Supplementary Materials

Table 1. Glucose tolerance tests for female and male mice aged 3 or 6 months with genotypes floxed-iPLA$_2$β, β-Cell-iPLA$_2$β-KO, or MØ-iPLA$_2$β-KO fed a regular or high-fat diet. Glucose tolerance tests (GTTs) were performed as in Figure 2, and the Areas Under the Curve (AUC) were computed as in Figure 3 for female (denoted "F") and male (denoted "M") floxed-iPLA$_2$β control mice, MØ-iPLA$_2$β-KO mice, and β-cell-iPLA$_2$β-KO mice aged 3 months or 6 months that had been fed a RD until age 8 weeks and then either RD or a HFD until age 3 months or 6 months. Values are displayed as means ± SEM (n = 6 to 25, as specified for each entry in the Table). Tabulated significance values pertain to the comparison between genotypes for the condition in question.

Entry	*Age (mos.)*	*Gender*	*Genotype*	*Diet*	*GTT AUC*	*SEM*	*n*	*p value*
1	3	F	Floxed-iPLA$_2$β	Regular	269	13	19	
2	3	F	MØ-iPLA$_2$β-KO	Regular	231	10	19	***0.028***
3	3	F	Floxed-iPLA$_2$β	High Fat	374	19	18	
4	3	F	MØ-iPLA$_2$β-KO	High Fat	352	18	18	0.414
5	3	F	Floxed-iPLA$_2$β	Regular	280	19	13	
6	3	F	β-Cell-iPLA$_2$β-KO	Regular	367	26	8	***0.008***
7	3	F	Floxed-iPLA$_2$β	High Fat	435	23	6	
8	3	F	β-Cell-iPLA$_2$β-KO	High Fat	514	34	6	0.083
9	3	M	Floxed-iPLA$_2$β	Regular	321	28	20	
10	3	M	MØ-iPLA$_2$β-KO	Regular	327	23	15	0.881
11	3	M	Floxed-iPLA$_2$β	High Fat	509	22	13	
12	3	M	MØ-iPLA$_2$β-KO	High Fat	508	28	16	0.988
13	3	M	Floxed-iPLA$_2$β	Regular	389	25	12	
14	3	M	β-Cell-iPLA$_2$β-KO	Regular	475	39	13	0.081
15	3	M	Floxed-iPLA$_2$β	High Fat	566	21	12	
16	3	M	β-Cell-iPLA$_2$β-KO	High Fat	583	42	12	0.72
17	6	F	Floxed-iPLA$_2$β	Regular	265	10	24	
18	6	F	MØ-iPLA$_2$β-KO	Regular	250	10	23	0.278
19	6	F	Floxed-iPLA$_2$β	High Fat	485	25	24	
20	6	F	MØ-iPLA$_2$β-KO	High Fat	414	22	24	***0.038***
21	6	F	Floxed-iPLA$_2$β	Regular	317	14	21	
22	6	F	β-Cell-iPLA$_2$β-KO	Regular	454	22	20	***4.14E-06***
23	6	F	Floxed-iPLA$_2$β	High Fat	549	42	12	
24	6	F	β-Cell-iPLA$_2$β-KO	High Fat	838	28	12	***1.45E-05***
25	6	M	Floxed-iPLA$_2$β	Regular	340	24	19	
26	6	M	MØ-iPLA$_2$β-KO	Regular	396	20	20	0.079
27	6	M	Floxed-iPLA$_2$β	High Fat	728	27	25	
28	6	M	MØ-iPLA$_2$β-KO	High Fat	645	31	25	***0.049***
29	6	M	Floxed-iPLA$_2$β	Regular	435	46	5	
30	6	M	β-Cell-iPLA$_2$β-KO	Regular	621	64	4	***0.0085***
31	6	M	Floxed-iPLA$_2$β	High Fat	756	37	12	
32	6	M	β-Cell-iPLA$_2$β-KO	High Fat	870	21	12	***0.014***

