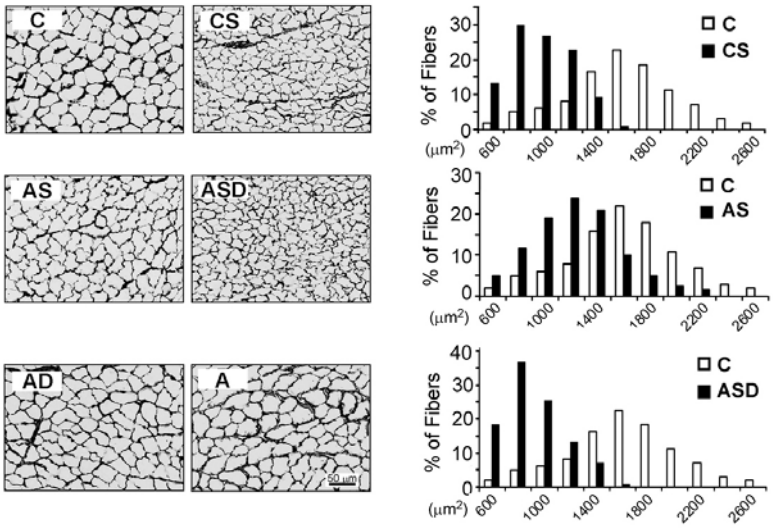
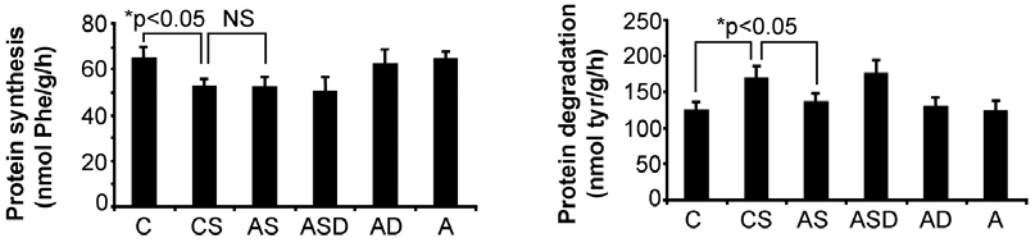
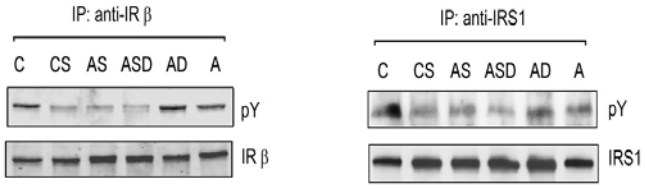
A

