FIGURE LEGENDS FOR SUPPLEMENTAL MATERIALS

Supplemental FIG. S1. mRNA expressions of the 3 ORM isoforms are increased during adipocyte differentiation of the 3T3-L1 cells. n = 2.

Supplemental FIG. S2. ORM expression is elevated in the adipocyte fractions from fat tissues of *db/db* mice. Total RNAs were isolated from the adipocytes, SVCs, and peritoneal macrophages and analyzed by Q-PCR for the expression of ORM1 (*A*), ORM2 (*B*), ORM3 (*C*), TNFα (*D*), and adiponectin (AdipoQ) (*E*).

Supplemental FIG. S3. Western blot analysis of ORM expression in the plasma of obese and/or diabetic human patients.

Supplemental FIG. S4. Acute LPS treatment induces ORM in liver, but not in adipose tissue. *A*, LPS increases plasma ORM expression. C57BL6 mice were intraperitoneally administered with LPS (5 μg), and ORM expression in the plasma was analyzed by western blot analysis. *B*-*C*, Q-PCR analysis of the three isoforms of ORM in epididymal adipose tissue (*B*) and liver (*C*) of mice administered with LPS at 4 h and 24 h after injection.

Supplemental FIG. S5. Nutritional regulation of ORM expression in adipose tissue. C57BL/6J mice were separated into 3 groups. One group of mice was maintained under ad libitum (C). Another group of mice were fasted for 24h (F). And the other group of mice was refed for 6 h after 24h fasting (R). *A*, mRNA levels of ORM isoforms in epididymal adipose tissue were measured by Q-PCR. *B*, Circulating ORM level was measured by western blot.

Supplemental FIG. S6. Effect of ORM siRNAs on basal and TNFα-induced inflammatory gene expression. *A*, Nucleotide sequences of 3 separate siRNA oligomers and their mutants. *B*-*E*, 3 separate siRNA oligomers and their mutants were transiently transfected into 3T3-L1 adipocytes. 2 days after the transfection, cells were treated with TNFα (10 ng/ml) and/or ORM (250 μg/ml) for 24 h, and harvested for measuring RNA expressions of ORM1 (*B*), IL-6 (*C*), MCP-1 (*D*) and iNOS (*E*) by Q-PCR.

Supplemental FIG. S7. ORM protein is detected around adipocytes and nonvascular stromal cells of adipose tissue. Epididymal adipose tissues from lean (control) or diet-induced obese (DIO, fed HFD for 3 months) mice were immunostained with FITC-conjugated BODIPY (green; adipocytes), and antibodies against ORM (red) and PECAM (blue on the left panel; blood vessel), and wholemounted for multiphoton fluorescence confocal microscopy.

