 [when Levi-Montalcini was working on her research at home in Turin], my question is, during that period, who supported you?

Levi-Montalcini: No one. I was working on my own. Not very much money, but I could do by myself, you know. It was not financed by anyone.

Chao: You did not have a fellowship?

Levi-Montalcini: It was in my bedroom. It was a period of persecution. I was not a victim of a personal persecution, but that was the time. I did not ask [for] any help. I did it with my personal, very little finances. Not very nice.

Chao: So your family supported you?

Levi-Montalcini: Yes. Very much so. Because they knew that I needed little money necessary to implant. Practically almost no money. I worked in my bedroom, and I just had my microscope, which I bought, it was very expensive, and a very minor gadget, not simple, it was very detailed. The amount of money necessary to do these experiments—I did it in my bedroom.

Chao: Your mother was there and she supported you?

[1]The Perspectives series in the *Annual Review of Physiology* focuses on eminent physiologists.

Levi-Montalcini: Yes, exactly so. My father was already dead. So later on, when the situation became very serious in Italy because of the bombing of the city, we moved to Asti, to a little house in the mountain near Turin. And there I continued my work and discovered the effect, not of NGF, but [cell death].

Chao: You told me a long time ago that during this period you observed cell death, massive cell death.

Levi-Montalcini: Yes. And it was in '72 I discovered the apoptosis, 30 years before it was discovered, because I saw also cells that die. Why do they die? What is the reason? And then in 1972 it was given the name of apoptosis.

Chao: During this period in Turin and also in the early '50s, you wrote many papers. Your observations you published in many papers. During that period, in the '40s and '50s, was it difficult to publish?

Levi-Montalcini: Italian papers would not accept, but the Vatican accepted. The Vatican was against Mussolini. The Italian papers did not accept because of my name, you know. So I could not publish in Italy; the only one was the Vatican. I published in that and also published in Belgium, in Switzerland. I could publish abroad, Belgium and Switzerland and, in Italy, Vatican.

Chao: So, because of your Jewish name, you were discriminated in publishing papers in scientific journals?

Levi-Montalcini: Yes. But not in Italian papers. I could not.

Chao: So this must have been very discouraging to have your papers rejected because of your name.

Levi-Montalcini: I did not care about it. No, Moses. I was totally indifferent. I did not expect to have a name or recognition. I was enthusiastic in the possibility "alla Robinson Crusoe." I was working for the beauty. What I was doing—totally indifferent of recognition. It made no difference to me. I never cared about it.

I was totally, I mean, I did not know if I could survive. I did not care about it. Many people, many friends of mine had already been brought to Auschwitz. Miraculously, we saved ourselves. We tried to go to Switzerland in the night, and it was a terrible mistake. By chance we were not taken by Germans or even Italian fascists. At the moment we arrived at the frontier I realized the danger. I did not know that Auschwitz was expecting me. But I knew the danger, so we decided at the last moment not to stay there but to go back to Italy because the danger was very, very high, I mean, to be immediately taken by the Germans or Italian fascists with my family with the luggage, they would have immediately taken us to Auschwitz.

Truly the most dangerous moment of my life.

Chao: When you went to St. Louis, and you worked with Viktor Hamburger, you developed a very important theory on the neurotrophic hypothesis, which is based on competition for NGF and other trophic factors.

Levi-Montalcini: Viktor Hamburger knew my work, not from Italy, but reading a Belgian paper. He was very impressed by my result, so he wanted to know how. We were so much different. He was a student of Spemann, was thinking the periphery acted through induction. I did say no, it is not induction. We had entirely different views. So he invited me, this was after the war, to work with him for about—he was the Chairman—about a few days, a few weeks. I stayed there 30 years because I found the Department of Zoology chaired by Viktor an excellent place to work.