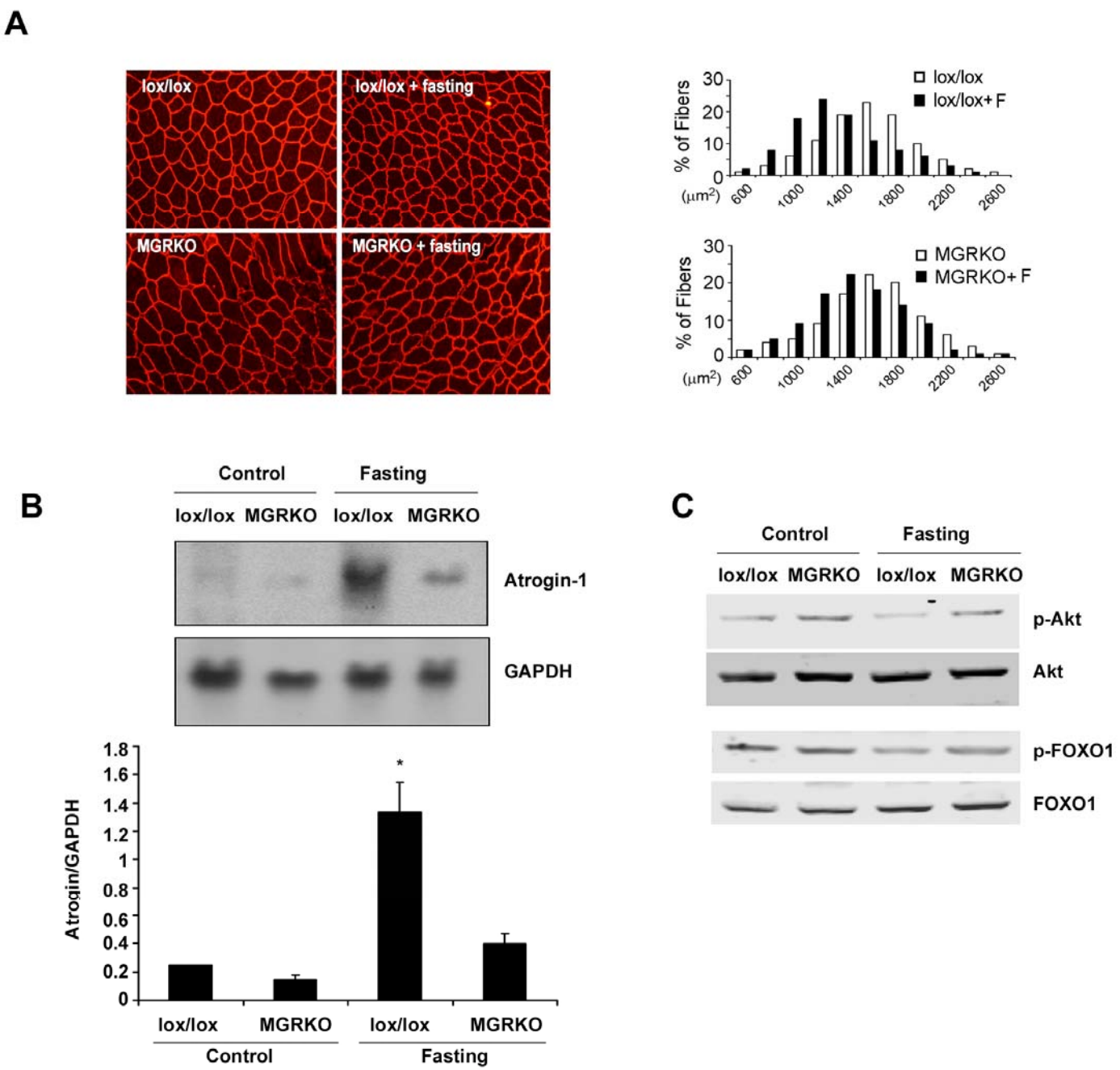

C
CS
AS
ASD
AD
A
% of Fibers
(μm²)
600
1000
1400
1800
2200
2600
C
CS
AS
ASD

B

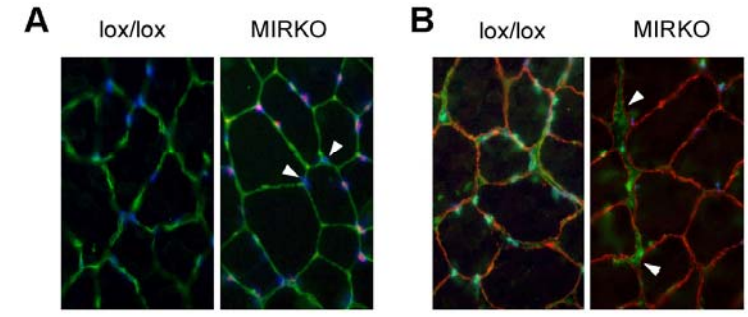

Protein synthesis
(nmol Phe/g/h)
*p<0.05
NS
C
CS
AS
ASD
AD
A
Protein degradation
(nmol tyr/g/h)
*p<0.05

