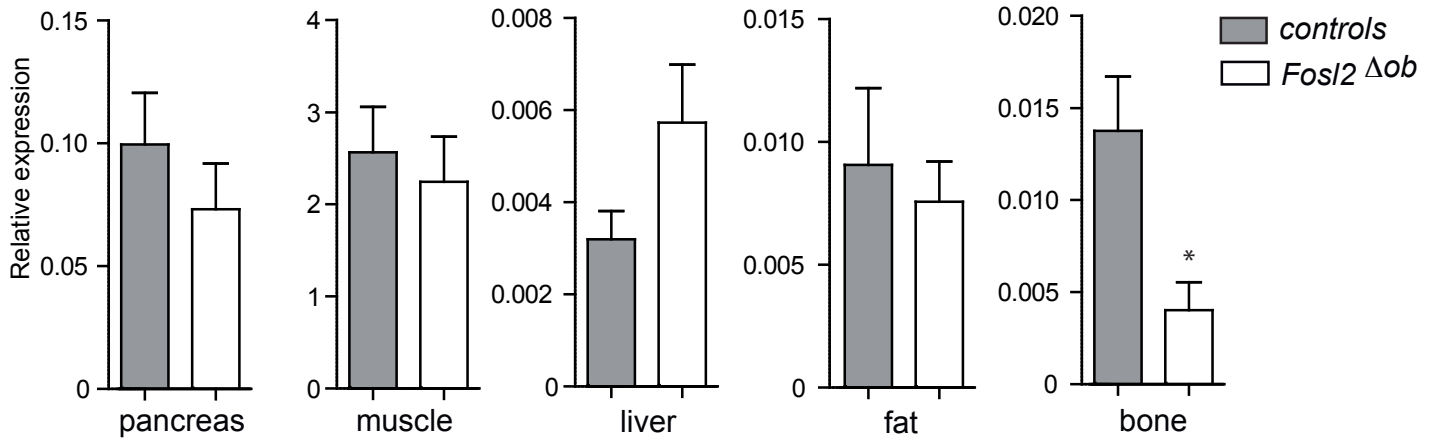
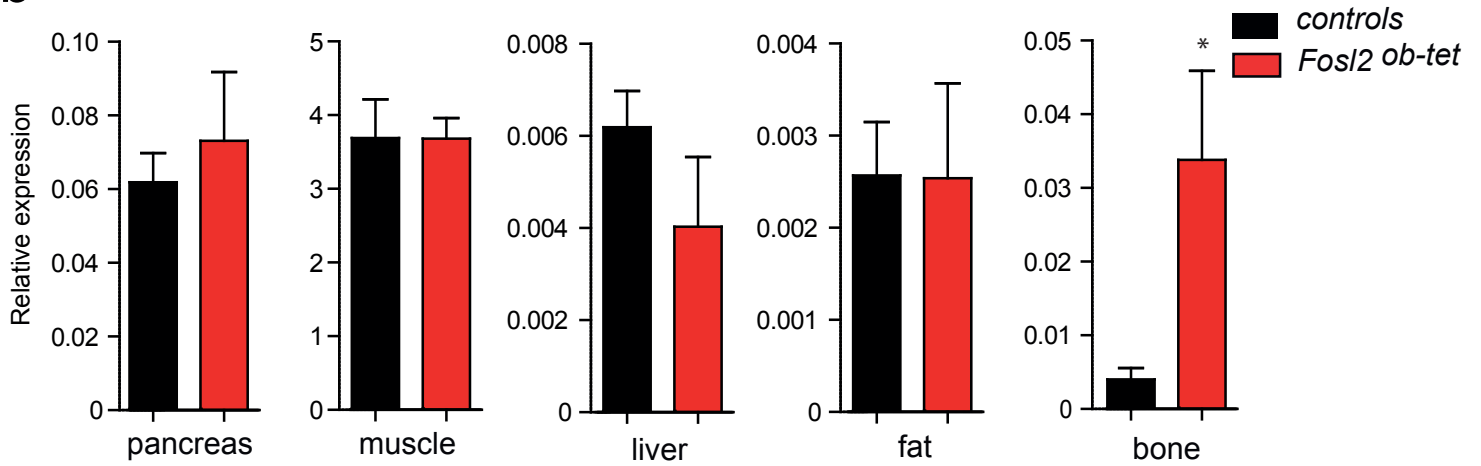


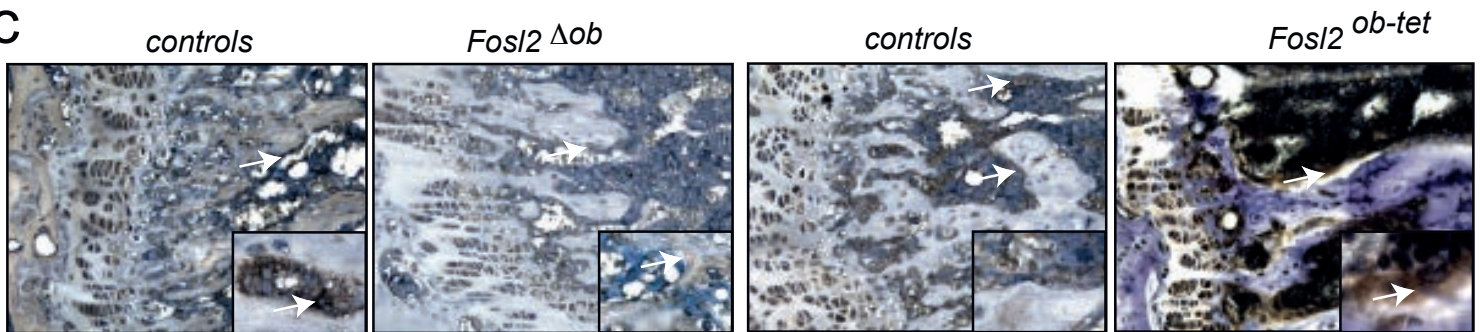
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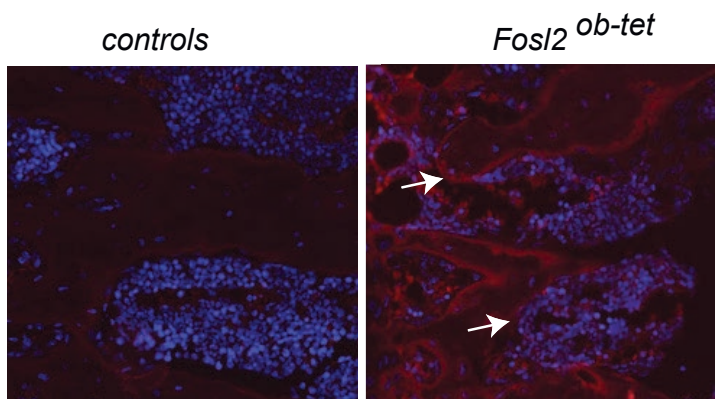
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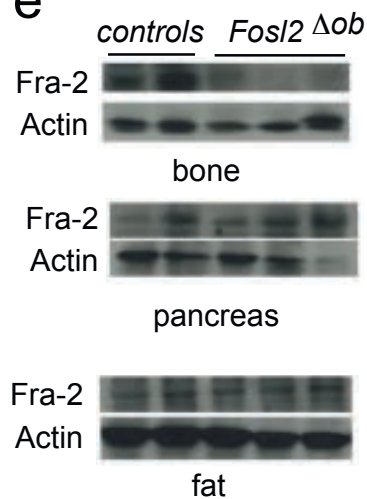
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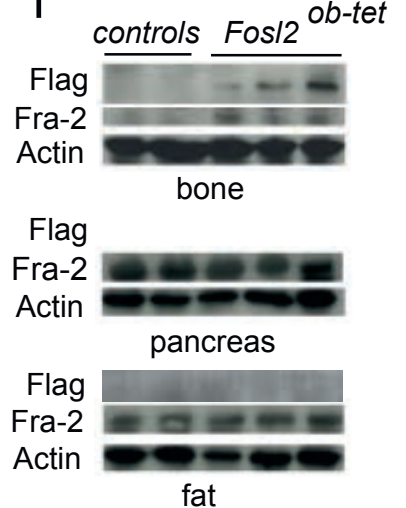