Stanley Cohen came to work with me because I discovered the in vitro effect alone, so I came to him. I did not know Stanley at the time. He was taken by Viktor Hamburger from another important laboratory. He was a young man, a biochemist, so he could not have discovered the nerve growth factor if I only worked on the embryos, so it was my idea to find a better possibility. I knew about tissue culture; I went to Rio de Janeiro and immediately discovered the in vitro effect.

First, I saw the effect on sensory, sympathetic nerve cells. A decade later, and not even me, it was also people who found that this factor acted also on the central nervous system. It was not my discovery, you know.

Chao: So, your career has now spanned seven decades at least, and I am wondering, if you were to start your career now, what would you want to work on?

Levi-Montalcini: I know that now there are wonderful new possibilities scientifically and technologically which were not available when I was a young person. So I believe I would start, as many people and students here too—is to become a biochemist, a molecular biologist, which I was not at the time. So I believe that now I would take advantage of these enormous developments, scientific and technological, which were not in my time. Not even Dulbecco, not even Luria, who received the Nobel Prize with me, a bit before me, had any advantage—they were, more than me, capable to work on viruses.

Chao: Your classmates Renato Dulbecco and Salvatore Luria were working in virology and also in phage genetics, but you actually created a whole field of neuroscience.

Levi-Montalcini: I was very much willing to leave the nervous system to work on Darwinism or genetics, but they told me no, continue to work on this. Speaking with Luria, I mean, it doesn't seem very important, don't change. At that moment, I wanted to change, you see, but there was nothing I can do anymore. It was a moment difficult because I did not know this important discovery. I knew it was important but not so much as to continue. So I was hesitant as to leave the nervous system to work with Luria or with Dulbecco, who were my close friends. Fortunately, I was assisted, and this was good.

Chao: So I am also wondering what advice would you give young people now. Many young people are not interested in science, and it's a very exciting time, as you mentioned.

Levi-Montalcini: I'd say, as I always say, that nothing is beautiful as to work on something scientific or social, to be very invested in what you do. I mean, not [to] be afraid, but knowing that you never will go ahead if you don't do it very seriously and then, as you say, the important [thing] is to be very engaged. What you do you should do well. I will say that it is not as important as scientific or social [work] because I'm also working on social problems, as you know, in Africa. So it is important to know what it is important in life, not just only very simple and stupid things, like being beautiful and successful, this is nonsense.

I always say so, and I have many followers you know. I work here, and I am delighted because excellent people work here, Antonino Cattaneo, Pietro Calissano, I mean, many people, not too many, but some people still understand the importance of being invested in important problems, not in futility.

Chao: You mentioned your work in Africa with women and—since you are such a strong role model for women scientists, and women scientists have usually more difficulty in getting a high position—why do you think it is so difficult for women?

Levi-Montalcini: Well, a dogma. I'd like to elaborate on this point, I mean, we are subjected to ideas which are preconceived ideas. The man is more intelligent than women, they say, because it's convenient, but it's nonsense. We are the victims of a program, genetic program—it is not true because we are far more epigenetic, not genetic. I mean, human beings are not like insects or invertebrates entirely acted [on] by a genetic program. Human beings and vertebrates in general have the possibility to adapt—not genetic, but epigenetic is far more important. The environment is important.

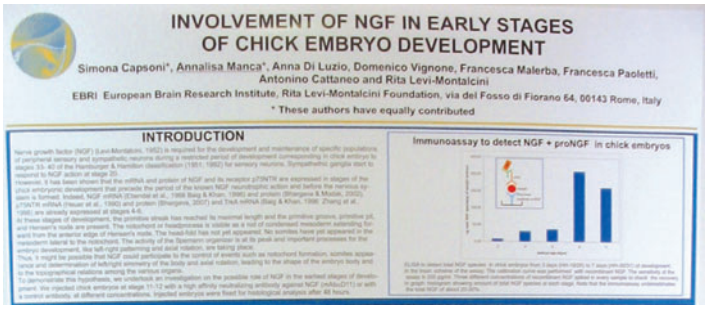
We are no more victims of dogma. The title of my new book is *The Destruction of Dogma for a Better Future*. We are still victims of dogma, you understand?

