

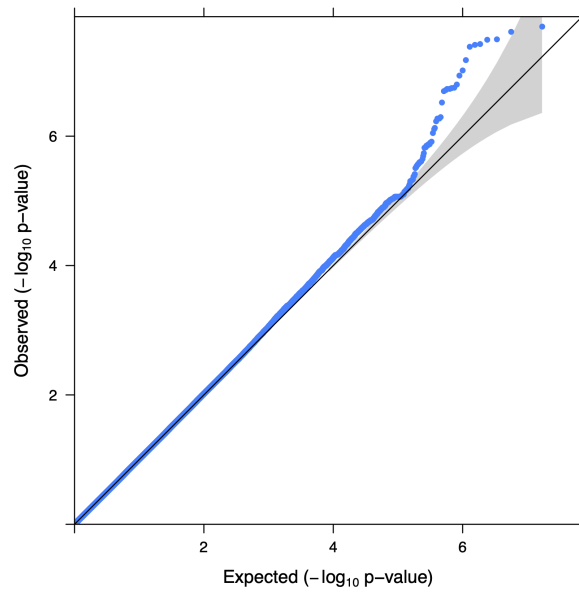


Figure S1. QQ-plot of p-values from a common variant GWAS of time to first peripheral neuropathy. Each point represents a single common variant. $\lambda_{gc}=1.004$

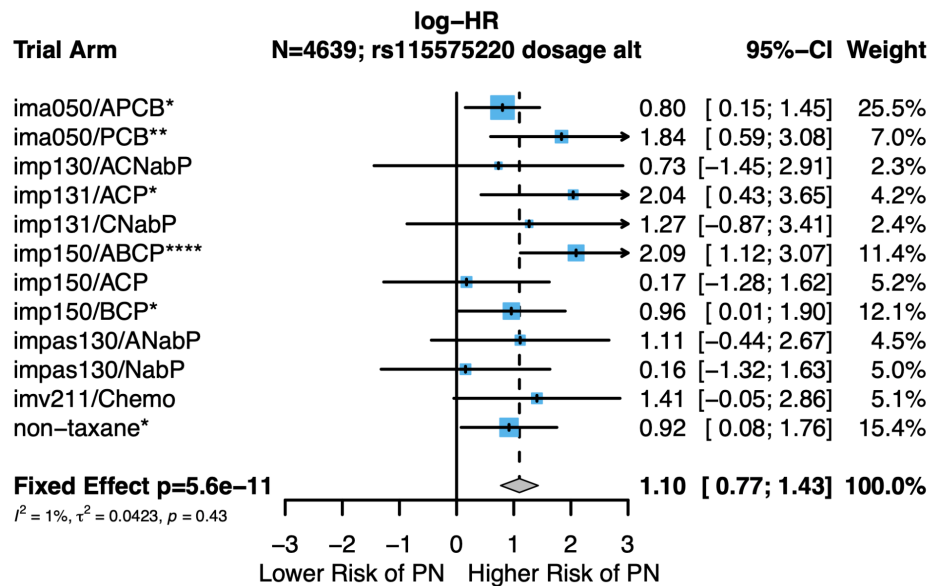


Figure S2. Effect size (HR) comparison across trials for rs115575220 (SCG2 locus) along with meta-analysis results.

