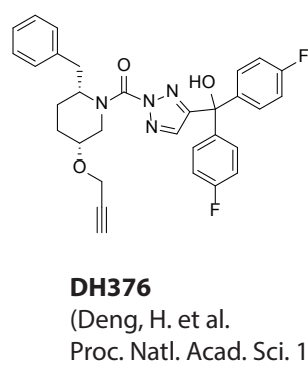
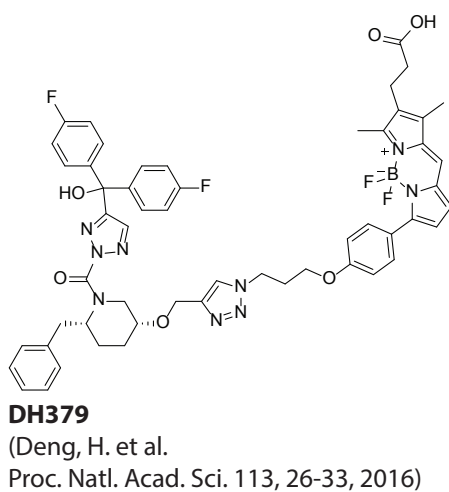
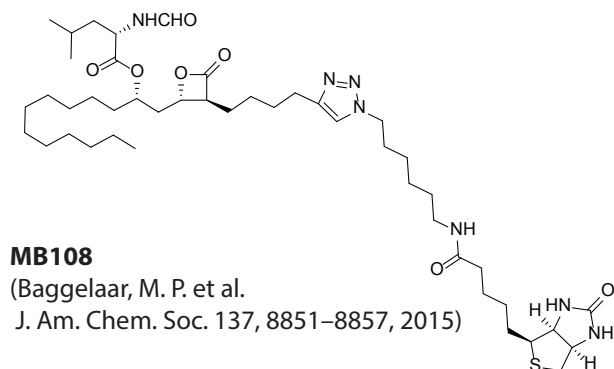
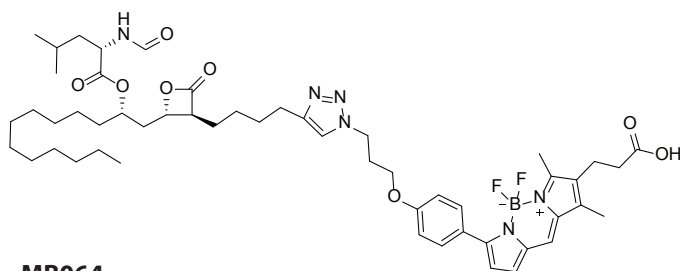
