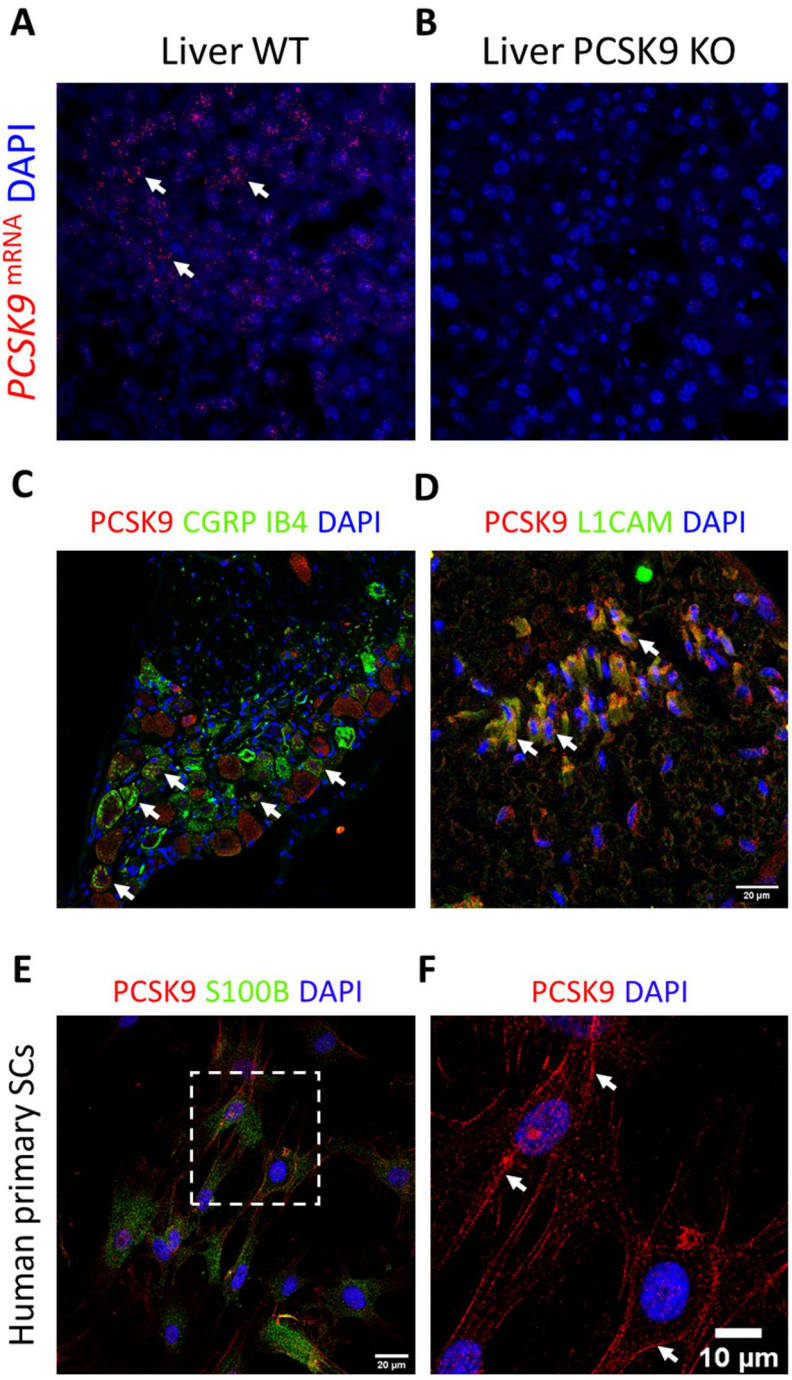
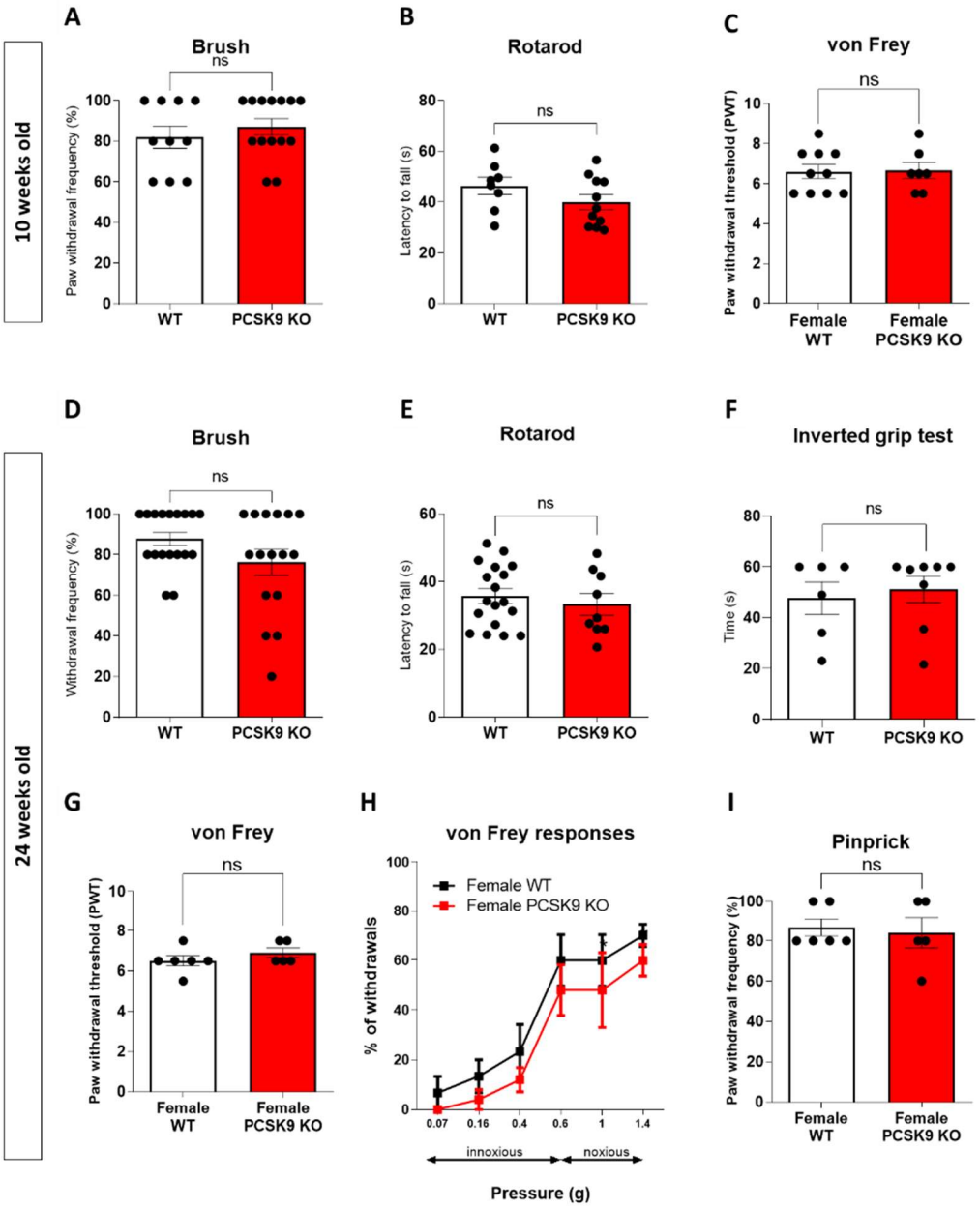


