Light-triggered ion channel regulation

Summary

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Supervisor:	PD Dr. Rainer Schindl
Availability:	This position is available.
Offered by:	Medical University of Graz
Application deadline:	Applications are accepted between August 01, 2018 00:00 and September 23, 2018 23:59 (CEST)

Description

Background: Optical techniques represent a powerful tool to precisely control signaling of excitable cells for neuroscience application. Electrical responses of neurons can be triggered and shaped by light, and enables interventions to treat neurological and psychiatric diseases. Recently, we have generated and used organic semiconductors that can be stimulated by laser light pulses[1]. These semiconductors have the size of single cells with thin needles in nanometer dimensions. These needles function as perfect contact sites with the plasma membrane of living single cells. A laser light beam is then focused on the semiconductor structure in order to stimulate the attached cell. The electrical signals Induced by laser stimulation are recorded in the target cells with the patch clamp technique. Hence, the developed organic semiconductors present a powerful and novel tool to manipulate electrical activity of cells by light.

Alternatively, we design photopharmacological tools for activation of specific ion channels. Herein, lipid messengers are modified to enable conformational changes in cation conductances by light and thereby to induce cellular Ca^{2+} signals. Specifically, the lipid messenger diacylglycerol was chemically modified with a light-sensitive molecular switch that can be efficiently controlled by the wavelength of the applied light pulse[2].

Hypothesis and Objectives: Optical control of ion channels: The goal of this PhD thesis is to efficiently induce ion channel regulation, and specifically voltage-gated ion channels and neuronal signaling by light. The opto-tools will include photoactive organic semiconductors and light controlled lipid messengers. The patch-clamp technique allows visualizing electrophysiological cell responses in a millisecond time range. Specific, voltage-gated ion channel will be heterologously expressed in single living cells to record their activation efficiency due to attached organic semiconductors or incubated photo-lipid messengers by light pulse. Successful stimulation of ion channel recordings will then be extended to primary cultured neurons. These cells generate action potentials, a transient depolarization to send the activation signal to the axon. Hence, the long term goal is to induce neuronal stimulation for physiological applications. These opto-tools will be designed to trigger visual responses in retinal ganglion cells or the recovery of neuronal networks after traumatic brain injury.

Methodology: The PhD student requires motivation and patience to perform single cell patch-clamp recordings. Additonally, the work of the PhD student will include fluorescence imaging, cell culture and neuronal tissue preparation. Prospective students should be able to plan experiments independently and like to work in an interdisciplinary research team. The PhD candidates with a technical master degree are prefered. Strength of the research team is intense collaboration with leading laboratories ranging of organic chemistry, computer simulations to neurosurgery. Experiments will be performed at the institute for biophysics and with collaboration partners within the Medical University of Graz. Semiconductors will be provided by two international collaboration partners and the Isolation of neuronal cells and cell culture will be important to achieve live cell recordings in contact with semiconductor structures.

References:

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2. An optically controlled probe identifies lipid-gating fenestrations within the TRPC3 channel. M. Lichtenegger, O. Tiapko, B. Svobodova, T. Stockner, T. N. Glasnov, W. Schreibmayer, D. Platzer, G. G. de la Cruz, S. Krenn, R. Schober, N. Shrestha, R. Schindl, C. Romanin, K. Groschner, *Nat Chem Biol* 14, 396-404 (2018)

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