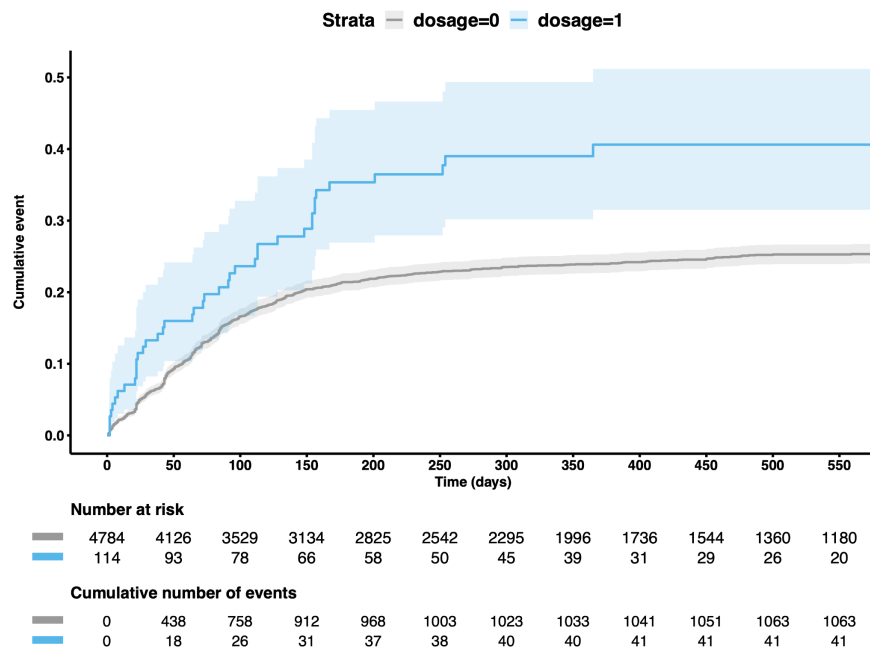


Figure S3. Kaplan Meier plot for PN events stratified by genotype dosage at rs115575220 (SCG2 locus).

