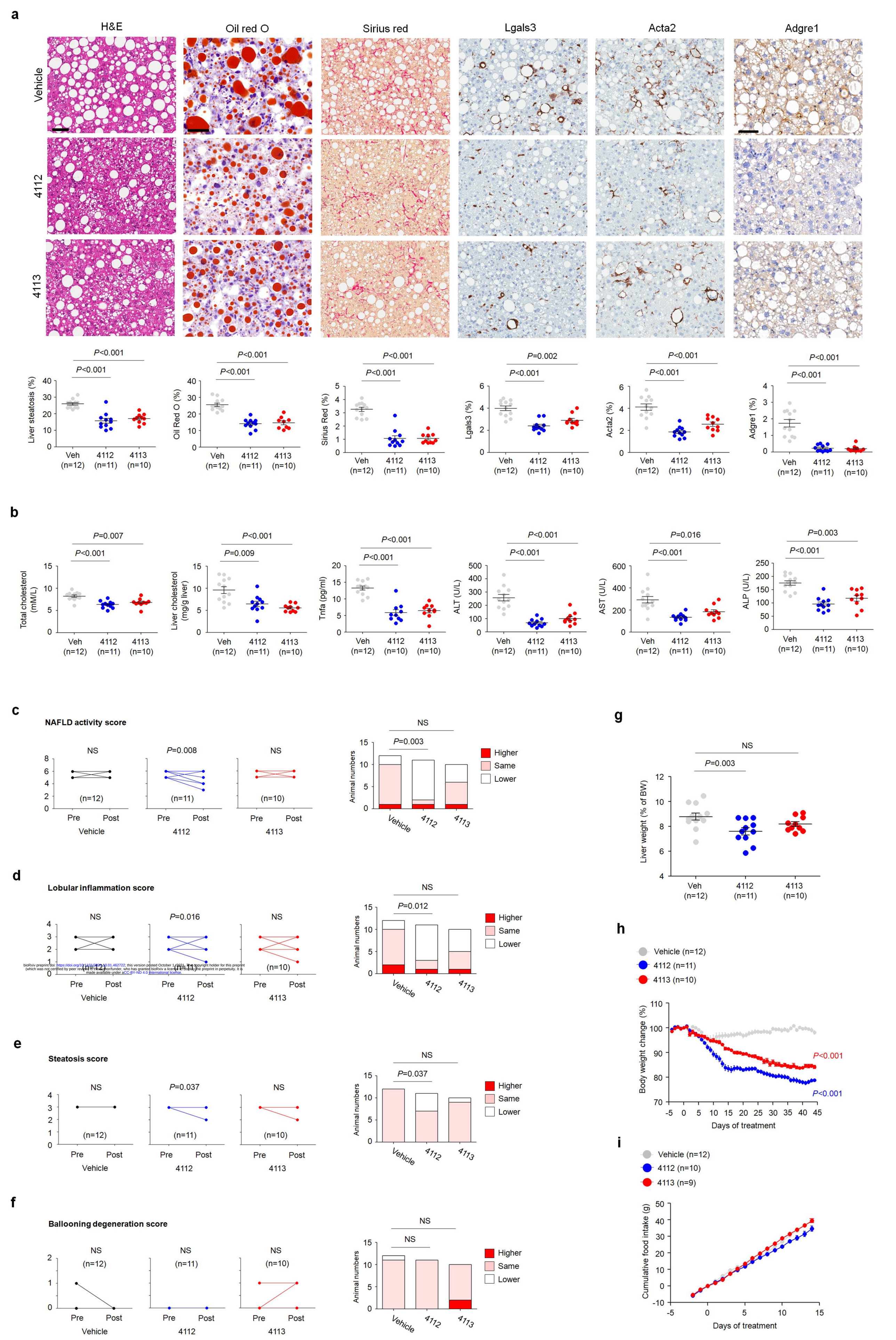

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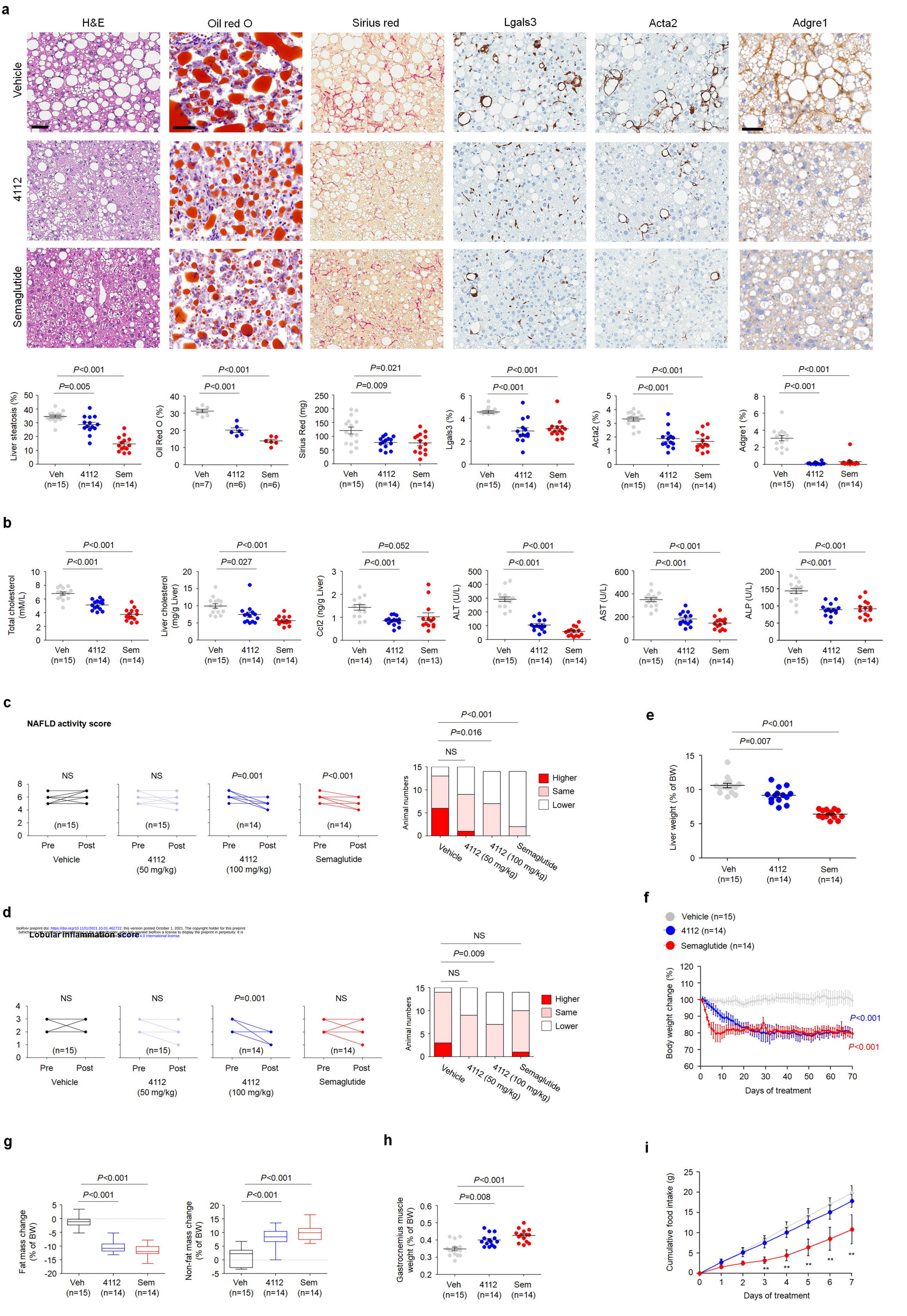

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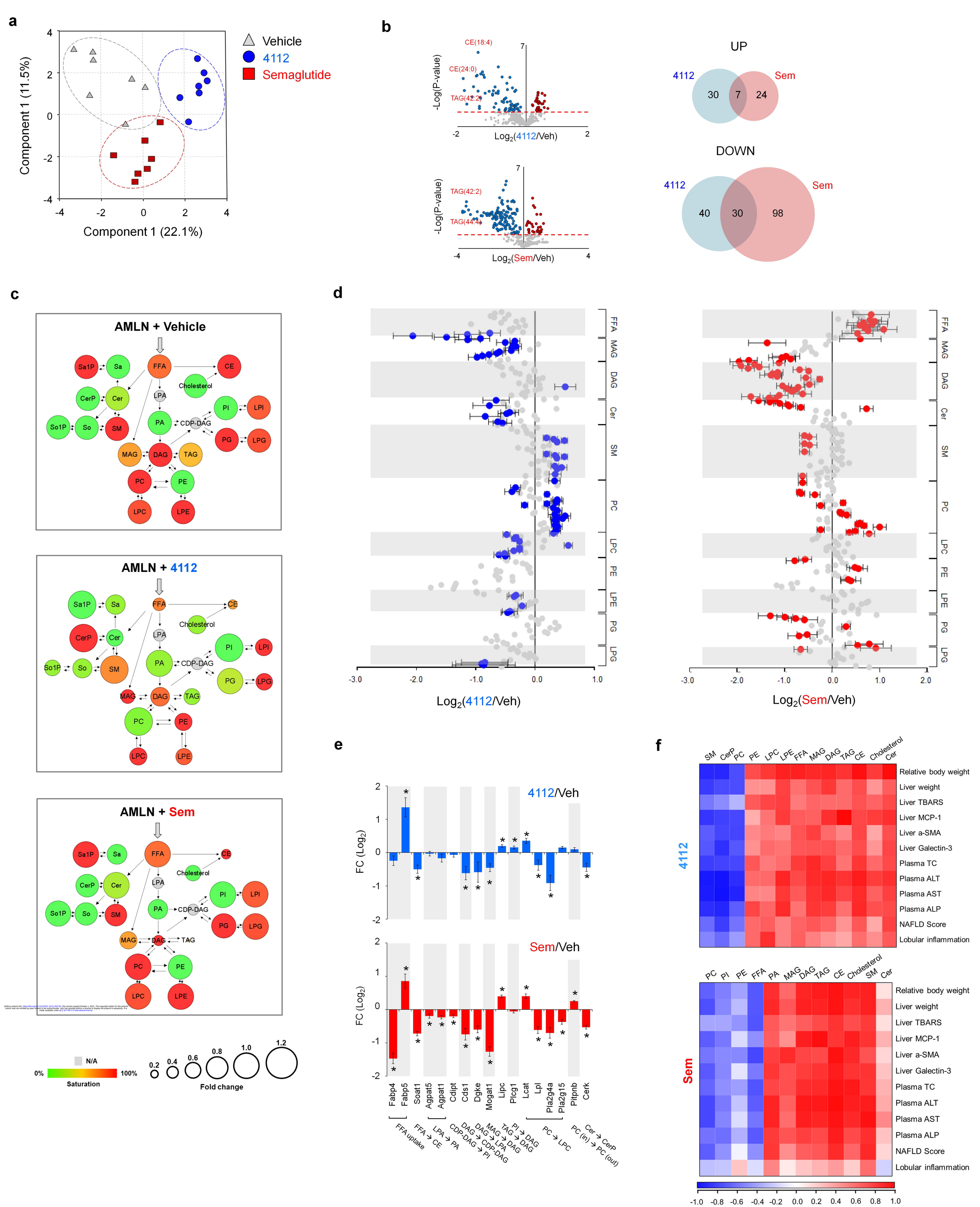
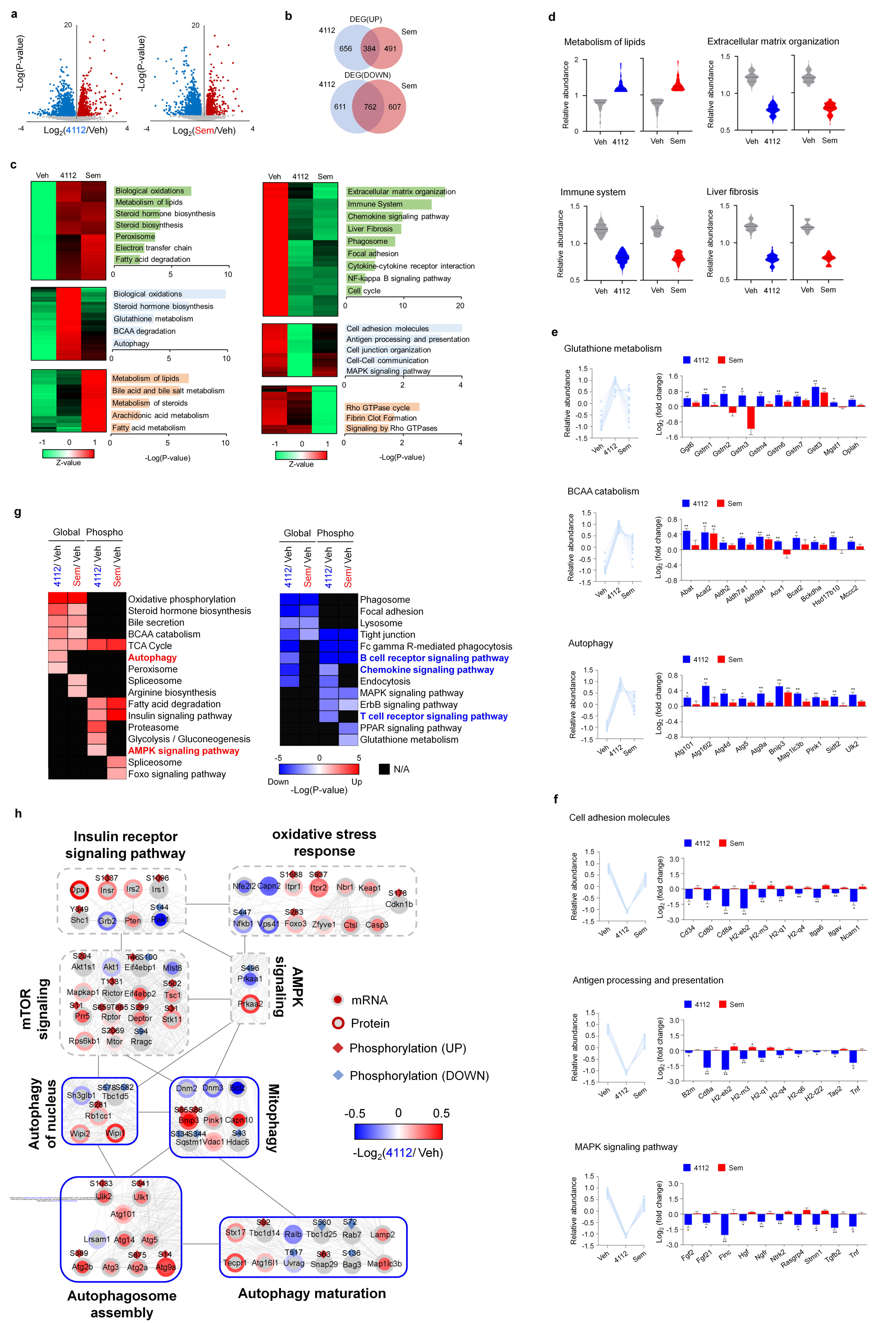
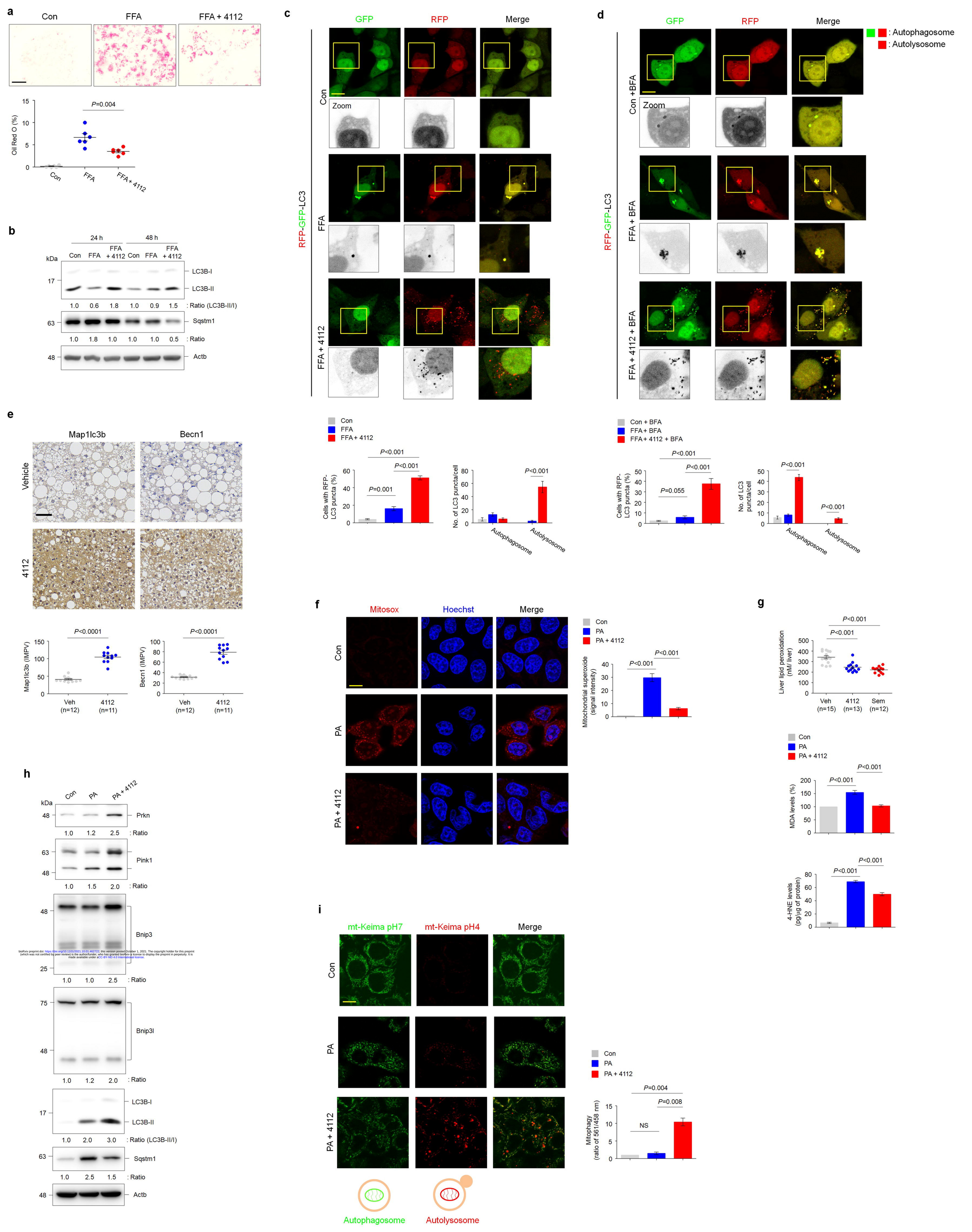

a
Vehicle
4112
Semaglutide
Component 1 (11.5%)
Component 1 (22.1%)
b
CE(18:4)
CE(24:0)
TAG(42:2)
TAG(44:4)
-Log(P-value)
Log2(4112/Veh)
Log2(Sem/Veh)
UP
4112
Sem
30
7
24
DOWN
40
30
98
c
AMLN + Vehicle
AMLN + 4112
AMLN + Sem