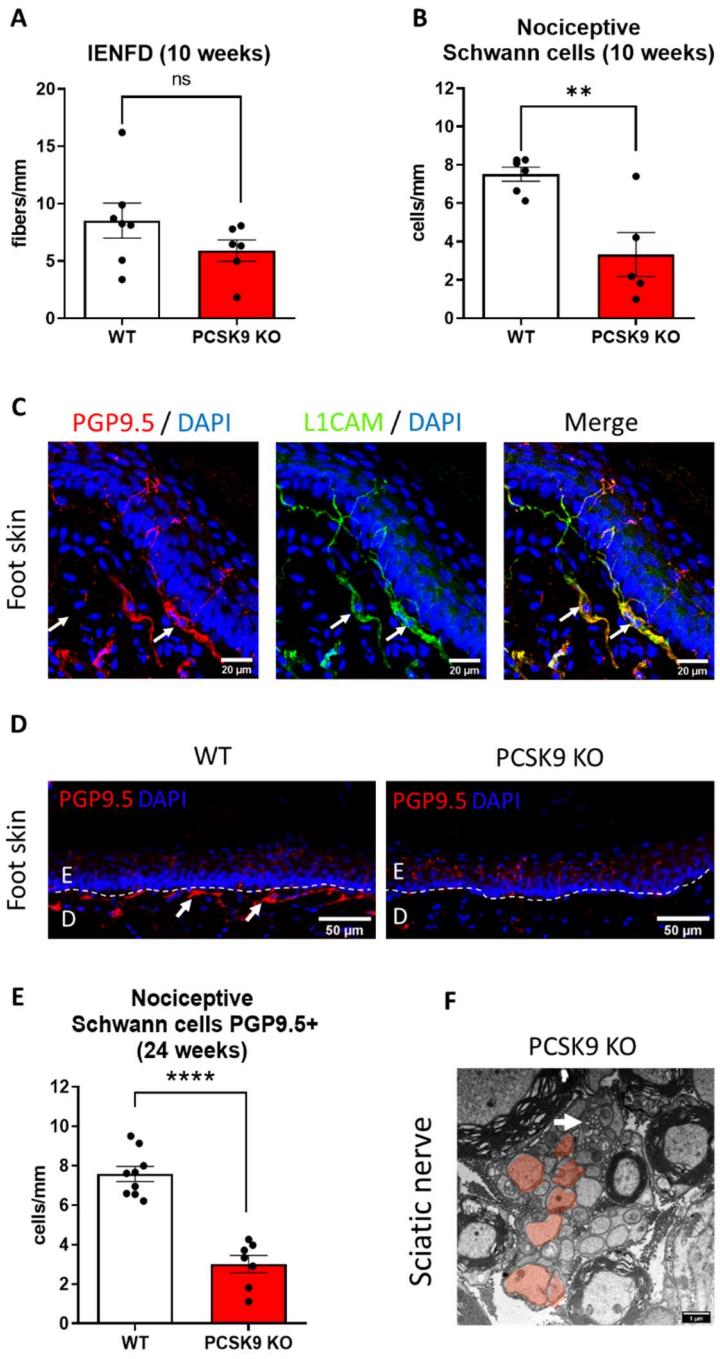
Supplemental Figure 1. *PCSK9* expression in the liver, DRG and primary SCs.