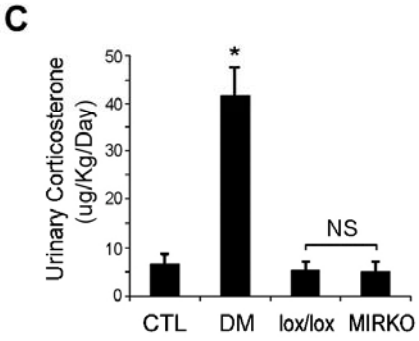
C

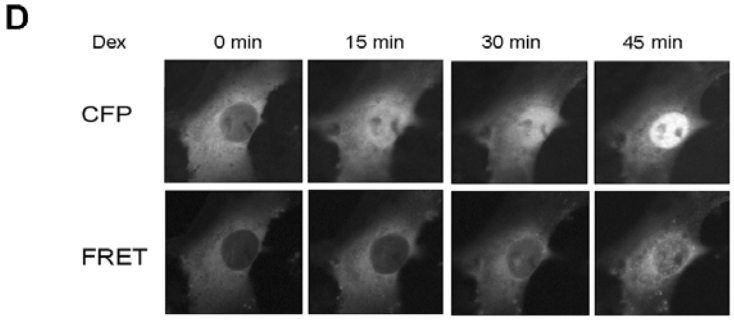

IP: anti-IR β
C CS AS ASD AD A
pY
IR β
IP: anti-IRS1
C CS AS ASD AD A
pY
IRS1

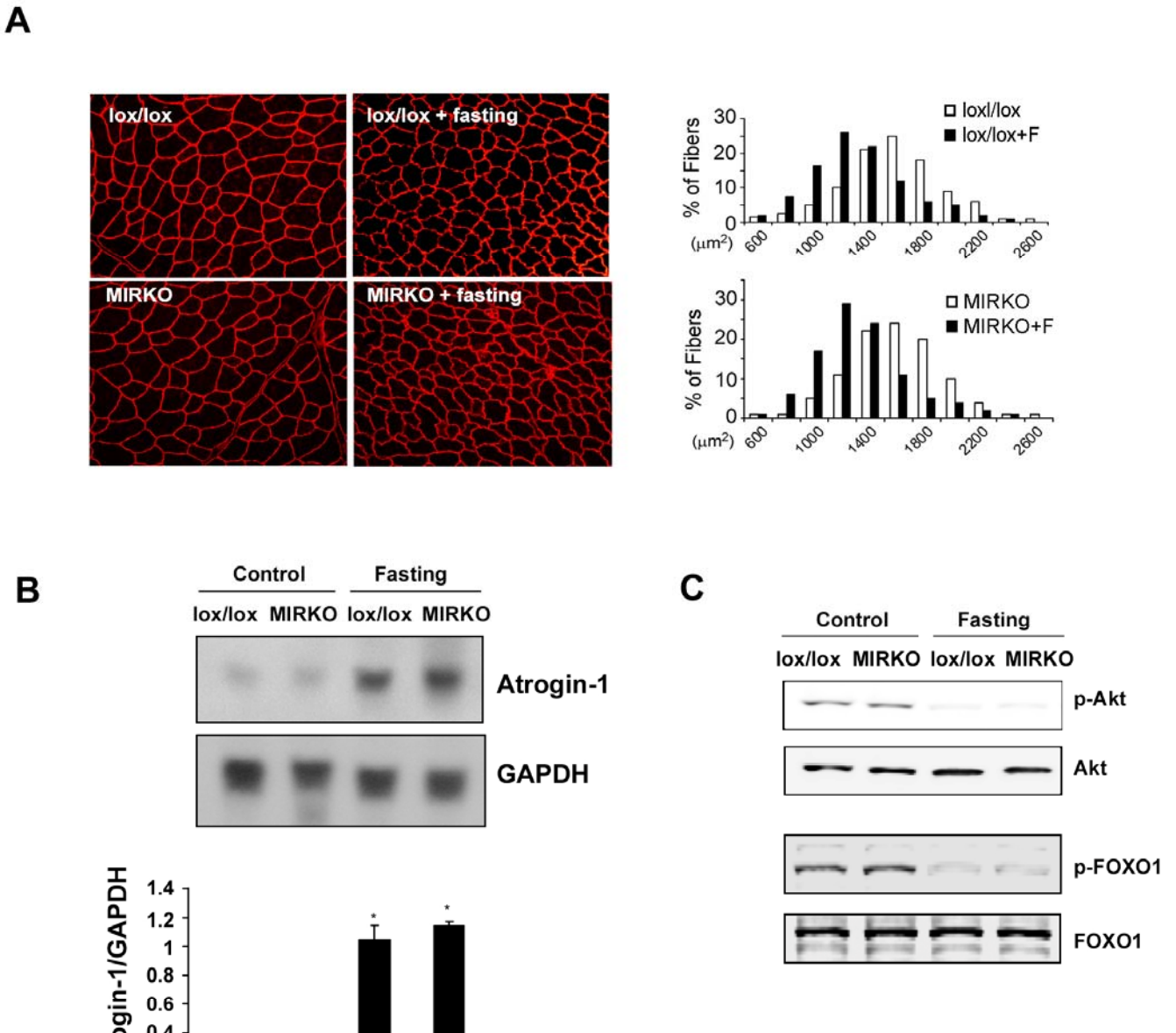

A
lox/lox
lox/lox + fasting
MGRKO
MGRKO + fasting
% of Fibers
lox/lox
lox/lox+ F
MGRKO
MGRKO+ F
(μm²)
600
1000
1400
1800
2200
2600
B
Control
Fasting
lox/lox
MGRKO
Atrogin-1
GAPDH
Atrogin/GAPDH
C
p-Akt
Akt
p-FOXO1
FOXO1