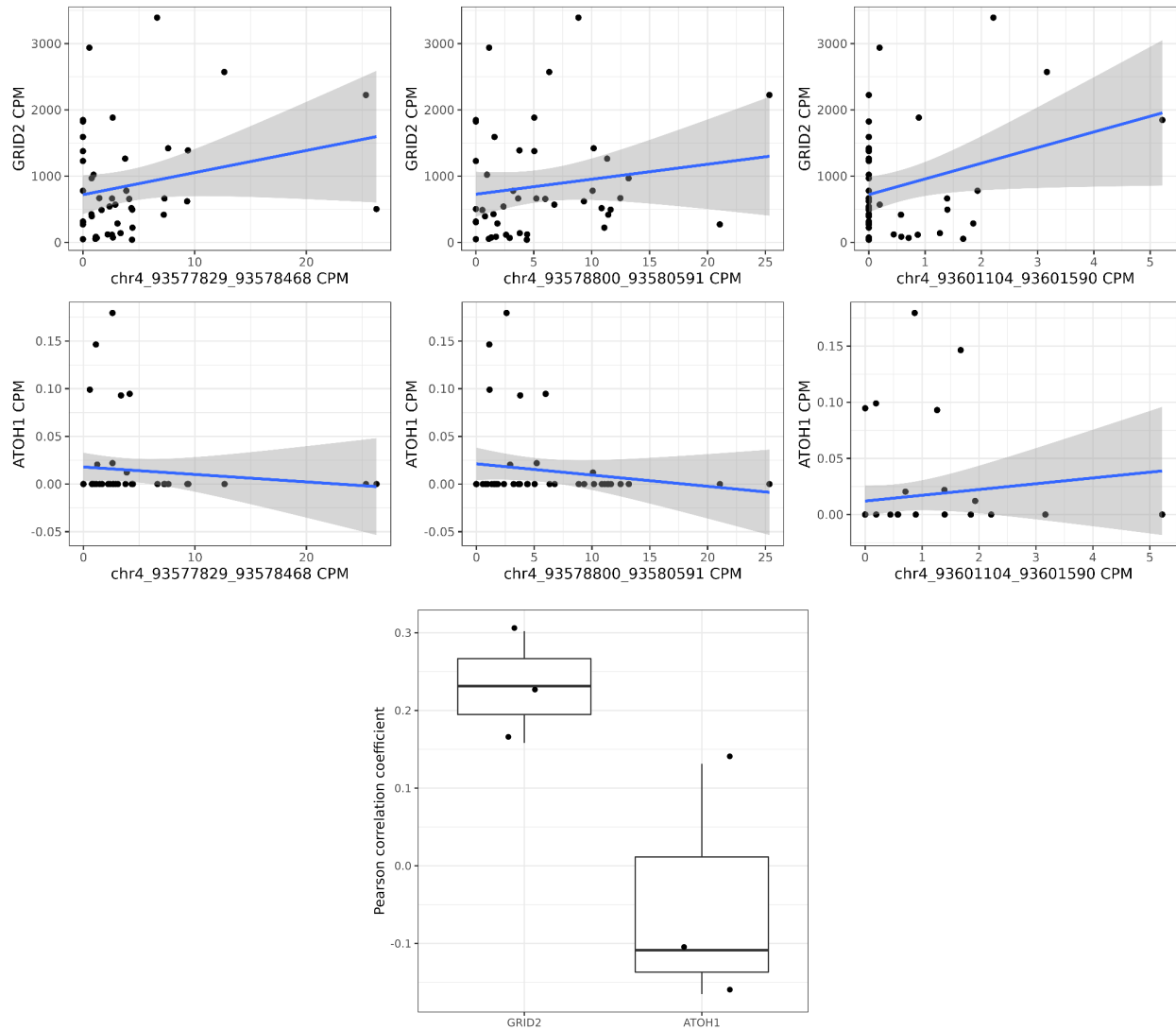


Figure S4. In the top panel, each point represents a cell type and each subpanel shows the relationship between gene expression and peak accessibility in the rs17020773/*GRID2* intron locus, which contains two protein-coding genes within 1MB (+/- 500KB) and three accessible chromatin peaks¹. For each cell type classified in the original publication, counts were summed across all genes and all peaks to generate pseudo-bulk profiles for gene expression and chromatin accessibility respectively, then profiles were normalized for read depth by dividing by the total and multiplying by 10^6 (CPM normalization). *GRID2* is highly expressed and has consistent positive correlations with chromatin accessibility across all peaks, summarized in the boxplot below.

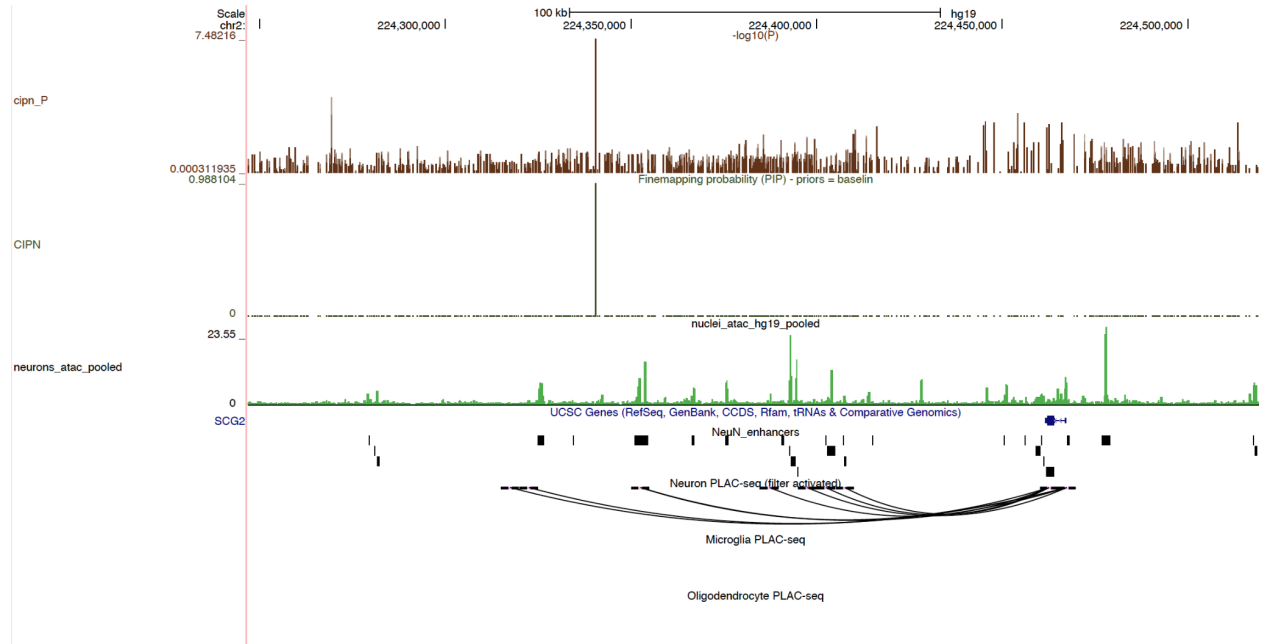


Figure S5. Top two panels show p-value, posterior causal probability respectively. Bottom four panels include data from and include ATAC-seq data in neurons, inferred locations of neuronal enhancers and chromatin interactions in neuronal, microglia, and oligodendrocyte PLAC-seq data, respectively². The index SNP (rs115575220) falls in a region enriched with neuron specific enhancers that show chromatin interaction with the promoter of *SCG2*.

