

SEMINAIRE

Dr. Michael Pusch

Biophysics Institute, Genova, Italy

Mardi 18 décembre 2018
à 12h15

Salle de séminaire n°107 au Bugnon 27

"Regulation of volume-sensitive LRRC8 channels by oxidation"

Abstract:

Most cells are able to regulate their volume upon a hypoosmotic extracellular challenge in a process called regulatory volume decrease (RVD). Key players in RVD are the ubiquitous volume regulated anion channels, VRACs. VRACs are heteromers composed of "Leucine-Rich-Repeat-Containing-8" (LRRC8) proteins containing the obligate LRRC8A (8A) subunit and one or more among the 8B-8E proteins. VRACs have long been known to be regulated by reactive oxygen species in many cell types but it was unknown if oxidation acts directly on the anion channel or on regulatory factors. We exploited our recently developed oocyte expression system to study direct oxidation effects on different subunit combinations. Interestingly, 8A-8E heteromers were dramatically activated by oxidizing reagents acting on intracellular cysteine residues, whereas 8A-8C and 8A-8D heteromers were inhibited by oxidation. Guided by recent cryo-EM structures we are in the course of identifying the residues responsible for the subunit-specific regulation of VRACs by oxidation.

Invité par : Dr. Stephan Kellenberger

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