SOCIETÀ ITALIANA DI FARMACOLOGIA

39° Congresso Nazionale della Società Italiana di Farmacologia

RICERCA
INNOVAZIONE
SOSTENIBILITÀ
APPROPRIATEZZA
FORMAZIONE

FIRENZE 20-23 NOVEMBRE 2019
PALAZZO DEI CONGRESSI

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Effetti della metformina e dell'esercizio aerobico sul muscolo scheletrico in un modello murino.

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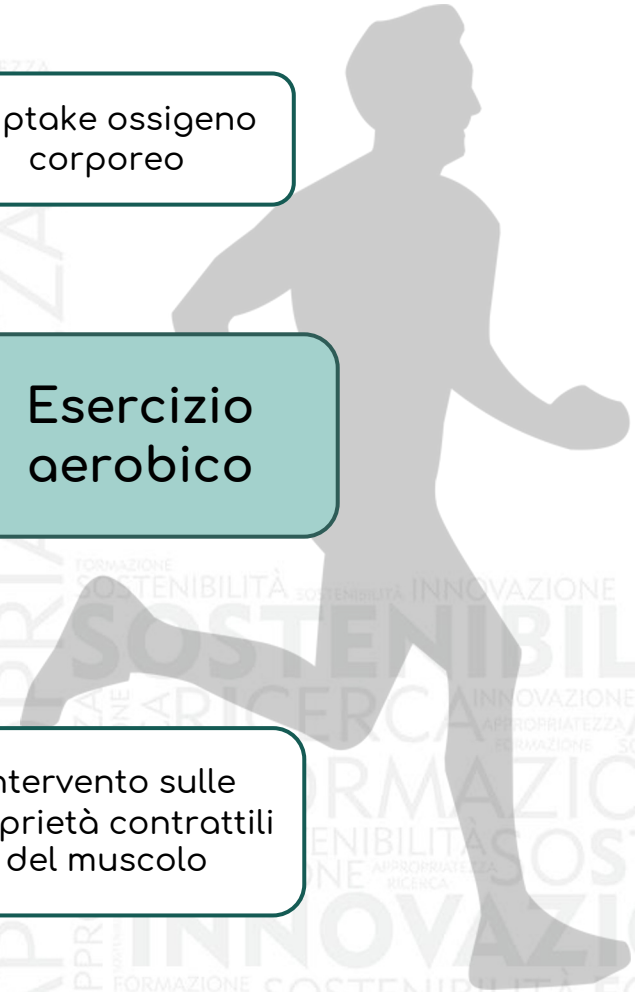
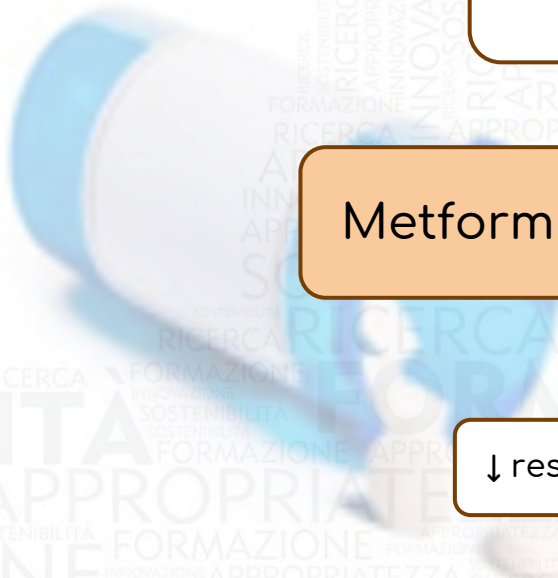


Esercizio aerobico

- ↑ uptake ossigeno corporeo
- rallentamento della progressione di molte malattie (obesità, diabete, ...)
- miglioramento della sensibilità all'insulina
- intervento sulle proprietà contrattili del muscolo

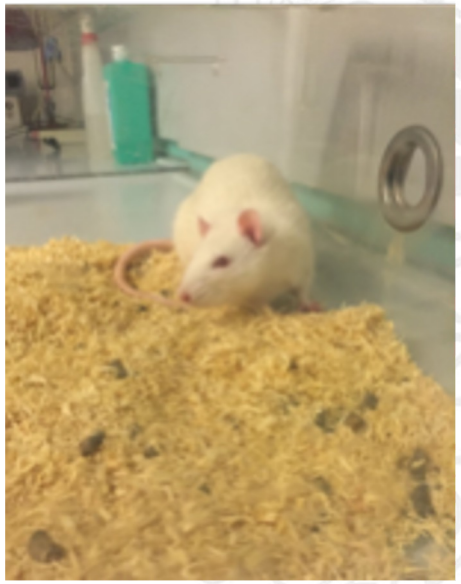


Metformina

- ↑ uptake glucosio nel muscolo scheletrico
- ↓ gluconeogenesi
- ↓ resistenza all'insulina

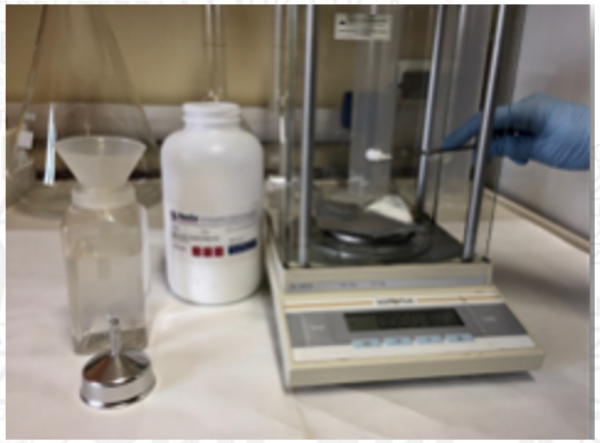

Metformina

Modello e protocollo sperimentale



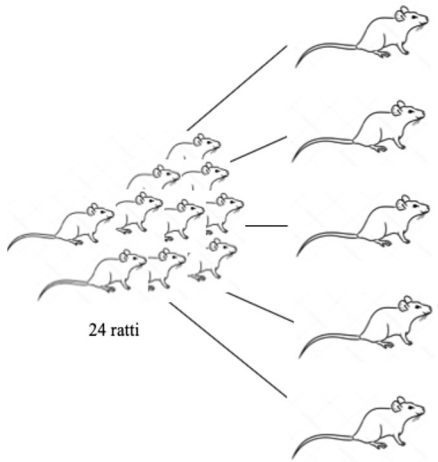
Ratto Wistar di sesso maschile
Peso: ~250 grammi

Treadmill a 5 vie



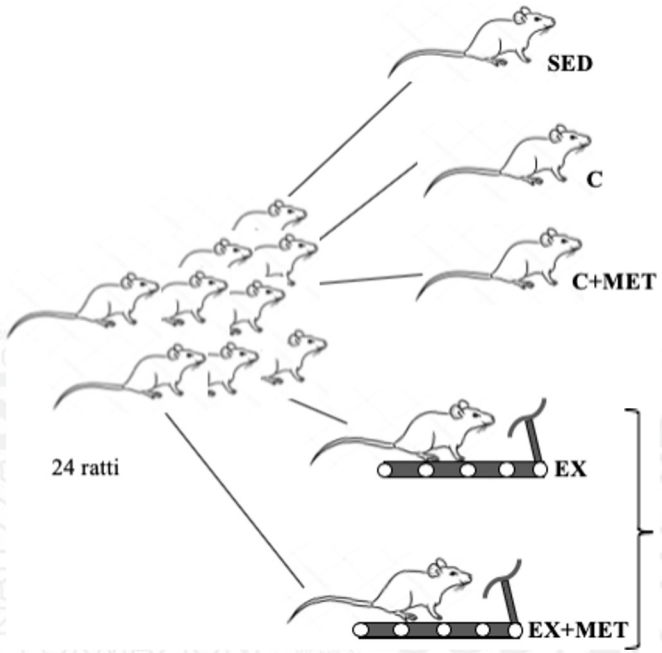
Metformina
Dose giornaliera: 250 mg/kg
peso corporeo