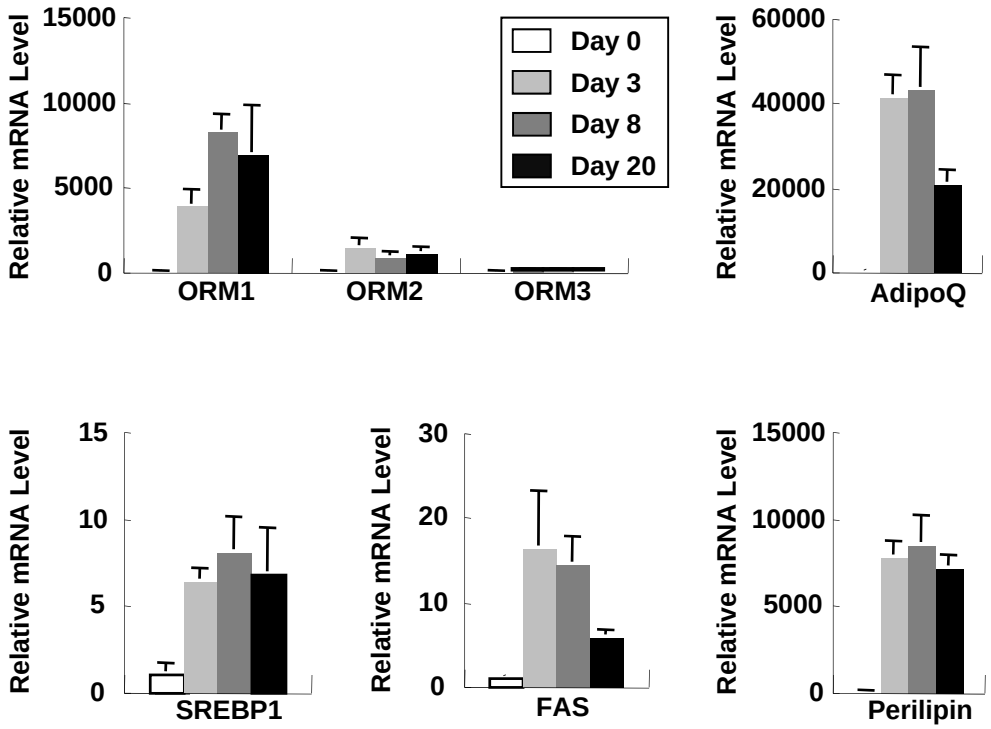
Supplemental FIG. S8. ORM suppresses ROS generation in THP-1 monocytes and RAW264.7 macrophages. *A*, THP-1 cells were treated with ORM for 24 h, and ROS levels were measured by flow cytometry after cell staining with DCFDA. *B*, RAW264.7 macrophages were treated with ORM for 6 h in the presence or absence of LPS. ROS levels were measured after DCF-DA staining.

Supplemental FIG. S9. Serum level of exogenous ORM protein after ORM infusion with osmotic pump. *A*, Western blot analysis with anti-human ORM antibody detected exclusively exogenous human ORM (purified from human serum). *B*, High affinity of ORM antibodies to human ORM protein. Mouse serum samples and/or purified human ORM protein samples were loaded on SDS-PAGE gel, and transferred to PVDF membrane. The membranes containing only mouse sera (Blot 1) or both mouse sera and human ORM protein (Blot 2) were hybridized with anti-human ORM antibodies separately. Anti-human ORM antibody detects only human ORM protein even in the presence of mouse ORM protein in western blots, whereas it detects mouse ORM protein when human ORM protein is absent.

