Figure S1. Macroscopic images of lower limb. Note the presence of a high amount of fat mass (asterisks) in ob/ob mice. Note that the color of skeletal muscle shifted from dark red in wild-type to pale red in ob/ob (arrows) which could be due to an increase in fat infiltration.
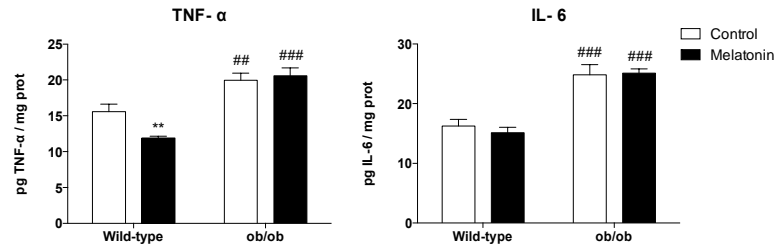
Figure S2. Leptin deficiency triggers an inflammatory response. Inflammation levels through the determination of TNF-α and IL-6 markers. Data are means ± SD. Statistical comparisons: [#] wild-type vs. ob/ob; [*] control vs. melatonin. The main effects of leptin deficiency and melatonin treatment were detected using a two-way ANOVA (n = 8). The number of symbols marks the level of statistical significance: one for $P < 0.05$, two for $P < 0.01$, and three for $P < 0.001$.
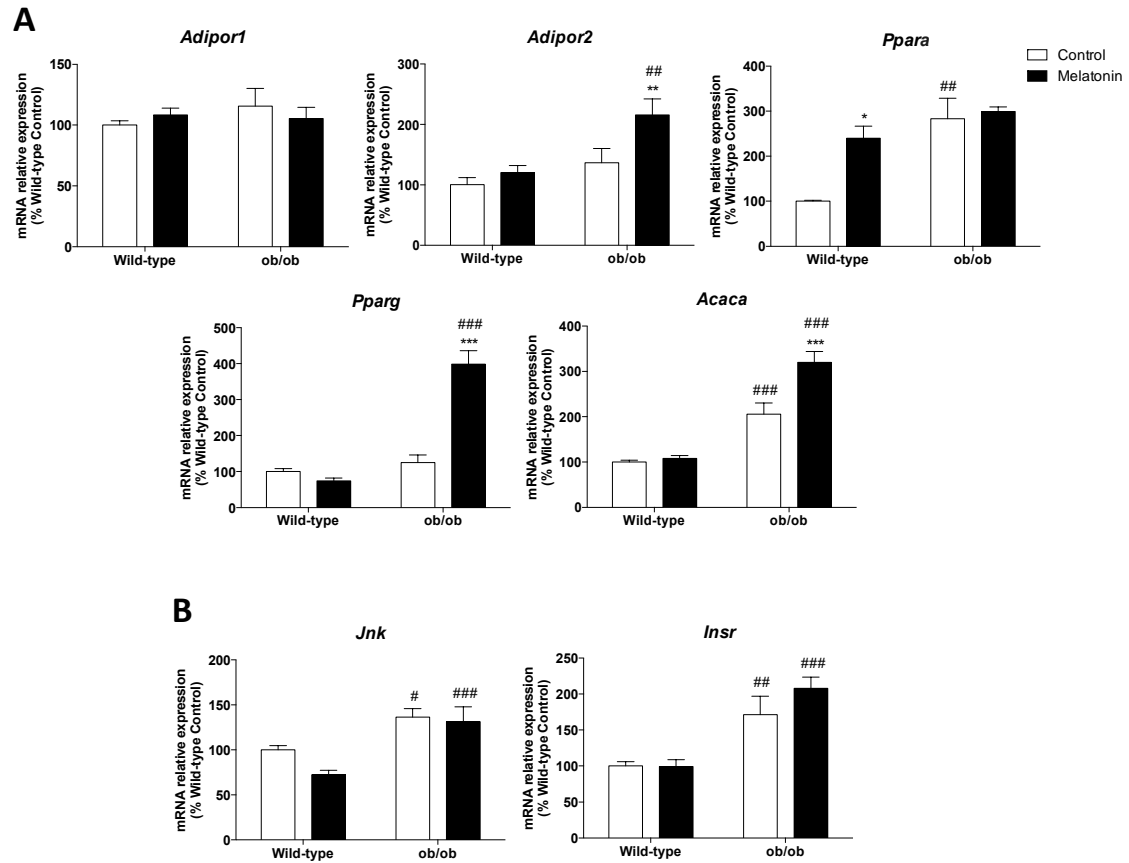
Figure S3. Melatonin remodels fatty acid metabolism in skeletal muscle from ob/ob mice. A, Relative mRNA expression of genes involved in β-oxidation (*Adipor1*, *Adipor2*, and *Ppara*) and in fatty acid synthesis (*Pparg* and *Acaca*) pathways. Data are means ± SD expressed as a percentage of wild-type control mice. B, Relative mRNA expression of genes implicated in insulin signaling (*Jnk* and *Insr*). Data are mean ± SD expressed as a percentage of wild-type control mice. Statistical comparisons: [#] wild-type vs. ob/ob; [*]Control vs. melatonin. The main effects of leptin deficiency and melatonin treatment were detected by two-way ANOVA (n = 8). The number of symbols marks the level of statistical significance: one for $P < 0.05$, two for $P < 0.01$ and three for $P < 0.001$.

Table S1. Anthropometric indicators of leptin-deficiency-induced obesity.

	Wild-type		ob/ob	
	Control	Melatonin	Control	Melatonin
N	8	8	8	8
Food intake (g/day)	3.27 ± 0.07	3.02 ± 0.22	4.82 ± 0.17 ###	5.17 ± 0.47 ###
Body weight at basline (g)	17.69 ± 1.37	17.69 ± 1.68	34.95 ± 2.93 ###	32.74 ± 2.67 ###
Body weight at sacrifice (g)	25.57 ± 0.94	23.98 ± 1.16	50.08 ± 3.82 ###	49.58 ± 2.59 ###
Body weight changes (g)	6.80 ± 1.54	6.30 ± 0.57	15.13 ± 1.85 ###	16.84 ± 2.01 ###
Muscle weight at sacrifice (g)	3.61 ± 0.36	3.66 ± 0.14	2.64 ± 0.07 ###	2.60 ± 0.19 ###
Peripheral Fat weight at sacrifice (g)	0.37 ± 0.06	0.38 ± 0.03	7.36 ± 0.54 ###	8.34 ± 1.10 ###
Lower limb perimeter (cm)	2.53 ± 0.24	2.68 ± 0.24	6.98 ± 0.67 ###	7.00 ± 0.66 ###
Body Mass Index (BMI) (kg/m^2)	3.53 ± 0.13	3.32 ± 0.16	6.18 ± 0.47 ###	6.21 ± 0.07 ###
Skeletal Muscle Index (SMI) (%)	13.08 ± 2.02	14.69 ± 1.46	4.98 ± 0.67 ###	5.11 ± 0.40 ###
Fat Mass Index (FMI) (g/m^2)	51.87 ± 8.66	53.15 ±3.62	948.15 ± 105.54 ###	1195.17 ± 231.32 ###
Limb-Appendicular Skeletal Muscle Mass Index (L-ASMI) (g/m^2)	461.82 ± 74.36	487.20 ± 49.06	308.64 ± 50.98 ##	320.10 ± 28.34 ###

Note: Data are means ± SD. Statistical comparisons: [#] wild-type vs. ob/ob; [##]$P < 0.01$, [###]$P < 0.001$.