Fase preliminare



Corsa sul tapis roulant
v = 25 cm/s, 5 minuti al giorno per 5 giorni

Fase sperimentale



giorno 0

v = 25 cm/s
t = 5 min

+2'-3' al giorno
+1 cm/s ogni 2 giorni

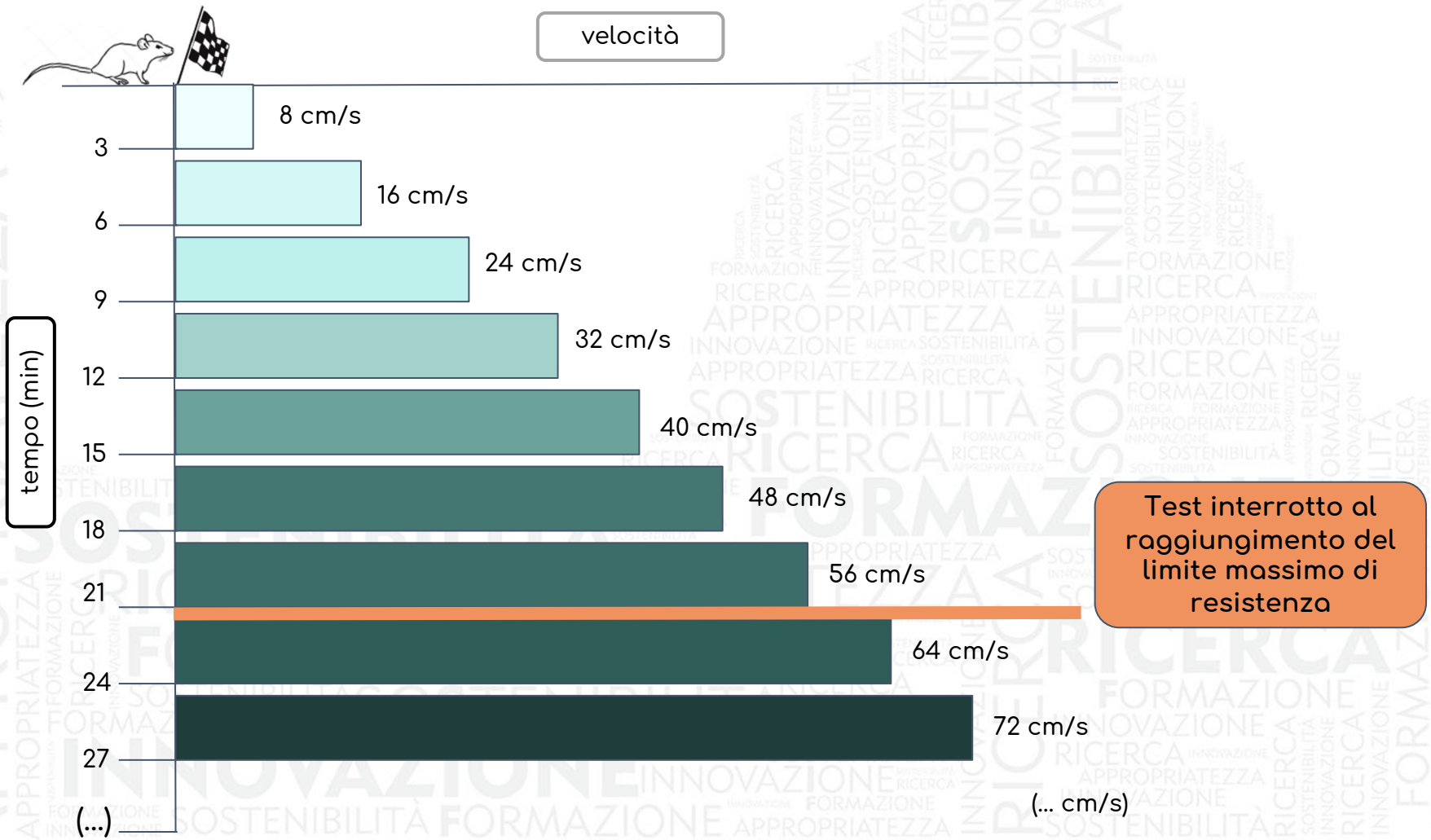
giorno 28 a 56

v = 34 cm/s
t = 60 min

giorno 57

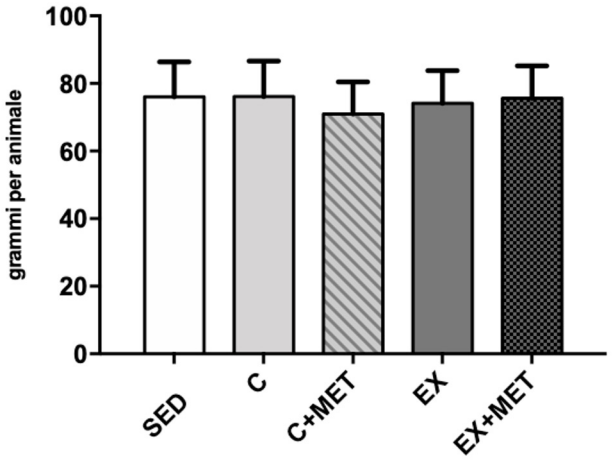
Sacrificio

Test di Massima Resistenza alla corsa (TRM)