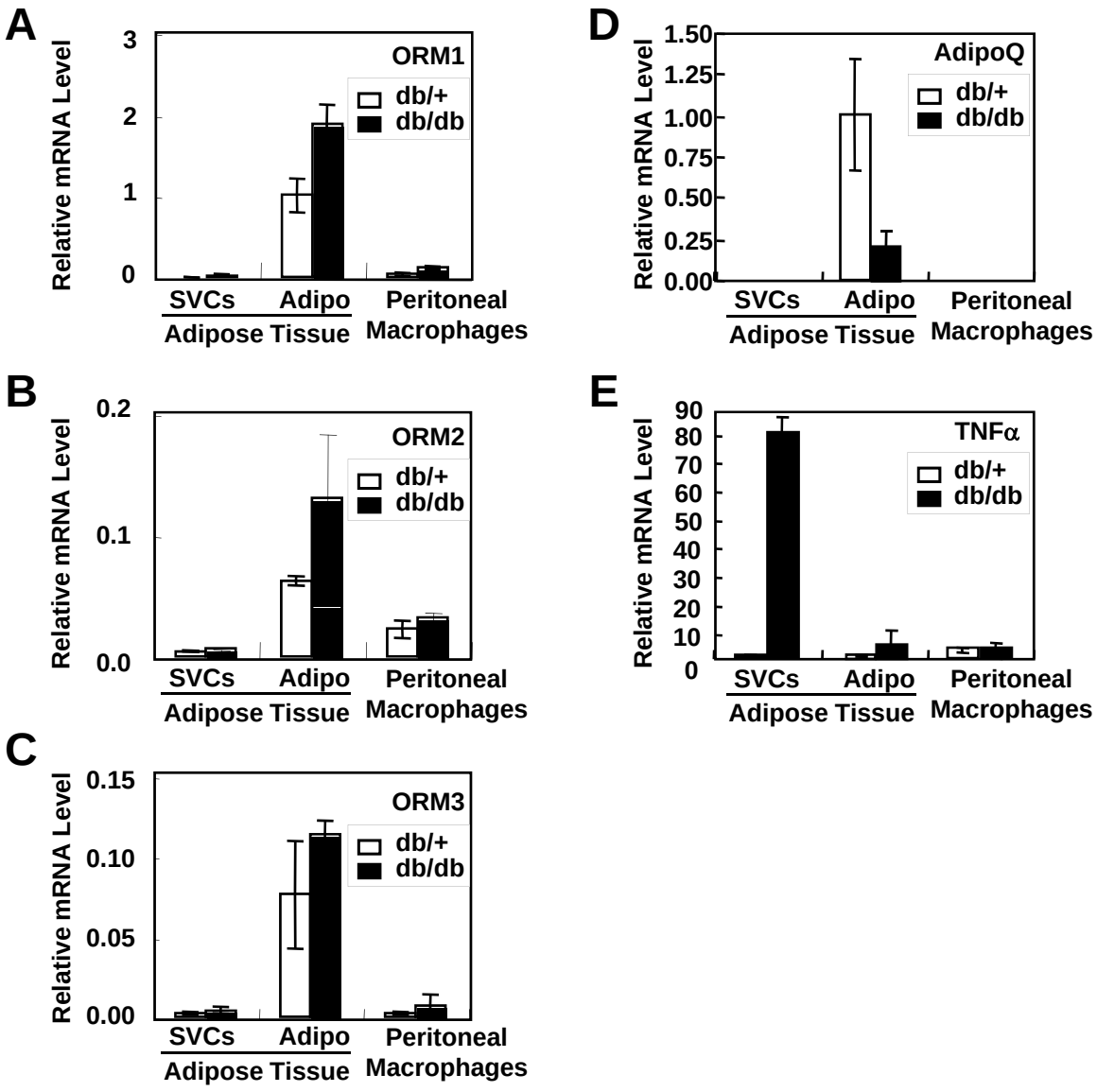
Supplemental FIG. S10. ORM1 overexpression improves glucose tolerance in *db/db* mice. ORM1 expressing adenovirus was i.v. injected (tail vein) into *db/db* mice. 1 and 2 week after injection, mice were subjected to glucose tolerance test and insulin tolerance test, respectively. *A*, ORM1 mRNA expression in the liver of GFP- and ORM1-adenovirus injected mice. *B*, Protein expression of ORM1 in serum of GFP- and ORM1-adenovirus injected mice. *C*, Oral glucose tolerance test (OGTT). *D*, Insulin tolerance test.

Supplemental FIG. S11. CCR5 and Siglec-E (mouse homologue of human Siglec-5) expressed in adipocytes and macrophages.

Supplement Figure S1



Supplement Figure S2



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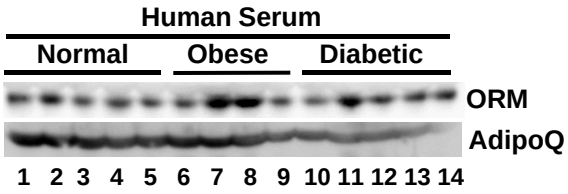

