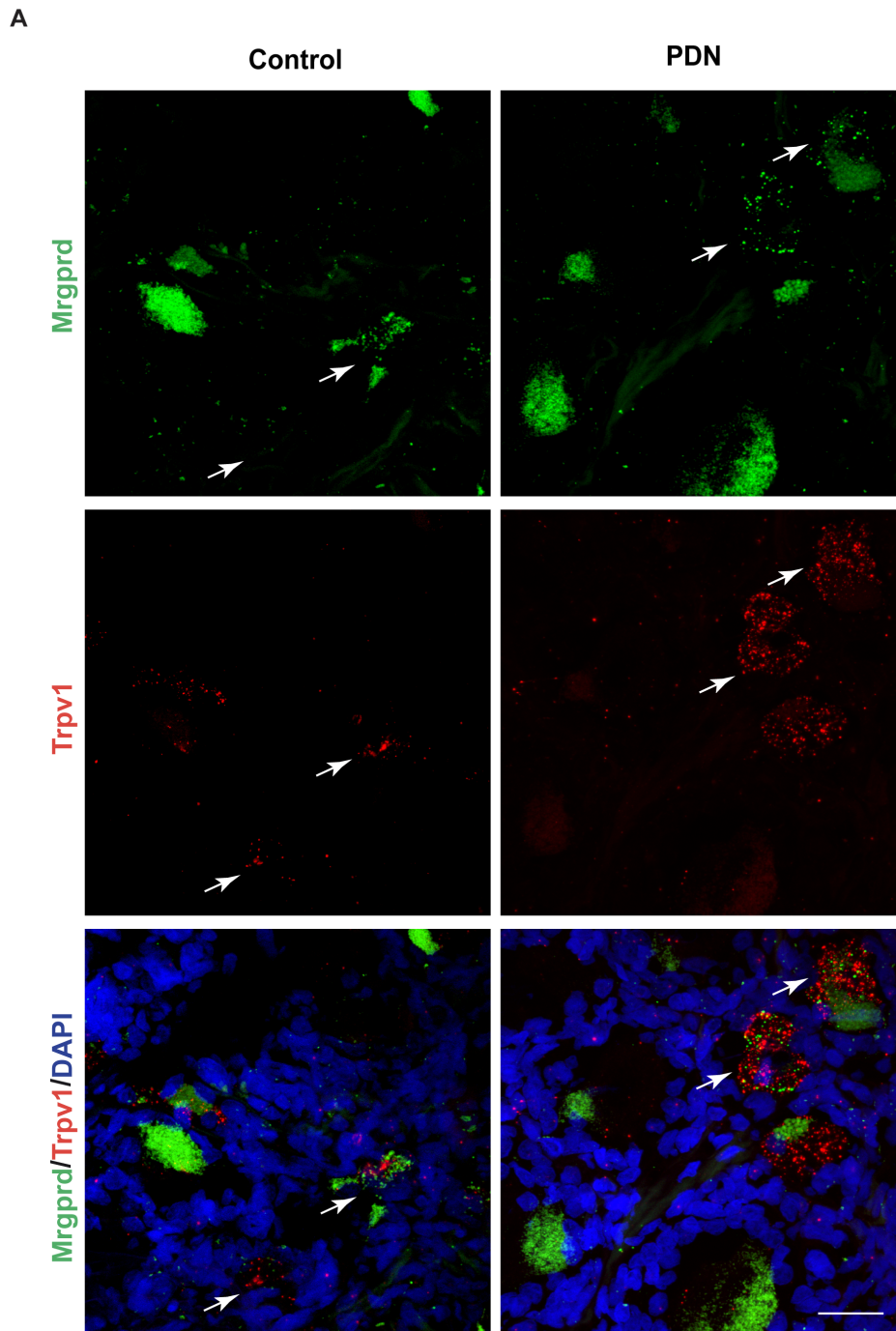