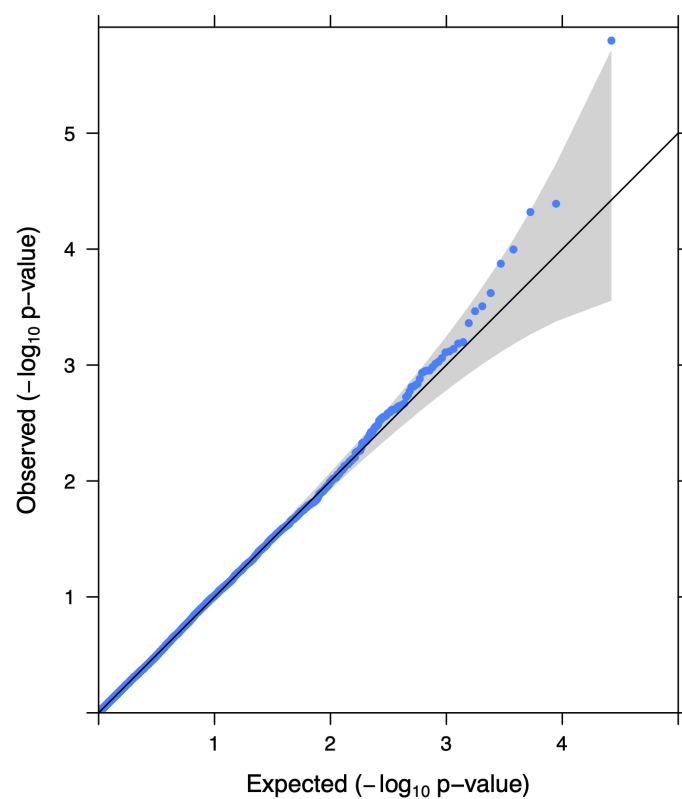


Figure S6. QQ-plot of p-values from a rare variant burden test of time to first peripheral neuropathy. Each point represents a gene. $\lambda_{gc}=1.009$.

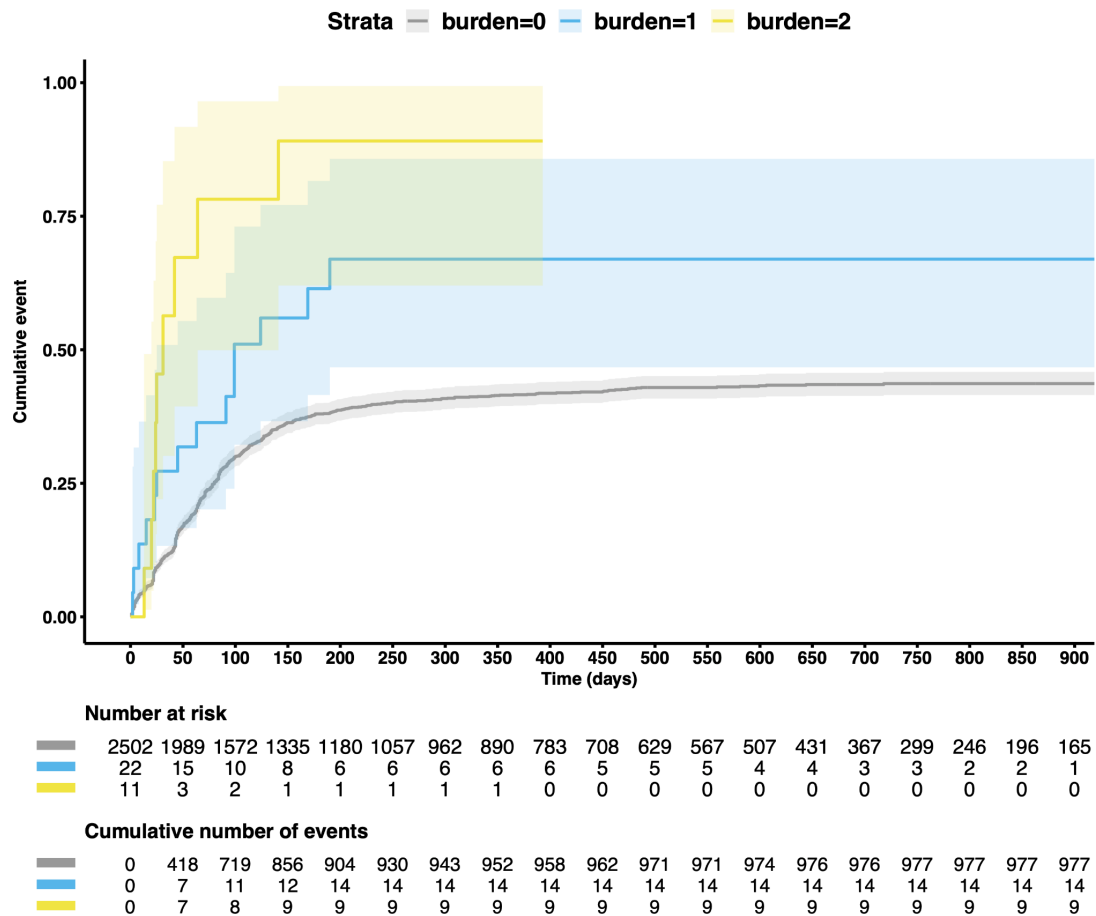


Figure S7. Cumulative incidence plot for PN events in taxane treated patients stratified by rare coding variant burden in *GPR68*.