(A) *PCSK9* mRNA expression in mouse liver of control (*WT*). **(B)** *PCSK9* mRNA expression in mouse liver of *PCSK9 KO* mice. **(C)** *PCSK9* expression in non- myelinated sensory neurons expressing *CGRP* and *IB4*. **(D)** *PCSK9* expression in Schwann cell subtypes in mouse sciatic nerve, showing colocalization of *PCSK9* with *L1CAM* positive non–myelinating Schwann cells. **(E)** Expression of *PCSK9* in Human primary Schwann cells culture. (**F**) High magnification of the dashed square in (E). Arrows indicate *PCSK9* expression.



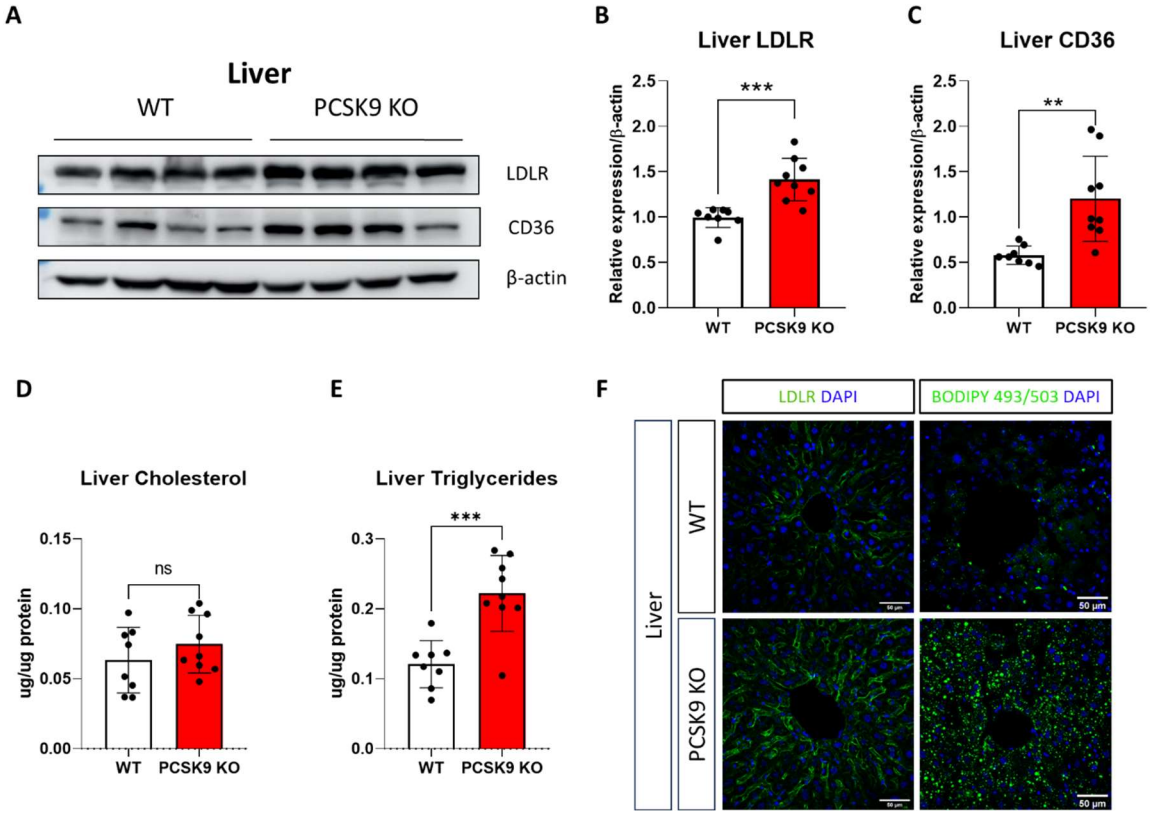
Supplemental Figure 2. Behavioral analysis of *PCSK9 KO* mice

