



Outstanding women scientists who have broadened the knowledge on biological photoreceptors-II

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Abstract

This part II is a continuation of the article published in *Photochemical and Photobiological Sciences* (2023) 22, 2799–2815, <https://doi.org/10.1007/s43630-023-00487-1>, which should be considered a work in progress. Now, two female scientists who have worked on different aspects of chronobiology, plus a younger colleague who recently and too prematurely died, are incorporated to the list of outstanding women who have expanded the knowledge in the field of biological photoreceptors.

Graphical Abstract



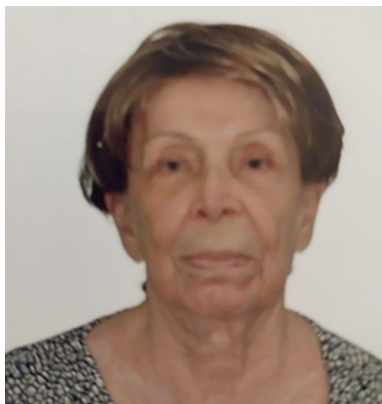
1 Ana Maria de Lauro Castrucci

Ana Maria Castrucci was born in São Paulo (Brazil) in 1948 and graduated in biological sciences at the University of São Paulo in 1969. She obtained her master's degree in 1973 and PhD degree in physiology in 1974 from the same university. Her post-doctoral stay in Prof. Mac Hadley's laboratory at the University of Arizona (USA) shaped her vocation as a comparative physiologist. Since 1992 until her retirement

in 2001, she was Full Professor at the University of São Paulo (USP) and until 2022 a Senior Professor at the Institute of Biosciences of the same University. Since 2022, she is Professor Emeritus from the USP. Ana Maria Castrucci has studied the regulation of gene expression and proteomics of opsins, clock genes and clock-controlled genes by light, temperature and hormones, and analyzed their signaling mechanisms in extra-ocular organs of crustaceans, fish, amphibians, birds and mammals.

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In 2002, Ana Maria Castrucci, together with Ignacio Provencio and Mark Rollag from the University of Virginia (USA), reported the discovery of an expansive photoreceptive 'net' in the mouse inner retina. The net was visualized by using an antiserum against melanopsin, a likely photopigment. This immunoreactivity was evident in a subset of retinal ganglion cells that morphologically resemble those that project to the suprachiasmatic nucleus (SCN), the site of the primary circadian pacemaker. The photoreceptive net is anatomically distinct from the rod and cone photoreceptors of the outer retina, and it was stated that it may mediate nonvisual photoreceptive tasks such as the regulation of circadian rhythms [1].

Later, Ana María Castrucci and his group in Brazil reported that, thanks to the presence of melanopsins, the skin cells of fish and amphibians are directly responsive to light. In amphibians, the response may be the migration of pigment granules within the pigment cell, causing a change in skin color, such as darkening [2].

In an interview with FAPESP, the funding agency of the State of São Paulo, Ana Maria Castrucci said: “In non-mammalian vertebrates, we showed that photons interact with melanopsins and trigger cellular signaling. This signaling is a cascade of events similar to that produced by light in the retina of mammals”. She added: “It is an evolutionarily conserved pathway. Melanopsin is an ancient opsin, in evolutionary terms. It is more primitive in that it does not form images: it is a photopigment only for the perception of light and dark. The fact that the cascade that light induces in the skin of these non-mammals is identical to the cascade that light induces in the human retina is an important finding in comparative physiology”.

In a recent publication, the group led by Ana Maria Castrucci, using functional proteomics associated with gene expression experiments, obtained data suggesting an important protective role of melanopsin (OPN4) in regulating skin physiology in the presence and absence of UVA

radiation [3]. They also demonstrated that melanopsin OPN4 is essential for UVA-induced murine pigmentation, signaling through the calcium calmodulin kinase CaM KII, nitric oxide (NO) and cyclic GMP [2]. Ana María Castrucci and co-authors revised recently the literature on the general role of opsins in skin physiology as well as in melanoma cancer [4].

Ana Maria Castrucci has published more than 120 papers in referred journals and has supervised numerous graduate students and post-doctoral fellows; she has certainly been the driving force for the studies on nonvisual photopigments in non-mammalian vertebrates in Brazil and Latin America. She is a member of the Brazilian Academy of Sciences, the Academy of Sciences of the State of São Paulo as well as of the Latin American Academy of Sciences. In 2005 she was awarded the National Order of Scientific Merit of the Minister of Science and Technology of Brazil.

2 Jennifer Loros

Born in 1950, Jennifer Loros set out to understand the molecular mechanisms, whereby circadian clocks regulate biological processes. She did so by advancing the understanding of fungi in general and their responses to their environment. At a time when circadian control mechanisms were untouched, she pioneered systematic identification of clock-regulated genes as central to circadian output.