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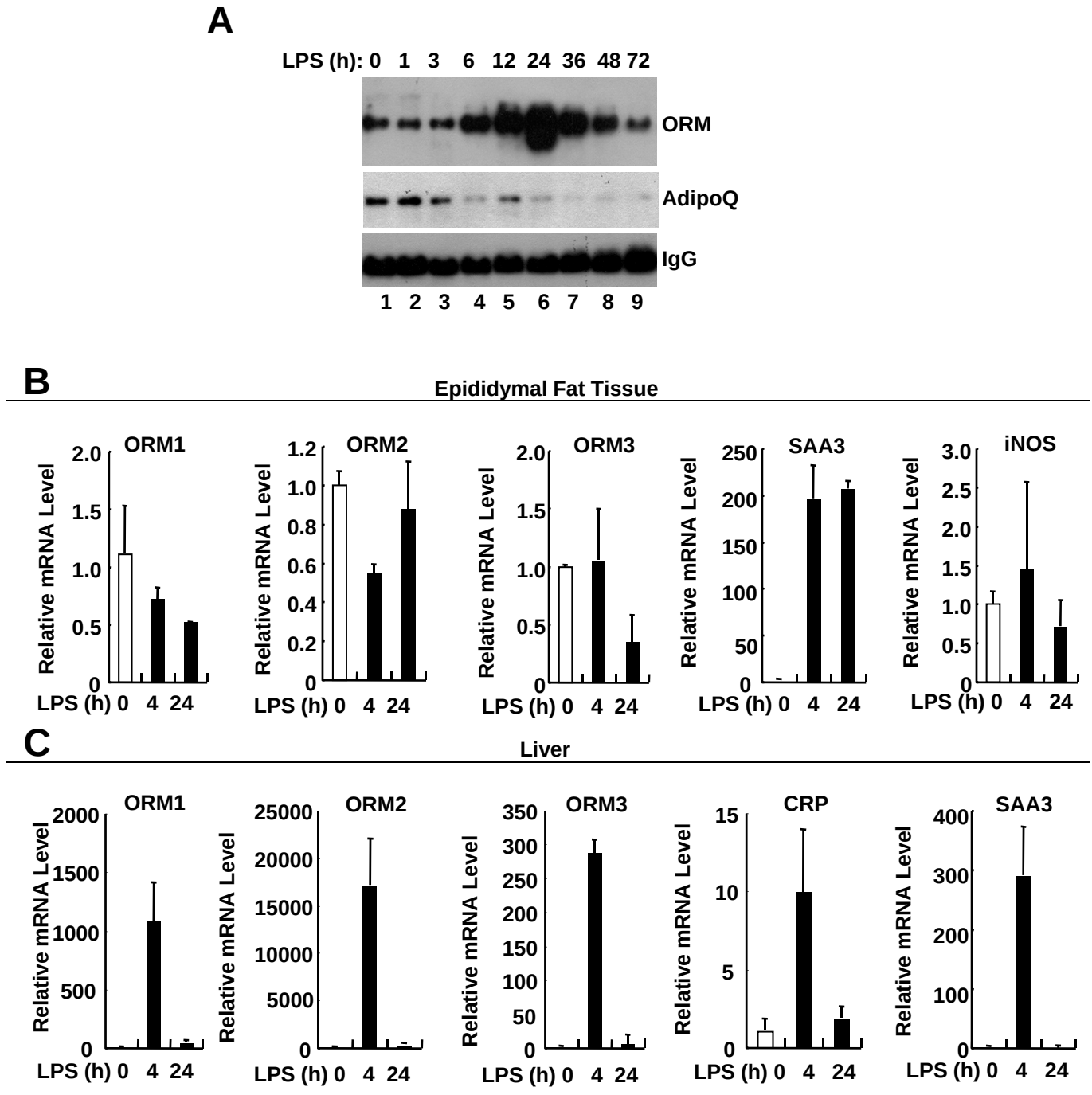

