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Obituary

Alberto Abbruzzese (1952–2011) Scientist who studied from amino acids to nanoparticles in anti-cancer therapy

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In the last 40 years, cancer research performed many steps forward to understanding the molecular basis of cancer, radically changing both diagnosis and treatment.

In this light, the regulation of protein synthesis machinery in the mechanisms of cell transformation was almost completely forgotten up to the last decades of 1900s. However, in the last 10 years data about the interaction between signalling and protein synthesis regulation have emerged and anti-cancer drugs raised against signalling components interacting with translational factors have reached the clinical setting (i.e. mTOR inhibitors). One of the most influential and prolific contributors in the study of relationship between translational and signal transduction factors was Alberto Abbruzzese, who died on 26 October at the age of 59. In the 1970s and early 1980s, Abbruzzese was involved in the study of the role of polyamines in the induction of cell transformation and in the regulation of proliferation of normal and eukaryotic cells. After his first studies in Italy at the School of Medicine of the University of Naples from 1983 to 1985, he reached the USA with a post-doctoral fellow position in Enzyme Chemistry Section of the Laboratory of Oral Biology and Physiology of the National Institute of Dental Research in Bethesda. He was involved in the study of the modifications induced by a polyamine (spermidine) on an initiation factor of protein synthesis, the eukaryotic initiation factor 5A (eIF-5A). Together with MH Park and J Folk, he found that the modification induced by spermidine on a lysine of eIF-5A caused the synthesis of a modified amino acid called hypusine that is located only on eIF-5A and that is essential for its function in protein synthesis. During these studies he found and characterized the enzymes responsible for this modification. In 1987, he came back in USA as visiting Associate at the same laboratory contributing to the discovery of the role of eIF-5A in the regulation of cellular transformation and proliferation pointing out that the inhibition of hypusine synthesis can affect cancer cell growth inducing retardation and/or complete arrest of cell cycle. In 1990s Abbruzzese was in Naples as an Associate Professor of Biochemistry and began to study the correlation between proliferative and survival signal transduction pathways and hypusine synthesis disclosing a new scenario in which cytokines, such as Interferon alpha, can block cell proliferation through the inhibition of hypusine synthesis in eIF-5A. During these years he found that the inhibition of hypusine synthesis in eIF-5A can potentiate the growth of inhibition and apoptosis induced by Interferon alpha in cancer cells and that the hyperactivation of the epidermal growth factor (EGF)-mediated pathway can counteract this effect, thus highlighting a cross-talk between proliferative signalling and the activity of protein synthesis factors. At the beginning of 2000 Abbruzzese reached the position of full professor of Biochemistry and participated to the identification of an escape pathway from apoptosis induced by interferons in cancer cells based on the overexpression and hyperactivation of the EGF-dependent pathway and on the Raf-dependent regulation of another factor of protein translation the eukaryotic elongation factor 1A (eEF1A). During the same years Abbruzzese focused his attention on the mechanisms of post-translational modifications of ras, a signalling factor downstream EGF and its receptor, and of the different ways to inhibit its isoprenylation. In details, he investigated the ras inhibitory activity of farnesyltransferase inhibitors, such as tipifarnib, and of farnesylpirophosphate synthase inhibitors, such as zoledronic acid (ZOL). Abbruzzese contributed to the setting of new pharmacological strategies based on the combination of ZOL and tipifarnib in the treatment of both human head and neck cancer and prostate adenocarcinoma. The last years of Abbruzzese were dedicated to the study of the nanotechnological modification of ZOL, which was performed in order to improve ZOL pharmacokinetic profile. These studies led to the deposit of patents of two different formulations of ZOL. These new drugs will be developed in the next years for the therapy of human cancers.

He also contributed to the development of the Department of Biochemistry and Biophysics of the Second University of

Naples and gave an important supply to the organization of educational programs at the School of Medicine of Naples. He took part to the Administrative Board of the Second University of Naples contributing to the building of a new Campus in Caserta.

Apart from his enduring efforts to an unprecedented era of cancer research, Abbruzzese trained a host of graduate students and postdoctoral fellows, many of whom have had notable scientific careers of their own. Abbruzzese had much to be proud of during his relevant scientific career. But perhaps his most enduring legacy will be his inspiration and nurturing of a generation of scientists who revered him for his sagacity, and for his warmth and quiet support. All his friends will remember him as a brother in life and science and they hope he will continue to help them from the place where he is now.

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