SEMINAR CYCLE

of the PhD in Neuroscience of Turin

8th Appointment

Prof. Fabio Benfenati

"A membrane-targeted photoswitch restores physiological retinal processing in the degenerate retina"

25th October 2024 h 2:00 PM-3:00 PM

The lecture will last 1 hour and it will be followed by discussion

Host: Prof. Serena Bovetti

Seminar Room, NICO - Neuroscience Institute Cavalieri Ottolenghi, Azienda Ospedaliero-Universitaria San Luigi Gonzaga; Regione Gonzole, 10 Orbassano

Link: https://bit.ly/3TPBKCz

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PROF. FABIO BENFENATI

Prof. Fabio Benfenati is graduated in Medicine and specialized in Neurology. He began his research path at the Department of Neuroscience of the Karolinska Institutet in Stockholm and at the Rockefeller University in New York. Prof. Benfenati has been full professor of Neurophysiology at the Faculty of Medicine of the University of Genoa since 2000 and Director of Research at the Italian Institute of Technology (IIT) since 2006. Within IIT, he founded the Department of Neuroscience and Brain Technologies and currently coordinates the Center for Synaptic Neuroscience and Technology. Prof. Benfenati is the author of over 400 scientific articles in international peer-reviewed journals, including several articles in Science, Nature and Cell journals, with an h-index of 81 and over 24,000 citations. He is co-inventor of 5 patents. He is currently President of the Federation of European Physiological Societies and member of the Council of Scientists of Human Frontiers Science Program Organization. In 2024 he won the Feltrinelli Prize of the Accademia Nazionale dei Lincei for Physiology and Neuroscience.

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ABSTRACT

The lack of effective therapies for visual restoration in Retinitis pigmentosa and macular degeneration has pushed the scientific community to pioneer therapeutical strategies to replace dead photoreceptors, including optogenetics and retinal prostheses. However, the resulting visual restoration is poor. Here, we show that a recently characterized membrane-targeted photoswitch, Ziapin2, is capable of reinstating, in degenerate retinas, the complexity of the physiological responses to light stimuli that are implemented by a healthy retina. We tested the ex vivo effects of Ziapin2 on blind retinal explants from rd10 mice and RCS rats, two distinct genetic models of photoreceptor degeneration, by recording light-evoked responses from retinal ganglion cells (RGCs) with patch-clamp and high- density multielectrode arrays. Thanks to its dual effect on intrinsic excitability, Ziapin2 reinstated brisk and sluggish ON, OFF, and ON-OFF responses in RGCs evoked by full-field or pattered stimuli, accompanied by the reactivation of excitatory and inhibitory conductances impinging on RGCs. When tested in vivo, a single intravitreal injection of Ziapin2 in fully blind 6-month-old rd10 mice restored light-driven behavior and optomotor reflexes, with a concomitant activation of RGC populations similar to sighted animals. The results indicate that Ziapin2 is a promising molecule for reinstating physiological visual responses at late stages of retinal degeneration, irrespective of the mutation causing degenerative blindness.

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