(A) Dynamic touch sensation evaluated with the brush test in 10-week-old *WT* (n=10) and *PCSK9 KO* (n=14) mice. **(B)** Gross motor coordination evaluated with the rotarod test in 10-week-old *WT* (n=8) and *PCSK9 KO* (n=11) mice. **(C)** Mechanical pain sensation evaluated with the von Frey test in 10-week-old female *WT* (n=10) and *PCSK9 KO* (n=7) mice. **(D)** Dynamic touch sensation evaluated with the brush test in 24-week-old *WT* (n=18) and *PCSK9 KO* (n=16) mice. **(E)** Gross motor coordination evaluated with the rotarod test in 24-week-old *WT* (n=18) and *PCSK9 KO* (n=9) mice. **(F)** Assessment of grip strength with the inverted grip test in 24-week-old *WT* (n=6) and *PCSK9 KO* mice (n=8). **(G)** Mechanical pain sensation evaluated with the von Frey test in 24-week-old female *WT* (n=6) and *PCSK9 KO* (n=5) mice. **(H)** Mechanical pain sensation evaluated with the von Frey test presented as withdrawal percentage in 24-week-old female *WT* (n=6) and *PCSK9 KO* (n=5) mice. **(I)** Acute mechanical pain sensation evaluated with the pinprick test in 24-week-old female *WT* (n=6) and *PCSK9 KO* (n=5) mice. Data are represented as mean ± SEM and statistically analyzed by unpaired t test. $P > 0.05$ (ns).



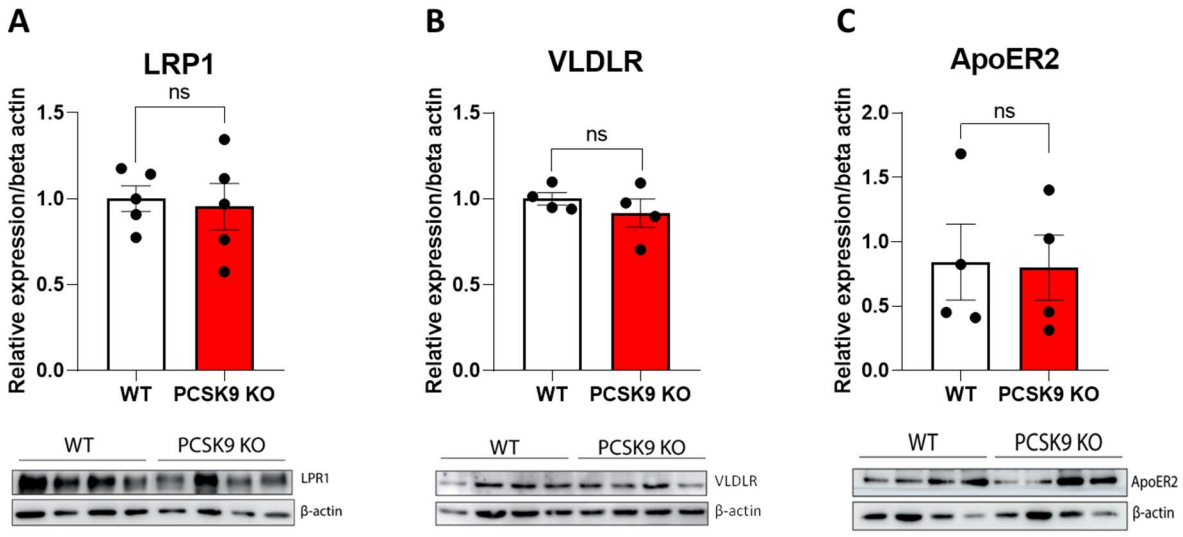
Supplemental Figure 3. IENFD and nociceptive SC in *PCSK9 KO* mice