S2


A
lox/lox
MIRKO
B
lox/lox
MIRKO


C
Urinary Corticosterone
(ug/Kg/Day)
50
40
30
20
10
0
*
NS
CTL
DM
lox/lox
MIRKO


D
Dex
0 min
15 min
30 min
45 min
CFP
FRET


A
lox/lox
lox/lox + fasting
MIRKO
MIRKO + fasting
% of Fibers
loxl/lox
lox/lox+F
(μm²) 600 1000 1400 1800 2200 2600
MIRKO
MIRKO+F
B
Control
Fasting
lox/lox MIRKO lox/lox MIRKO
Atrogin-1
GAPDH
Atrogin-1/GAPDH
C
p-Akt
Akt
p-FOXO1
FOXO1

Supplemental figure 1: A: Acute diabetes induces muscle atrophy (CS vs C) as indicated by a left shift in the distribution of myofiber sizes. Adrenalectomy ameliorated diabetes-induced muscle atrophy (AS vs C). Adding DEX restored the diabetes-induced muscle atrophy in adrenalectomized mice (ASD vs C). B: Protein synthesis (Left panel) in muscles from control mice (C) was suppressed by acute diabetes (CS). Adrenalectomy did not eliminate the diabetes-induced in protein synthesis (AS). Adding DEX did not change muscle protein synthesis (ASD or AD) (*, $p< 0.05$; n=6 mice in each group). Right panel: the increase in protein breakdown in muscles of acutely diabetic mice (CS) was blocked by adrenalectomy (AS) and restored by DEX replacement (ASD). DEX (AD) or adrenalectomy (A) alone did not affect protein breakdown (*, $p<0.05$; n=6). C: DEX (n=3) did not change tyrosine phosphorylation of either the insulin receptor (left panel) or IRS-1 (right panel).

Supplemental figure 2: MGRKO mice are resistant to fasting-induced muscle atrophy. A. comparison of the distribution of the cross sectional areas of myofibers in fasted and non fasted lox/lox, control and MGRKO mice. B. Atrogin-1/MAFbx mRNA values in muscles from lox/lox mice were higher in response to fasting compared to results in MGRKO mice. C. Fasting of lox/lox mice reduced p-Akt and p-FoxO1 levels in muscle more than in muscles of MGRKO mice (n = 5 in each group; $p<0.05$).

Supplemental figure 3: A: By immunofluorescence analysis, the Cre recombinase (Red) was expressed in nuclei of myofibers from MIRKO mice but not in satellite cell nuclei (arrows). Green staining is for dystrophin; blue staining of nuclei is by DAPI. B. Insulin receptor expression (green staining) was markedly decreased in myofibers of

MIRKO mice; insulin receptors were expressed in satellite/vascular cells (arrows). C . In control mice, acute diabetes (DM) markedly increased corticosterone production. In MIRKO mice, defective insulin signaling in muscle did not stimulate corticosterone production (*, $p<0.001$, $n=3$). D: A fluorescence resonance energy transfer (FRET) analysis (lower panel) confirmed that GR and p85 of PI3K interact. DEX caused GR-CFP to translocate to the nucleus but abundant GR-CFP remained in the cytosol (upper panel). Cytosolic GR-CFP (donor) interacted with p85-YFP (recipient) resulting in an increase of FRET in the cytoplasma.

Supplemental figure 4: MIRKO mice develop muscle atrophy with fasting. A. comparison of the distribution of cross sectional areas of myofibers with and without fasting of lox/lox, control and MIRKO mice. B. Atrogin-1/MAFbx mRNA values in muscles from lox/lox and MIRKO increased to a similar degree when mice were fasted. C. Fasting reduced p-Akt and p-FoxO1 levels in muscles of lox/lox and MIRKO mice to a similar degree ($n = 5$ in each group; $p<0.05$).