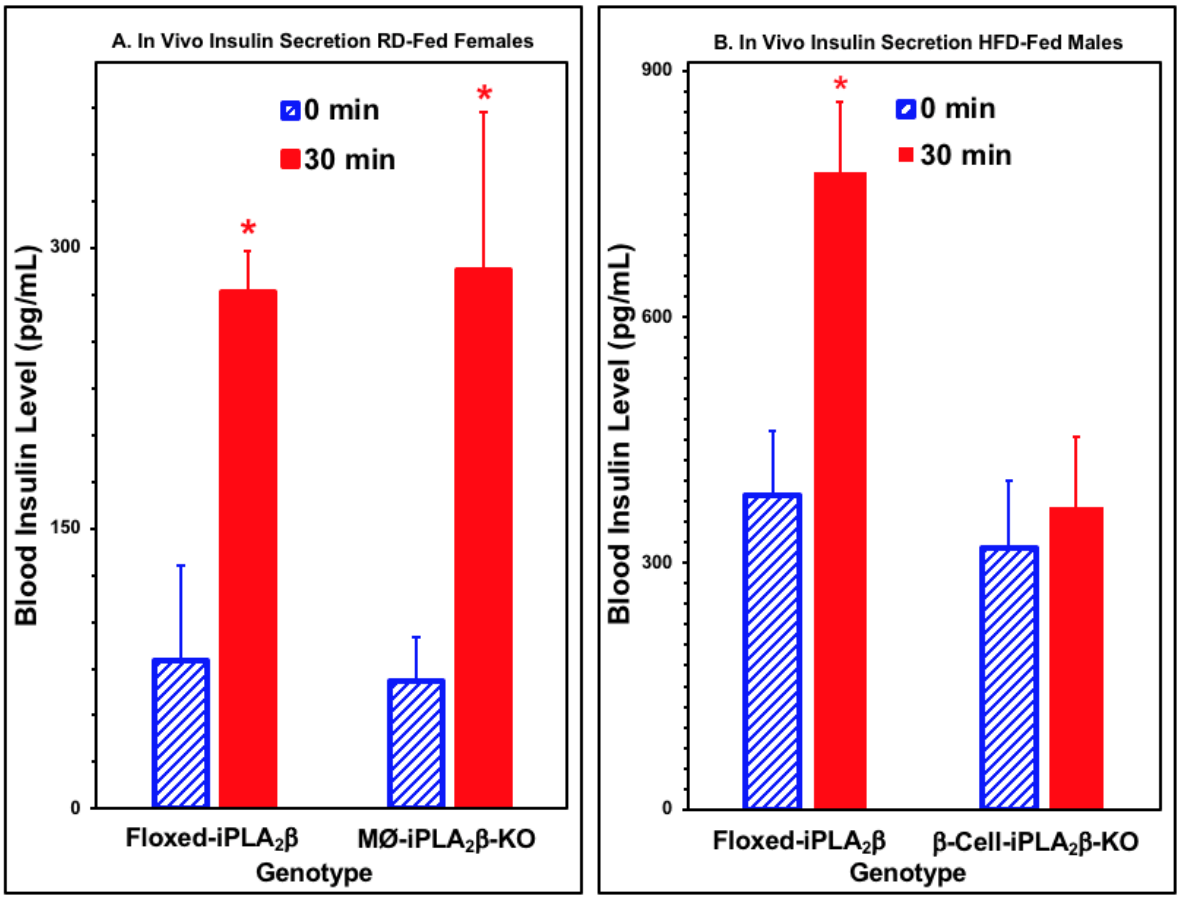

Figure S1. In vivo insulin secretion for iPLA$_2$β conditional knockout and floxed- iPLA$_2$β control mice fed a regular or high-fat diet. After an overnight fast, baseline blood samples were obtained from the saphenous vein of female (**A**) or male (**B**) MØ-iPLA$_2$β-KO mice (**A**), β-cell-iPLA$_2$β-KO mice (**B**), or floxed-iPLA$_2$β control mice 6 months of age that had been fed a regular diet (RD, **A**) or high-fat diet (HFD, **B**) after 8 weeks of age. D-glucose (3 mg/kg body weight) was administered by intraperitoneal injection, and a blood sample was obtained 30 min thereafter. The insulin content of the baseline (cross-hatched bars) and 30 min (solid bars) samples was then measured by enzyme-linked immunosorbent assay, as described [23,24,57]. Displayed values represent mean ± SEM. An asterisk (*) denotes $p < 0.05$ for the comparison between the time 0 and 30 min values (n = 5 to 7).