(A) Quantification of IENFD in 10 weeks old *WT* (n=7) and *PCSK9 KO* (n=6) mice. **(B)** Quantification of numbers of nociceptive Schwann cells in 10 weeks old *WT* (n=6) and *PCSK9 KO* (n=5) mice. **(C)** Images of terminal nociceptive Schwann cells with colocalization between *PGP9.5* and *L1CAM*. **(D)** Representative images of nociceptive Schwann cells identified by immunostaining against *PGP9.5*/DAPI in the foot skin of *WT* and *PCSK9 KO* mice. **(E)** Quantification of the number of nociceptive Schwann cells in *WT* (n=9) and *PCSK9 KO* (n=7) mice. **(F)** Electron microscopy picture of sciatic nerve showing structural abnormalities in axonal circularity in *PCSK9 KO* mice (red highlight). Arrow shows vacuoles inside the nerve. Data are represented as mean ± SEM and statistically analyzed by unpaired t test. $P > 0.05$ (ns), $^{**}P < 0.01$, $^{****}P \leq 0.0001$.



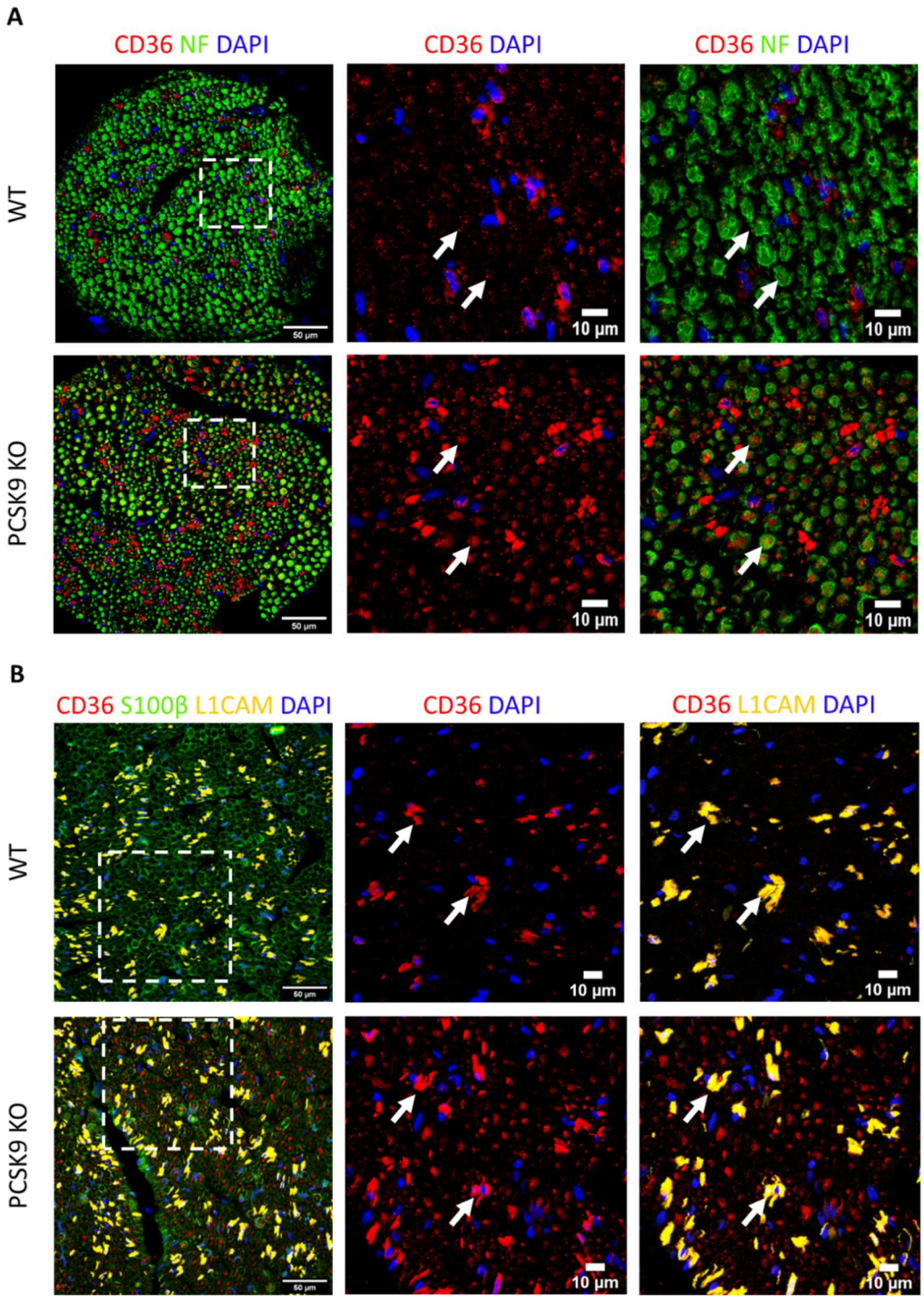
Supplemental Figure 4. *LDLR* and *CD36* expression in the liver of control and *PCSK9 KO* mice.