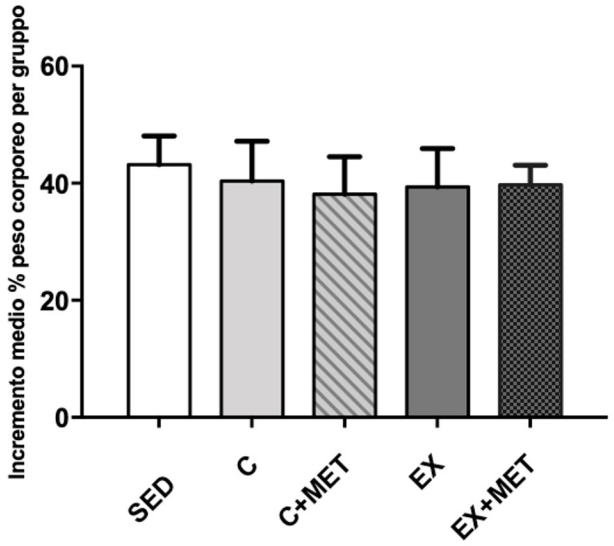


Risultati

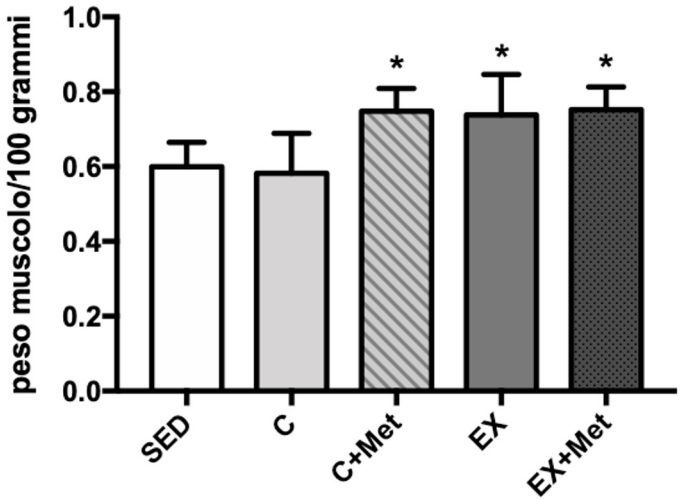
Consumo di cibo



Incremento del peso corporeo



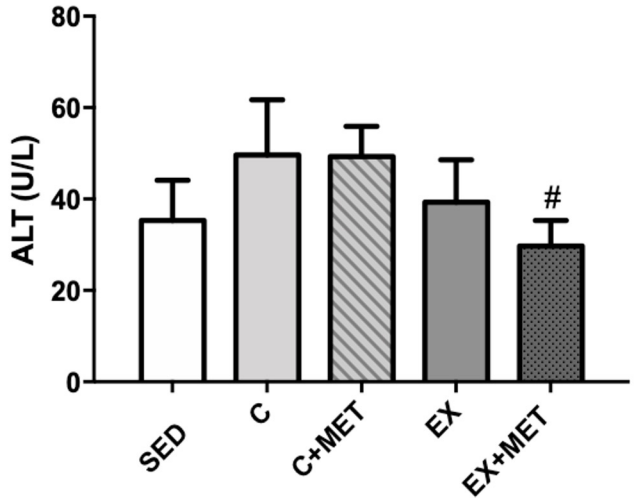
Peso muscolo/peso corporeo
(gastrocnemio)



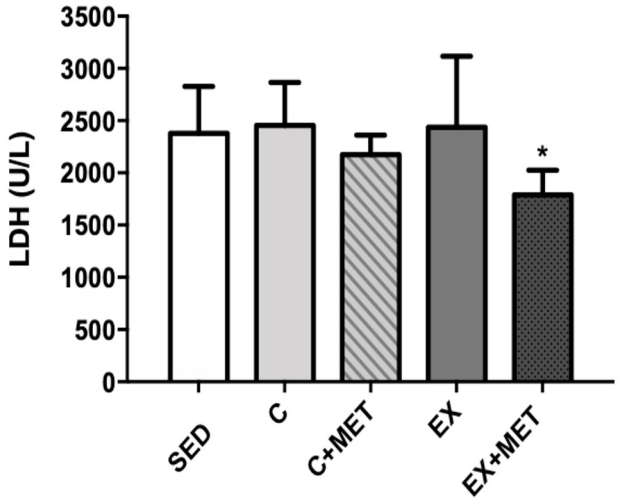
* $p < 0,05$ vs SED e C

Parametri ematochimici

- ALT
- AST
- Colesterolo totale
- Colesterolo HDL
- Creatinina
- Glucosio
- LDH
- Mioglobina
- Proteina C-reattiva
- Trigliceridi
- Urea



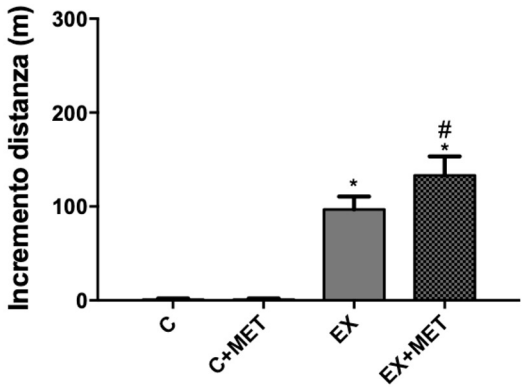
ρ < 0,001 vs C e C+Met



* ρ < 0,05 vs C ed EX

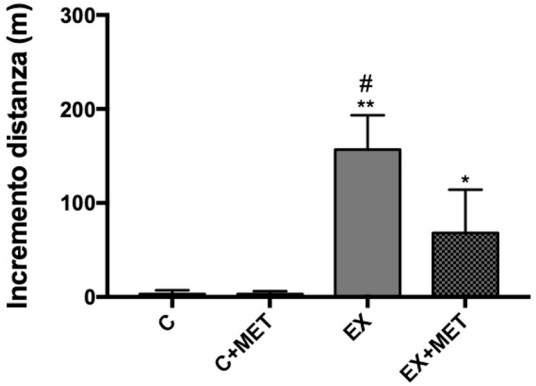
Test di Massima Resistenza alla corsa

I TRM vs II TRM



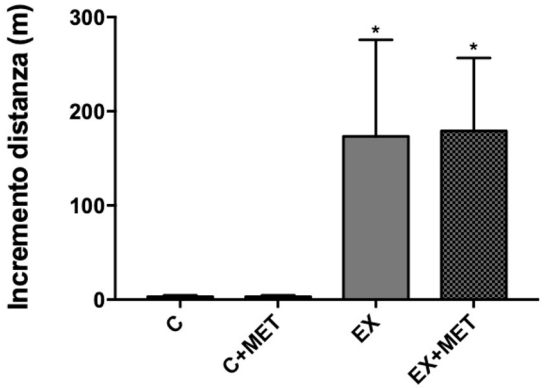
ρ < 0,001 vs C e C+Met
** ρ < 0,01 vs EX