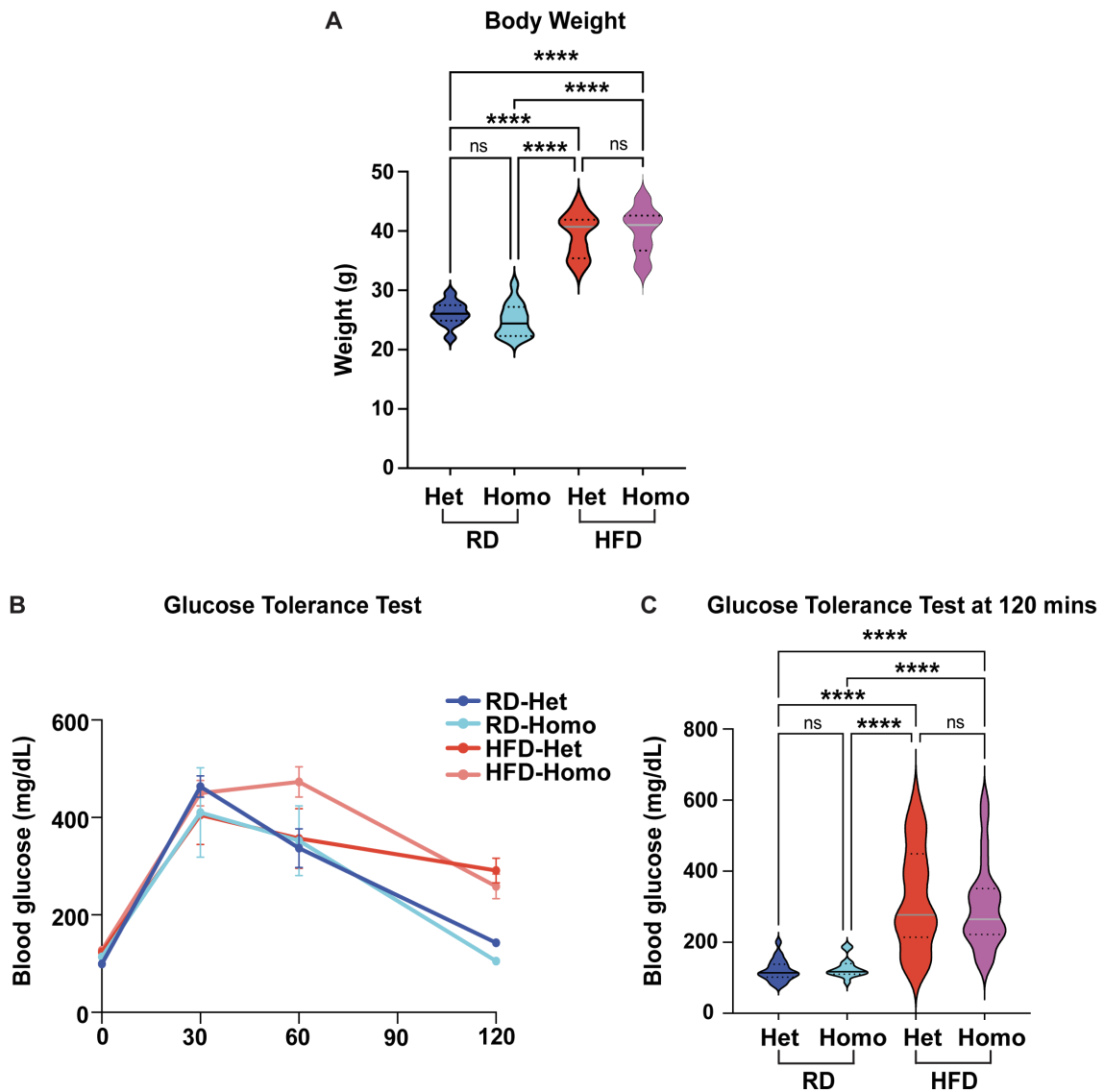


