The Doctoral Program

ION CHANNELS AND TRANSPORTERS AS MOLECULAR DRUG TARGETS („MolTag“)

is pleased to invite you to the following lecture

“Cell signaling and secretion in adrenal chromaffin cells: Specific roles for Na^+, K^+ and Ca^{2+} channel gating”

by Prof.Dr. Emilio CARBONE

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on: Thursday, May 18th, 05:00 pm (17:00)

at: UZA 2, Althanstr. 14, 1090 Vienna, LECTURE HALL 6

Abstract:. The chromaffin cells (CCs) of the adrenal medulla are the main source of circulating catecholamines (CAs) that regulate body responses to stressful situations. CAs are secreted in response to splanchnic nerve discharges, acetylcholine release and subsequent CCs depolarization associated with nicotinic and muscarinic receptors activation. Cell depolarization causes increased Ca^{2+}-entry through open voltage-gated Ca^{2+} channels and robust exocytosis from CA-containing vesicles. CCs depolarization occurs in various forms: as trains of single action potentials (APs) or as prolonged depolarizations, which originate AP trains in form of “tonic” or “burst” firing [1]. This “neuron-like” mode of firings of CCs is ensured by the expression of high densities of Ca^{2+}, Na^+ and K^+ channels that warrant rapid AP responses and sufficient Ca^{2+}-influx to drive CA secretion during basal or sustained stimulation.

Rat and mouse CCs express high densities of neuronal Cav1.3 L-type Ca^{2+} channels that activate at relatively low membrane potentials and are spatially and functionally coupled to Ca^{2+}-activated BK and SK channels [2, 3]. In this way, Cav1.3 channels control Ca^{2+} entry and cell excitability at potentials near rest and are thus critical to sustain spontaneous firing and CA release during basal conditions. Using KO [2, 3] and KI [4] Cav1.3 mouse models it has been possible to highlight the critical role of these Ca^{2+} channels in setting AP firing modes (tonic vs. bursts) and thus, in CA secretion. The functional role of burst firing is mostly evident during metabolic conditions in which the extracellular pH is lowered from 7.4 to 6.6 [5], mimicking muscle fatigue acidosis and the associated release of CA from the adrenal gland.

References: 1. Vandael, D.H., A. Marcantoni, and E. Carbone, *Cav1.3 Channels as Key Regulators of Neuron-Like Firings and Catecholamine Release in Chromaffin Cells.* Curr Mol Pharmacol, 2015. **8**(2): p. 149-61.; 2. Marcantoni, A., et al., *Loss of Cav1.3 Channels Reveals the Critical Role of L-Type and BK Channel Coupling in Pacemaking Mouse Adrenal Chromaffin Cells.* Journal of Neuroscience, 2010. **30**(2): p. 491-504.; 3: Vandael, D.H.F., et al., *Ca(V)1.3-Driven SK Channel Activation Regulates Pacemaking and Spike Frequency Adaptation in Mouse Chromaffin Cells.* Journal of Neuroscience, 2012. **32**(46): p. 16345-16359.; 4. Scharinger, A., et al., *Cell-type-specific tuning of Cav1.3 Ca2+-channels by a C-terminal automodulatory domain.* Frontiers in Cellular Neuroscience, 2015. **9**: p. 18.; 5. Guarina, L., et al., *Low pHo boosts burst firing and catecholamine release by blocking TASK-1 and BK channels while preserving Cav1 channels in mouse chromaffin cells.* J Physiol, 2017.

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