II TRM vs III TRM



* ρ < 0,05 vs C e C+Met
# ρ < 0,001 vs C e C+Met
** ρ < 0,01 vs EX+Met

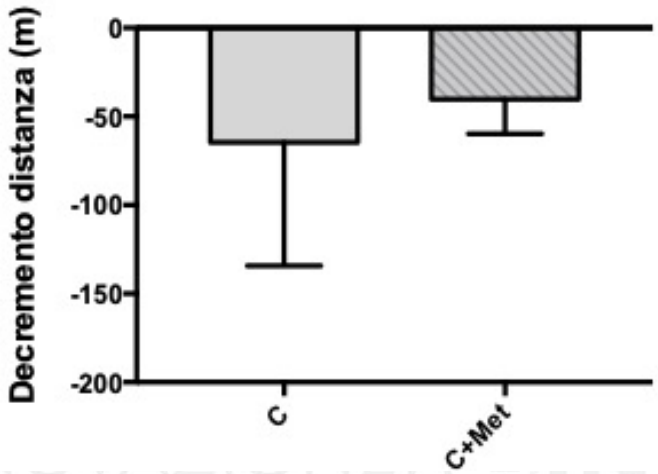
I TRM vs III TRM

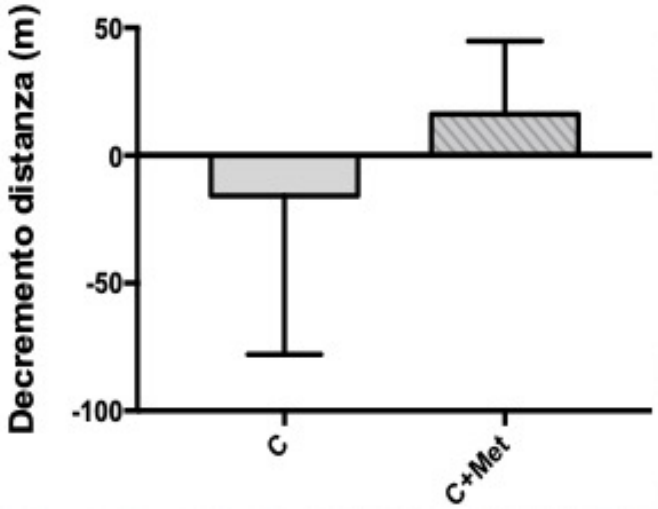


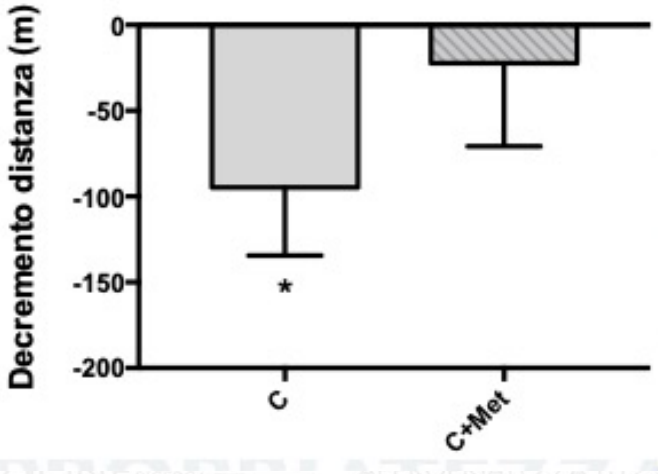
** ρ < 0,01 vs C e C+Met

Test di Massima Resistenza alla corsa – confronto C e C+Met

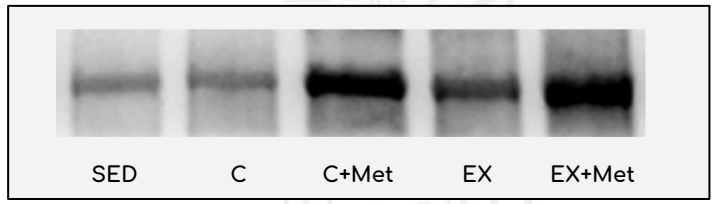
I TRM vs II TRM — II TRM vs III TRM — I TRM vs III TRM