Supplemental Figure 1 :



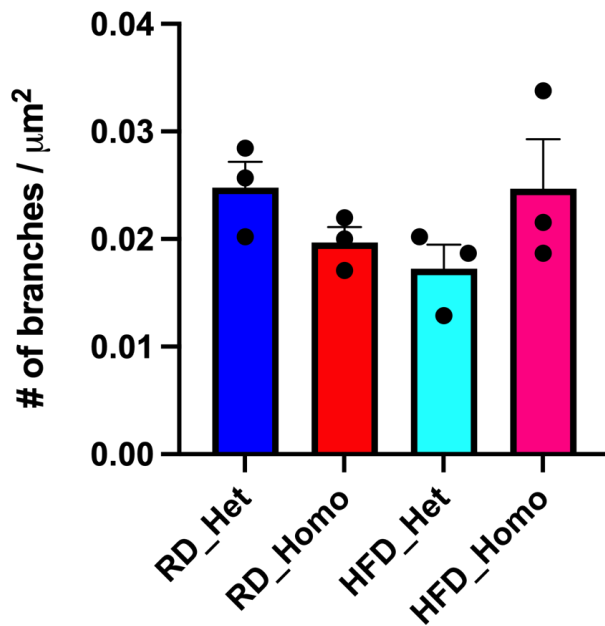
**Supplemental Figure 1: (A)** MRGPRD (green), TRPV1 (red) and DAPI expression in human DRG samples from control and patients with PDN. Scale bar represents 25  $\mu$ m. Control (n=1) and PDN patient (n=1), three sections were imaged for each group.

Supplemental Figure 2:



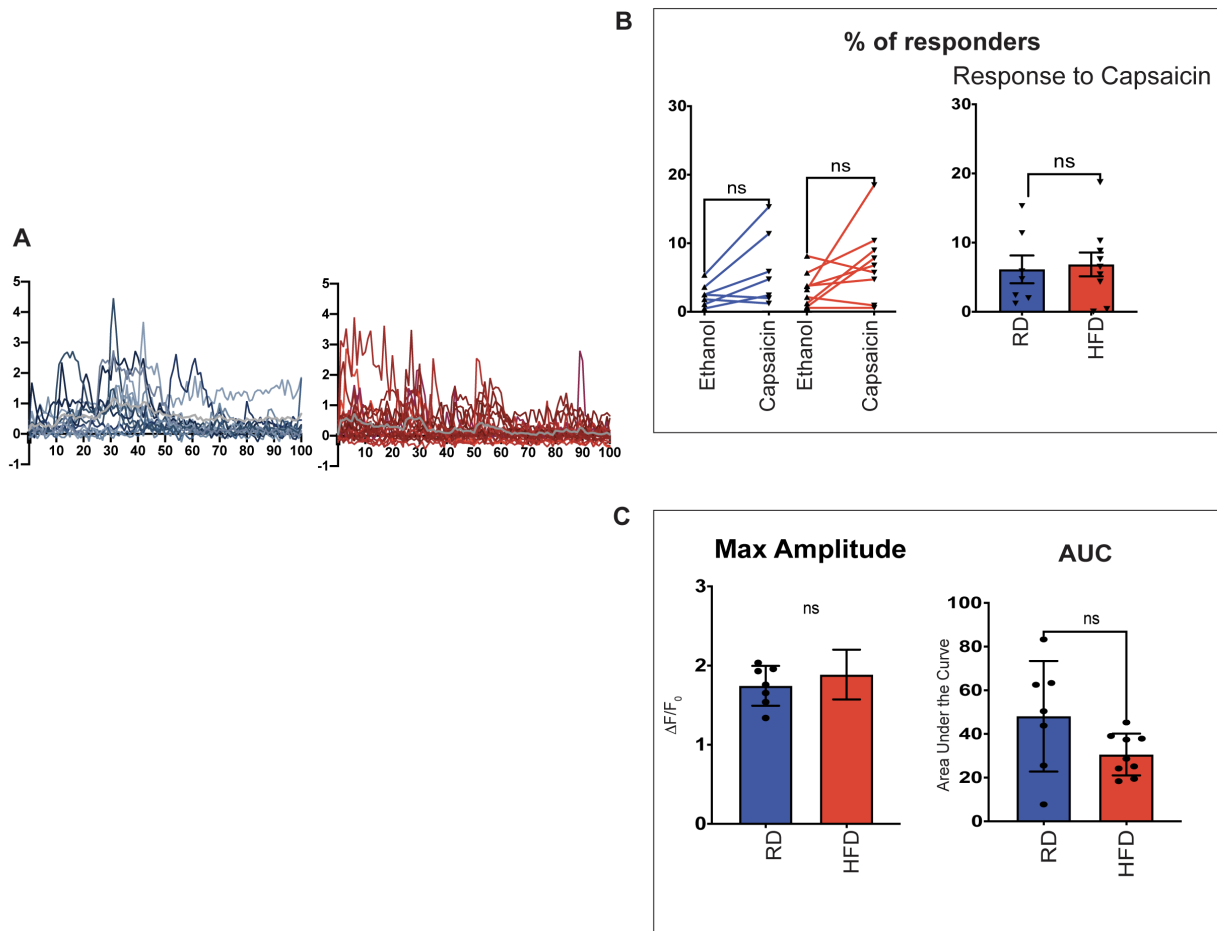
**Supplemental figure 2: Deletion of *Mrgprd* does not alter the metabolic profile. (A)** Body weight of *Mrgprd* heterozygous (+/-) and homozygous (-/-) mice fed either RD or HFD at ten weeks. **(B)** Blood glucose levels of the same mice at fasting, 30-, 60- and 120-minutes post glucose injection. **(C)** Area under the curve (AUC) for measurements in (B). RD-Het n = 10 mice; RD-Homo n = 8 mice; HFD-Het n = 17 mice; HFD-Homo n = 16 mice). \*\*\*\*p < 0.0001. Blood glucose was analyzed using One-way ANOVA followed by Tukey's test.