Sa1P
Sa
FFA
CE
Cholesterol
CerP
Cer
LPA
PI
LPI
So1P
So
SM
PA
CDP-DAG
PG
LPG
MAG
DAG
TAG
PC
PE
LPC
LPE
N/A
0%
100%
Saturation
0.2
0.4
0.6
0.8
1.0
1.2
Fold change
d
FFA
MAG
DAG
Cer
SM
PC
LPC
PE
LPE
PG
LPG
Log2(4112/Veh)
Log2(Sem/Veh)
e
4112/Veh
Sem/Veh
FC (Log2)
Fabp4
Fabp5
Soat1
Agpat5
Agpat1
Cdipt
Cds1
Dgke
Mogat1
Lipc
Plcg1
Lcat
Lpl
Pla2g4a
Pla2g15
Pitpnb
Cerk
FFA uptake
FFA → CE
LPA → PA
CDP-DAG → PI
DAG → CDP-DAG
MAG → LPA
TAG → DAG
PI → DAG
PC → LPC
Cer → CerP
PC (in) → PC (out)
f
SM
CerP
PC
PE
LPC
LPE
FFA
MAG
DAG
TAG
CE
Cholesterol
Cer
Relative body weight
Liver weight
Liver TBARS
Liver MCP-1
Liver a-SMA
Liver Galectin-3
Plasma TC
Plasma ALT
Plasma AST
Plasma ALP
NAFLD Score
Lobular inflammation
4112
PC
PI
PE
FFA
PA
MAG
DAG
TAG
CE
Cholesterol
SM
Cer
Sem


a
-Log(P-value)
Log2(4112/Veh)
Log2(Sem/Veh)
b
DEG(UP)
4112
Sem
656
384
491
DEG(DOWN)
611
762
607
c
Veh
4112
Sem
Biological oxidations
Metabolism of lipids
Steroid hormone biosynthesis
Steroid biosynthesis
Peroxisome
Electron transfer chain
Fatty acid degradation
Glutathione metabolism
BCAA degradation