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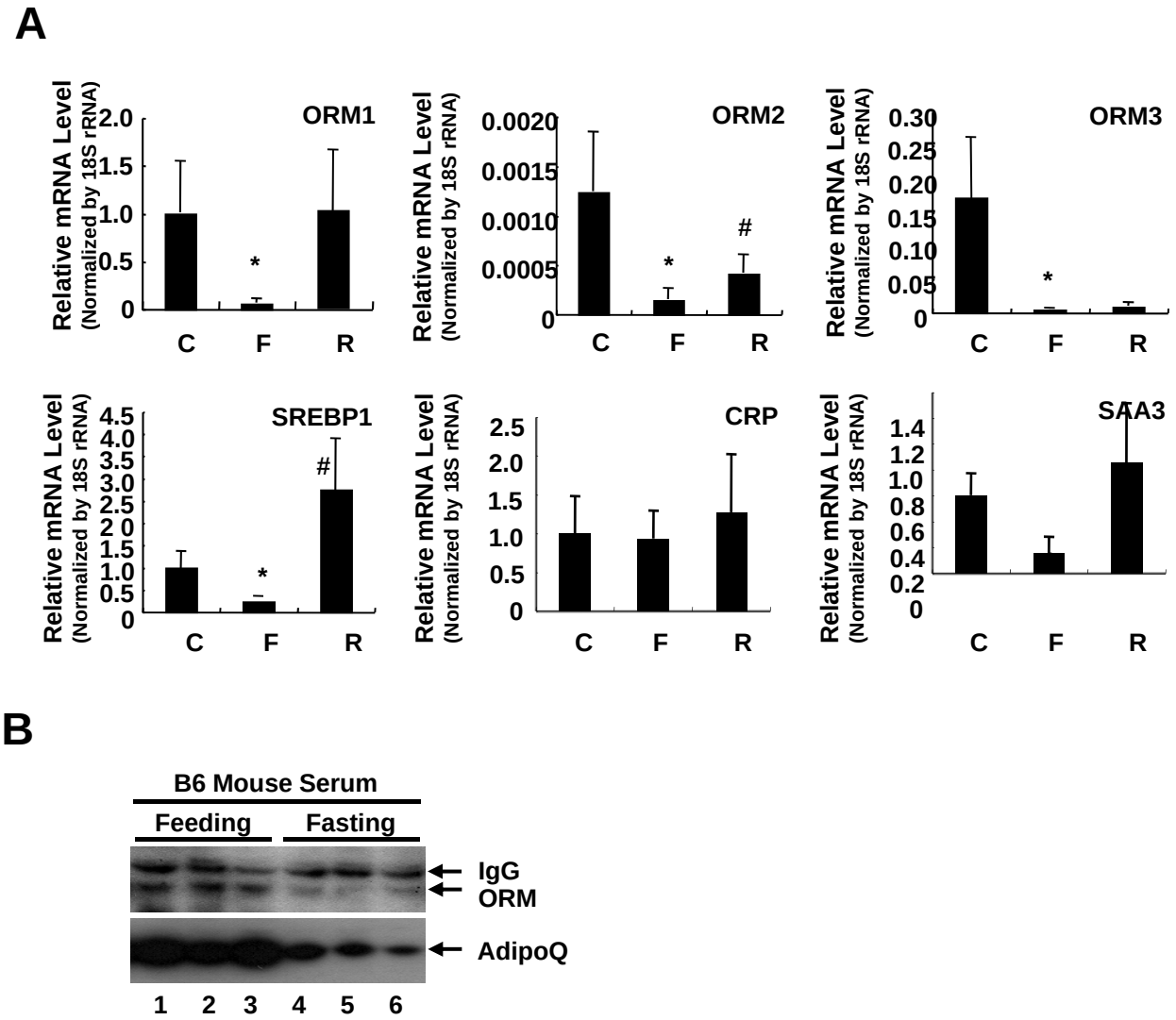
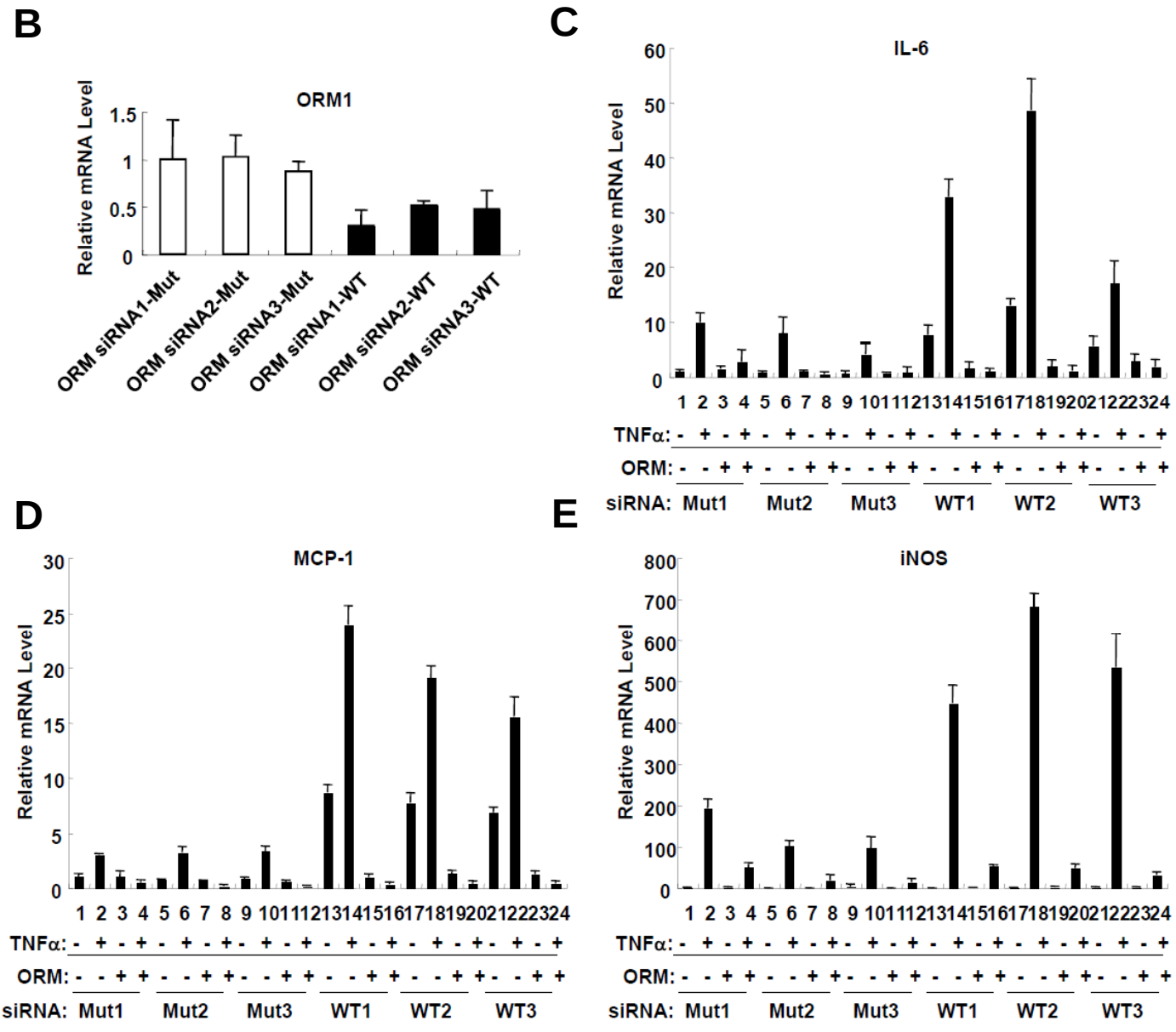