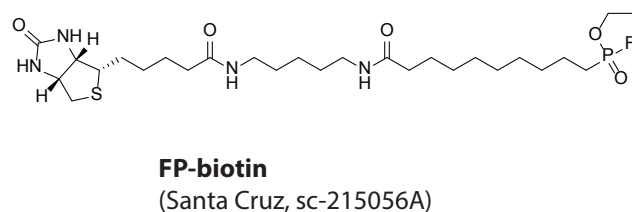
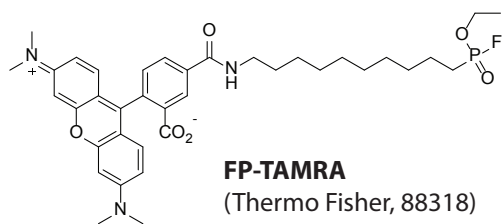
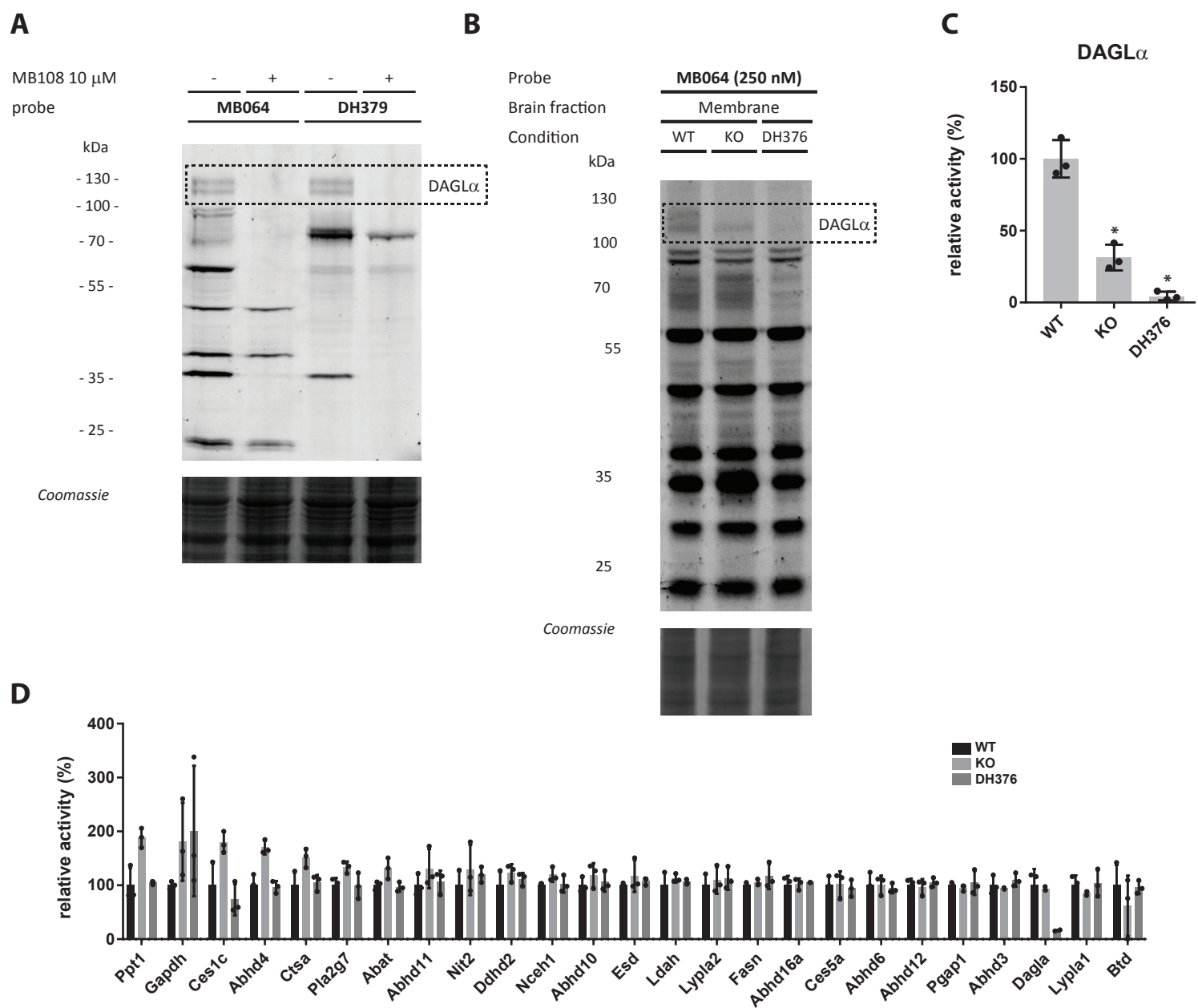