Autophagy
Bile acid and bile salt metabolism
Metabolism of steroids
Arachidonic acid metabolism
Z-value
-Log(P-value)
Extracellular matrix organization
Immune System
Chemokine signaling pathway
Liver Fibrosis
Phagosome
Focal adhesion
Cytokine-cytokine receptor interaction
NF-kappa B signaling pathway
Cell cycle
Cell adhesion molecules
Antigen processing and presentation
Cell junction organization
Cell-Cell communication
MAPK signaling pathway
Rho GTPase cycle
Fibrin Clot Formation
Signaling by Rho GTPases
d
Metabolism of lipids
Extracellular matrix organization
Immune system
Liver fibrosis
Relative abundance
e
Glutathione metabolism
BCAA catabolism
Autophagy
4112
Sem
Relative abundance
Log2 (fold change)
Ggt6
Gstm1
Gstm2
Gstm3
Gstm4
Gstm6
Gstm7
Gstt3
Mgst1
Oplah
Abat
Acat2
Aldh2
Aldh7a1
Aldh9a1
Aox1
Bcat2
Bckdha
Hsd17b10
Mccc2
Atg101
Atg16l2
Atg4d
Atg5
Atg9a
Bnip3
Map1lc3b
Pink1
Sidt2
Ulk2
f
Cell adhesion molecules
Antigen processing and presentation
MAPK signaling pathway
Cd34
Cd80
Cd8a
H2-eb2
H2-m3
H2-q1
H2-q4
Itga6
Itgav
Ncam1
B2m
H2-q6
H2-t22
Tap2
Tnf
Fgf2
Fgf21
