ELSC-ICNC Seminar: Baruch Minke

February 28, 2013

On the topic of: TRP channels: what are they, how they are activated and why are they important for understanding brain damage

ELSC & ICNC cordially invite you
to the lecture given by:

Baruch Minke
Departments of Medical Neurobiology, the Institute of Medical Research Israel-Canada (IMRIC), the Edmond and Lily Safra Center for Brain Sciences (ELSC)

On the topic of:

"TRP channels: what are they, how they are activated and why are they important for understanding brain damage"

The lecture will be held on Thursday, February 28, 2013 at 17:00, at ELSC-ICNC: Silverman Bldg., 3rd Wing, 6th Floor, Edmond J. Safra Campus

Light refreshments at 16:45

Abstract:

In Drosophila, a PLC-mediated signaling cascade links photo-excitation of rhodopsin to the opening of the Transient Receptor Potential (TRP) and TRP-Like (TRPL) channels. A lipid product of phospholipase C (PLC), diacylglycerol (DAG) and its metabolite(s), polyunsaturated fatty acids (PUFAs) may function as second messengers of channel activation. However, how can one separate between the increase in the above lipids, change in pH and PI(4,5)P2 depletion, when exploring the gating mechanism? To dissect PLC activation of TRPL into its molecular components, we used a powerful method which reduced plasma membrane associated PI(4,5)P2 in HEK cells, within seconds, without activating PLC. Upon addition of a dimerizing drug, PI(4,5)P2 was selectively hydrolyzed in the cell membrane without producing DAG, IP3, or calcium signals. We show that PI(4,5)P2 is not an inhibitor of TRPL channel activation. While PI(4,5)P2 hydrolysis combined with either acidification or application of DAG analogs failed to activate the channels, while PUFA did. A further insight on TRP channel gating came from our studies on the effects of anoxia on fly photoreceptors. Anoxia rapidly and reversibly depolarized the photoreceptors and induced Ca2+ influx into these cells in the dark. We further found that openings of the light sensitive channels, which mediate these effects, could be obtained by mitochondrial uncouplers or by depletion of ATP in photoreceptor cells while the effects of illumination and all forms of metabolic stress were additive. Effects similar to those found in wild type flies were also found in mutants with strong defects in rhodopsin, Gq-protein or...
phospholipase C, thus indicating that the metabolic stress operates at a late stage of the phototransduction cascade. Genetic elimination of both TRP and TRPL channels prevented the effects of anoxia, mitochondrial uncouplers and depletion of ATP thus demonstrating that the TRP and TRPL channels are targets of metabolic stress. These results shed new light on the properties of the TRP and TRPL channels by showing that a constitutive ATP-dependent process is required to keep these channels closed in the dark, a requirement that would make them vulnerable to metabolic stress. Since mammalian TRP channels are heavily expressed in the brain, neuronal death due to ischemia may involves activation of TRP channels.

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