Chao: I think NGF is for humans evolved evolutionarily to not only be involved in development of the nervous system but also in higher-order behavior, because you know in *Drosophila* and *C. elegans*, you can make a nervous system without NGF. So NGF has other properties.

Levi-Montalcini: My paper—the vital role of NGF is from preembryonic to the last part of vertebrate [development]. It is a vital role, and it is present before the formation of the embryo in the oocyte and the sperm. The zygote is due to NGF, which makes connections, and NGF is active long before the formation of the organism.

Chao: I understand you are still doing research on this idea that there are early events affected by NGF. Is that correct?

Levi-Montalcini: Just before the oocyte and spermatozoa we've proved that is already present there, the early part of the embryo found before the nervous system is formed. It's not that the NGF is necessary, for it is already present before. It is a universal molecule which is very important for vital roles, the vital role of NGF, which is not only neurogenetic. [In Rita's recent research, her colleagues have been following the effects of NGF at quite early times during chick development (stages 11–12). She presented this work at the International NGF meeting in 2008; see **Figure 5**.] We proved it with experiment of monoclonal antibody to NGF in a very early stage in the very beginning of formation, and we found out that with removal, you have not the death, but a very bad development of the embryo, which eventually dies. This is because it is necessary; I mean, NGF is not an organizer. If you take away the organizer, you have no organism to form. If you take [it] away by interjecting mouse or if you take it away by antibody to NGF, the embryo is formed but is very badly formed, and it's doomed to die because there's not a capacity of proliferation, so it will slowly die, not like it will be no formation of the embryo. The embryo is very poorly built.


INVOLVEMENT OF NGF IN EARLY STAGES
OF CHICK EMBRYO DEVELOPMENT

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INTRODUCTION

Immunoassay to detect NGF + proNGF in chick embryos

Figure 5

A poster presented by Rita Levi-Montalcini's group at the Katzir Conference on Life and Death in the Nervous System at Kfar Blum, Israel, September 2008.

Chao: So I have to ask you. All the experiments that you did with Stanley Cohen using antibodies against NGF, the original experiment with sympathetic ganglia. How did you get the idea to do this experiment?

Levi-Montalcini: Cohen was an excellent biochemist; do you know him?

Chao: Yes.

Levi-Montalcini: Excellent scientist and human being too. So it is very much his merit to have found that it was necessary to destroy NGF to find out what is its action. So we found out that we destroy with antibodies. You don't have anymore all the sensory and sympathetic neurons, which do not develop.

Chao: But this experiment was very, very important, and it preceded a knockout experiment, it preceded by 40 years the mouse knockout experiment which got the same results. So it was a very key experiment that was done at that time to establish the importance of NGF, and I think it reflects a lot of creativity and also interpretation to do the experiment and also interpret the results.

Levi-Montalcini: *Certo*! (Of course!) It is true. I say so in my new book. The two identical results but different kind. Transgenic mice, you don't have transgenic chick. I mean, it's the same. I mean, you can destroy the NGF in transgenic mice knock me out, but you can also destroy it by antibodies. It's two different ways of destroying. So in the chick embryo you have only the possibility of antibody because we don't have transgenic chick, but you have so with the mouse. So the mouse offers to us the possibility of studying the actual role of NGF, not only [in] very early stages but throughout the lifetime, also later on the Alzheimer's, consequence of NGF. So,

everything came out because we transferred our interest from the chick embryo to the mouse.

Chao: After 50 years of studying NGF, there's still a lot of interest.

Levi-Montalcini: Very much so.

Chao: What do you think in the future will be the future of NGF?

Levi-Montalcini: Yes, I can see, Moses. My title, vital role, I have to find out because a new scenario is open now. I mean, you know that the NGF is not only working on neurotrophins, it is also neurotrophic, but far more. So what we have now is a new scenario ahead of us. We know that NGF has an active, vital role from early oocyte, sperm, zygote, from very very early on. It is a universal important factor came to existence; we are still open to find out new ways of looking at NGF. NGF, I mean, its trophic term is to some extent one of the actions of the trophin, as we found out.