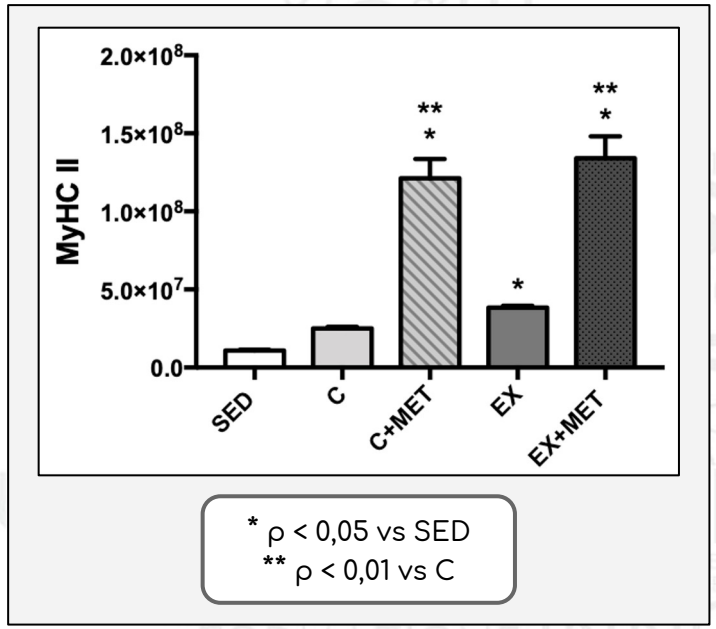


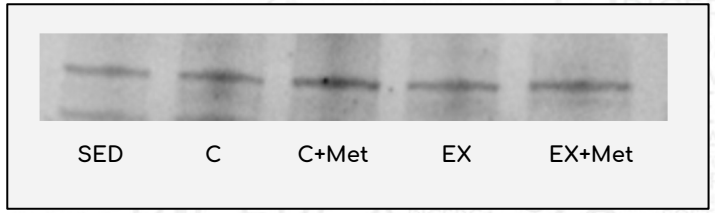


MyHC II e fattori di trascrizione del differenziamento muscolare

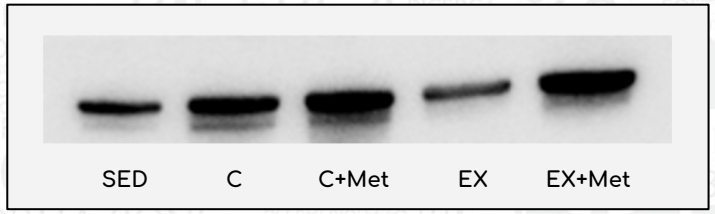


MyHC II

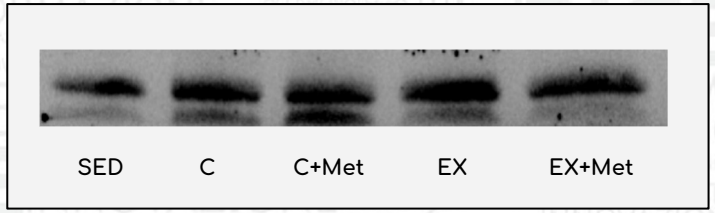




PAX 7



Myf 5



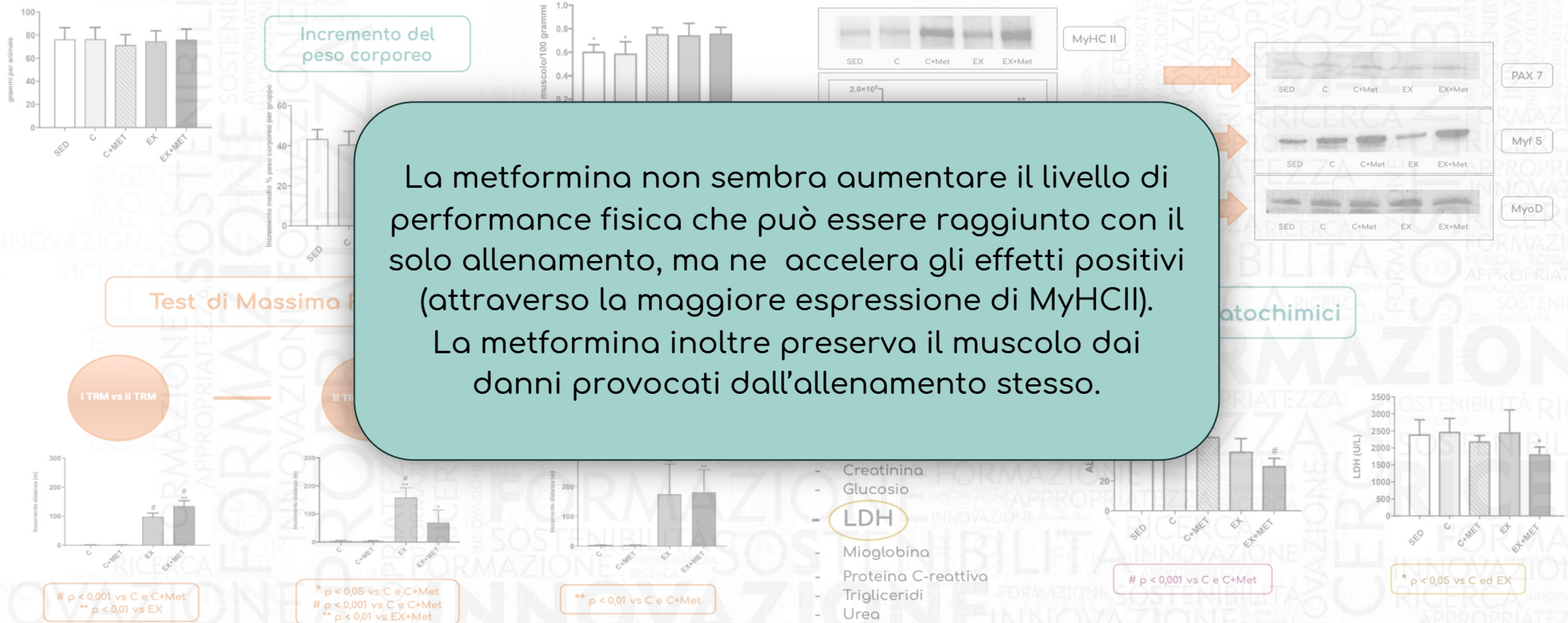
MyoD

Consumo di cibo

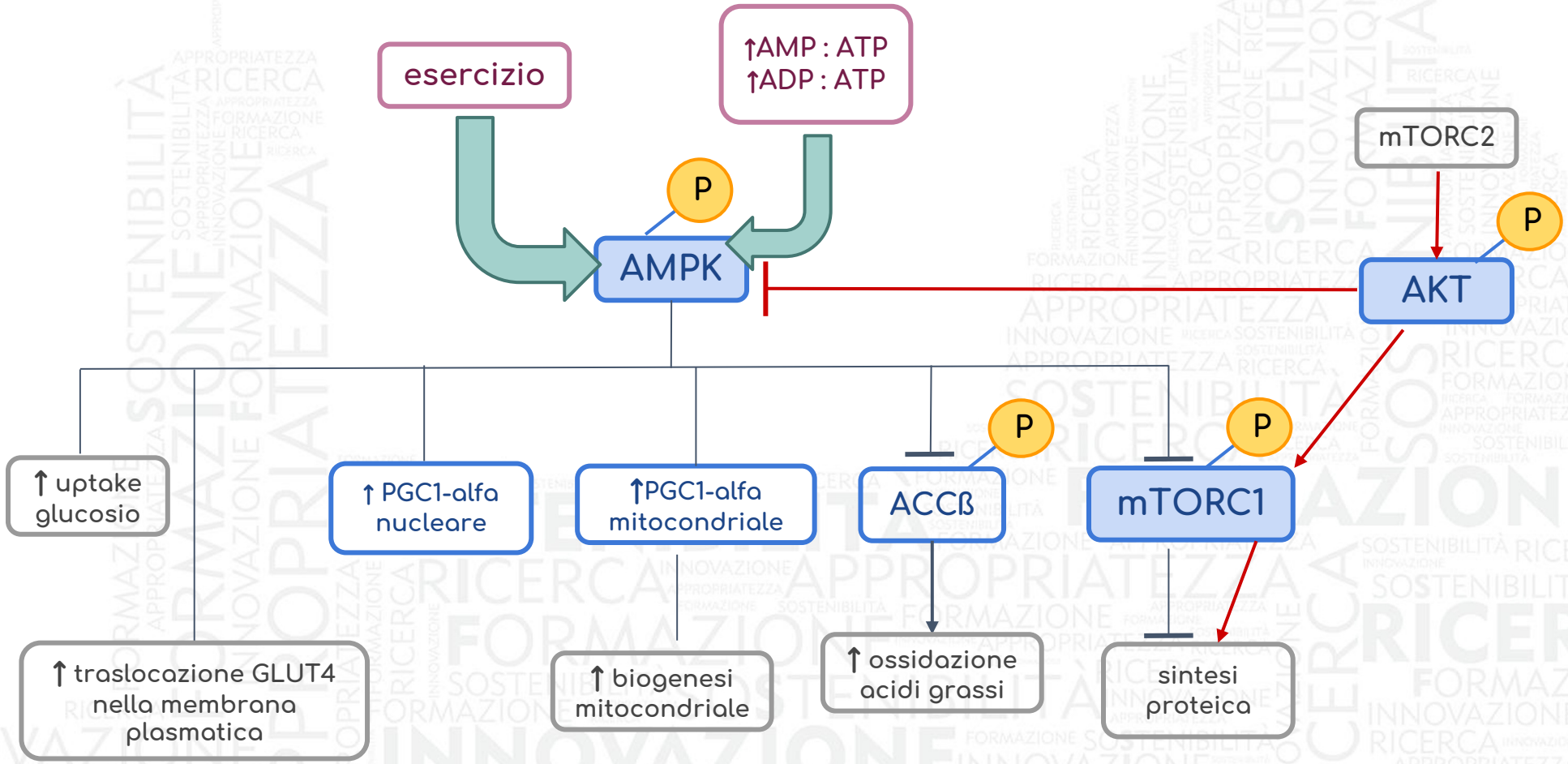
Peso muscolo/peso corporeo

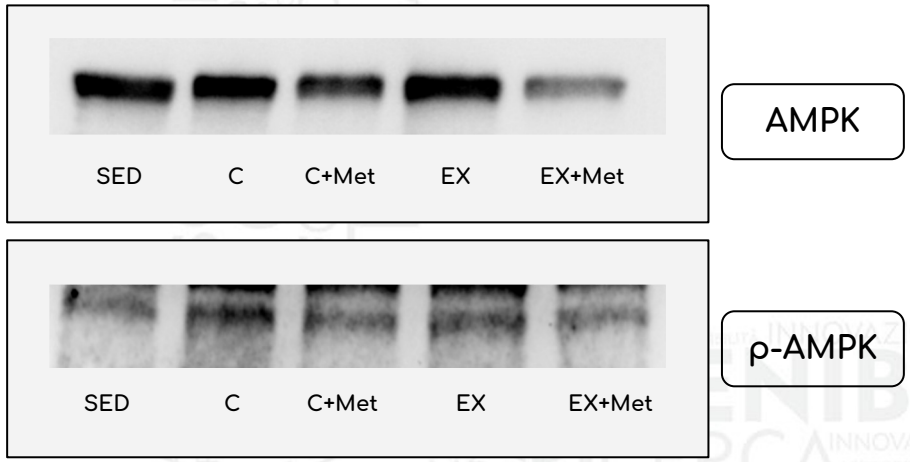
MyHC II e fattori di regolazione delle cellule satelliti

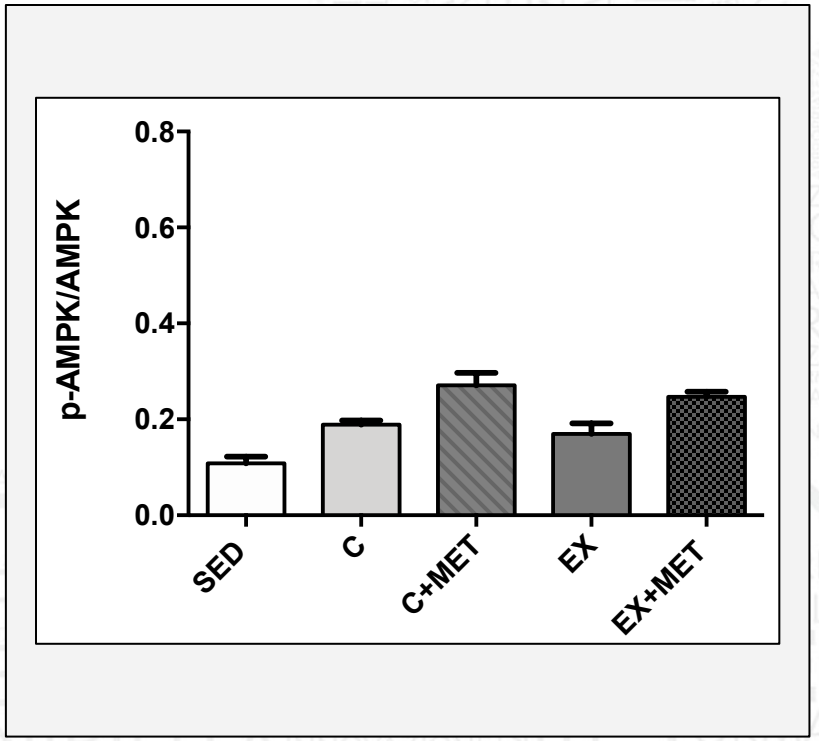
Incremento del peso corporeo

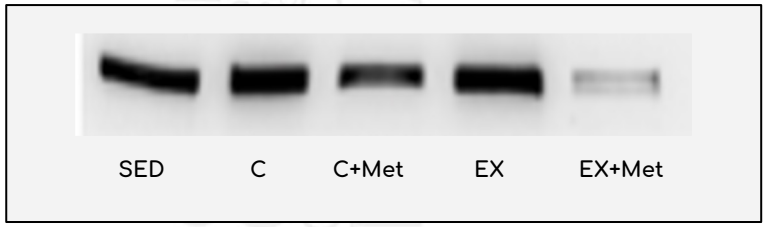


La metformina non sembra aumentare il livello di performance fisica che può essere raggiunto con il solo allenamento, ma ne accelera gli effetti positivi (attraverso la maggiore espressione di MyHCII).
La metformina inoltre preserva il muscolo dai danni provocati dall'allenamento stesso.