(A) *LDLR* and *CD36* expression in the liver by immunoblotting. **(B)** Quantification of *LDLR* liver expression in 24-week-old *WT* (n=9) and *PCSK9 KO* (n=9). **(C)** Quantification of *CD36* liver expression in 24-week-old *WT* (n=8) and *PCSK9 KO* (n=9). **(D)** Cholesterol levels in the liver of 24-week-old *WT* (n=8) and *PCSK9 KO* (n=9) mice. **(E)** Triglycerides levels in the liver of 24-week-old *WT* (n=8) et *PCSK9 KO* (n=9) mice. **(F)** *LDLR* expression and bodipy staining in section of liver from 24-week-old *WT* and *PCSK9 KO* mice. Data are represented as mean ± SEM and statistically analyzed by unpaired t test. $P > 0.05$ (ns), $^{**}P < 0.01$, and $^{***}P < 0.001$.



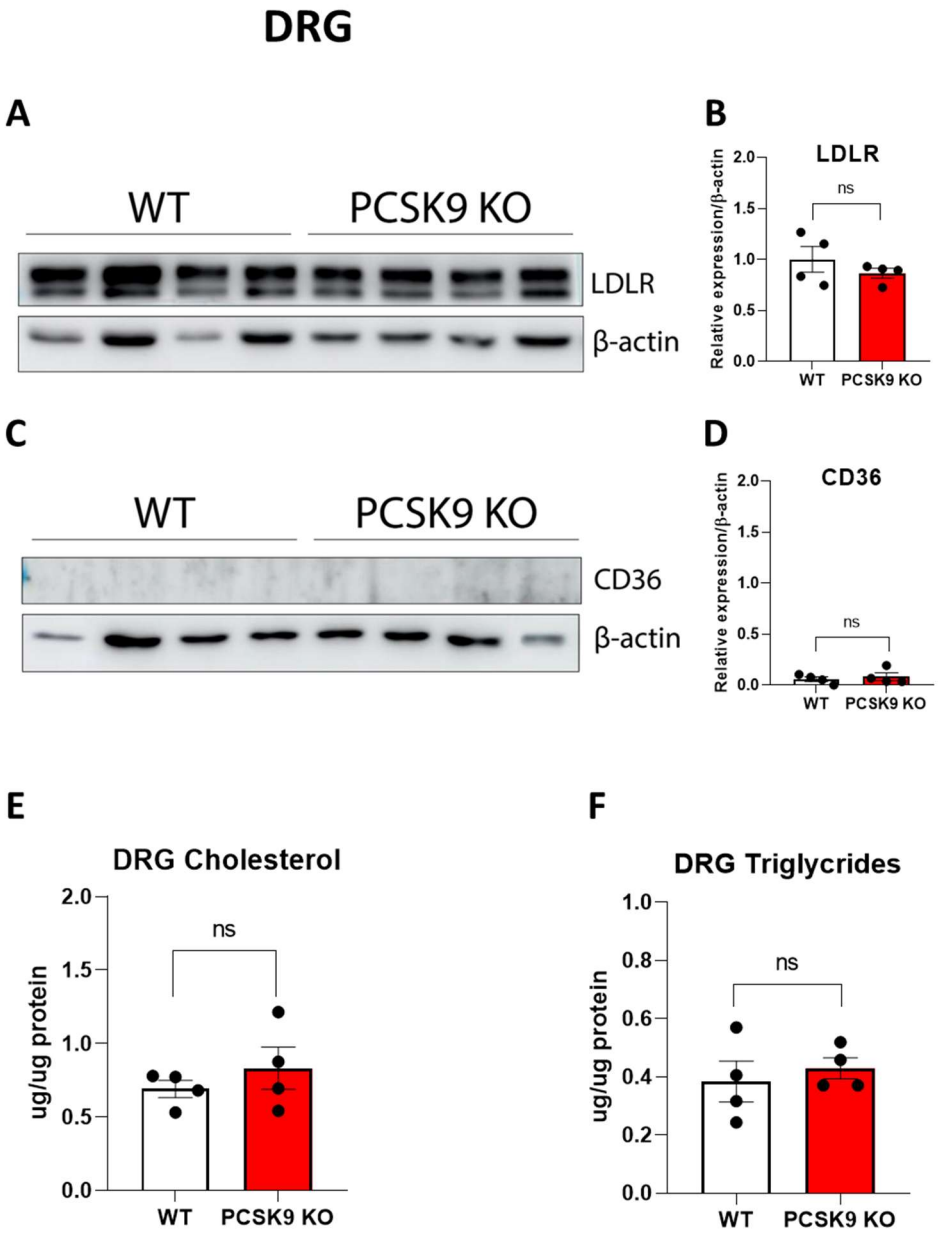
Supplemental Figure 5. *LRP1*, *VLDLR* and *ApoER2* expression in the sciatic nerve of control and *PCSK9 KO* mice

