Al collegio docenti del Dottorato in Medicina Molecolare
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Introduction. Small ankyrin 1.5 (sAnk1.5) is the most abundant muscle-specific isoform of *ANK1* gene. sAnk1.5 is localized in the sarcoplasmic reticulum (SR) membrane and binds to the giant sarcomeric protein obscurin, tethering the SR around the myofibrils. Characterization of sAnk1.5 knockout (KO) mice showed a reduction of the longitudinal SR volume, responsible for Ca ions storage. With ageing, sAnk1.5 KO mice developed additional structural damages and were characterized by a reduced muscle contractile performance.
Ca^{2+}, in addition to its pivotal role in muscle contraction, also regulates several signaling pathways involved in metabolic processes, such as PI3K/AKT pathway, that is critical in regulating insulin dependent membrane translocation of glucose transporter GLUT4. Interestingly, recent studies indicate that sAnk1.5 can be consider a novel regulator of SERCA1, the main calcium pump in skeletal muscle.
Methods. Total protein lysates from gastrocnemius muscle were prepared from 4, 12 months old sAnk1.5 KO and WT mice either in basal condition and following insulin (1U/Kg) intraperitoneal administration. **Expression levels of p85α, AKT, pAKT(ser473), pAKT(Thr308), PTEN, FOXO1** and pFOXO(ser256) were then evaluated by western blot analysis.

Results. In 4 months old mice, we observed a significant increase of both phosphorylated forms of AKT in sAnk1.5 KO mice compared to WT in basal conditions. Accordingly, expression levels of PTEN were significantly decreased in sAnk1.5 KO mice with respect to WT mice. Expression levels of all proteins evaluated following insulin injection showed the same difference observed in basal conditions.
Protein expression levels from 12 months old mice did not show differences in sAnk1.5 KO mice compared to WT, in basal conditions. After insulin injection pAKT(ser473) was significantly increased in sAnk1.5 KO mice with respect to WT. Moreover, PTEN and **p85α levels were** significantly decreased in sAnk1.5 KO mice compared to WT.
To evaluate whether sAnk1.5 would regulate SERCA1 pump activity, measurements of Ca^{2+}-dependent ATPase activity and Ca^{2+} uptake activities of muscle membrane fractions isolated form sAnk1.5 KO mice and controls are now in progress.