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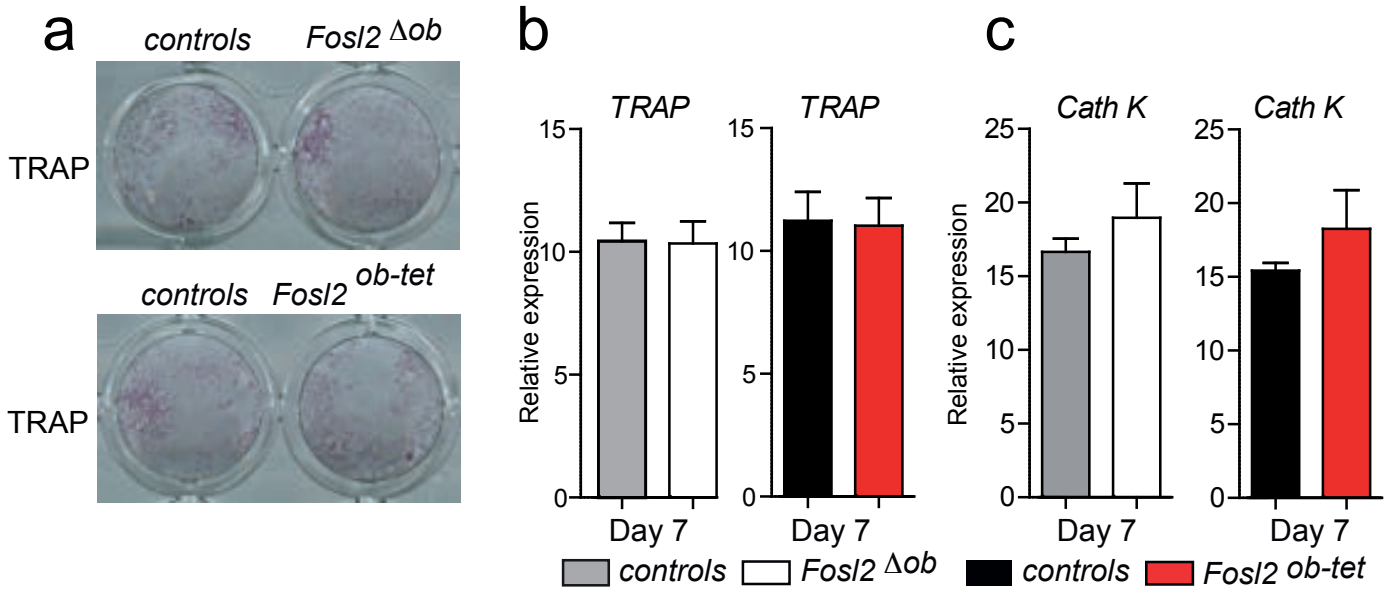
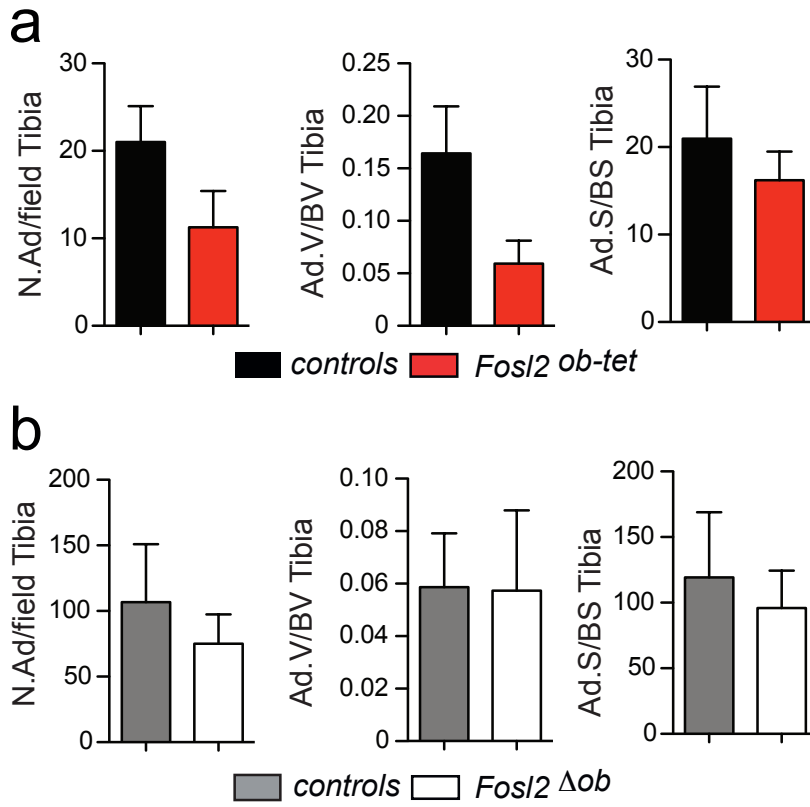


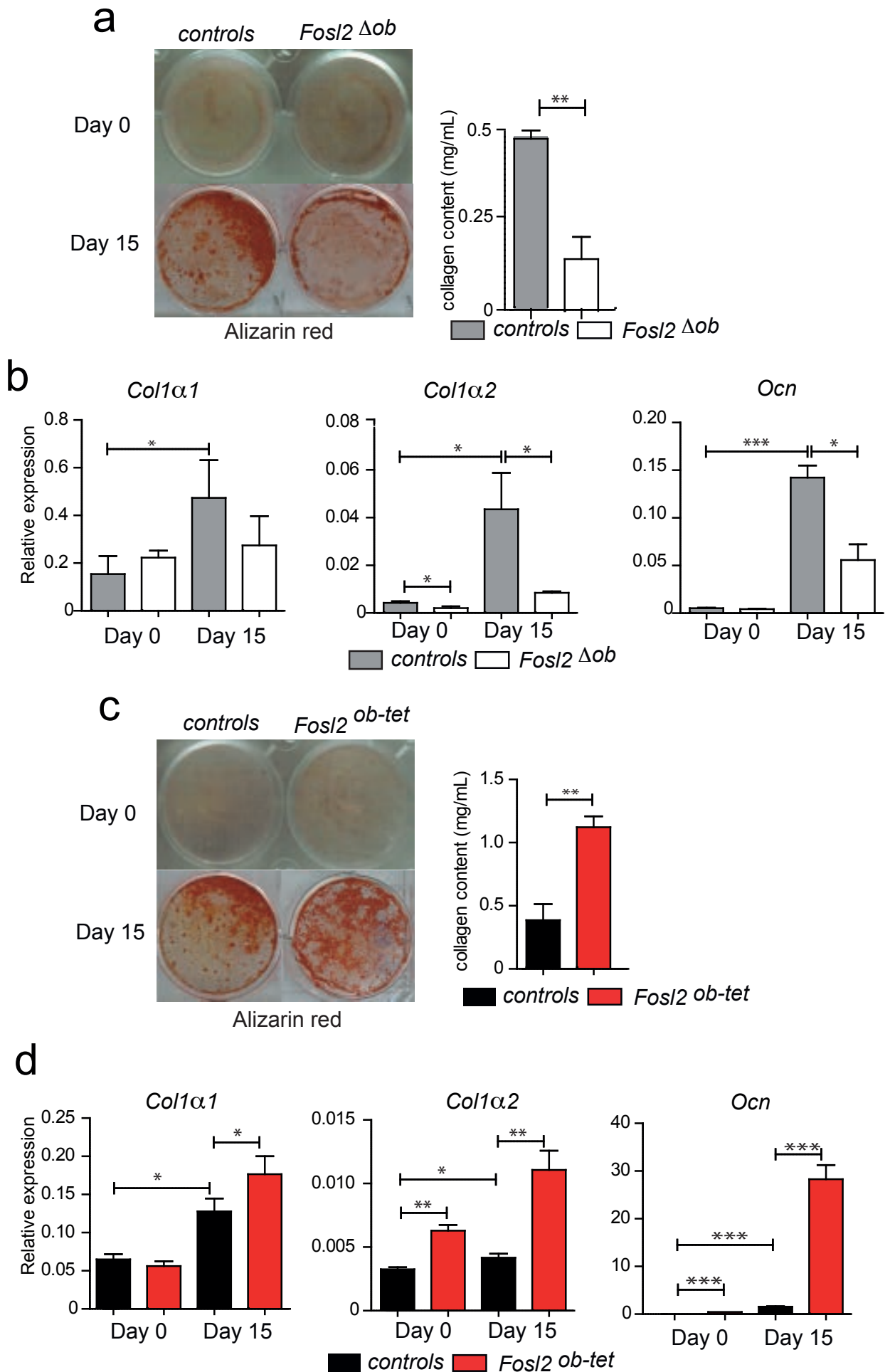
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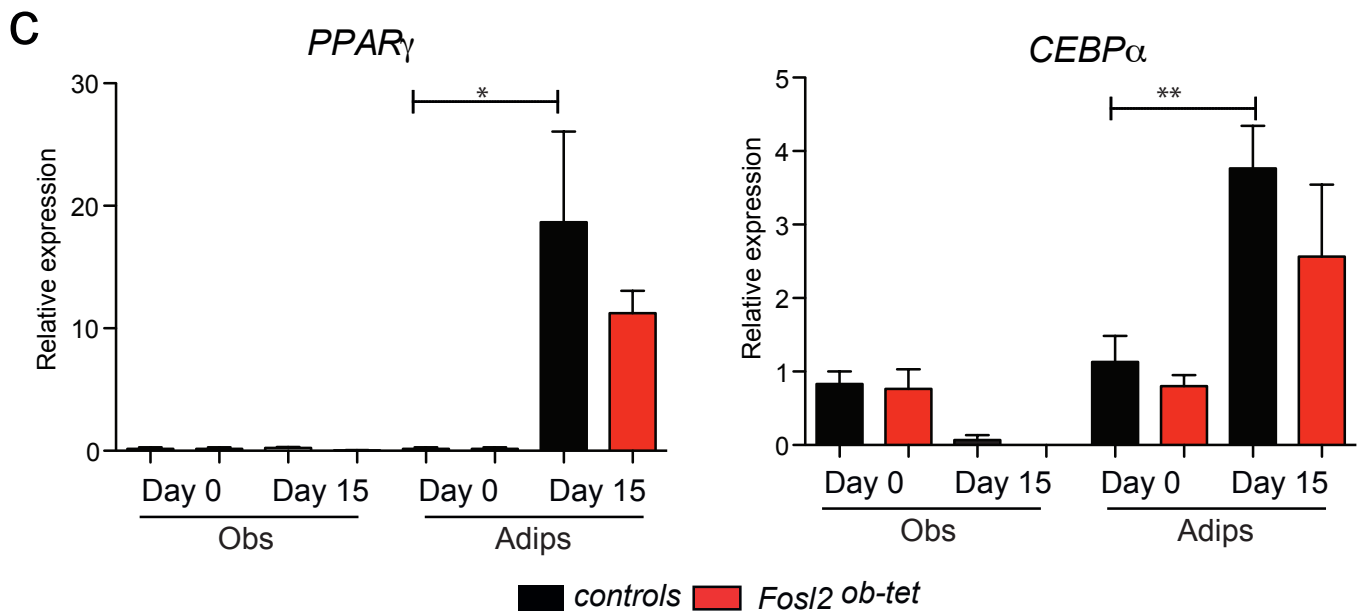
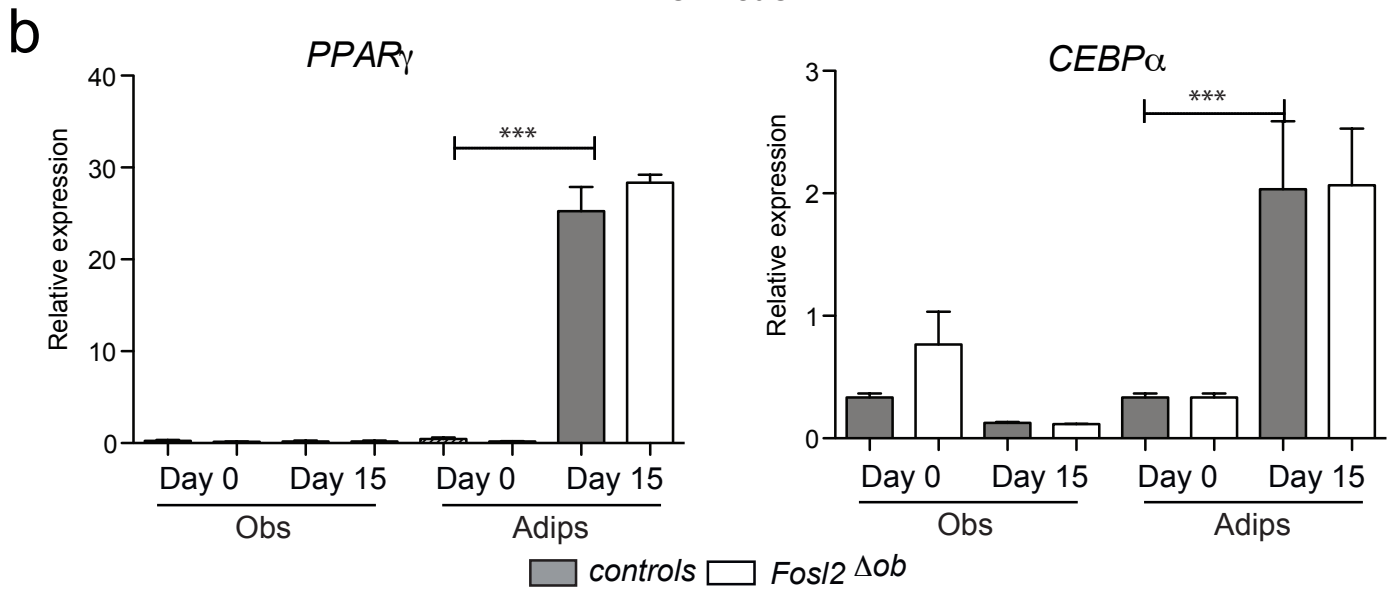
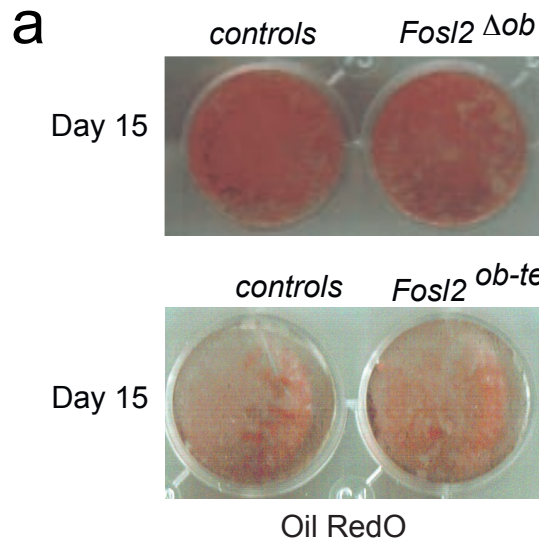