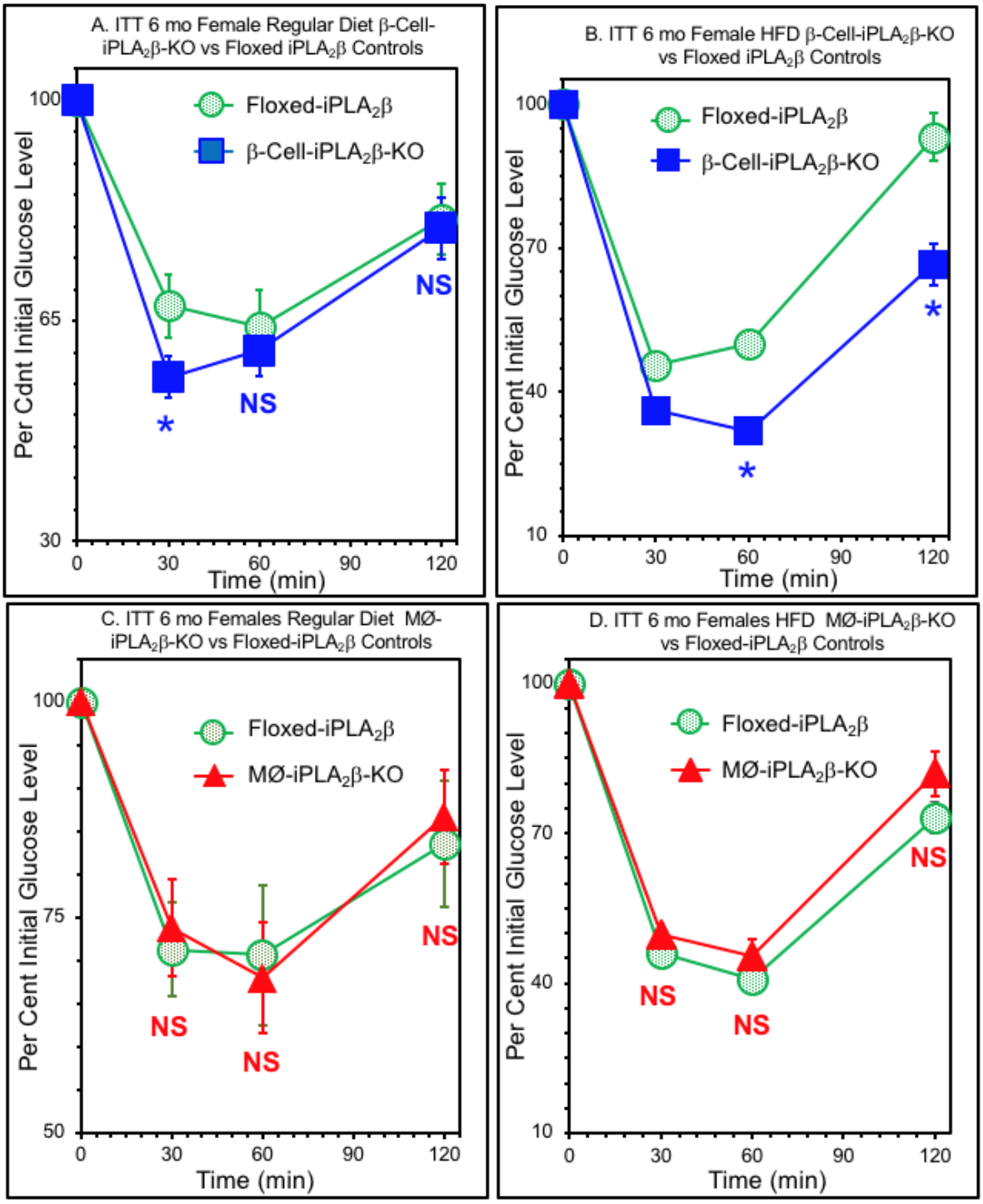

Figure S2. Insulin tolerance tests of 6-month-old female conditional iPLA2β-knockout mice and floxed-iPLA2β controls fed a regular or high-fat diet (HFD). Female floxed-iPLA2β control mice (circles), β-cell-iPLA2β-KO mice (squares, **A,B**) mice, or MØ-iPLA2β-KO mice (triangles, **C,D**) were fed a RD after weaning until they were 8 weeks of age and were then fed a HFD until 6 months of age. Insulin tolerance tests were then performed in mice with free access to water and chow until human regular insulin (0.75 U/kg; Lilly, Indianapolis, IN) was administered by intraperitoneal injection. Blood specimens were collected at 0, 30, 60, and 120 min thereafter for glucose concentration measurements, which were expressed as a percentage of the time zero blood glucose concentration, as described in [23,24,57]. Displayed values represent mean ± SEM (n = 13 to 26). An asterisk (*) denotes $p < 0.05$ for the comparison between genotypes.

