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Seminar Title:

Unravelling the Mechanisms of Fight or Flight: It's All About the Neighborhood

Abstract:

Increased cardiac contractility during fight-or-flight response is caused by β-adrenergic augmentation of the cardiac $Ca_V1.2$ channels. It is assumed that this iconic regulation involves phosphorylation of $Ca_V1.2$ α_1/β-subunits. In transgenic murine hearts expressing fully PKA phosphorylation-deficient mutant α_{1C}/β subunits, this regulation persists, however, suggesting involvement of extra-channel factors. I will discuss our recent studies using peroxidase-catalyzed labeling in mice hearts expressing ascorbate peroxidase conjugated- α_{1C} or β_{2B} with multiplexed quantitative proteomics, which allowed tracking of thousands of proteins in proximity of $Ca_V1.2$. I will discuss how the $Ca_V1.2$ micro-environment is altered upon β-adrenergic stimulation, and how this alteration in the macromolecular complex is the mechanism by which β-adrenergic agonists stimulate $Ca_V1.2$.