

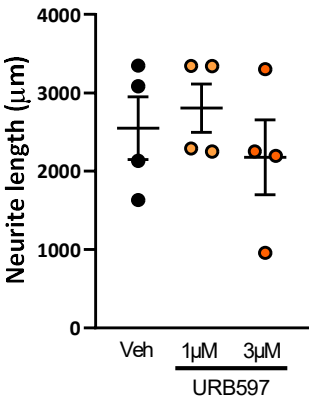
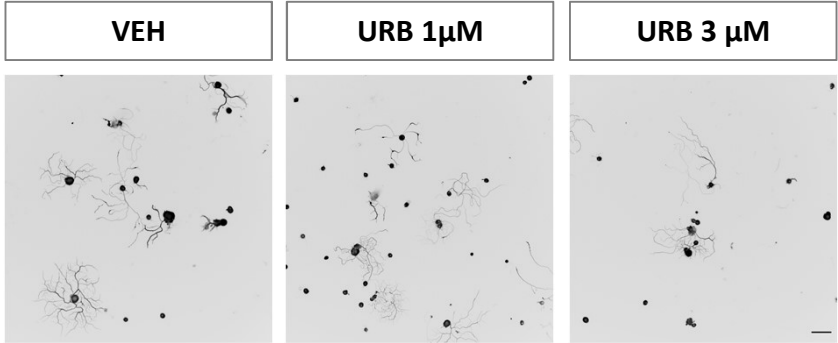
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Supplemental information

**Injury-induced activation
of the endocannabinoid system
promotes axon regeneration**

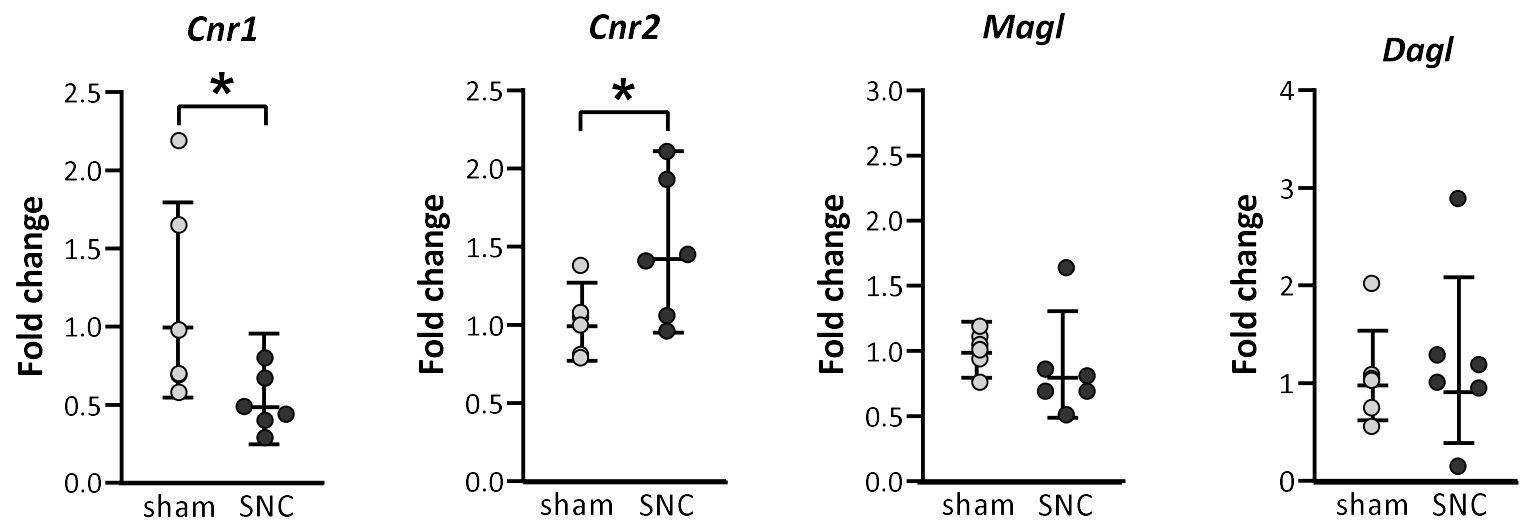
Sara Martinez-Torres, Francina Mesquida-Veny, José Antonio Del Rio, and Arnau Hervera

Supplementary Fig 1.



