



On November 21st 2021 in Florence Giancarlo Pepeu, Emeritus Professor of Pharmacology at the University of Florence and Hon. Fellow of the British Pharmacological Society, suddenly passed away leaving family, friends and colleagues with the feeling of a very strong loss.

Born in Milan in a family with long Hapsburg roots (his father graduated in Medicine in Vienna), he graduated in Medicine in Florence (1954) and soon entered into an academic career that spanned many decades. A very important phase of his scientific growth were the years he spent at the Department of Pharmacology of Yale University where he started his love and passion for Neuropharmacology, a subject that accompanied him for the rest of his life. His early appointments were at the Universities of Sassari (Sardinia), Pisa and Cagliari where he held the chair of Pharmacology up to his 1974 appointment as Professor Pharmacology at the Faculty of Medicine of the University Florence, a post he vacated on his retirement on 2005, though continuing his research activity until recently as shown by his last paper published 3 years ago. In Florence, for many years, Giancarlo Pepeu was head of the Pharmacology Department and Dean for research and international relations. He received many international prizes and accolades for his research and was a former president of the Italian Pharmacological Society.

In the late fifties and early sixties several labs around the world developed studies of new brain neurotransmitters like glutamate and GABA alongside transmitters such as acetylcholine (ACh) and biogenic amines known to have major effects on the autonomic nervous system. At Yale Giancarlo Pepeu started his love affair with ACh working on whether psychotropic drugs can alter ACh concentrations and its release as a mechanism of action underlying EEG and behavioral changes. With Nick Giarmenou he showed that antimuscarinic drugs like atropine and scopolamine decreased the level of ACh in the cerebral cortex, suggesting this phenomenon may be responsible for the amnesic action of these drugs (Br J Pharmacol Chemother, 1964, 23,123-130). In a seminal paper published in Br J Pharmacol Chemother. 1967 ;31:66-73

together with A. Bartolini, he demonstrated the basic properties of ACh release from the cerebral cortex, thus laying the platform for a series of further studies of drugs and afferent inputs from subcortical structures modulating this process. In Florence Giancarlo Pepeu's interest strongly developed his studies of ACh release in vivo and in vitro and extended them to investigations into the release of glutamate, GABA and adenosine. Giancarlo Pepeu's work clearly indicated that cortical networks operating via complex neurotransmitter interactions are responsible for drug effects on memory. His later activity turned to the involvement of central cholinergic pathways in the pathophysiology of Alzheimer's disease and was at the forefront of research demonstrating the principal role of neuroinflammation in animal models of this disease.

Giancarlo Pepeu was a highly productive scientist as he published over 300 papers, edited several books and was on the editorial board of many international journals. His own personal role in research was always intense: he loved to be in his lab and even published his work as a sole author in *Nature* 1963 (Nov 30;200:895). He trained many students and postdocs who went on to important academic posts or industrial roles. He was also a passionate teacher who started his lectures of Pharmacology from the original experimental data to explain the drug mode of action and therapeutical applications.

The scientific legacy that Giancarlo Pepeu has left us is based on the fundamental pillars of his academic personality. The first one is the importance of maximal experimental rigor with well-planned research protocols, very careful observations and measurements, and critical evaluation of different hypotheses for data interpretation. The second one is the firm belief that research must be based on international collaborations that should operate bidirectionally with exchange of people and ideas between labs as demonstrated by the flow of Italian as well as foreign scientists coming to work in his lab in Florence.

Following these principles will be the best way to remember Giancarlo Pepeu as a great contributor to Pharmacology. Giancarlo Pepeu is survived by his wife Ileana to whom we express our condolences.

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