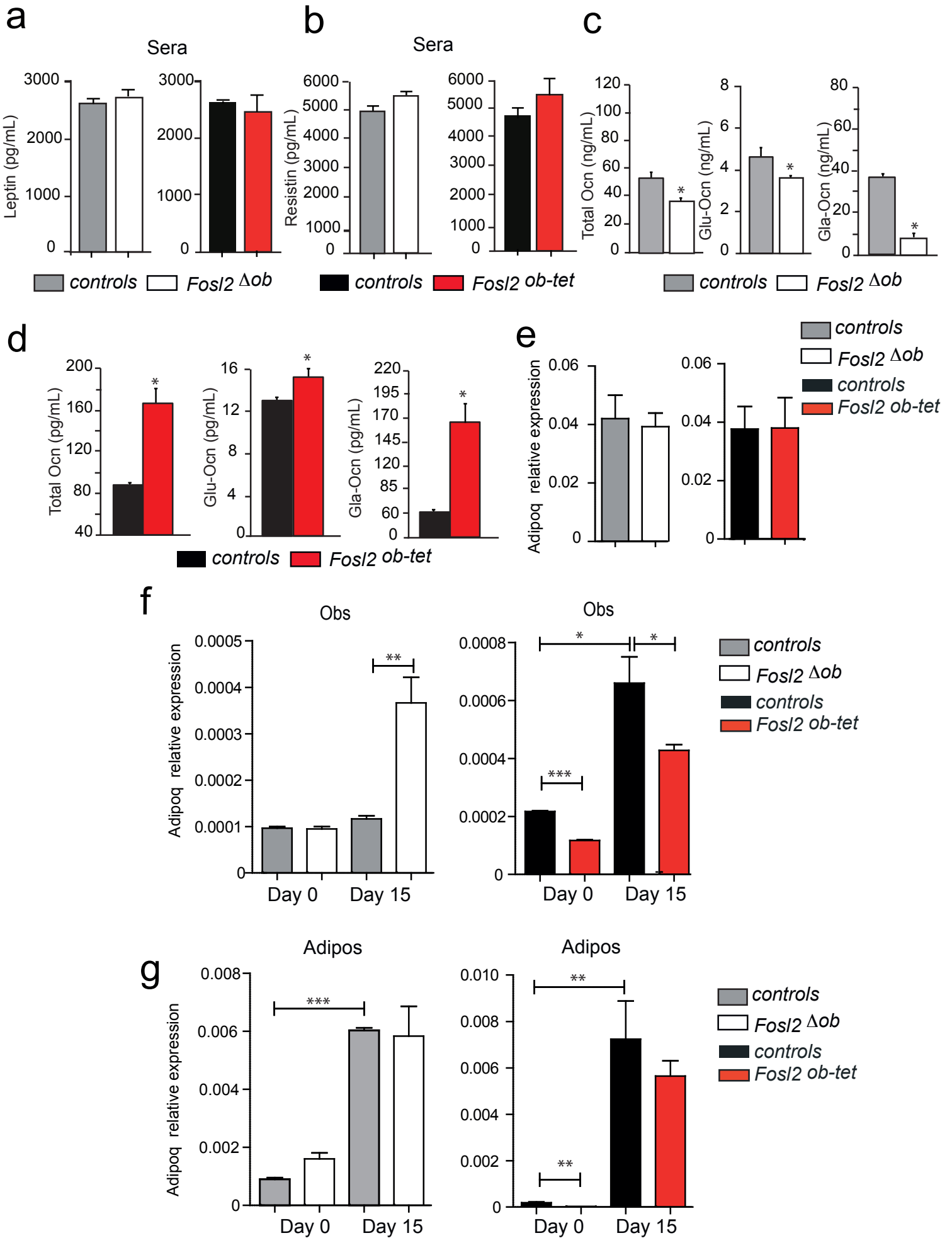
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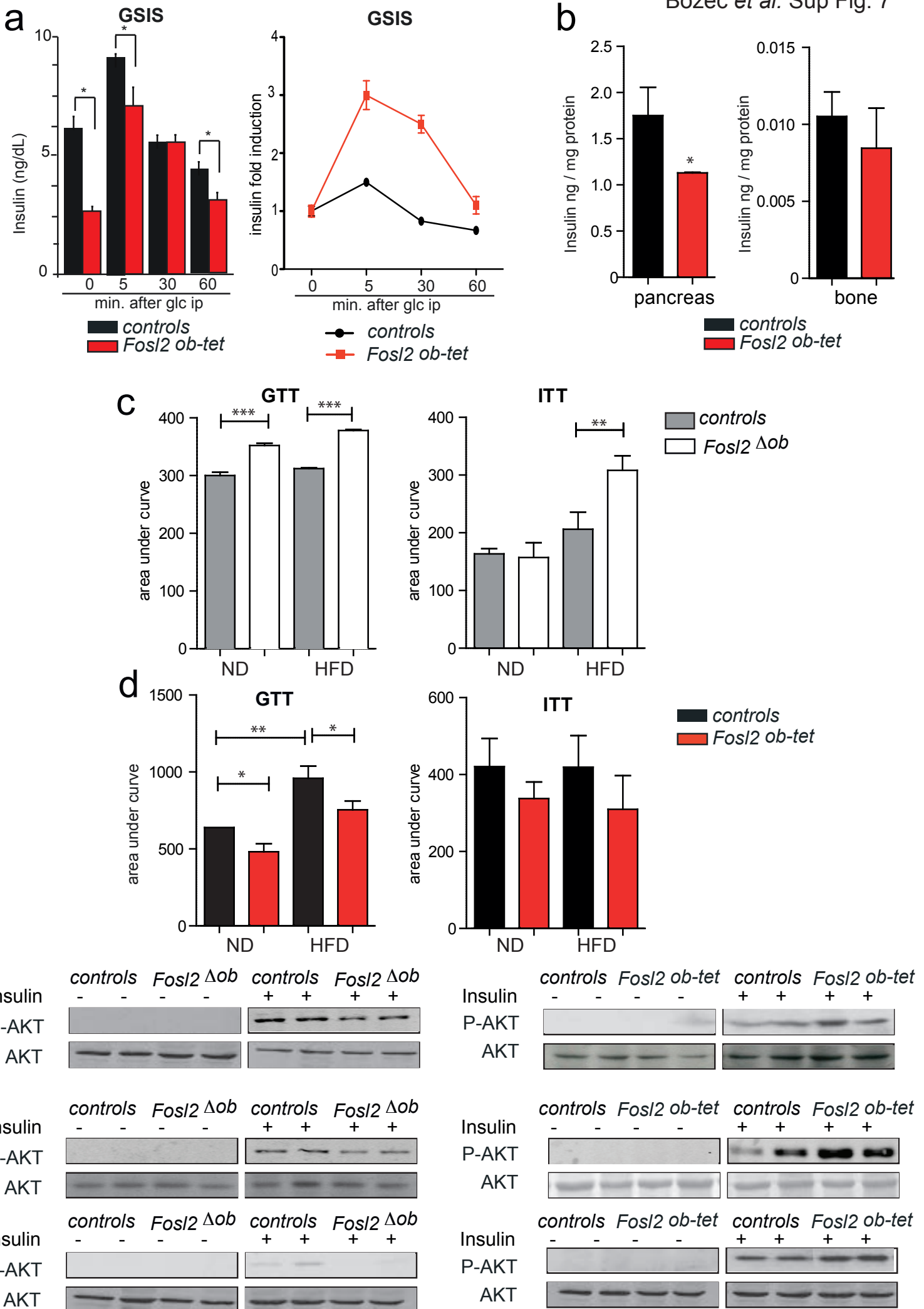












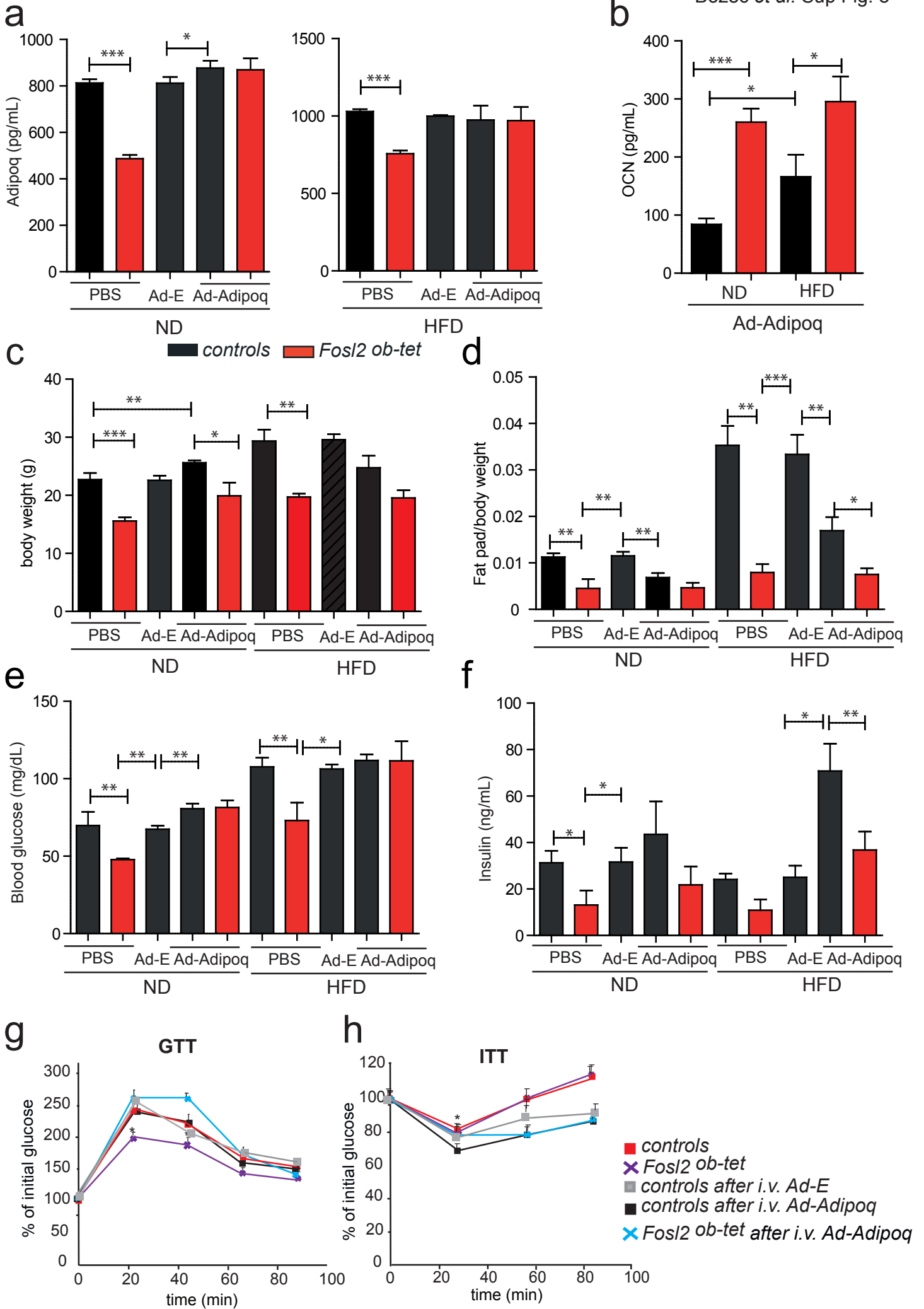


Fig. S1. Fra-2 expression in *Fosl2*^{Δob} and *Fosl2*^{ob-tet} mice. a, b: qPCR analyses of Fra-2 in pancreas, muscle, liver, fat and bone from *Fosl2*^{Δob} (a) and *Fosl2*^{ob-tet} (b) mice