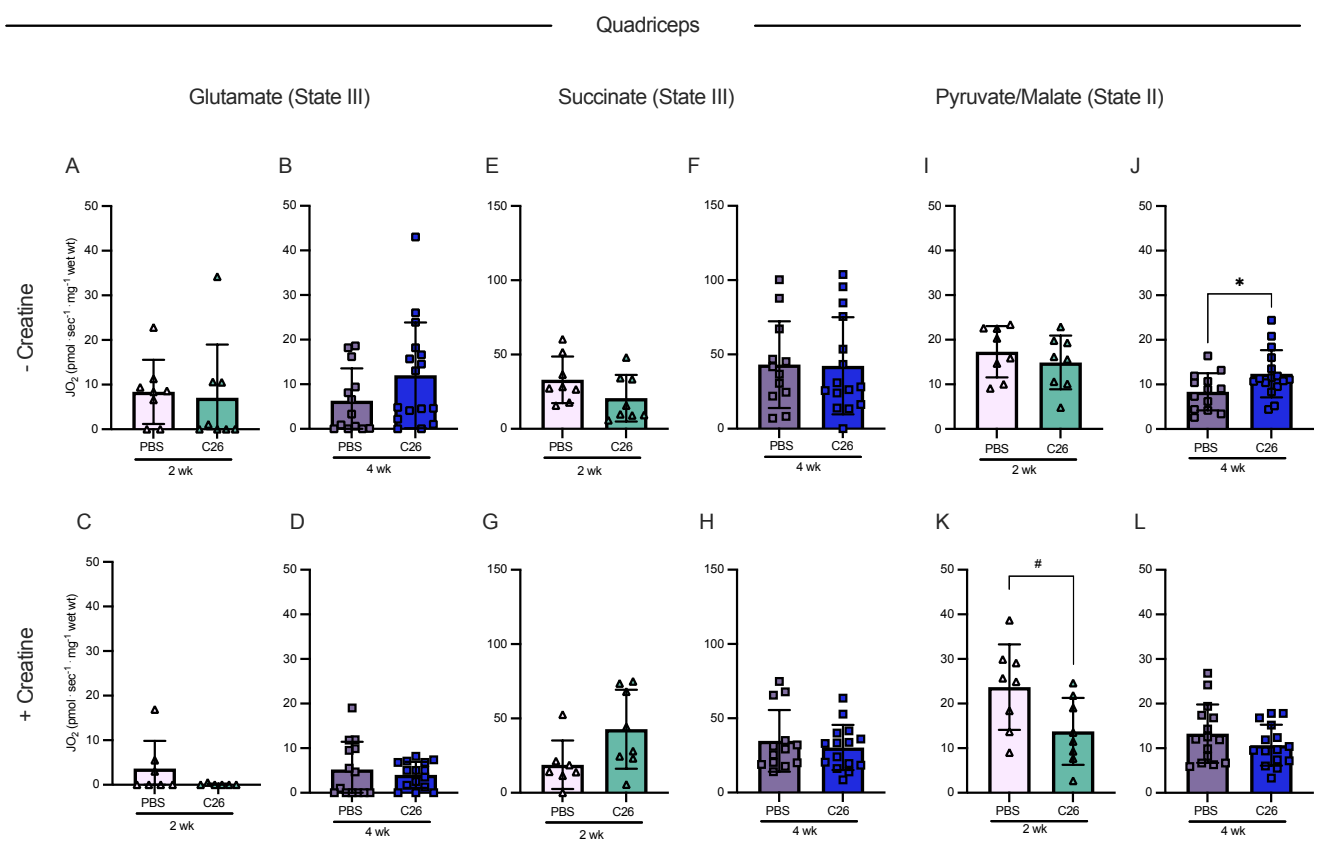
