22 APRIL: RLM DAY AS RELATED TO THE BEAUTY OF THE HUMAN CAPITAL

On behalf of the Bulgarian Society
for Cell Biology (BGSCB)

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Some people are so much known that it is sufficient
to mention their initials to recognize them:

L – Carl Linnaeus

N – Napoleon Bonaparte

FDR – Franklin Delano Roosevelt

JFK – John Fitzgerald Kennedy

TS Eliot – Thomas Stearns Eliot

RLM – Rita Levi-Montalcini

As a homage to Her great contributions to modern neuroscience, we have announced 22 April (the day she was born) as Rita Levi-Montalcini Day (RLM Day) - to be celebrated globally.

Rita Levi-Montalcini was born April 22, 1909 in Turin, Italy, where received her medical degree from the University of Turin in 1936. The same year she entered the Institute of Anatomy as postgraduate student of Professor Giuseppe Levi, a well-known neuroanatomist and tutor of two other future Nobel Prize winners in Physiology or Medicine, Salvatore Luria (in 1969) and Renato Dulbecco (in 1975).

At the end of the nineteenth century, it was envisaged by Santiago Ramon y Cajal but has not been proven that life at

The Nobel Prize Award Ceremony, 10 December 1986, Stockholm: Rita Levi-Montalcini receives the Nobel Prize from King Carl Gustaf XVI of Sweden.

the neuronal level requires trophic support. The proof was obtained by work initiated by Rita Levi-Montalcini in 1949. In 1951, in her initial published work with Victor Hamburger, she prospected the hypothesis that the nerve-target interactions are reciprocally competitive in the sense that developing neurons depend on feedback (retrograde) signals from the peripheral tissues that are required for neuronal survival. These seminal observations and hypothesis paved the way to the discovered of programmed cell death (in the today's context, the apoptosis). In 1951 at Washington University in St. Louis, Missouri Rita Levi Montalcini discovered nerve growth factor (NGF). In 1986, 35 years after the discovery of NGF, Rita Levi-Montalcini was

awarded the Nobel prize for medicine (1) with Stanley Cohen - discoverer of epidermal growth factor (EGF).

Later, in her book *The Saga of the Nerve Growth Factor* (2, 3) she described the magic to *predict the unpredictable*: from mouse tumor grafted on chicken embryos through snake venom and mouse salivary glands to find a biomolecule that stimulates the differentiation and growth of nerve cells is an exciting example of heuristics.

Rita Levi-Montalcini's NGF provided a conceptual framework for the formulation of the neurotrophic hypothesis: particular neuronal types require trophic ("nutritional") factor(s) for neurite growth and neurotransmitter production for proper function and survival. Her data on the prototype neurotrophic factor, NGF, triggered an unprecedented search for a family of related proteins now commonly called neurotrophins. More importantly, Levi-Montalcini's NGF determined a new concept of biology, that cells require specific protein signals for differentiation and survival, that is, *the general theory of cell growth factors*. All this resulted in the discovery of hundreds of growth factors that affect almost all facets of cell biology. In analogy with Mendelevium (Md), Einsteinium (Es) and Fermium (Fm) in Dimitri Mendeleev's Periodic Table of Chemical Elements, we may now introduce NGF as Montalcinium (Mt) in the Periodic Table of Biomolecules.

Originally identified as neurite outgrowth-stimulating factor, later studies revealed that non-neuronal cells, including immune cells, endothelial cells, cardiomyocytes, pancreatic beta cells,

This photograph was taken during the One Day Meeting on Nerve Growth Factor dedicated to RLM's 100th birthday held on 21 April 2009 in Rome, Italy. From left to right: Luigi Aloe, Rita Levi-Montalcini and George Chaldakov.

prostate epithelial cells and adipose tissue cells, are also targets for and/or sources of NGF. Nerve growth factor is well recognized at present to mediate multiple biological phenomena, ranging from the neurotrophic through immunotrophic and epitheliotropic to metabotropic effects. Consequently, NGF and other members of the neurotrophin family are implicated in the pathogenesis of a large spectrum of neuronal and non-neuronal diseases, ranging from Alzheimer's and other neurodegenerative

Gala dinner: Rita Levi-Montalcini and participants of the Rome-2009 meeting dedicated to Her 100th birthday.

diseases to atherosclerosis and other cardiometabolic diseases (4). Recent studies demonstrated the therapeutic potentials of NGF in these diseases including ocular and cutaneous diseases. Whereas NGF TrkA receptor antagonists emerged as novel drugs for pain, prostate and breast cancer, and urinary bladder syndromes.

On 21 April 2009 in Rome, Italy, Luigi Aloe, the most devoted, productive and long lasting coworker of RLM, organized One Day Meeting on Nerve Growth Factor dedicated to RLM. Amazingly, she, at the age of 100 years, took active part in all the events related to the Meeting, two of them illustrated by the following photographs.

Professor Levi-Montalcini was the first Nobel Prize-winner to reach the age of 100. With her 103 years of life (1909-2012) and vast experience and erudition of a scholar and teacher she did contribute very much to the progress of scientific and public life of Italy and the world. Truly, RLM's centennial life created the scientific bridge between two millenia, a path followed by many generations (5-9).

Noteworthy, in a paper entitled *Is this the secret of eternal life?* published on 23 April 2009 in the British newspaper *The Independent* has quoted one of RLM's great messages: *I say to the young, be happy that you were born in Italy because of the beauty of the human capital of this country... No other country has such human capital.*

This is the guarantee of her "presence in the absence", also indicated by Her message "Life does not finish with death...", shown herein.

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"La vita non finisce con la morte. Quello che resta, è quello che trasmetti. L'immortalità non è il tuo corpo, che un giorno morirà. Non m'importa di morire... La cosa importante è il messaggio che lasci agli altri. Questa è l'immortalità."

Rita Levi-Montalcini