

P005 AKAP-complex regulates the Ca^{2+} reuptake into heart sarcoplasmic reticulum

Birgitte Lygren^{*}, Cathrine R. Carlson^{*}, Katja Santamaria[§], Valentina Lissandron[‡], Theresa Mcsorley[§], Walter Rosenthal[§], Manuela Zaccolo[‡], Kjetil Taskén^{*} and Enno Klussmann[§].

^{}Biotechnology Centre of Oslo, University of Oslo, Norway,*

[§]Forschungsinstitut für Molekulare Pharmakologie, Berlin, Germany

[‡]Dulbecco Telethon Institute and Venetian Institute of Molecular Medicine, Padova, Italy

Phospholamban (PLB) is a key regulator of cardiac contraction and modulates sarcoplasmic reticulum (SR) Ca^{2+} sequestration by inhibiting the SR Ca^{2+} -ATPase (Serca2) in its dephosphorylated state. Upon beta-adrenergic stimulation which mediates cAMP-dependent protein kinase (PKA) phosphorylation of PLB Ser16, the inhibitory effect of PLB on the function of Serca2 is released. In failing hearts Serca2 has reduced Ca^{2+} -reuptake activity because PLB is just partly phosphorylated. We have identified an A-kinase anchoring protein (AKAP) in SR that is in complex with PLB and recruits PKA to its substrate. By peptide array mapping, the binding site in PLB was unveiled. Disruption of AKAP-PLB interaction leads to decreased PKA phosphorylation of PLB.