In remembrance of Professor Eugenio Müller (1933–2015)

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Published online: 3 May 2015

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With the death of Eugenio Müller world science has lost one of its more influential leaders. Eugenio, born in 1933, obtained his Medical Degree at the University of Milano in 1958. As a brilliant student, during the University years, he had been working first in the Department of Anatomy and subsequently in the Polyclinic Medical Center. After graduating, he followed a Postgraduate Course in Endocrinology and Metabolic Diseases at the University of Torino and joined the Institute of Pharmacology of the University of Milano, which became, with growing success and responsibilities, his home for the rest of his scientific life.

As it was traditional in those times, the first publications of Eugenio appeared in several Italian medical journals. His first international paper (Growth hormone-releasing activity of hypothalamic extracts at different ages) appeared in *Endocrinology* (volume 77, pages 241–246) in 1965. The co-authors were Antonio Pecile and myself. The paper described the presence, in the hypothalamus of the rat, of a principle which was able to decrease the content of growth hormone (GH) in the pituitaries of recipient rats as measured by “the tibia test” method. At that time, it was obviously impossible to measure pituitary hormones directly in blood. The paper also suggested that the principle involved was disappearing in the hypothalamus of old rats. These experiments were obviously performed to investigate the validity of the hypothesis, formulated by Geoffrey Harris, that the anterior pituitary is under hypothalamic control and that this control is mediated by the production of several principles, specific for each anterior pituitary

hormone, transported to the gland via the pituitary portal vessels. At that time, there were discussions on the existence of a specific corticotropin releasing factor (CRF) which would cooperate with vasopressin in stimulating the release of ACTH, and of possible factors controlling, respectively, the secretion of pituitary luteinizing (LH) and thyrotropic (TSH) hormones. The two hypothalamic factors were referred to as LRF and TRF. Eugenio’s paper was the first to suggest that a similar mechanism might be operating also for the control of the secretion of GH. This paper put Eugenio immediately on the fore front in the new field of neuroendocrinology.

After having clarified, in subsequent experiments, that the GH releasing activity of the hypothalamus was not linked to the presence of known neurotransmitters (posterior pituitary hormones, adrenergic and cholinergic principles, etc.), Eugenio decided to apply for an NIH scholarship which allowed him to go to work, as a Postdoctoral Fellow, at the “Endocrine and Polypeptides Laboratory” created by Andrew V. Schally in new Orleans. As every endocrinologist knows, Schally received the Nobel Prize in Medicine and Physiology for the structure of LHRH in 1978, sharing it with Roger Guillemin for the structure of TRH. It is interesting to recall that the structure of GHRH was eventually obtained by Wiley Vale and his co-workers in 1982. During his stay in New Orleans, Eugenio was extremely productive and published more than 10 original papers in very qualified Journals. Obviously, he became one of the most respected friends of Andrew Schally.

After his return to Italy, Eugenio Müller was promoted to the role of Assistant Professor (1967), a position that provided him the first permanent salary of his life. In 1975 he became Full Professor of Pharmacology at the University of Cagliari in Sardinia, but was allowed to maintain his laboratory in Milano, where, in the meantime, he had been joined by a growing group of qualified students and

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Postdoctoral Fellows. In 1980 he was asked to become Professor of Chemotherapy and Pharmacology at the Medical Faculty of the University of Milano. After the conversion of the original Institute into the Department of Pharmacology, Chemotherapy and Medical Toxicology, he became Director of this new structure for several terms of service (1988–1994).

The load of teaching and administrative responsibilities did not interfere too much with his devotion to research, which continued to be the illuminating center of his professional interests. GH remained “his” hormone but, in subsequent years, he became interested also in the mechanisms controlling the secretion of prolactin. In this new area, he was very influential in elucidating the mechanism(s) of action of several dopaminergic drugs still in use for the medical treatment of prolactinomas and the ensuing infertility.

In those years he also started with several clinical friends a fruitful collaboration which rapidly allowed to transfer to humans most of the results obtained in animal experiments, consequently enabling the development of innovative drugs for the diagnosis and therapy of disturbances of the somatotrophic axis. As an example we may recall the demonstration that, in acromegalic patients, dopaminergic drugs decrease (and do not stimulate like it happens in normal people) the secretion of GH. These observations prompted the introduction of dopaminergic drugs for the medical treatment of acromegaly.

Eugenio must also be remembered for the successful campaign he started, very early in his career, for creating a Pituitary Bank to collect human pituitaries for the extraction of human (hGH) to be used to treat hypophyseal

dwarfism. Of significant interest are also his studies on psychiatric diseases linked to alimentary problems (e.g., anorexia nervosa) for which he proposed and developed several approaches for the early detection and, consequently, for a precocious therapy.

Because of his scientific success, Eugenio was requested to give his inputs to several national and international organizations. He was one of the creators of the Italian Society of Neurosciences and, personally, took on his shoulders the formation of a very diversified group of scientists for collecting modern information on “age-related cerebral defects”.

In addition to his original papers, he was also the author and/or the Editor of several volumes which have enriched the international neuroendocrine library.

The spirit of innovation, native in Eugenio, was the basis of his endeavors for more than half a century. But this was possible only because it was linked to deep and critical meditations, which were proper of his personality. His scientific honesty has been, and will continue to be, an example for everybody.

All the above explain why Professor Eugenio Müller was able to create a special school formed by all the co-workers who joined him from the beginning of his career. The number of his associates and Postdoctoral Fellows, both Italians and foreigner (coming from countries such as Spain, Israel, Mexico, Libano, Japan, and China), has increased during the years, creating, around him, a real scientific and dedicated family. Many of his associates are presently respected members of several faculties here and abroad.