Exploring istaroxime effects on storage-operated calcium entry in non-cardiac cells

Metallo A.[1], **Volonterio L.**[1], Arici M.[1], Rocchetti M.[1]
E-mail: l.volonterio@campus.unimib.it
[1] University of Milano-Bicocca, Italy

Keywords: istaroxime, proliferation, sodium-potassium pump, SERCA, SOCE

Abstract:

Beside acting on heart as a safe inotropic drug due to the Na+/K+ ATPase (NKA) inhibition coupled with SERCA2a stimulation, istaroxime has been shown to possess anti-proliferative and anti-migratory properties towards cancer cells. This effect seems to depend on FAK dephosphorylation and transcriptional repression of ORAI1 and STIM1, canonical effectors of storage-operated calcium entry (SOCE), which was inhibited. My thesis aims to characterize istaroxime's influence on this calcium handling pathway in healthy non-cardiac cells. Experiments in isolated rat pulmonary artery smooth muscle cells (PASMCs) confirmed that the drug was able to reduce the amplitude of SOCE, both following chronic treatment and upon acute superfusion. Moreover, drug-induced SOCE inhibition was associated to significant reduction of resting calcium levels in PASMCs. Overall, the molecular scenario of SOCE inhibition by istaroxime is still unclarified; though istaroxime could in principle have otherunknown targets in addition to NKA and SERCA, involvement of NKA-dependent pathways (i.e. Src/FAK signalling) seems plausible.