(A) Quantification of *LRP1* expression in the sciatic nerve of 24-week-old *WT* (n=5) and *PCSK9 KO* (n=5) mice. **(B)** Quantification of *VLDLR* expression in the sciatic nerve of 24-week-old *WT* (n=5) and *PCSK9 KO* (n=5). **(C)** Quantification of *ApoER2* expression in the sciatic nerve of 24-week-old *WT* (n=5) and *PCSK9 KO* (n=5). Data are represented as mean ± SEM and statistically analyzed by unpaired t test. $P > 0.05$ (ns).



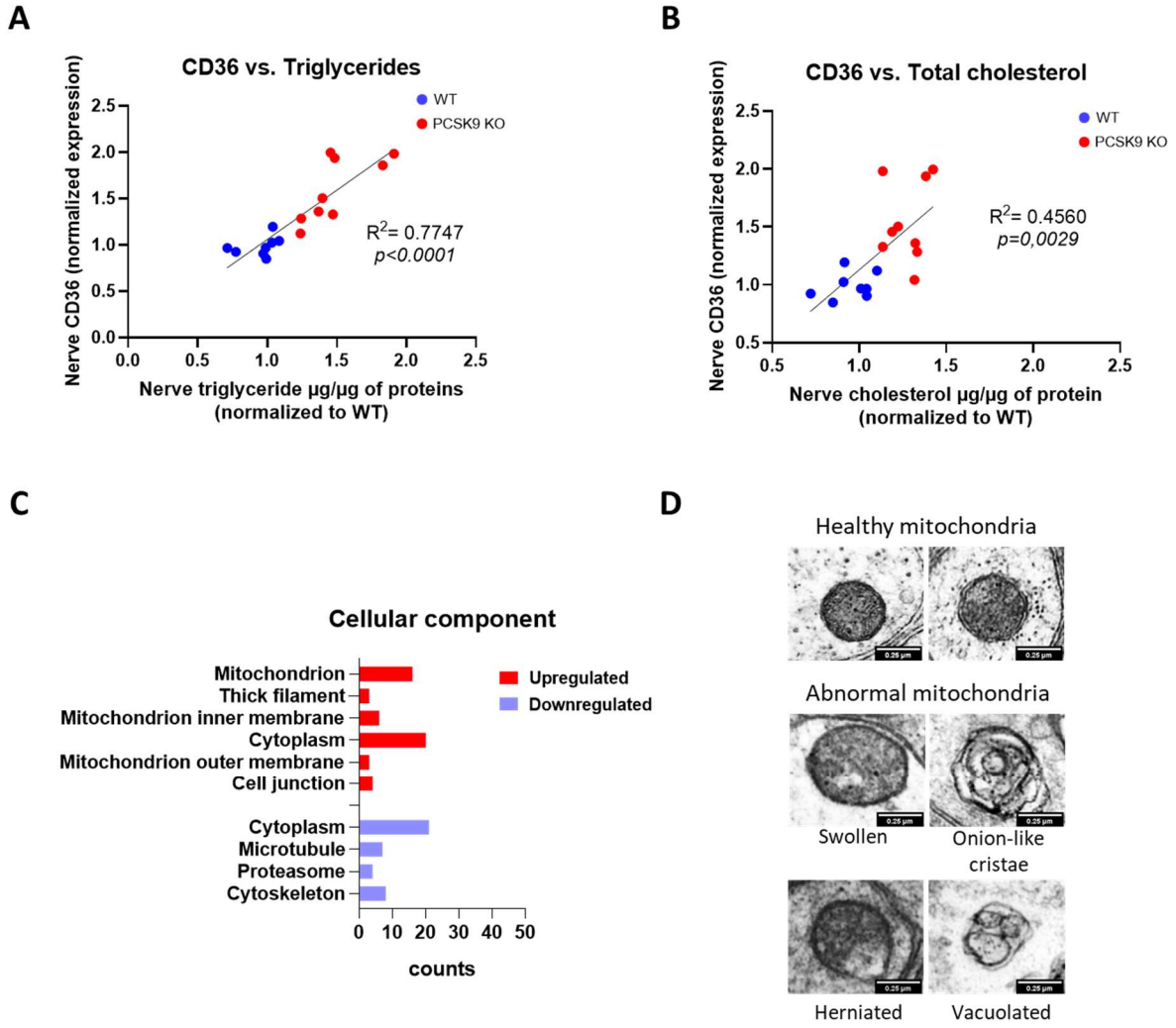
Supplemental Figure 6. *CD36* expression in the sciatic nerve of control and *PCSK9 KO* mice.