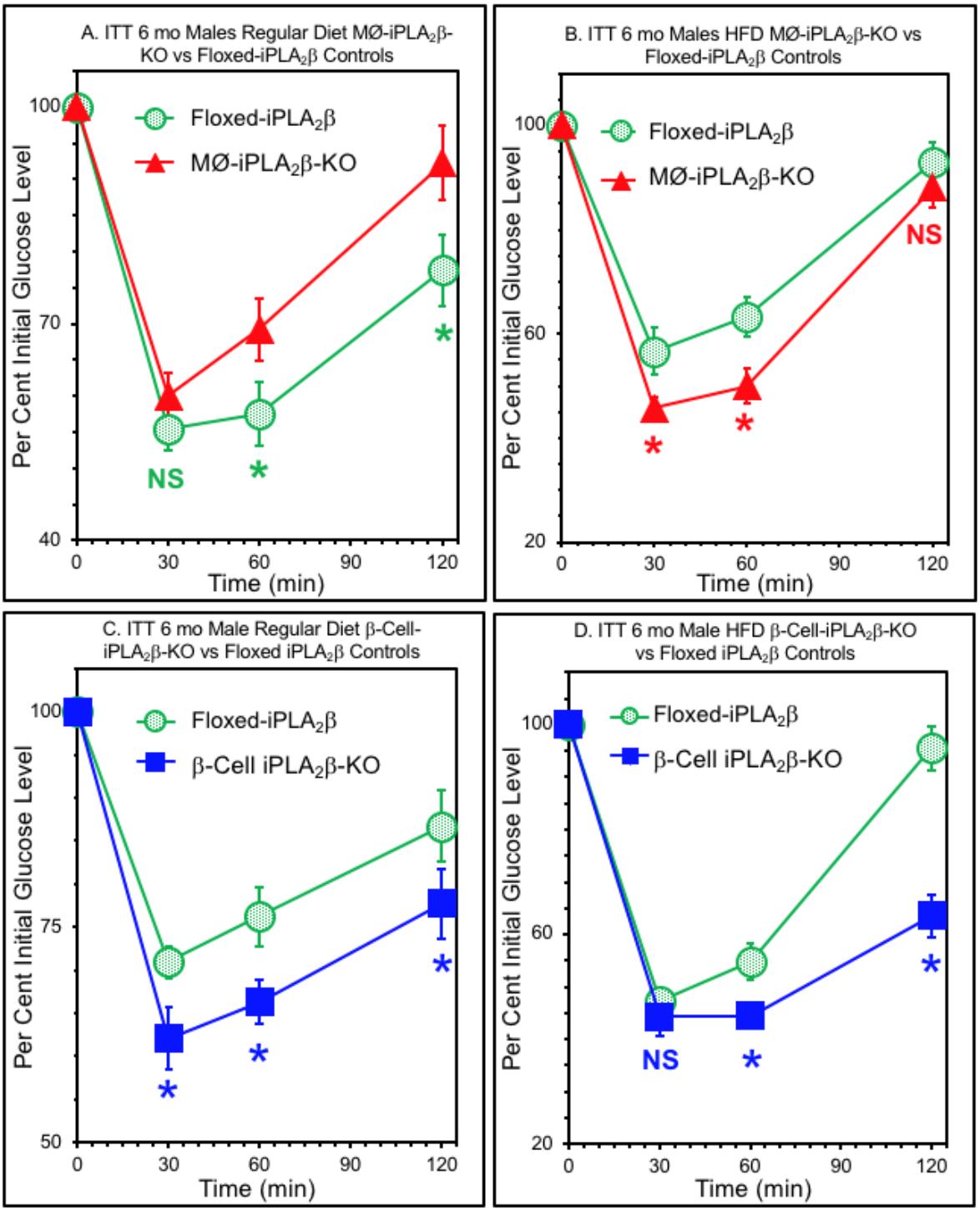

Figure S3. Insulin tolerance tests of 6-month-old male conditional iPLA2β-knockout mice and floxed-iPLA2β Controls Fed a Regular or High-Fat Diet (HFD). Male floxed-iPLA2β control mice (circles), MØ-iPLA2β-KO mice (triangles, **A,B**), or β-cell-iPLA2β-KO mice (squares, **C,D**) mice were fed a RD after weaning until they were 8 weeks of age and were then fed a HFD until 6 months of age. Insulin tolerance tests were then performed in mice with free access to water and chow until human regular insulin (0.75 U/kg body weight; Lilly, Indianapolis, IN) was administered by intraperitoneal injection. Blood specimens were collected at 0, 30, 60, and 120 min thereafter for glucose concentration measurements, which were expressed as a percentage of the time zero blood glucose concentration, as described in [23,24,57]. Displayed values represent mean ± SEM (n = 13 to 26). An asterisk (*) denotes $p < 0.05$ for the comparison between genotypes.