Mon 12. Aug 2019
Time: 11:00 h

Institute of Biochemistry and Molecular Medicine (IBMM)
Seminar Room
Gertrud-Woker-Str. 5,
3012 Bern

Everybody is welcome

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This lecture is hosted by Prof. Christine Peinelt (IBMM).

NCCR TransCure Lecture in Biology
by Indu Ambudkar

STIM2 co-ordinates assembly and function of Orai1/STIM1 in specialized ER-PM junctions

Stromal interaction molecules (STIMs), STIM1 and STIM2, reside within the ER and undergo a conformational change that causes remodeling of the cytosolic C-terminal domain. As a consequence, STIMs multimerize and translocate to the cell periphery where the plasma membrane (PM) and ER are tightly apposed, which enables STIM-interaction with plasma membrane-PIP_2. Orai1 is recruited and activated by the STIM proteins at these ER-PM junctions. Orai1-mediated Ca^{2+} entry generates distinct spatial and temporal Ca^{2+} signals that are sensed and decoded by different sensors and effector proteins. STIM1 is a strong activator of Orai1 and loss of the protein eliminates channel function as well as downstream Ca^{2+}-dependent cell functions. STIM2 is induces weak activation of the channel and has been proposed to regulate resting $[Ca^{2+}]_i$ in cells. Further, due to the relatively low Ca^{2+} affinity of its EF-hand domain, STIM2 senses small decreases in $[Ca^{2+}]_{ER}$. Our previous findings demonstrated that STIM2 modulates the cell response to low stimulus intensities by promoting assembly of Orai1/STIM1 and facilitating STIM1 activation under conditions when $[Ca^{2+}]_{ER}$ is not low enough to activate STIM1. Despite its small contribution to SOCE, STIM2 has unique physiological relevance as loss of STIM2 in mice causes death within 4-6 weeks of age. Also, STIM2-deficient T cells have a small decrease in SOCE but display significantly greater decrease in cytokine production due to a defect in nuclear translocation of NFAT1. Our new findings regarding the role of STIM2 in regulation of Ca^{2+}-dependent gene expression and our previous data showing role of STIM2 in Orai1/STIM1 assembly will be discussed.

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