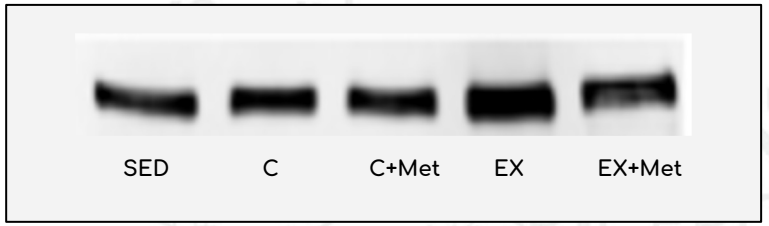

esercizio
↑AMP : ATP
↑ADP : ATP
P
AMPK
mTORC2
P
AKT
↑ uptake glucosio
↑ PGC1-alfa nucleare
↑PGC1-alfa mitocondriale
P
ACCß
P
mTORC1
↑ traslocazione GLUT4 nella membrana plasmatica
↑ biogenesi mitocondriale
↑ ossidazione acidi grassi
sintesi proteica


SED
C
C+Met
EX
EX+Met
AMPK
SED
C
C+Met
EX
EX+Met
p-AMPK

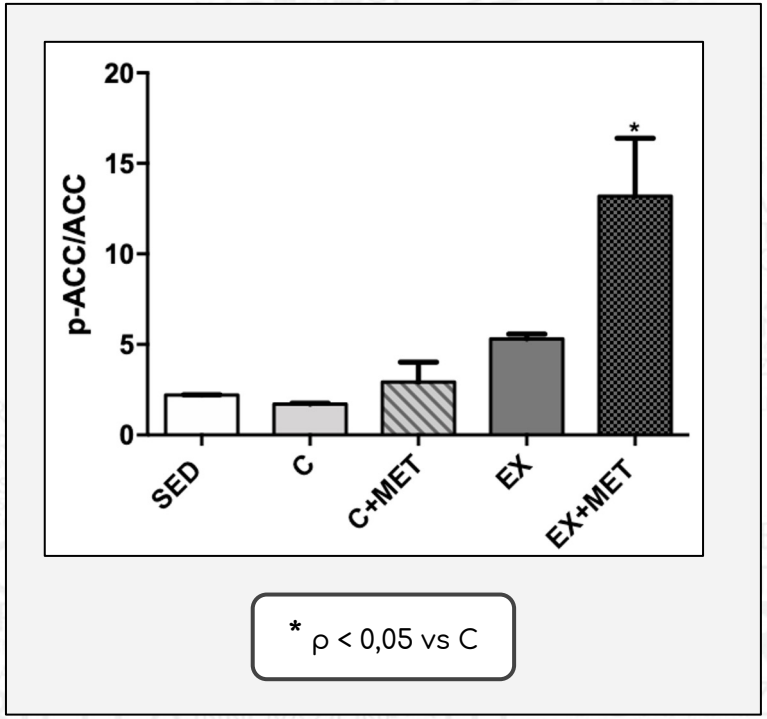

p-AMPK/AMPK
0.8
0.6
0.4
0.2
0.0
SED
C
C+MET
EX
EX+MET



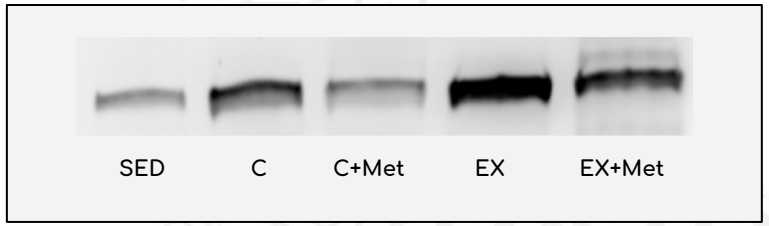
ACCß



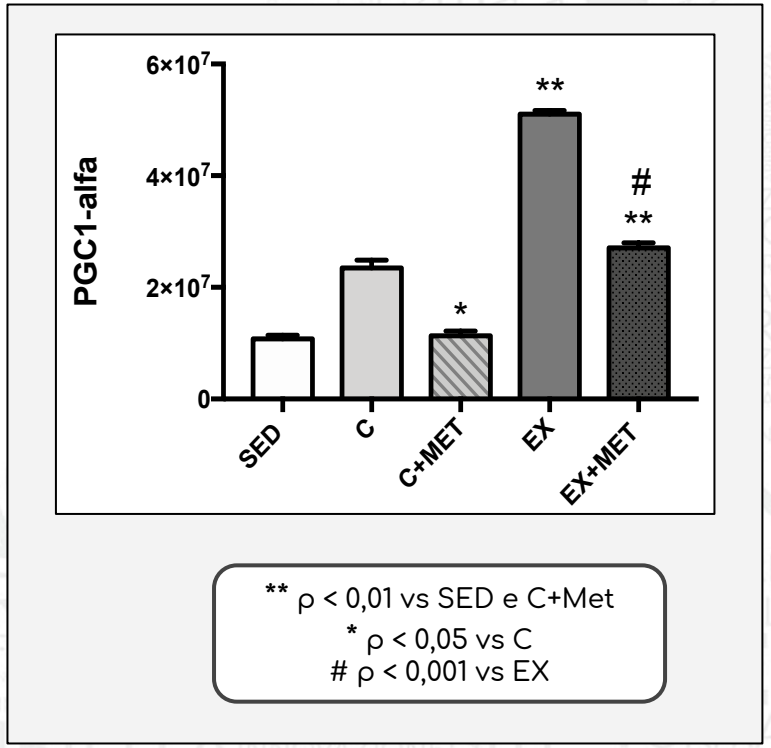
ρ-ACC



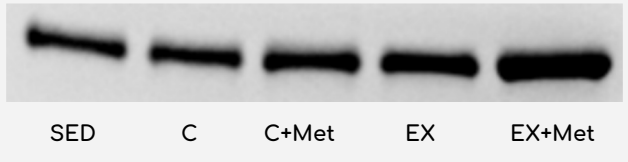
* ρ < 0,05 vs C



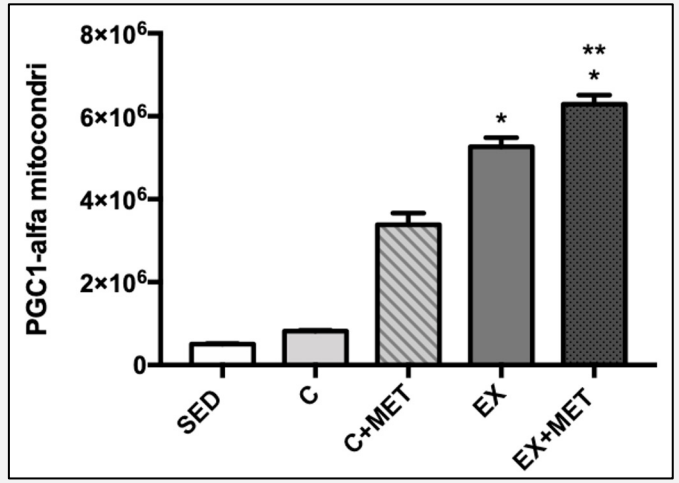
PGC1-alfa



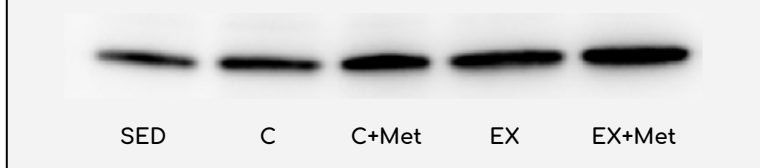
** ρ < 0,01 vs SED e C+Met
* ρ < 0,05 vs C
# ρ < 0,001 vs EX