Chao: I know you are heavily involved as a Senator in the Italian Senate, and I wonder how you feel about politics?

Levi-Montalcini: No. I do not like politics. I like problems, social problems, and naturally I am from the left, not from the right, because all the problems can be developed and solved by [an] open mind, not by being the right. I mean, people are better? No, we are all the same, but it's the way how we work which may be different.

Chao: Very few scientists are involved in politics.

Levi-Montalcini: And also I believe that with the people of Africa, women, if you give them instructions—this is what I am doing—they do it as well and better than men.

Chao: You definitively are a role model. How do you feel being involved in politics, in Italian politics?

Levi-Montalcini: Not too happy. But when there was the previous government I was very much in favor and I still am, I thought that this was the only way, democracy, not totalitarian systems, this is against the possibility of development. So I became interested in trying to follow this, and I worked very much in the Senate. And I work now in Africa, you know, to give women all possibilities of instruction, which is more important than anything.

Chao: I understand you are the longest-living Nobel laureate—nobody else has lived as long as you have who has the Nobel Prize—and I just wondered, what's the secret to your longevity?

Levi-Montalcini: Because I never think of myself. I am totally indifferent. I mean, my life, I am, to some extent, indifferent if it will end tomorrow or longer. I have no problem with my health; I don't care about it. I'm totally indifferent.

Chao: You are thinking about others, you are thinking about problems. . .

Levi-Montalcini: I do not know if this is [why] I live so long, but at night I do not sleep but I think. Because there's wasting time in sleeping. All the night I think, and in the morning I have new ideas, but this is because I am totally indifferent to food and indifferent to sleep, never cared. I believe we give too much importance to sleep and food.

Chao: So, you don't sleep at all at night, just a few hours?

Levi-Montalcini: Normally, I don't sleep in the night. I take half an hour, not every day, but sometimes in the afternoon, that's all. I've no interest in sleeping. It is wasting time and I don't need food, more than very little.

Chao: So maybe the caloric restriction contributes to longevity. But I think it is also the fact that you are very active. I also think that since you are so active at this age that it has an effect on your plasticity and increases neurotrophic factors in the CNS and helps you to be more creative.

Levi-Montalcini: You know, I've also something to tell you: I use every day my factor NGF in the cornea. Now we know that cornea immediately goes to the brain and works on the cells,

so it's also possible that my vitality is in part due to the fact that three times a day I use the cornea in my eye because I've lost the vision and it goes to the brain. It is a hypothesis.

Chao: One more question. What is the happiest time of your life?

Levi-Montalcini: This one! Well, it was very good when I realized the importance of the discovery of the nerve growth factor, but all together the very end of my life gives me the possibility of work, not only scientifically but socially, what I wanted when I was 20 years old. I did not believe I would be a scientist. I wanted to go to Africa to fight leprosy. This was my idea of life. At the very end I work scientifically, but I work also to help women in the end. So I do believe that the best period of my life is the present.

Chao: Wonderful. That's wonderful!

Levi-Montalcini: Yes. I had an excellent time with Hamburger, with Stanley Cohen. He was an excellent biochemist, and I had an excellent relationship also with him.

Chao: Thank you so much. *Grazie*.

Levi-Montalcini: Thank you, Moses. I am delighted.

Chao: You had a remarkable career.

Levi-Montalcini: It is an honor more than I deserve, you speaking about me. I don't believe I merit it; it is your kindness and generosity. It is not my merit. It just happened. It was a pleasure of a long life, and the end is even better than the beginning. You know, when I was a child I was a very unhappy child because my family was totalitarian, I mean a Victorian kind, my father. So I could not go to high school, but I studied by myself. So I resented it, and I was very unhappy. After this, my life has become better and better.

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