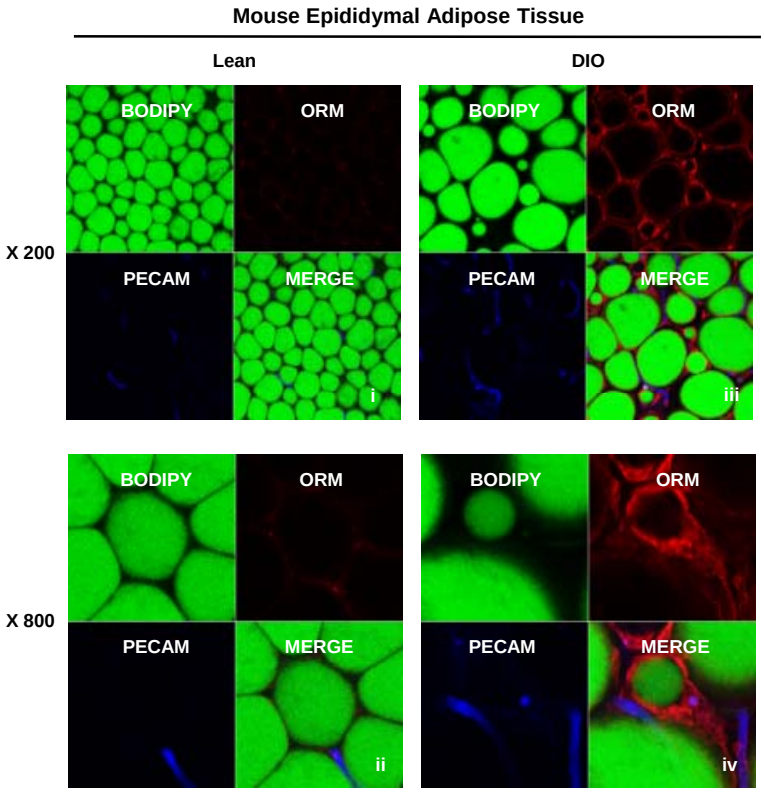
Supplement Figure S6

A

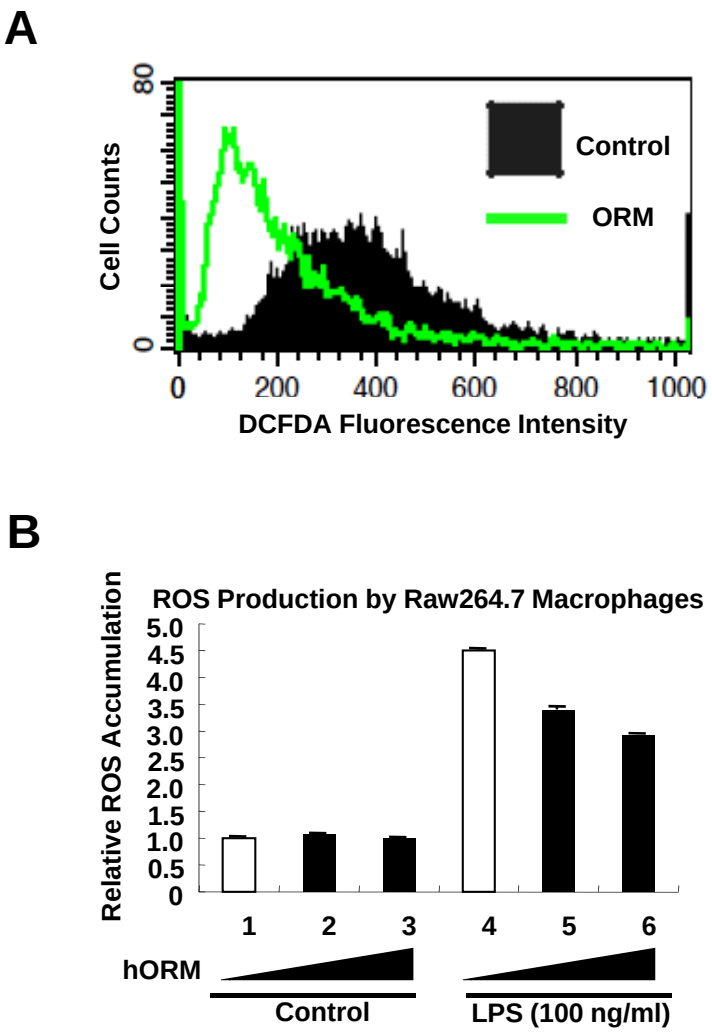
ORM1 siRNA 1-WT:	CCACCCAUCUAGGAUUCCA(dTdT)
ORM1 siRNA 1-Mut:	CCACCCAUCUAGUCUCACA(dTdT)
ORM1 siRNA 2-WT:	AGAGAGAAAAUGGGACCUU(dTdT)
ORM1 siRNA 2-Mut:	AGAGAGAAAAUGACGUCUU(dTdT)
ORM1 siRNA 3-WT:	GUUUUUCAUGGGUGCAGCU(dTdT)
ORM1 siRNA 3-Mut:	GUUUUUCAUGGGACGUGCU(dTdT)



