



METFORMIN REGULATES MYOBLAST DIFFERENTIATION THROUGH AMPK



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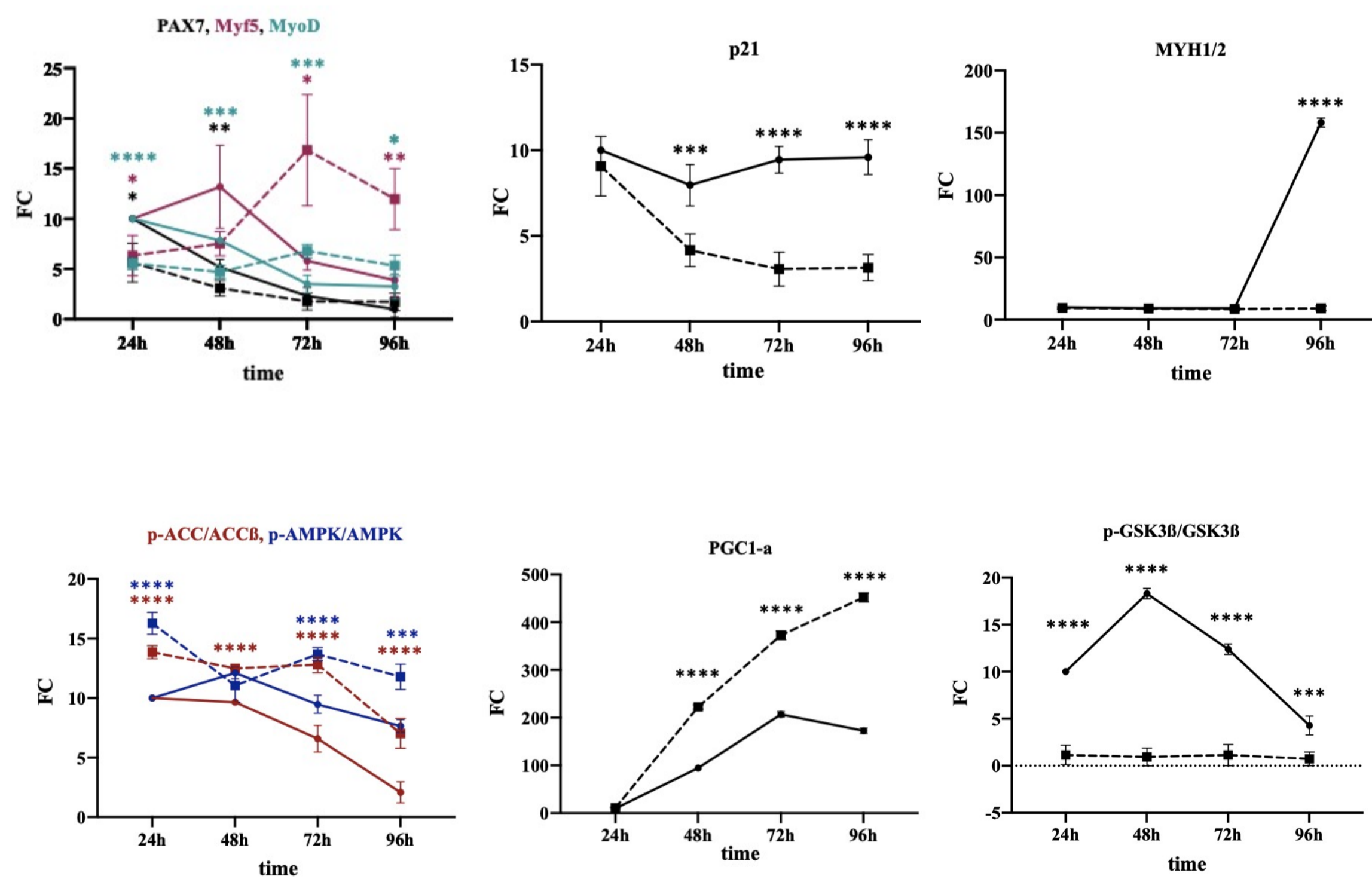
INTRODUCTION AND STATE OF ART

Metformin is an oral antidiabetic drug commonly used to treat type II diabetes, reducing insulin resistance and gluconeogenesis. Other pharmacological effects of clinical interest have been attributed to metformin, including anti-age effects on skeletal muscle and contrast to ischaemia-reperfusion cardiac injury. The underlying signaling cascade is not completely clear, although it has been demonstrated that the drug inhibits the Complex I of the mitochondrial respiratory chain, leads to AMP cellular accumulation and activates the cellular energy sensor AMP-Kinase. Moreover, an association between AMPK activation and inhibition of differentiation toward a muscle phenotype has been reported.