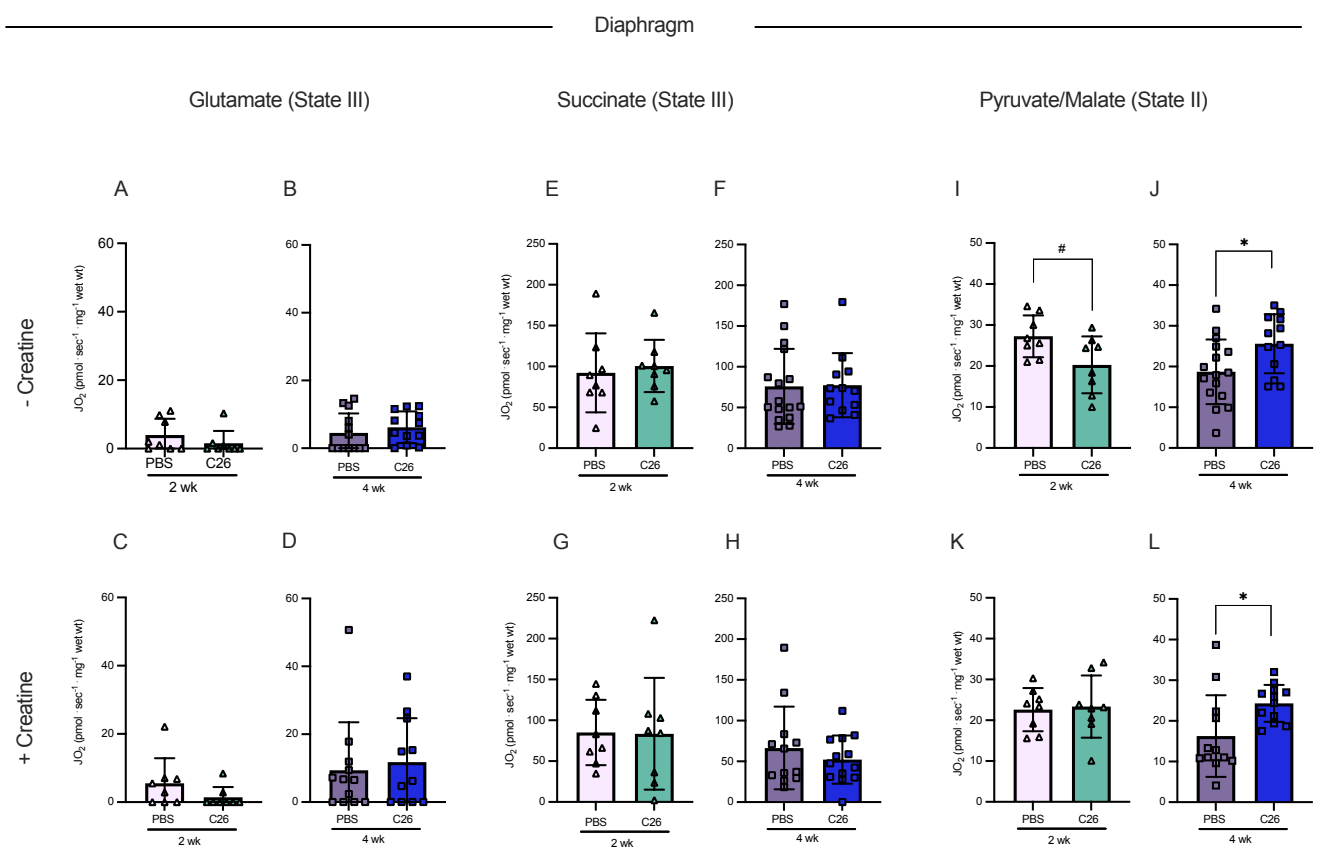
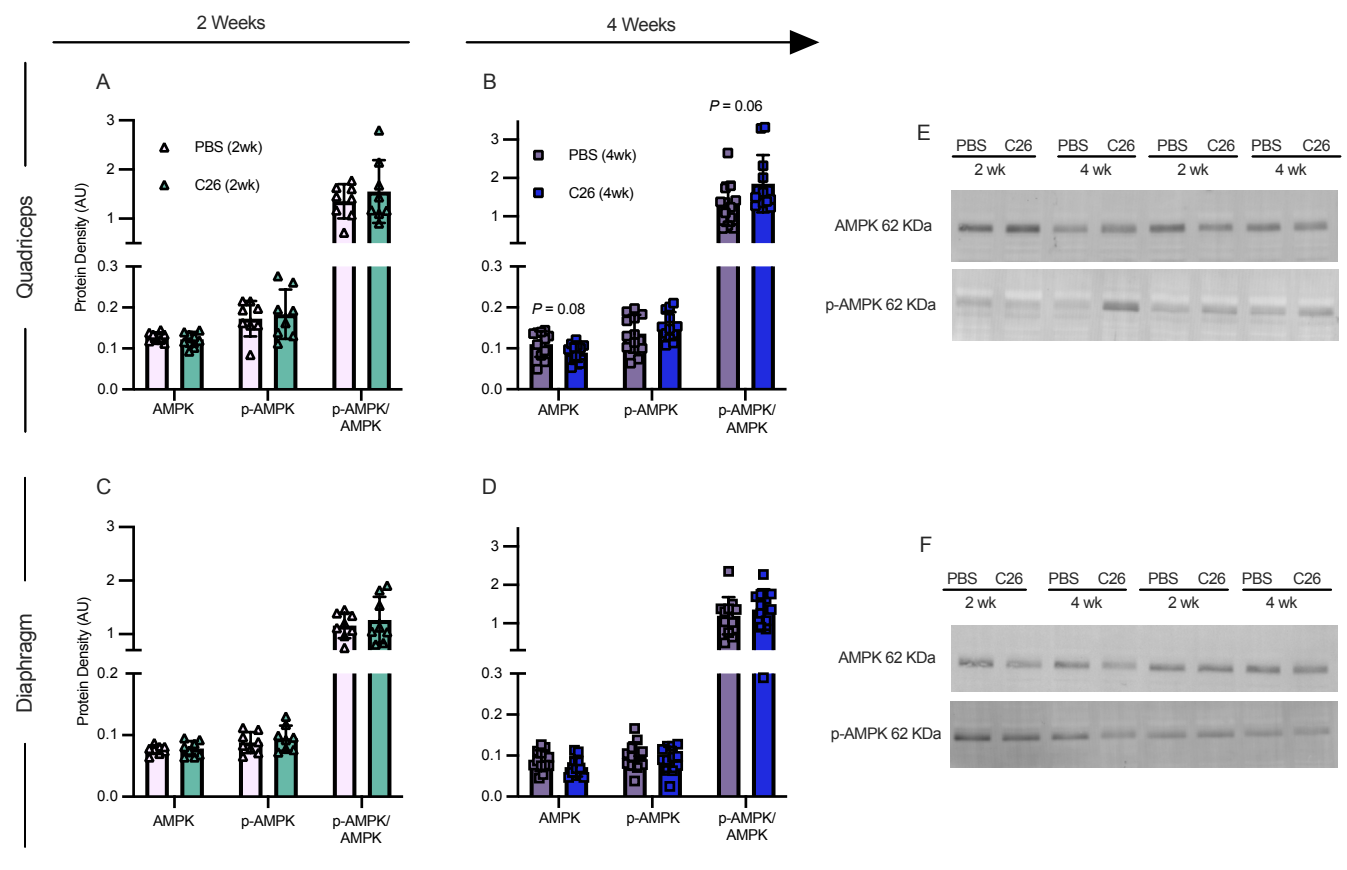