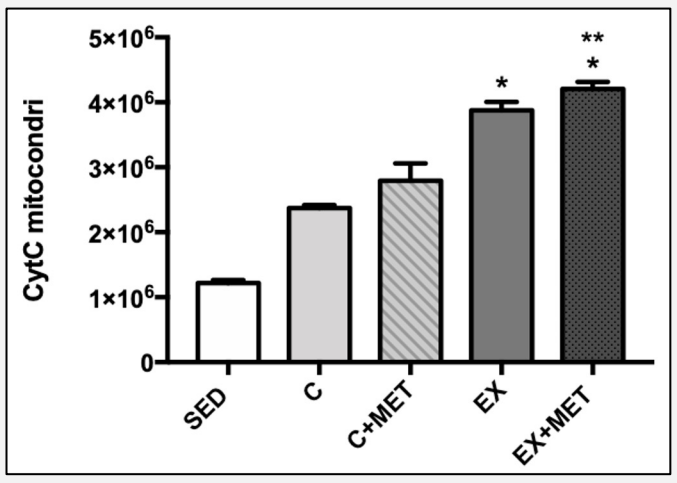
PGC1-alfa
(mitocondri)



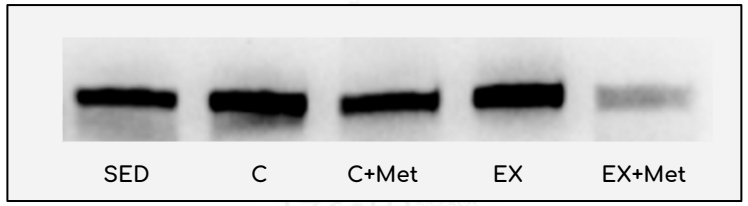
* ρ < 0,05 vs SED
** ρ < 0,01 vs C



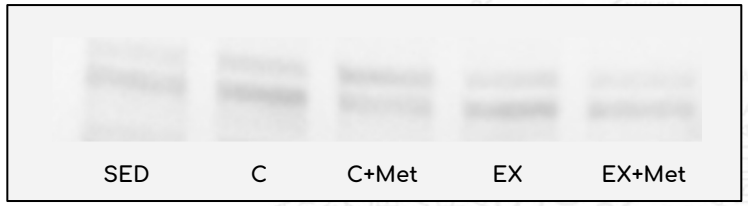
Cyt C
(mitocondri)