AIM

To investigate the effects of metformin (MET) on muscle differentiation process and on differentiated cells, using a specific cell line of immortalized murine myoblasts (C2C12) that differentiate into myotubes upon appropriate incubation.

10mM METFORMIN AFFECTS C2C12 DIFFERENTIATION PROCESS



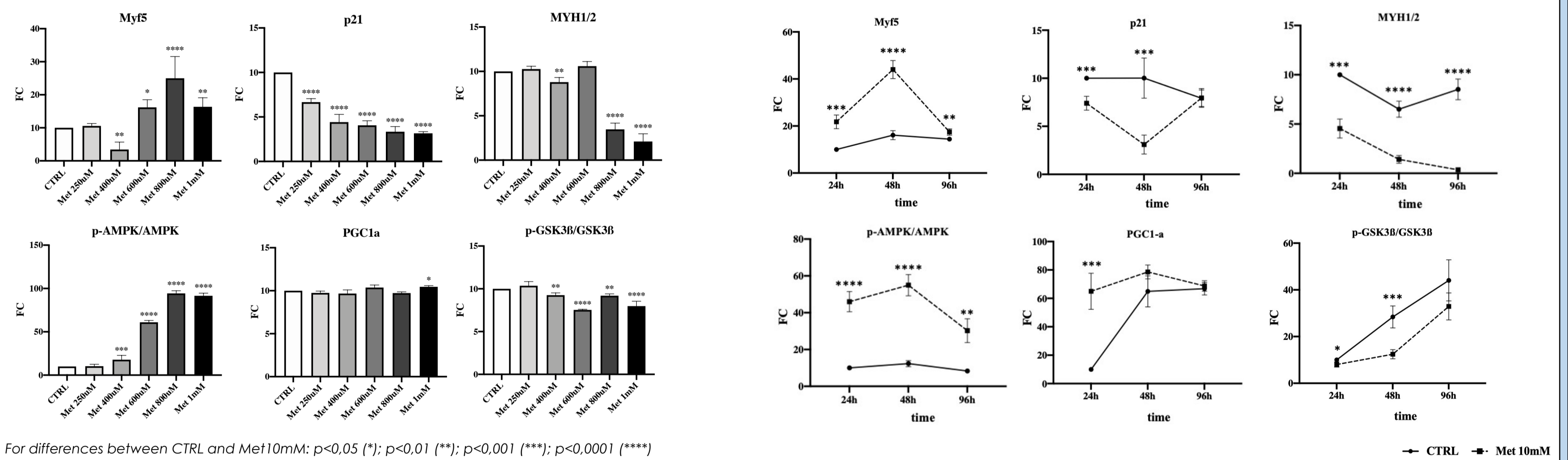
For differences between CTRL and Met10mM: p<0,05 (*); p<0,01 (**); p<0,001 (***)

→ CTRL → Met 10mM

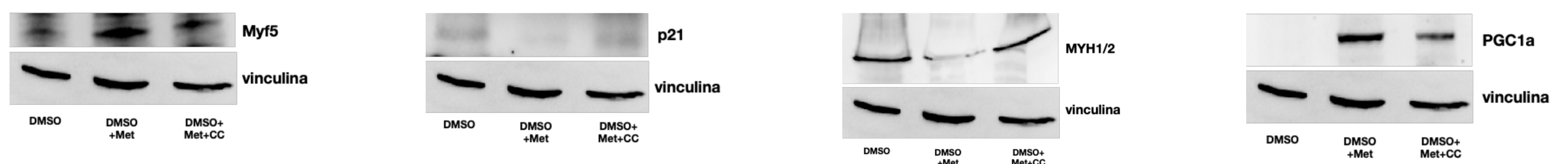
CONCENTRATION- AND TIME-DEPENDENT EFFECTS OF METFORMIN ON DIFFERENTIATED C2C12

Myotubes treated with 250uM, 400uM, 600uM, 800uM, 1mM metformin for 24h

Myotubes treated for 24h, 48h and 96h with 10mM metformin



MYOTUBES TREATED WITH 10mM METFORMIN IN PRESENCE OR ABSENCE OF 10µM COMPOUND C (Western Blot analysis)



Compound C reverses the effects of metformin analyzed until now

DISCUSSION and CONCLUSION

Our results confirm that metformin inhibits the myogenic differentiation from myoblasts into myotubes and we propose that metformin negatively affects myogenic differentiation through AMPK pathway.