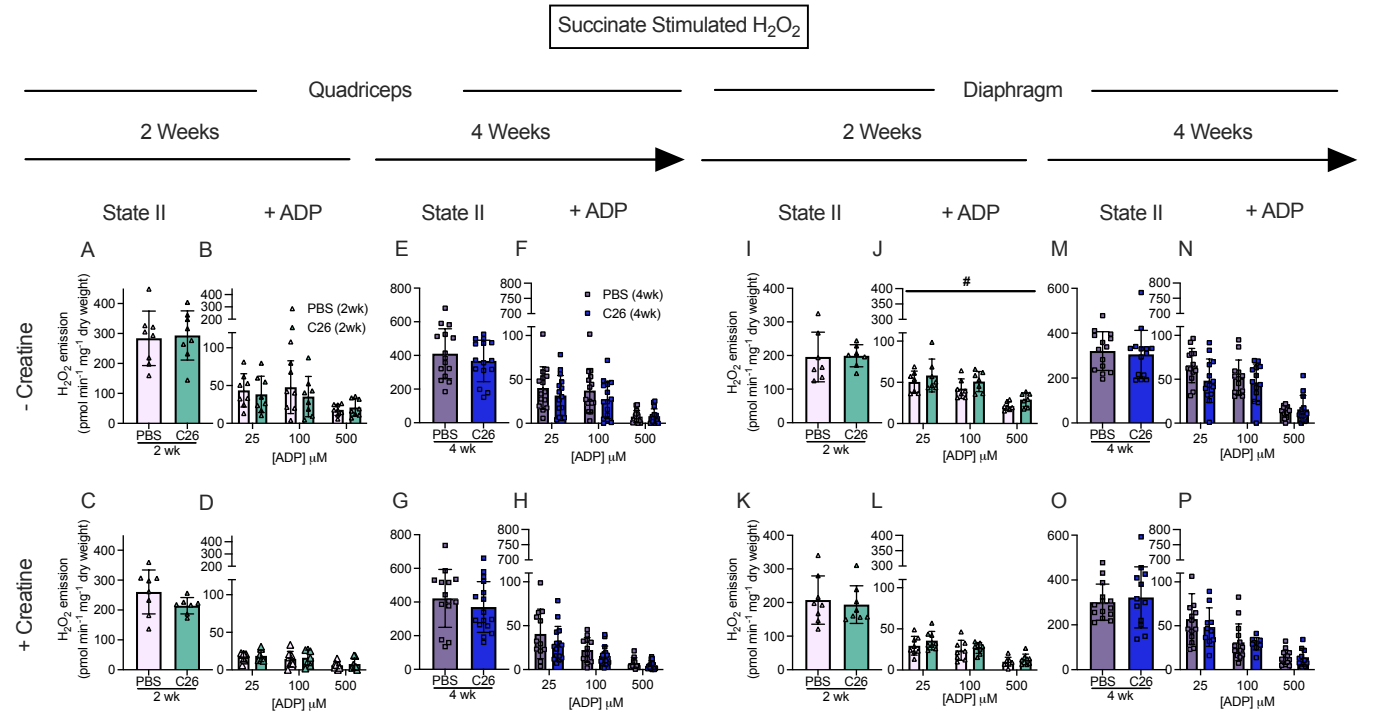

