UNIVERSITÀ DEGLI STUDI DI UDINE
hic sunt futura

Dott. CLARISSA GISSI
Prof. BRUNO GRASSI – Dott.ssa MARINA COMELLI
Email : gissi.clarissa@spes.uniud.it

Ph.D. course in :
Biomedical Sciences and Biotechnology

Increased MtCK and ANT in aging Pin1 KO mice as a basis of augmented ADP sensitivity of mitochondrial respiration

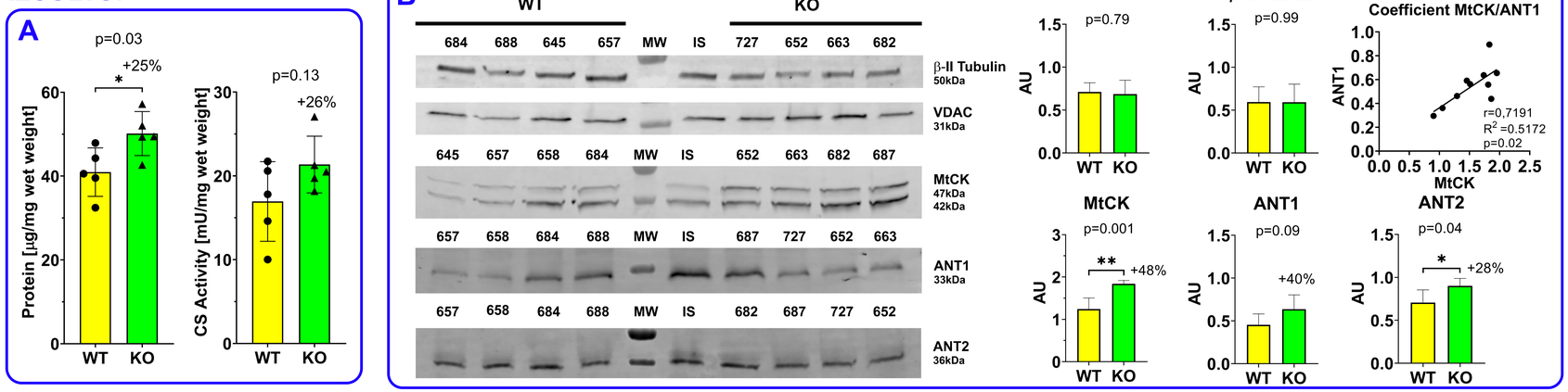
Gissi C.[a], Zuccarelli L.[a], Comelli M.[a], Brocca L.[b], Rossi M.[b], Battini R.[c], Uchida T.[d], Pellegrino M.A.[b], Bottinelli R.[b], Grassi B.[a], Molinari S.[c], Mavelli I.[a].

[a] Dept. of Medicine, University of Udine, Piazzale M. Kolbe 4, Udine, Italy; [b] Dept. of Molecular Medicine University of Pavia, Via Forlanini 6, Pavia, Italy; [c] Dept. of Life Sciences, University of Modena and Reggio Emilia, Via Campi 287, Modena, Italy; [d] Molecular Enzymology, Graduate School of Agricultural Science, Tohoku University, Miyagi 981-8555, Japan.

INTRODUCTION: Mitochondrial impairment associated to a severe motor neuron loss occurs frequently during aging, causing muscle wasting and sarcopenia. Pin1, Peptidyl-prolyl cis-trans isomerase NIMA-interacting 1, is a prolyl isomerase that binds to and isomerizes specific phosphorylated Ser/Thr-Pro motifs of target phosphoproteins, thereby affecting the stability and activity of numerous signalling proteins and transcription factors. Thus, Pin1 plays a crucial role in numerous cellular processes. Importantly, a role of Pin1 was recently suggested as a regulatory mechanism of the adult myogenesis[1].

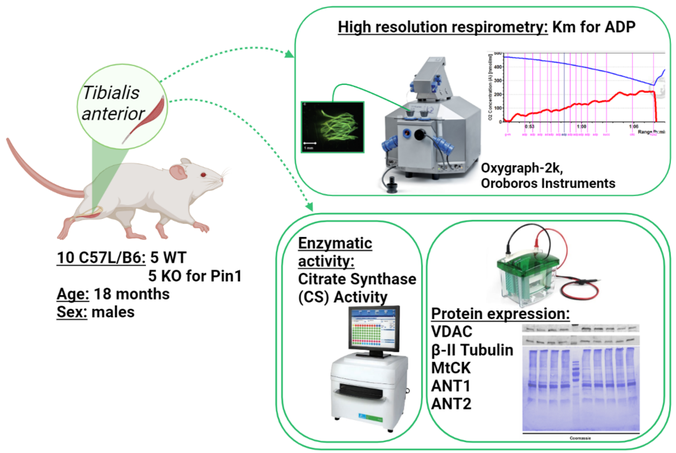
AIM: To assess the effects of Pin1 loss on mitochondria structural/functional aspects, in order to evaluate if they might counteract loss of skeletal muscle function in aging mice. To this aim, we quantified some proteins residing in different mitochondrial sub-compartments, as well as responsible for regulation of the ADP sensitivity of respiration, in the skeletal muscle of *in vivo* Pin1 KO mature adult mice.

RESULTS:



The increase observed in KO for CS activity, a mitochondrial matrix marker, mirrored the increment of the protein quantity in total muscle homogenates (**A**). The expression levels of VDAC and its interactor β-II Tubulin did not differ between KO and WT. Instead, higher expression levels in KO *vs.* WT were observed for MtCK, ANT1 and ANT2. The 40% increase of ANT1 expression did not result statistically significant, but a Pearson's correlation analysis revealed a moderate positive correlation between MtCK and ANT1 or ANT2 variations (**B**). The apparent Km for ADP decreased (increased ADP sensitivity of mitochondrial respiration) by 73% in KO compared to WT, although the difference did not reach the statistical significance. (* $p<0.05$; ** $p<0.005$)

EXPERIMENTAL DESIGN AND METHODS:



CONCLUSION: These preliminary data suggest that the selective increase observed in Pin1 KO for MtCK, ANT1 and ANT2 may explain the increased sensitivity of mitochondrial respiration to submaximal ADP, by favouring ADP recycling from the inter-membrane space to the matrix. The data also show that, while there was no change in proteins residing in the mitochondrial matrix and outer membrane, there was a selective increase in proteins associated to the inner membrane, suggesting a remodelling of such membrane improving mitochondria function.

REFERENCE: [1] A. Magli, C. Angelelli, M. Ganassi, F. Baruffaldi, V. Matafora, R. Battini, A. Bachi, G. Messina, A. Rustighi, G. Del Sal, S. Ferrari, S. Molinari, J Biol Chem (2010), 285(45), 34518-27.

ACKNOWLEDGEMENT: This work was supported by the Ministero dell'Istruzione dell'Università e della Ricerca, PRIN Project 2017CBF8NJ.