Supplement Figure S7



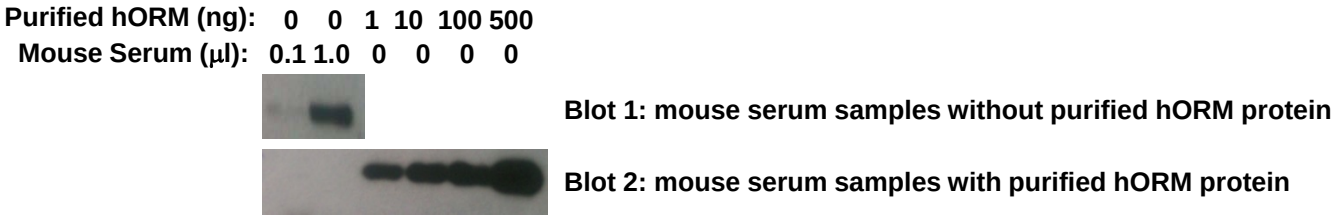
Supplement Figure S8



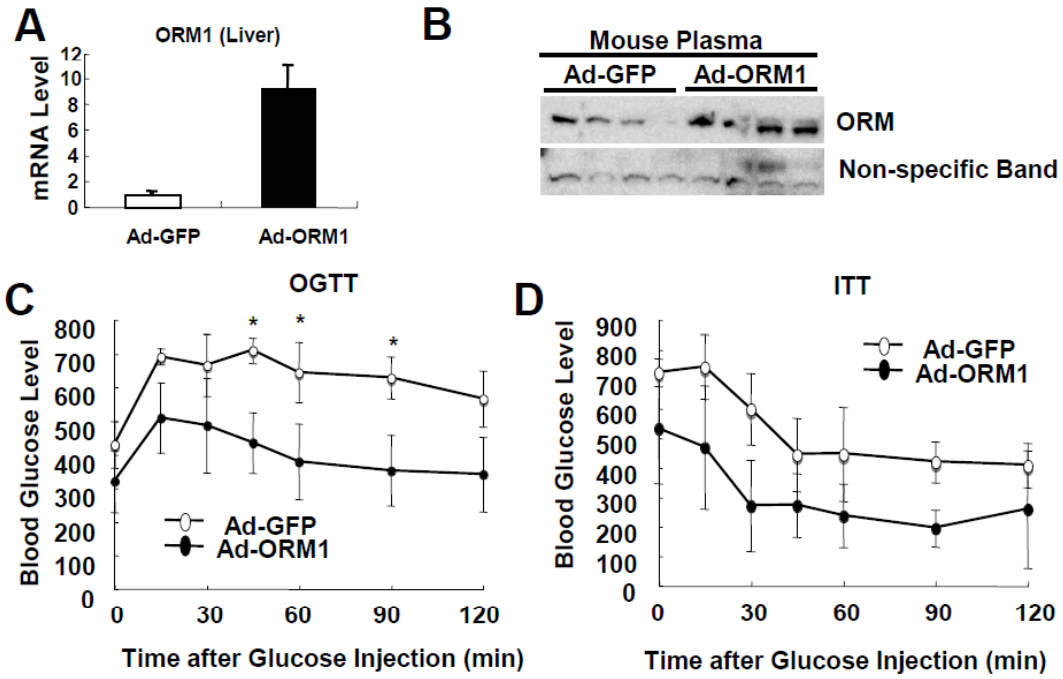
Supplement Figure S9

A

B



Supplement Figure S10



Supplement Figure S11