Supplemental Information

Enhanced GLP-1- and Sulfonylurea-Induced Insulin Secretion in Islets Lacking Leptin Signaling

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Materials and Methods

Long-term treatment of mouse islets with free fatty acid.

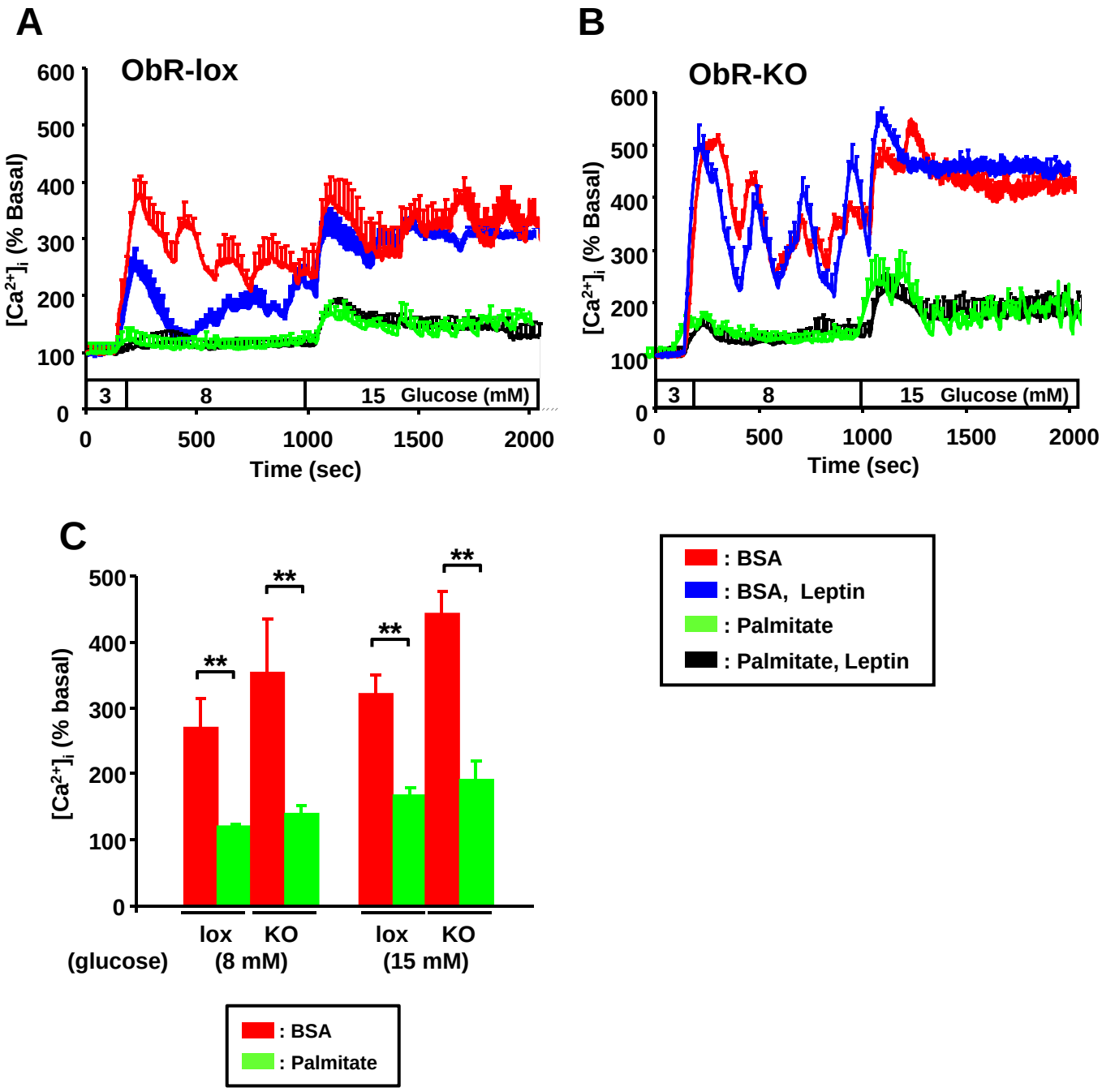
Mouse islets were isolated from ObRlox or ObRKO mice and incubated with control media with 5% FBS and 0.25% BSA or 0.5 mM palmitate (Sigma) for 48 hours. Subsequently, a single islet was perfused in a microfluidic chamber with different concentrations of glucose, with or without 10 nM leptin, as indicated. The $[Ca^{2+}]_i$ and insulin release in islet were measured as described in Materials and Methods.

