Editorial

On rat brain pumps and persistence: Dr. Stylianos Tsakiris as a brain researcher and mentor

Apostolos Zarros

Institute of Cancer Sciences, University of Glasgow, Glasgow, Scotland, UK

Correspondence to: Dr. Apostolos Zarros, physician, MRes, PhD, PhD. Lab 112, L1, Wolfson Wohl Cancer Research Centre, Institute of Cancer Sciences, University of Glasgow, Glasgow, G61 1QH, Scotland, UK. Email: azarros@gmail.com; apostolos.zarros@glasgow.ac.uk.

Received: 17 September 2019; Accepted: 09 October 2019; Published: 01 November 2019.

doi: 10.21037/arh.2019.10.01

View this article at: http://dx.doi.org/10.21037/arh.2019.10.01

This focused issue of the *Annals of Research Hospitals* is dedicated to Dr. Stylianos Tsakiris: a brain researcher, university teacher and mentor who retired as Associate Professor of Physiology after serving the academic community of the National and Kapodistrian University of Athens for more than 35 years. Dr. Tsakiris has taught physiology to undergraduates in medicine, dentistry and pharmacy, and has worked in a systematic manner on cellular physiology, with emphasis on the mechanisms through which metabolic diseases, oxidative stress, heavy metals and ageing affect the functionality of critical enzymatic parameters of the cell membrane. His published work includes more than 120 articles indexed in PubMed, and several other published works. This issue honours not only his scientific contribution as a cellular physiologist, but also the mentorship that many of us enjoyed and treasure.

Dr. Tsakiris was born in 1950 in Keratsini, Greece. He studied natural sciences at the National and Kapodistrian University of Athens, before fulfilling his military duties during a troublous period for both Greece and Cyprus (1973–1975). In 1976 he gained a scholarship that allowed him to undertake doctoral studies at the Nuclear Research Centre "Demokritos" under the supervision of Dr. George Akoyunoglou. His PhD thesis on the dynamic regulation of the photosynthetic membrane of the common bean (*Phaseolus vulgaris*) chloroplasts was successfully defended at the Aristotle University of Thessaloniki in 1982. Later that same year, Dr. Tsakiris was appointed as a Lecturer at the Medical School of the National and Kapodistrian University of Athens, embarking on a 35-year-long journey of research and teaching at the Laboratory of Physiology, where he was subsequently promoted to Assistant Professor and Associate Professor of Physiology (1996 and 2003, respectively).

As a member of staff in a historical and research-oriented department that is the Laboratory of Physiology (formerly known as "Laboratory of Experimental Physiology"), Dr. Tsakiris developed an interest in cellular physiology and rapidly moved on in establishing his own research projects. In his relatively small lab space that could barely fit four people at the same time, he established an array of neurochemical techniques that would be systematically employed in his fascinating projects. Ageing, neurodevelopment, oxidative stress, exercise, toxic and metabolic encephalopathies, inborn errors of metabolism, would become some of the recurring themes of his research. Of particular importance has been his work on sodium-potassium adenosine triphosphatase (Na^+,K^+-ATPase); a major consumer of adenosine triphosphate (ATP) in the brain that maintains the neuronal membrane potential, regulates neuronal excitability and can alter the uptake and release of major neurotransmitters in response to simple or complex external stimuli. Commonly referred to as "the brain pump", Na^+,K^+-ATPase is now considered as a key transmembrane enzyme (EC 3.6.3.9, formerly EC 3.6.1.3) for the assessment of brain injury following acute and chronic toxic and metabolic insults; a concept that Dr. Tsakiris began to explore quite early in his career (1,2) by studying the enzyme's activity—its most informative, sensitive and technically-challenging parameter. He did so along with other neurochemical parameters (such as the activity of acetylcholinesterase; AChE), and by employing translationally-sound *in vitro* conditions aiming to simulate

clinical conditions such as phenylketonuria (3) and galactosaemia (4), as well as by setting up collaborations that would provide him access to brain tissue from animals subjected to experimental interventions of varying complexity (5-10).

Dr. Tsakiris had a prolific collaboration with Dr. Kleopatra Schulpis of the Institute of Child Health (Athens), as well as with members of staff of the Laboratory of Experimental Pharmacology of the Medical School of Athens, such as Dr. Haris Carageorgiou and Professor Charis Liapi. Dr. Schulpis played a key role in defining the *in vitro* conditions employed for the simulation of inborn errors of metabolism on rat synaptosomal membranes (4,11), and she facilitated access to patient blood samples that led to the publication of seminal papers (12,13). Noteworthy are also the projects that Dr. Carageorgiou led on the neurotoxic effects of cadmium (14) and hypothyroidism (15) on the adult rat, both followed up by projects shifting the focus from adulthood to neurodevelopment, for which Dr. Tsakiris collaborated with Professor Liapi (16,17). Moreover, a series of projects designed and led by Professor Liapi on the neurotoxic effects of dietary-induced choline-deprivation in neurodevelopment (18) as well as in the absence (19) and presence of comorbidities such as diabetes (20) in adulthood, resulted in the characterization of several novel *in vivo* disease models in rats.

In parallel to the aforementioned projects, Dr. Tsakiris has worked on the *in vitro* neurotoxic effects of aspartame and its metabolites on the postnatal rat hippocampus (21), on the effects of forced swimming on crucial rat brain enzyme activities (22), as well as on a number of projects focusing on membrane-bound enzymatic modulation in athlete- (23) and patient-derived (12,13,24) erythrocytes. Although interested in the improvement of the teaching of physiology (25) and a driving force behind the elective course of "Physiology of Ageing" offered to undergraduate medical students, Dr. Tsakiris would commonly self-identify solely as a researcher.

His dedication in maintaining high standards in his research practice has not obstructed him from introducing an important number of undergraduate medical students to translational research, and from successfully supervising a significant number of doctoral (PhD) projects. In recent years, this dedication took the form of unwavering persistence when a promotion to full professorship became unlikely and retirement loomed.

A nightmare for procrastinating administrators on the other end of the line, humble and hard-working, Dr. Stylianos Tsakiris has also been a caring and fair mentor for all of us who were fortunate to work under his supervision. To those of us who systematically volunteered as undergraduate research assistants in his lab, co-authorship on publications was assured, and his analytical, tedious and reliable research practice would make a lasting impression. Dr. Tsakiris has been an attentive and encouraging mentor to his students, making sure that we would not only gain insight into the research performed, but we would also have access to material that would broaden our understanding of the translational reasoning behind the witnessed work.

I write on behalf of all contributors in affirming that his legacy is inspiring, and that this Honorary Issue serves as a token of gratitude for his work and mentorship.

Acknowledgments

This is the editorial for the focused issue entitled "Molecular Functions in Disease and their Translational Interpretation: an Honorary Issue for Dr. Stylianos Tsakiris". I am grateful to the journal's editorial staff as well as to all contributing authors and reviewers. I am particularly grateful to Professor Michael Koutsilieris (Director of the Laboratory of Physiology at the Medical School of the National and Kapodistrian University of Athens) for his support.

Footnote

Conflicts of Interest: The author has no conflicts of interest to declare.

Ethical Statement: The author is accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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doi: 10.21037/arh.2019.10.01
Cite this article as: Zarros A. On rat brain pumps and persistence: Dr. Stylianos Tsakiris as a brain researcher and mentor. Ann Res Hosp 2019;3:16.