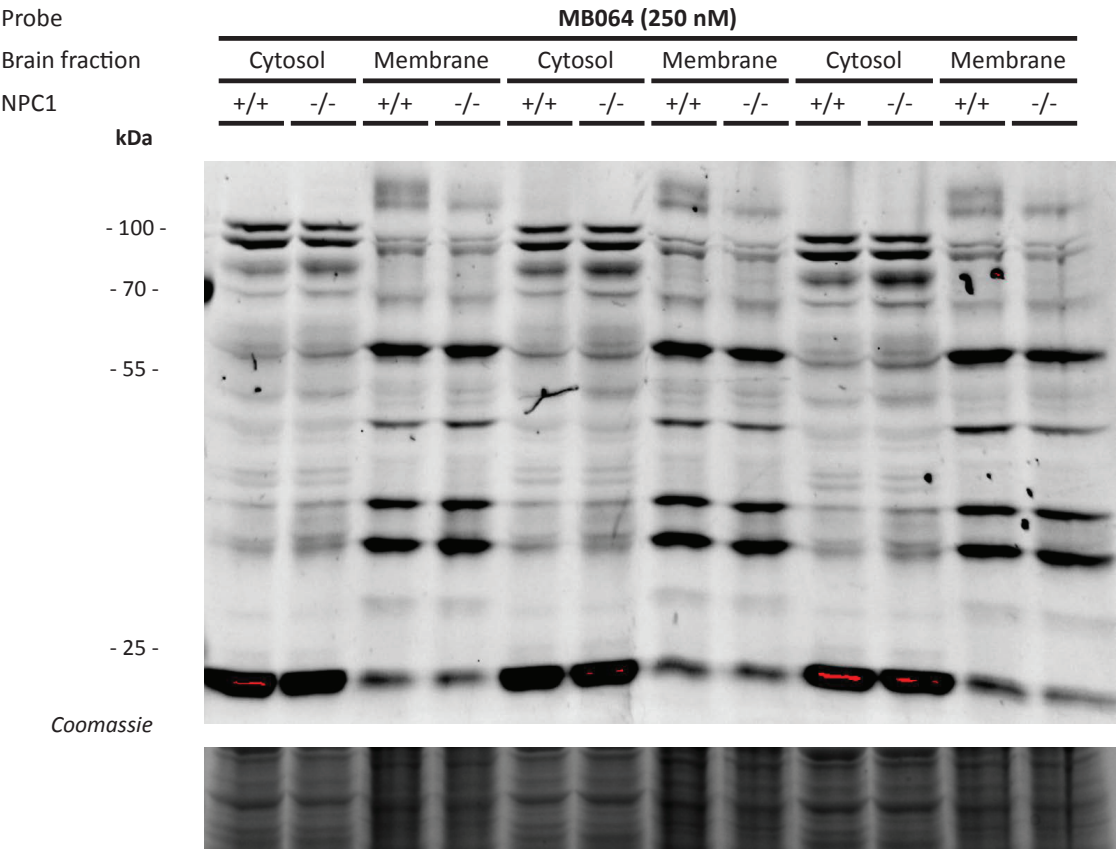
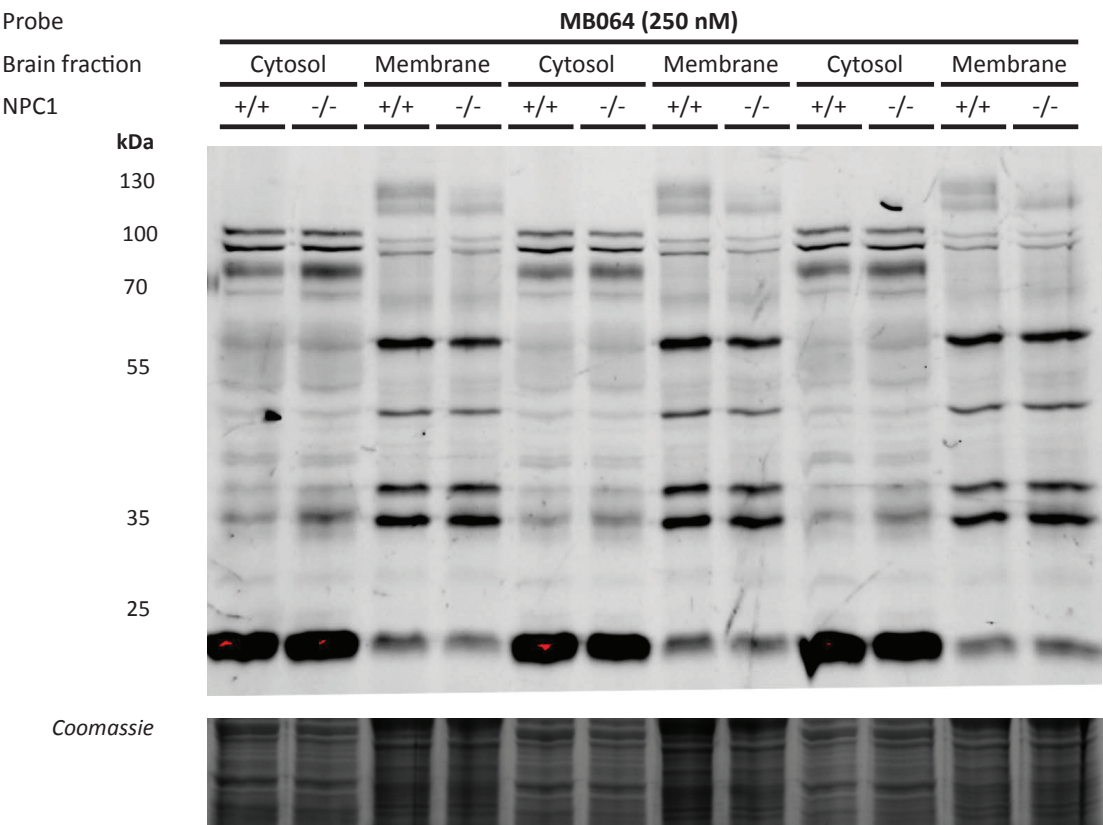