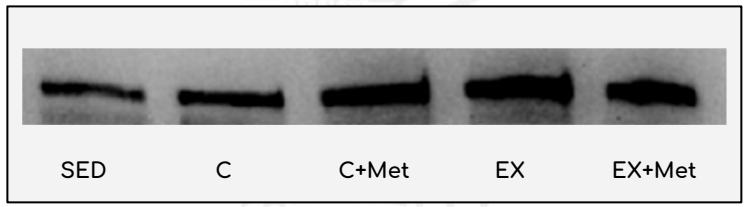
* ρ < 0,05 vs SED
** ρ < 0,01 vs C



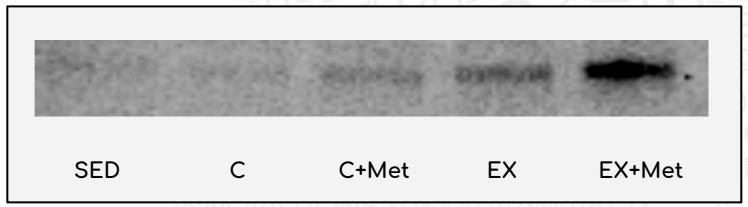
mTORC1



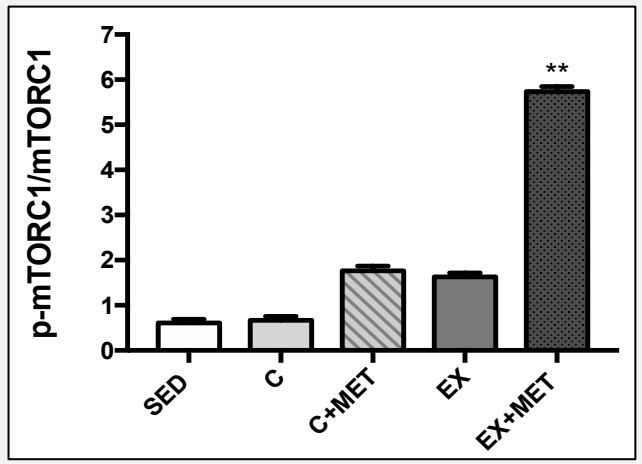
ρ70S6K



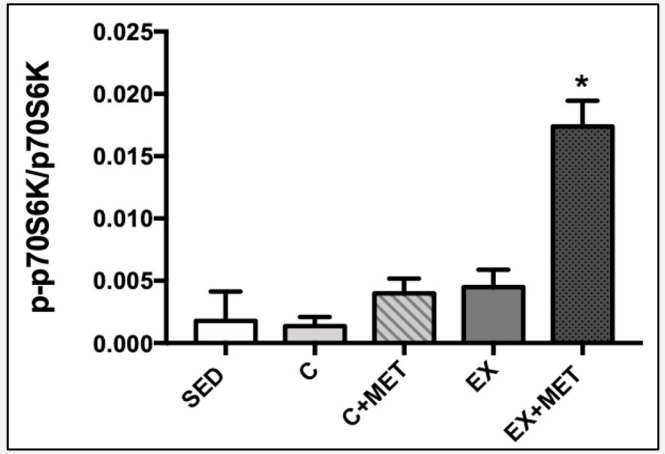
ρ-mTORC1



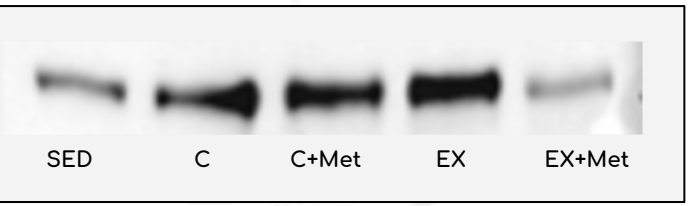
ρ-ρ70S6K



** ρ < 0,01 vs SED e C

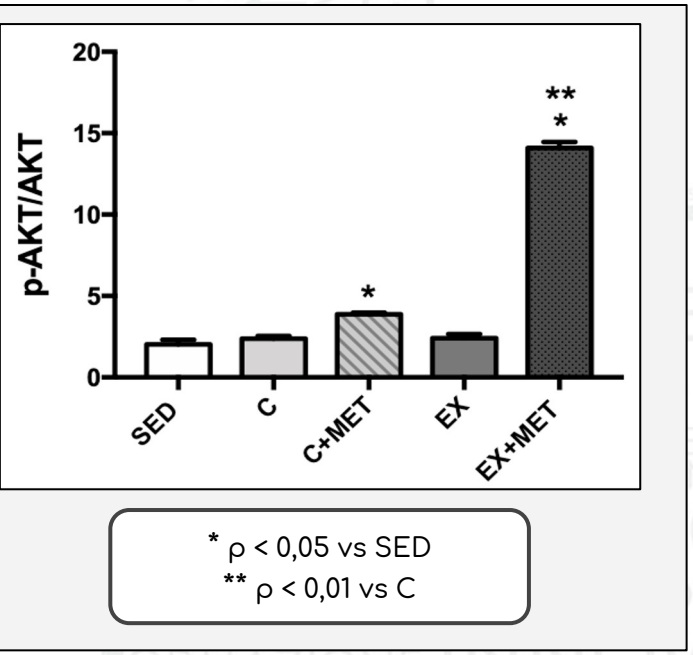


* ρ < 0,05 vs SED, C e C+Met

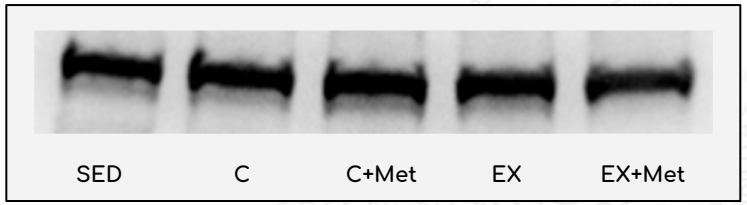


AKT

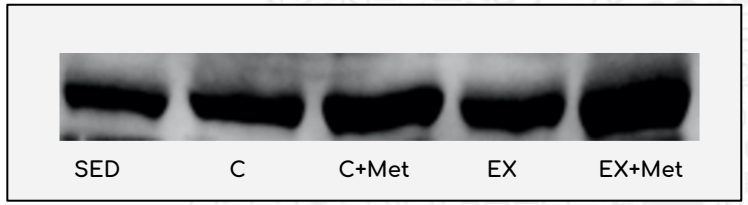
ρ-AKT
Ser473



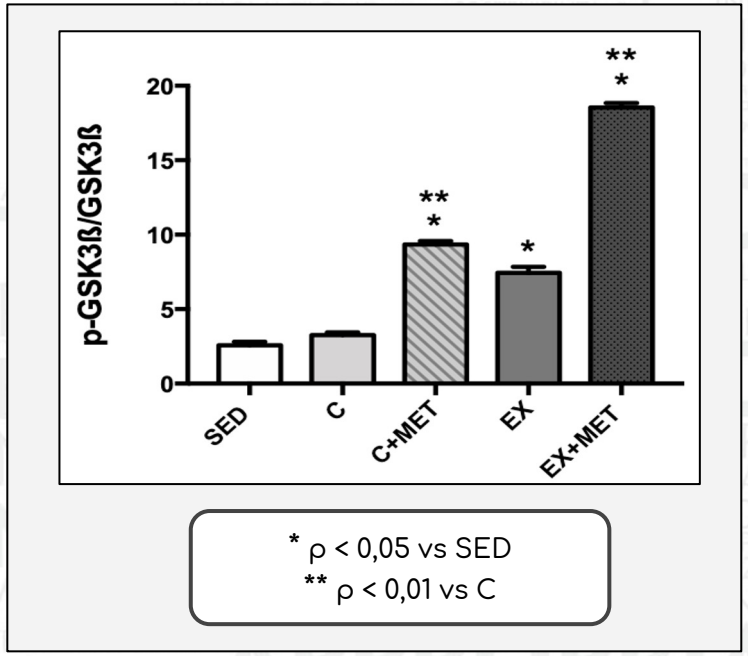
* ρ < 0,05 vs SED
** ρ < 0,01 vs C



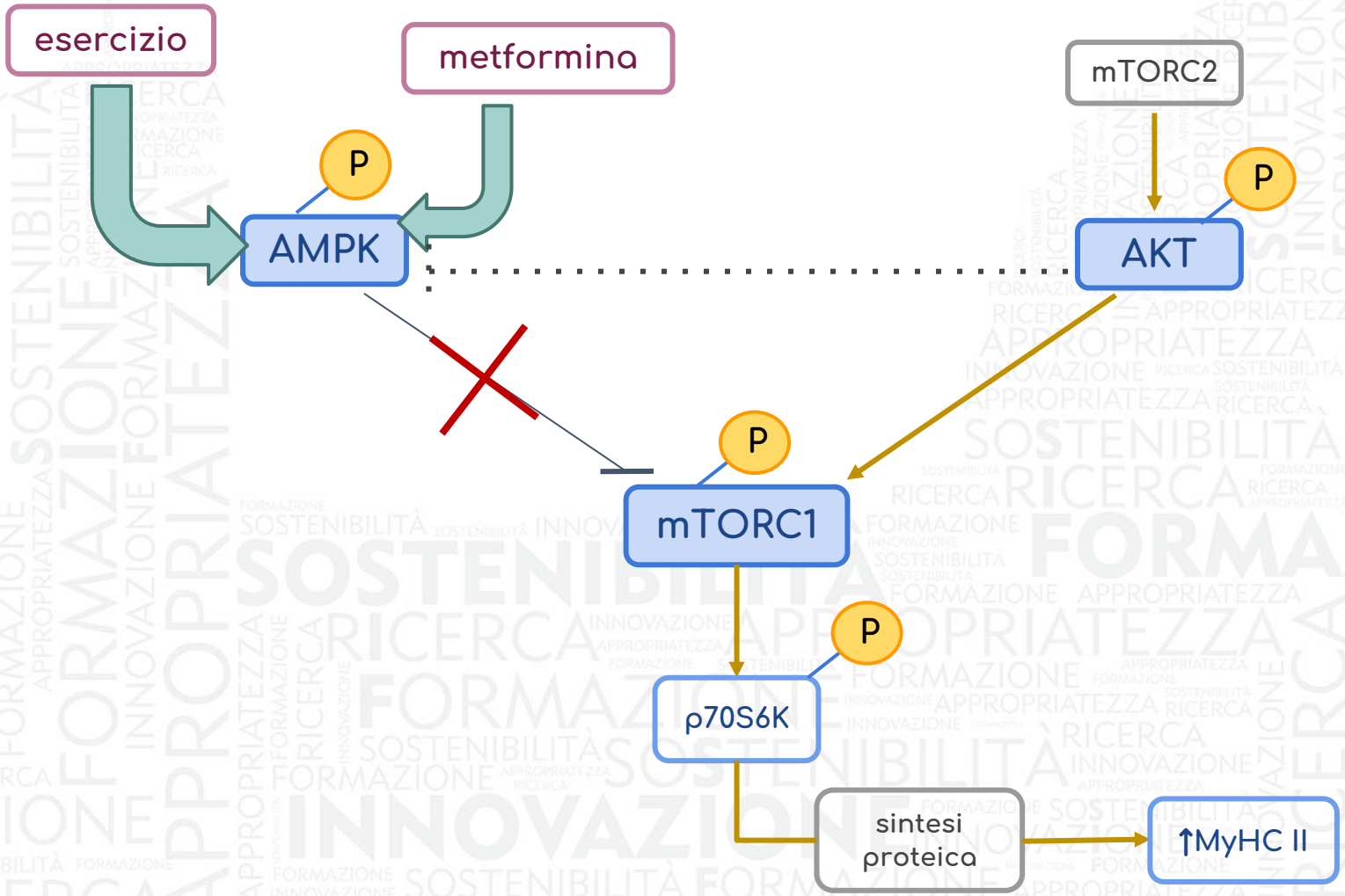
GSK3ß



ρ-GSK3ß
Ser 9



* ρ < 0,05 vs SED
** ρ < 0,01 vs C


esercizio
metformina
mTORC2
P
P
AMPK
AKT
P
mTORC1
P
p70S6K
sintesi proteica
↑MyHC II

Grazie per l'attenzione.