This yielded the first “*clock-controlled genes*” (ccgs) [5], thereby coining a universal term in the circadian lexicon: she led the study of *ccg* regulation [6–8]. In collaboration, she defined the identity and mechanism of the fungal circadian photoreceptor, WC-1, prototype for the principal blue light photoreceptor of the fungal kingdom [9] and was first to associate, in any organism, specific biochemical activities (DNA binding and transcriptional activation) with clock molecules (WC-1 and WC-2) [7] and to connect DNA damage to clock resetting [10], a signaling pathway conserved in mammals. She pioneered global analysis of light-responsive genes [7, 11], determined the mechanism for photoadaptation [12, 13] and used photobiology to probe fungal pathogenesis [14].

Federally funded in the USA as the principal investigator on her own research grants from 1985 until 2022, she has published 155 articles and co-authored “*Chronobiology: Biological Timekeeping*” [15], a widely used textbook on chronobiology and circadian rhythms.

For 15 years, Loros served as the course director and as a lecturer for the year-long core “Biochemistry, Cell, and Molecular Biology” course for the Molecular and Cellular Biology graduate Program at Dartmouth. She has hosted numerous undergraduates in her laboratory, trained 18 graduate students, and 22 out of 41 of her post-doctoral fellows

have entered faculty positions, now holding positions ranging from assistant professor to department head and institute director. In 2019, she was awarded the Graduate Faculty Mentoring Award from Dartmouth.

She has chaired and/or served on numerous NSF and NIH study sections and external advisory boards, including the Fungal Genetics Stock Center (2008 to present), as an associate editor of *GENETICS* (1996–2011) and the *Journal of Biological Rhythms* (2000–present). She was awarded the Aschoff's Rule Award (1996), received MERIT (2001) and Creativity (1998) Awards from NSF, was elected AAAS Fellow (2006) to the American Academy of Microbiology in 2013, and to council of the AAAS in 2016, and received the Pioneer Award from the Society for Research on Biological Rhythms in 2021 and the B.O. Dodge Award, delivering the Dodge Lecture in 2023.



3 Ulrike Alexiev

Ulrike Alexiev was born in 1964 and unexpectedly died on December 29th, 2023, when she was at the height of her very productive scientific life. This short biography is a homage to her multifaceted life. Joachim Heberle and Holger Dau [16] review in the recent obituary: “After completing her diploma studies (1983–1988) in biophysics at the Humboldt University Berlin and working at the Max Delbrück Center in Berlin-Buch, Ulrike joined the Department of Physics at the Freie Universität in 1990 as a doctoral student, where she received her doctorate in 1994 under Prof. Maarten P. Heyn. During her doctorate, she worked closely with the laboratory of Nobel Prize winner Har Gobind Khorana (MIT, USA)..... Her dissertation was awarded the Tiburtius Prize of the Berlin universities.”

“After research stays at the University of Virginia (USA) and the Massachusetts Institute of Technology (MIT), she completed her habilitation in biophysics at the Department of Physics in 2002.” Heberle and Dau: “Ulrike's field of research was molecular biophysics with a focus on

biological photoreceptors. This research began with bacteriorhodopsin and led via rhodopsin and channelrhodopsin to phytochromes.” “Ulrike also became increasingly interested in biomedical issues...” “Based on her interdisciplinary expertise, she and her colleagues successfully operated molecular genetics laboratories at the Department of Physics. Her particular methodological biophysical expertise lied in the use of fluorescence probes for spectroscopic, imaging and time-resolved methods, which has been reflected in numerous publications” [16, 17].



An important review on the knowledge acquired on rhodopsins by using fluorescence spectroscopies, exemplified by the results of their own laboratories, was written by Ulrike Alexiev and David Farrens [18]. A recent publication by several laboratories, including Ulrike's, brings better understanding of the impact of the transmembrane voltage on retinal protein dynamics and fluorescence [19]. Another multilaboratory publication on a canonical phytochrome produced information on the role of protons in controlling the structure and function in these photosensors [20]. More recently, the group of Ulrike Alexiev, in collaboration with colleagues at the Justus Liebig University in Giessen, combined mutations known to enhance fluorescence in the cyanobacterial phytochrome Cph1, to derive a series of highly fluorescent variants from near-infrared fluorescent proteins (NIR-FPs) engineered from biliverdin-binding bacteriophytochromes. The obtained variants, with fluorescence quantum yield exceeding 15%, have the potential to be successfully used in *in situ* imaging [21].

Heberle and Dau [16] add: “Ulrike's outstanding research achievements and her wide-ranging interest in various fields of research have led her to become a member of an extraordinary number of Collaborative Research Centers (or Networks)”. She was not only a founding member of the SFB (special research network of the German Research

Foundation, DFG): “Protonation Dynamics in Protein Function”, but also the dedicated head of its graduate school (Research Training Group) for the last 11 years. Supporting younger scientists was always particularly important to Ulrike. In addition, she was deputy spokesperson of the research network “Structure and Function of Membrane Receptors” and project leader in the research networks “Nanocarriers: Architecture, Transport and Targeted Delivery of Drugs for Therapeutic Applications” and “Dynamic Hydrogels at Biological Interfaces”, all financed by the German Research Foundation (DFG).

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Declarations

Conflict of interests The author states that there is no conflict of interest.

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