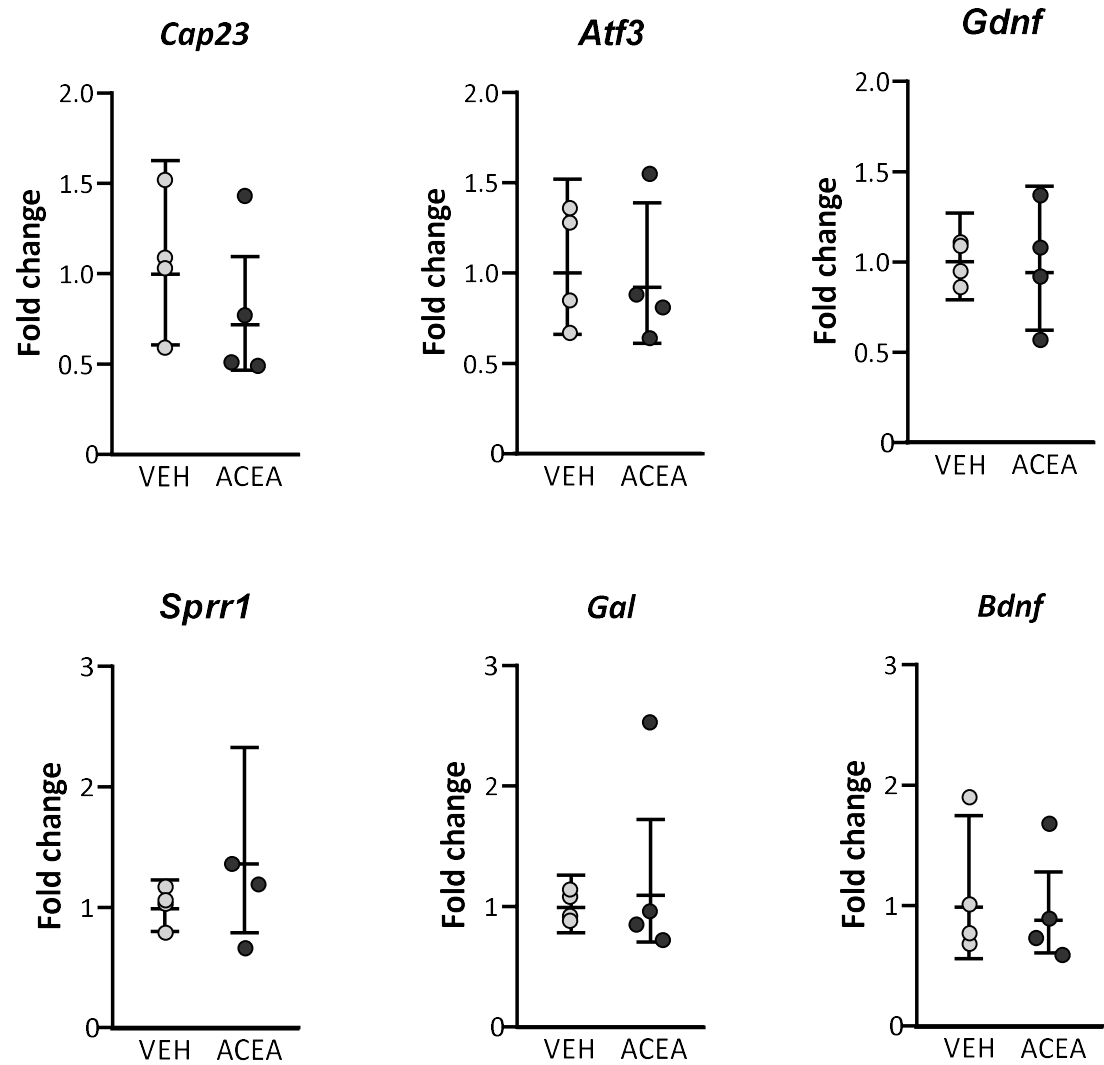
Supplementary Figure 1. FAAH inhibition does not affect neurite outgrowth. Related to Figure 1. Representative images and graphs of *in vitro* DRG neurite outgrowth (Tuj-1 positive cells) 24h after vehicle (VEH), 1 μ M or 3 μ M of FAAH inhibitor (URB597) (n = 4 different wells per group). Data are expressed as mean $\pm$ S.E.M.. Scale bars 100 μ m.

