

EDITORIAL

Rita Levi Montalcini and research

"If I were to die tomorrow or in a year's time, it would be the same: what counts is the message you leave behind you. It's the only way to prevent that our passing on Earth doesn't exhaust in a big nothing" R.L.M.

It is thanks to her passing, to her light but determined footsteps, that the world is now richer and more fertile.

The life, work, commitment and the many years dedicated to scientific research by Rita Levi Montalcini are difficult to summarise. Her intense existence, marked by historic events, has been illustrated with extreme competence in *Nature* (www.nature.com; *Nature* 458, 564-567, 2009) on the occasion of her 100th birthday.

The great riches she has delivered to the world consist in her scientific discoveries: the discovery of NGF (Nerve Growth Factor) and its role in the immune system, its increase in states of anxiety, the protective effect against Alzheimer's, a therapy for ocular ulcers and much more.

In 1986, at the age of 77, Rita Levi Montalcini was awarded the Nobel prize for medicine, together with the American Stanley Cohen, for the discovery in the early 1950s of the **Nerve Growth Factor (NGF)**; a discovery which represents a milestone in biology. At that time, studies on chemical neurotransmitters were practically non-existent and the brain was considered on a par with an electrical circuit.

Rita Levi Montalcini discovered a powerful growth "factor", that was called NGF. It was sufficient to inject an infinitesimal quantity into a test tube along with a few nervous cells and wait one day. After 24 hours an aureola started

to develop so rich with filaments that it appeared similar to a sun with many rays. The growth factor of the nervous cells was just the first of the many ingredients that living organisms use to transmit information to their interior. Hundreds of other similar molecules were subsequently discovered. NGF is a crucial protein for the growth and maintenance of neurons in the sympathetic and sensorial nervous systems, without which the brain cells die.

These pioneering studies, carried out on chicken embryos, demonstrated therefore that the brain can 'regenerate' itself, contrary to previous belief. True, after birth new neurons do not form and those that die are gone for ever, but it is also true that new connections, or alternative circuits, do form. And the 'director' of this extraordinary neuronal plasticity is, in fact, NGF.

Over thirty years later in Stockholm, on awarding her the prize along with her colleague Stanley Cohen, the Nobel Committee explained: "*The discovery of NGF is an example of how an acute observer can elaborate a concept from apparent chaos*". Rita Levi Montalcini was one of just 10 women, versus 189 men, to win the coveted award.

When NGF was discovered on 11 June 1951, its importance seemed related to the nervous system alone.

In actual fact, after having identified NGF and studied its effects on the growth of nervous tissue, R.L.M. took her research further and arrived at a second conclusion: that **the nervous, immune and endocrine systems are not separate entities.**

In 1977, she demonstrated for the first time that the nerve growth factor has a sphere of influence well beyond the peripheral or central nervous

system; it affects the cells belonging to the immune system (mastocytes), and is produced by a variety of defensive cells (lymphocytes) and glandular cells (especially salivary). The term 'Nerve Growth Factor' is simplistic – NGF is a modulator which acts synergically upon the three systems on which the balance of the organism depends. Without it, general disaster looms.

A further aspect of the biological activity of NGF was discovered in 1986. A study carried out on young recruits experimenting parachute launches showed an 84% increase in NGF levels in the blood before jumping and an additional increase of as much as 107% twenty minutes after landing.

This increase of NGF in the blood stream puts it in directly proportional relation to **aggressive and anxious behaviour**.

In 2005 the link between NGF and stress was experimented and demonstrated on an astronaut aboard the International Space Station.

Studies conducted by R.L.M.'s European Brain Research Institute over the last 15 years, in collaboration with The Institute of Neurobiology and Molecular Medicine of the CNR (Italian National Research Centre), resulted in the discovery of **the key role played by NGF in preventing the onset of Alzheimer's disease**. The protein blocks the production of beta-amiloid proteins, mainly responsible for Alzheimer's, and contrasts the degenerative process. At present, studies for possible therapeutic applications are under way both for Alzheimer's and for other serious diseases of the nervous system (Parkinson's, Amyotrophic Lateral Sclerosis, ...).

In Italy, the molecule has been experimented in collyrium form for the **treatment of corneal ulcers**, lesions which can lead to loss of sight.

The initial clinical trials at the Institute of Neurobiology of the CNR in Rome suggest that the administration of NGF-based collyrium is efficacious in repairing damaged tissue after just a few weeks of treatment. In trials, this treatment has also shown to be effective against

glaucoma, a degenerative and irreversible condition of the optic nerve.

Lastly, NGF is also the first "lovers' molecule". Research at the University of Pavia has in fact demonstrated that the level of this protein is higher in the early phases of falling in love. At more than sixty years from its discovery, it is ever clearer that this protein comes into play even in controlling phenomena which until now have escaped any biochemical formula, such as falling in love.

NGF has proved to be a 'vital molecule', which R.L.M. has always considered important both in the development of the individual and that of the human species.

It is likely that in a few decades the therapeutic potential of this "factor" will have achieved even more therapeutic goals in the treatment of other degenerative diseases, and all thanks to the fertile legacy of Rita Levi Montalcini.

I would like to conclude this article by recalling her words when collecting her *honoris causa* degree at the Bicocca: "*My intelligence? More than mediocre. My only merits have been commitment and optimism*", but also worthy of note is what she was never tired of requesting from Italian governments: "*Do not jeopardize the future of all those young researchers who cultivate the hope to work in Italy*".

Researchers not only in the field of pure basic research, but also in that applied to odontology.

It is sufficient to consider the regenerative medicine in dentistry, with the studies on the use of stem cells, local modulators and the growth factors for tissue regeneration. Not least, research regarding odontological materials in continuous advancement and the technological applications, with particular attention to the development of innovative systems in the field of implantology and the advanced technologies applied to bone reconstruction.

Researchers who ask that their future "*doesn't exhaust in a big nothing*".

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