Flnc
Hgf
Ngfr
Ntrk2
Rasgrp4
Stmn1
Tgfb2
g
Global
Phospho
4112/ Veh
Sem/ Veh
Oxidative phosphorylation
Steroid hormone biosynthesis
Bile secretion
BCAA catabolism
TCA Cycle
Autophagy
Peroxisome
Spliceosome
Arginine biosynthesis
Fatty acid degradation
Insulin signaling pathway
Proteasome
Glycolysis / Gluconeogenesis
AMPK signaling pathway
Spliceosome
Foxo signaling pathway
Phagosome
Focal adhesion
Lysosome
Tight junction
Fc gamma R-mediated phagocytosis
B cell receptor signaling pathway
Chemokine signaling pathway
Endocytosis
MAPK signaling pathway
ErbB signaling pathway
T cell receptor signaling pathway
PPAR signaling pathway
Glutathione metabolism
Down
Up
-Log(P-value)
N/A
h
Insulin receptor signaling pathway
oxidative stress response
mTOR signaling
AMPK signaling
Autophagy of nucleus
Mitophagy
Autophagosome assembly
Autophagy maturation
mRNA
Protein
Phosphorylation (UP)
Phosphorylation (DOWN)
-Log2(4112/ Veh)



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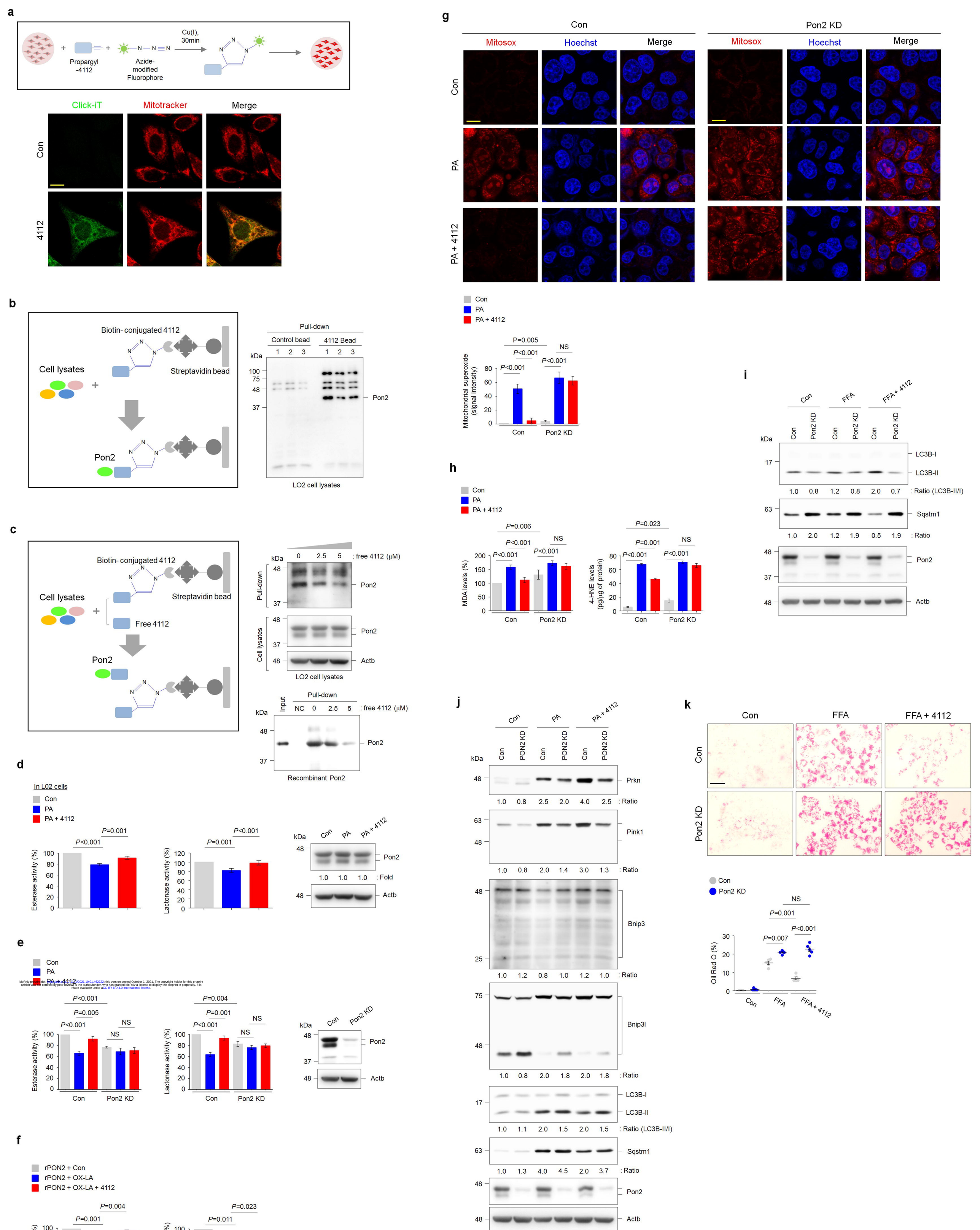

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