Supporting figure 1. Probes and inhibitors used in this study.



Supporting figure 2. Control experiments with MB108 and DAGL α inhibitor DH376 in mouse brain membrane proteome (A) Gel-based *Npc1*^{+/+} (WT) pre-treatment with MB108 and labelling with MB064 and DH379. (B) Gel-based *Npc1*^{+/+} (WT) vs *Npc1*^{-/-} (KO) comparison and competition with inhibitor DH376. (C) Quantification of relative enzyme activity for DAGL α (average WT is set to 100%), N = 3. * P < 0.05 (Student's t-test). (D) Chemical proteomics comparison of *Npc1*^{+/+} (WT) vs *Npc1*^{-/-} (KO) and competition with inhibitor DH376. Activity was measured in the membrane fraction using MB108 (10 μ M). Label-free quantification with IsoQuant. Statistical analysis by means of student's t-test (KO and inhibitor conditions compared to WT) and the resulting p-values were subjected to Benjamini-Hochberg correction, setting the false discovery rate at 10% (* indicates significant difference).

Full gels



Probe

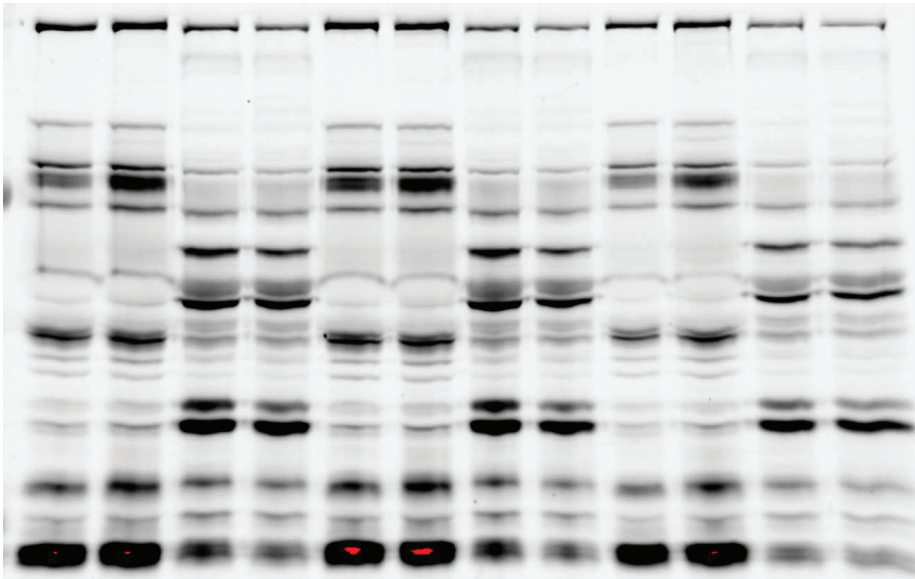
FP-TAMRA (500 nM)

Brain fraction

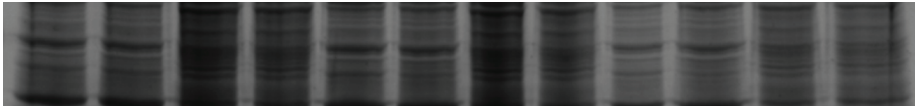
NPC1

Cytosol		Membrane		Cytosol		Membrane		Cytosol		Membrane	
+/+	-/-	+/+	-/-	+/+	-/-	+/+	-/-	+/+	-/-	+/+	-/-

kDa
- 130 -
- 100 -
- 70 -
- 55 -
- 35 -
- 25 -



Coomassie



Probe

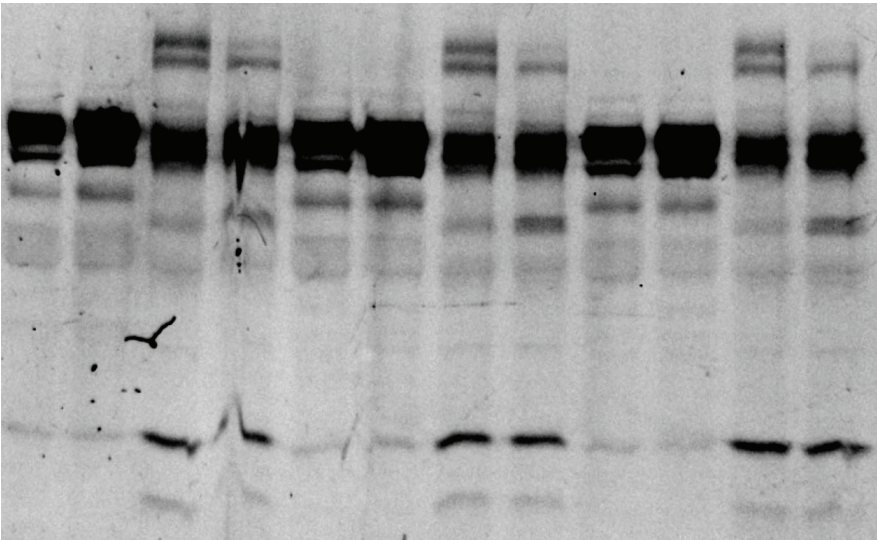
DH379 (1 μ M)

Brain fraction

NPC1

Cytosol		Membrane		Cytosol		Membrane		Cytosol		Membrane	
+/+	-/-	+/+	-/-	+/+	-/-	+/+	-/-	+/+	-/-	+/+	-/-

kDa
- 100 -
- 70 -
- 55 -
- 35 -



Coomassie