Supplementary Fig 2.



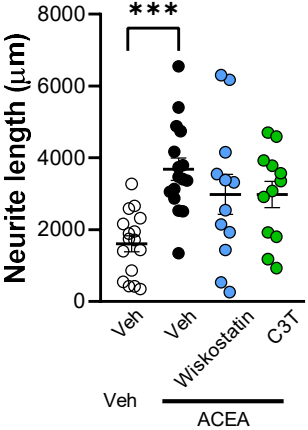
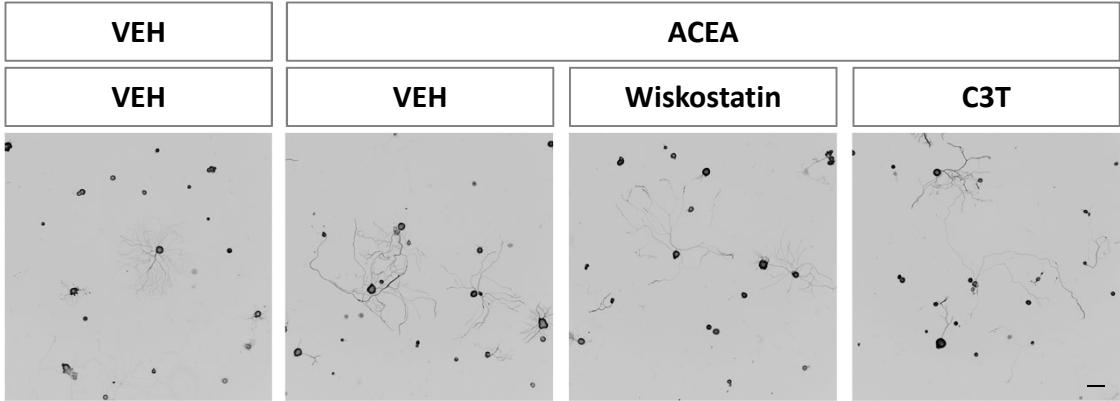
Supplementary Figure 2. Sciatic nerve injury changes cannabinoid receptor expression but not 2-AG synthesis enzymes. Related to Figure 1. DRG mRNA levels of *Cnr1*, *Cnr2*, *Magl* and *Dagl* 24h after sham or sciatic nerve crush (SNC). Data are expressed as $2^{-\Delta\Delta Ct} \pm \text{upper } (2^{-(\Delta\Delta Ct + SD)}) / \text{lower } (2^{-(\Delta\Delta Ct - SD)})$ limits. * $p < 0.05$ denotes significant difference between $\Delta\Delta Ct$ s after Student's T test. (n = 5-6 animals per group).

Supplementary Fig 3.



Supplementary Figure 3. ACEA does not induce increase in RAG expression. Related to Figure 4. DRG neuron mRNA levels of RAGS: *Cap23*, *Atf3*, *Gdnf*, *Sprr1*, *Gal* and *Bdnf* after *in vitro* vehicle (VEH) or ACEA administration. Data are expressed as $2^{-\Delta\Delta Ct} \pm \text{upper } (2^{-(\Delta\Delta Ct + SD)}) / \text{lower } (2^{-(\Delta\Delta Ct - SD)})$ limits. (n= 3-4 biological replicates).

Supplementary Fig 4.



Supplementary Figure 4. ACEA-induced outgrowth is not affected by actin cytoskeleton dynamics inhibition. Related to Figure 4. Representative images and graphs of *in vitro* DRG neurite outgrowth (Tuj-1 positive cells) 24h after VEH or ACEA combined with n-WASP (Wiskostatin) or RhoA (C3T) inhibitors. Data are expressed as mean±S.E.M. ***p<0.001 denote significant difference after ANOVA followed by Bonferroni post-hoc test. (n = 12 different wells per group) Scale bars 100µm.