Supplemental Figure 3:



**Supplemental figure 3: Quantification of the number of nerve terminal branches in the epidermis.** The graph represents the total number of branches in the epidermis between Mrgprd $\Delta$ EGFP heterozygous and homozygous mice (n=3 per group with 3 different sections counted per animal) fed either a RD or HFD. There was no statistical significance and the data were compared using One-way ANOVA followed by Tukey's test.

## Supplemental Figure 4:



**Supplemental figure 4: In vivo calcium response to capsaicin. (A)** All responses to capsaicin from representative RD and HFD mice. The gray line indicates the average change in fluorescence intensity over time. **(B)** Paired analysis showing the percentage of responses to ethanol and capsaicin treatment in RD (blue) and HFD (red) and percentage of neurons responding to capsaicin, each black triangle represents one animal. **(C)** Graphs showing maximum amplitude and **(D)** area under the curve (AUC).

**Supplemental Table 1 :**

<b>FIGURE</b>	<b>PANEL</b>	<b>COMPARISON</b>	<b>p- value</b>
3	A-E	RD vs HFD: Nav1.8 % expression	0.1143
		RD vs HFD: Nav1.8-Mrgprd % expression	0.8857
3	B-F	RD vs HFD: Nefh % expression	>0.9999
		RD vs HFD: Nefh-Mrgprd % expression	0.4000
3	C-G	RD vs HFD: Lpar3 % expression	0.5556
		RD vs HFD: Lpar3-Mrgprd % expression	0.9048
3	D-H	RD vs HFD: Trpv1 % expression	0.0571
		RD vs HFD: Trpv1-Mrgprd % expression	0.2857

**Supplementary Table 1:** Statistical results (Unpaired Two-tail T-test, RD n= 3-4, HFD n= 4-5 mice).