at 6 weeks of age; bars represent mean values ± SD (n=6). c: Immuno-histochemical (IHC) analyses of Fra-2 in *Fosl2*^{Δob} and *Fosl2*^{ob-tet} long bones at 2 months of age; magnification 20x. Inserts: 40x. White arrows indicate osteoblasts. d: Immuno-fluorescence analyses of Fra-2 in *Fosl2*^{ob-tet} long bones at 2 months of age; magnification 20x. White arrows indicate osteoblasts. e: Western blot analyses of Fra-2 in bone, pancreas and fat pad from controls and *Fosl2*^{Δob} mice at 6 weeks of age (n=2/3); actin was used as loading control. f: Western blot analyses of Flag and Fra-2 in bone, pancreas and fat pad from controls and *Fosl2*^{ob-tet} mice at 6 weeks of age (n=2/3); actin was used as loading control. Statistical analyses: *P<0.05, **P<0.01, ***P<0.001.

Fig. S2. *In vivo* adipocyte phenotypes in osteoblast-specific Fra-2 mutant mice. a, b: Quantification of number of adipocytes per field Tibia (N.Ad/field Tibia), adipocyte volume per bone volume (Ad.V/BV Tibia) and adipocyte surface per bone surface (Ad.S/BS Tibia) in *Fosl2*^{Δob} (a) and *Fosl2*^{ob-tet} (b) mice at 2 months of age (n=8).

Fig. S3. *In vitro* analyses of osteoclasts from osteoblast-specific Fra-2 mutant mice. a: TRAP staining in *Fosl2*^{Δob} and *Fosl2*^{ob-tet} osteoclasts during differentiation at day 7 after addition of M-CSF and Rankl (n=3). b, c: qPCR analyses of *TRAP* (b) and *CathK* (c) in *Fosl2*^{Δob} and *Fosl2*^{ob-tet} osteoclasts during differentiation at day 7 after addition of M-CSF and Rankl (n=3).