(A) Transverse section of mouse sciatic nerve of 24-week-old *WT* and *PCSK9 KO* labeled with an antibody against *CD36* (red) and neurofilament (*NF*) (green) as well as nuclear DAPI staining (blue). **(B)** Triple immunostaining of transverse section mouse sciatic nerve of 24-week-old *WT* and *PCSK9 KO* with antibody against *CD36* (red), *S100B* a pan-Schwann cell marker (green) and *L1CAM* a non-myelinating Schwann cell marker (yellow) as well as nuclear DAPI staining (nuclear staining blue). (Arrows show the colocalization of *CD36* with the different markers).



Supplemental Figure 7. *LDLR* and *CD36* expression in DRG of control and *PCSK9 KO* mice.

(A) Immunoblot of *LDLR* expression in DRG of 24-week-old *WT* and *PCSK9 KO* mice. **(B)** Quantification of *LDLR* expression level in DRG of *WT* (n=4) and *PCSK9 KO* (n=4) mice. **(C)** Immunoblot of *CD36* expression in DRG of 24-week-old *WT* and *PCSK9 KO* mice. **(D)** Quantification of *CD36* expression level in DRG of *WT* (n=4) and *PCSK9 KO* (n=4) mice. **(E)** Quantification of cholesterol level in DRG of 24 weeks *WT* (n=4) and *PCSK9 KO* (n=4) mice. **(F)** Quantification of triglycerides levels in DRG of 24-weeks-old *WT* (n=4) and *PCSK9 KO* (n=4) mice. Data are represented as mean ± SEM and statistically analyzed by unpaired t test. $P > 0.05$ (ns).



Supplemental Figure 8. Correlation between *CD36* expression and nerve triglyceride and cholesterol concentration.

(A) Scatter plot displaying the correlation between nerve *CD36* expression and nerve triglyceride levels in *WT* (n=8) and *PCSK9 KO* (n=9). **(B)** Scatter plot displaying the correlation between nerve *CD36* expression and nerve cholesterol levels in *WT* (n=8) and *PCSK9 KO* (n=9). **(C)** Gene ontology annotation of the top upregulated (red) and downregulated (blue) in terms of molecular function and (D) cellular component sorted by P-value. **(D)** Representative images of healthy mitochondria and abnormal mitochondria.

Target antigen	Vendor or source	Catalog #	Experiments
Rabbit anti human pro-PCSK9 N-terminal domain	Abcam	ab135647	IF
Goat anti human PCSK9 C-terminal domain	Abcam	ab28770	IF
Rabbit anti-mouse PCSK9	Cayman	10240	IF
Mouse anti-S100β	Sigma-Aldrich	S2532	IF
Rat anti- L1CAM	Merck milipore	MAB5272	IF
Goat anti-LDLR	R&D	AF2255	IF,WB
Mouse anti-ApoER2	Abnova	H00007804-M01	IF,WB
Rabbit anti-LRP1	Abcam	ab92544	IF,WB
Goat anti-VLDLR	R&D	AF2258	IF,WB
Chicken anti-NF	Merck milipore	AB5539	IF
Rabbit anti-β-actin	Abcam	ab8227	WB
Rabbit anti-PGP9.5	Merck milipore	AB1761	IF
Rabbit anti-CD36	Abcam	ab124515	IF,WB
Donkey anti-Rabbit Alexa 594	ThermoFisher	A-21207	IF
Donkey anti-Mouse Alexa 594	ThermoFisher	A-21203	IF
Donkey anti-Rat Alexa 488	ThermoFisher	A-21208	IF
Donkey anti-Goat Alexa 594	ThermoFisher	A-11058	IF
Donkey anti-Chicken Alexa 488	Invitrogen	A78948	IF
Donkey Anti-Goat IgG H&L (HRP)	Abcam	ab205723	WB
Peroxidase AffiniPure™ Donkey Anti-Rabbit IgG (H+L)	Jackson ImmunoResearch	711-035-152	WB
Peroxidase AffiniPure™ Donkey Anti-Mouse IgG (H+L)	Jackson ImmunoResearch	715-035-150	WB

Table 1: List of all antibodies used (IF: immunofluorescence, WB: western blot)