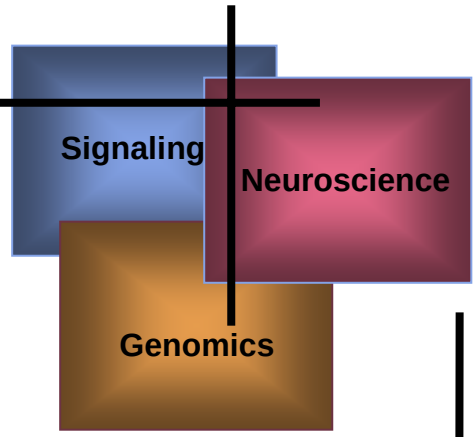
Department of Pharmacology



Proudly Presents the
Seminar Series:

Frontiers in Pharmacology

Reinhold Penner, MD, Ph.D.

Center for Biomedical Research
The Queen's Medical Center & University of Hawaii

"CRACking the molecular components of store-operated calcium entry"

Receptor-mediated Ca2+ signals are caused by inositol 1,4,5-trisphosphate-induced Ca2+ release from intracellular stores, followed by Ca2+ entry through plasma membrane Ca2+ channels that are activated as a result of store depletion. This process of store-operated Ca2+ entry has been extensively studied and the current mediating Ca2+ entry (termed Ca2+ release--activated Ca2+ current, or ICRAC) has been thoroughly characterized. However, the molecular components involved in this mechanism have been identified only recently, when extensive RNAi screens revealed stromal-interacting molecule (STIM1) and the CRAC Modulator CRACM1 (Orai1) as required components of store-operated Ca2+ entry and ICRAC. The single membrane spanning STIM1 protein likely senses ER Ca2+ levels by virtue of its luminal facing EF-hand domain and accumulates into ER puncta close to the plasma membrane in response to store depletion, whereas CRACM1 represents the pore-forming unit of the channel itself. Overexpression of both proteins is required to reconstitute store-operated CRAC currents and results in massive CRAC channel activation and store-operated Ca2+ entry in response to store depletion. The presentation will highlight the most recent advances in our understanding of the molecular components of store-operated Ca2+ entry.

Contact: Heike Wulff, Ph.D; email: *hwulff@ucdavis.edu*

Friday, January 26, 2007
2:00 pm (please note time change)

Auditorium (Room 1005) in GBSF