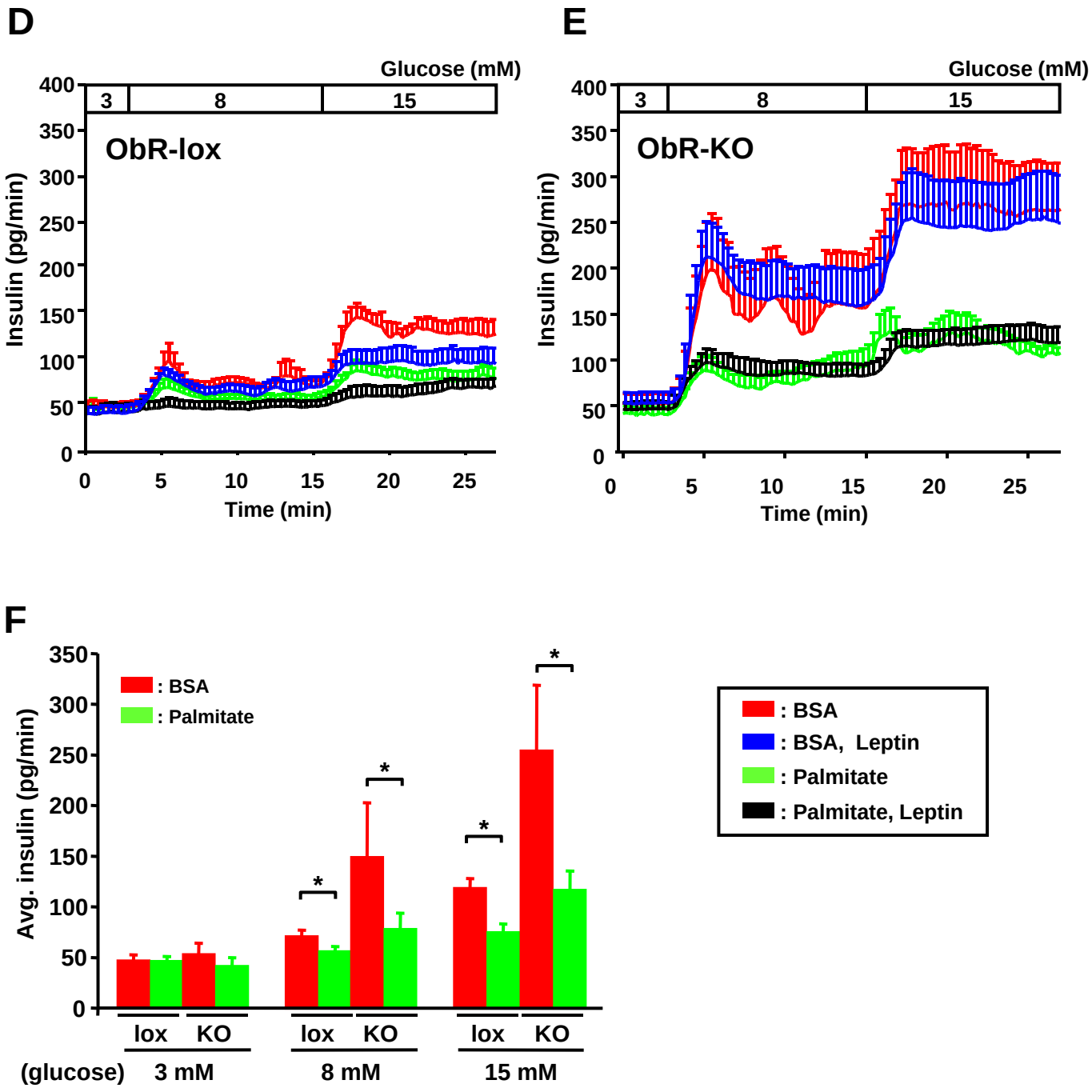
Figure Legends

Supplemental Fig. 1: Islets lacking leptin receptor exhibit impaired glucose-stimulated $[Ca^{2+}]_i$ increase and insulin release induced by long-term fatty acid treatment. A, B, D and E, Representative traces of $[Ca^{2+}]_i$ (A and B) and insulin release (D and E) measured in primary, size-matched islets isolated from 6-month-old male ObRlox (A and D) and ObR-KO (B and E) mice in different glucose concentrations with or without 10 nM leptin after 48-hour pre-incubation with 0.5 mM palmitate or 0.25 % BSA. C, Average $[Ca^{2+}]_i$ is expressed as % basal (mean ± SEM, **, $P < 0.01$; $n = 5$). F, Average insulin release value (pg/min) (mean ± SEM, *, $P < 0.05$; $n = 5$).

Supplemental Fig. 2: Mouse islets exhibiting significant first-phase insulin secretion in response to glucose and GLP-1. Representative traces of insulin release measured in primary size-matched islets isolated from 6-month-old male ObRlox (left) and ObR-KO (right) mice and treated with 8.0 mM glucose and 10 nM GLP-1 (7-36) amide.

Supplemental FIG. 1.




D
Glucose (mM)
3
8
15
ObR-lox
Insulin (pg/min)
Time (min)
E
Glucose (mM)
3
8
15
ObR-KO
Insulin (pg/min)
Time (min)
F
Avg. insulin (pg/min)
: BSA
: Palmitate
lox
KO
(glucose)
3 mM
8 mM
15 mM
: BSA
: BSA, Leptin
: Palmitate
: Palmitate, Leptin

Supplemental FIG. 2.