Quadriceps
Glutamate (State III)
Succinate (State III)
Pyruvate/Malate (State II)
- Creatine
+ Creatine
A
B
C
D
E
F
G
H
I
J
K
L
JO2 (pmol sec-1 mg-1 wet wt)
PBS
C26
2 wk
4 wk
*
#


Diaphragm
Glutamate (State III)
Succinate (State III)
Pyruvate/Malate (State II)
- Creatine
+ Creatine
A
B
C
D
E
F
G
H
I
J
K
L
JO2 (pmol sec-1 mg-1 wet wt)
PBS
C26
2 wk
4 wk
#
*


2 Weeks
4 Weeks
Quadriceps
Diaphragm
A
B
C
D
E
F
PBS (2wk)
C26 (2wk)
PBS (4wk)
C26 (4wk)
Protein Density (AU)
P = 0.06
P = 0.08
AMPK
p-AMPK
p-AMPK/ AMPK
PBS C26 PBS C26 PBS C26 PBS C26
2 wk 4 wk 2 wk 4 wk
AMPK 62 KDa
p-AMPK 62 KDa


Succinate Stimulated H_2O_2
Quadriceps
Diaphragm
2 Weeks
4 Weeks
2 Weeks
4 Weeks
State II
+ ADP
State II
+ ADP
State II
+ ADP
State II
+ ADP
A
B
E
F
I
J
M
N
C
D
G
H
K
L
O
P
- Creatine
+ Creatine
H_2O_2 emission (pmol min^{-1} mg^{-1} dry weight)
PBS (2wk)
C26 (2wk)
PBS (4wk)
C26 (4wk)
#
PBS
C26
2 wk
4 wk
[ADP] μM
25
100
500

Supplemental Figure Legends

Figure S1 Multiple substrate evaluation of oxygen consumption in quadriceps permeabilized muscle fibre bundles. Oxygen consumption was evaluated in the absence of creatine at 2 weeks and 4 weeks post C26 implantation or PBS injections in permeabilized muscle fibres when stimulated with glutamate (*A, B*), succinate (*E, F*) and pyruvate/malate (*I, J*). This was repeated in the presence of 20mM Creatine (*C, D, G, H, K, L*). Results represent mean ± SD; n=8-16; # $P<0.05$ PBS (2wk) vs C26 (2wk); * $P<0.05$ PBS (4wk) vs C26 (4wk)

Figure S2 Multiple substrate evaluation of oxygen consumption in diaphragm permeabilized muscle fibre bundles. Oxygen consumption was evaluated in the absence of creatine at 2 weeks and 4 weeks post C26 implantation or PBS injections in permeabilized muscle fibres when stimulated with glutamate (*A, B*), succinate (*E, F*) and pyruvate/malate (*I, J*). This was repeated in the presence of 20mM Creatine (*C, D, G, H, K, L*). Results represent mean ± SD; n=8-16; # $P<0.05$ PBS (2wk) vs C26 (2wk); * $P<0.05$ PBS (4wk) vs C26 (4wk).

Figure S3 Muscle-specific changes in markers of growth in C26 tumour-bearing skeletal muscle. Protein content of AMPKα and P-AMPKα were quantified at in the quadriceps at 2 weeks (*A*, $n=8$) and 4 weeks (*B*, $n=12$). Markers were also quantified at in the diaphragm at 2 weeks (*C*, $n=8$) and 4 weeks (*D*, $n=12$). *E*, representative image for quadriceps and *F*, representative image for diaphragm. Results represent mean ± SD.

Figure S4 Succinate stimulated mH_2O_2 emission in quadriceps and diaphragm muscle of C26 tumour bearing mice. At 2 and 4 weeks, quadriceps mH_2O_2 emission supported by succinate

(10mM) ($FADH_2$) was assessed under maximal State II (no ADP) conditions in the absence of creatine (*A, E*) and in the presence of 20mM Creatine (*C, G*). State III (range of [ADP] to model metabolic demand) was also assessed in the absence of creatine (*B, F*) and in the presence of 20mM creatine (*D* and *H*). These measures were repeated in the diaphragm (I-P). Results represent mean ± SD; n=7-16; # $P<0.05$, PBS (2wk) vs C26 (2wk); * $P<0.05$, PBS (4wk) vs C26 (4wk).