Fig. S4. *In vitro* analyses of osteoblasts from osteoblast-specific Fra-2 mutant mice. a: Alizarin red staining and collagen content of mineralized osteoblasts derived from calvariae of *Fosl2*^{Δob} mice at day 0 and 15 of *in vitro* differentiation (n=5). b: qPCR analyses of *collα1*, *Collα 2* and *Ocn* in osteoblasts from *Fosl2*^{Δob} cultures at day 0 and 15 of *in vitro* differentiation; error bars represent SD (n=6) c: Alizarin red staining and collagen content of mineralized osteoblasts derived from calvariae of *Fosl2*^{ob-tet} mice at day 0 and 15 of *in vitro* differentiation (n=5). d: qPCR analyses of *collα1*, *Collα 2* and *Ocn* in osteoblasts from *Fosl2*^{ob-tet} cultures at day 0 and 15 of *in vitro* differentiation; error bars represent SD (n=6). Statistical analyses: *P<0.05, **P<0.01, ***P<0.001.

Fig. S5. *In vitro* analyses of adipocytes from osteoblast-specific Fra-2 mutant mice. a: Oil RedO staining of adipocytes derived from calvariae of *Fosl2*^{Δob} and *Fosl2*^{ob-tet} at day 15 of *in vitro* differentiation (n=3). b, c: qPCR analyses of *PPARγ* and *CEBPα* in osteoblasts and adipocytes from *Fosl2*^{Δob} (b) and *Fosl2*^{ob-tet} (c) cultures at day 0 and 15 of *in vitro* differentiation; error bars represent SD (n=6). Statistical analyses: *P<0.05, **P<0.01, ***P<0.001

Fig. S6. Adiponectin expression in Fra-2 mutant mice. a, b: Leptin (a) and Resistin (b) levels in sera from controls and *Fosl2*^{Δob} or *Fosl2*^{ob-tet} mice at 3 months of age; error bars represent SD (n=4/6). c, d: Total, Glu and Gla Ocn levels in sera from controls, *Fosl2*^{Δob} (c) and *Fosl2*^{ob-tet} (d) mice (n=10). e: qPCR analyses of *Adipoq* in fat from *Fosl2*^{Δob} or *Fosl2*^{ob-tet} mice at 3 months of age; error bars represent SD (n=6). f, g: qPCR analyses of *Adipoq* in osteoblasts (f) and adipocytes (g) from *Fosl2*^{Δob} and *Fosl2*^{ob-tet} cultures at day 0 and 15 of *in vitro* differentiation; error bars represent SD (n=5). Statistical analyses: *P<0.05, **P<0.01, ***P<0.001.

Fig. S7. Metabolic phenotype of Fra-2 mutant mice. a: Glucose-stimulated insulin secretion (GSIS) graph and curve measured by insulin fold induction where time 0=1 in 3 months old controls and *Fosl2*^{ob-tet} mice (n=6). b: Insulin content per mg protein of pancreas or bone from 3 months old *Fosl2*^{ob-tet} mice; error bars represent SD (n=3). c, d: Area under curve analyses of the GTT and ITT tests after 6h or 3h fasting from *Fosl2*^{Δob} (c) and *Fosl2*^{ob-tet} (d) mice following 6 weeks of ND or HFD; error bars represent SD (n=6/7). e-g: Western blot analyses of p-AKT and AKT in fat (e), liver (f) and muscle (g) from controls and *Fosl2*^{Δob} (left panel) or *Fosl2*^{ob-tet} (right panel) mice 15 min after vehicle or insulin injection (n=4). Statistical analyses: *P<0.05, **P<0.01, ***P<0.001

Fig. S8. Injection of Adeno-Adipoq into *Fosl2*^{ob-tet} mice partially rescues the metabolic phenotype. a: Adipoq levels in sera from controls and *Fosl2*^{ob-tet} mice, under ND or HFD for 6 weeks, 12 days after i.v. injection of PBS (Co), Adeno-Empty (Ad-E) or Adeno-Adipoq (Ad-Adipoq); error bars represent SD. (n=6/8). b: Total Ocn levels in sera from controls and *Fosl2*^{ob-tet} mice under ND or HFD for 6 weeks, 12 days after i.v. injection of Adeno-Adipoq (Ad-Adipoq); error bars represent SD (n=6). c: Weight of controls and *Fosl2*^{ob-tet} mice, under ND or HFD for 6 weeks, 12 days after i.v. injection of PBS (Co), Adeno-Empty (Ad-E) or Adeno-Adipoq (Ad-Adipoq); error bars represent SD. (n=6/8). d: Fat pad/total weight of controls and *Fosl2*^{ob-tet} mice, under ND or HFD for 6 weeks, 12 days after i.v. injection of PBS (Co), Adeno-Empty (Ad-E) or Adeno-Adipoq (Ad-Adipoq); error bars represent SD. (n=6/8). e, f: Blood glucose (e) and insulin (f) levels from controls and *Fosl2*^{ob-tet} mice, under ND or HFD for 6 weeks, 12 days after i.v. injection of PBS (Co), Adeno-Empty (Ad-E) or Adeno-Adipoq (Ad-Adipoq); error bars represent SD. (n=6/8). g, h: Glucose tolerance (GTT) (g) and insulin tolerance (ITT) (h) tests after 6h or 3h fasting from 3 months old controls and *Fosl2*^{ob-tet} mice, 12 days after i.v. injection of PBS (Co), Adeno-Empty (Ad-E) or Adeno-Adipoq (Ad-Adipoq) (n=6/8). Statistical analyses: *P<0.05, **P<0.01, ***P<0.001