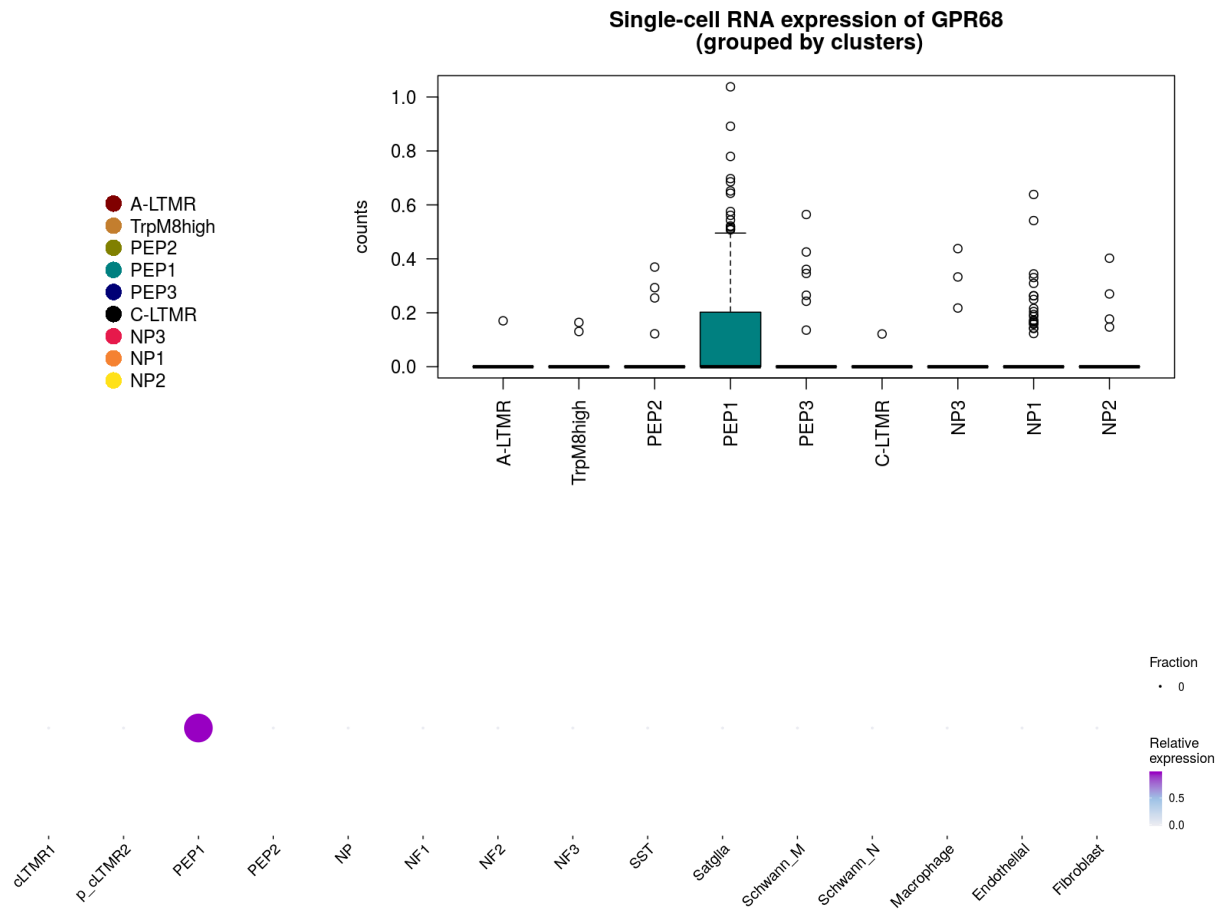


Figure S8. (top) Relative expression patterns *GPR68* in different DRG cell types in macaque (top from <https://ernforsgroup.shinyapps.io/macaqueDRG/>)³ and in mouse (bottom from <https://painseq.shinyapps.io/publish/#>)⁴ indicates a similar expression pattern to *GPR68* in human DRG. PEP1 neurons show relatively high expression of *GRP68* in both organisms.

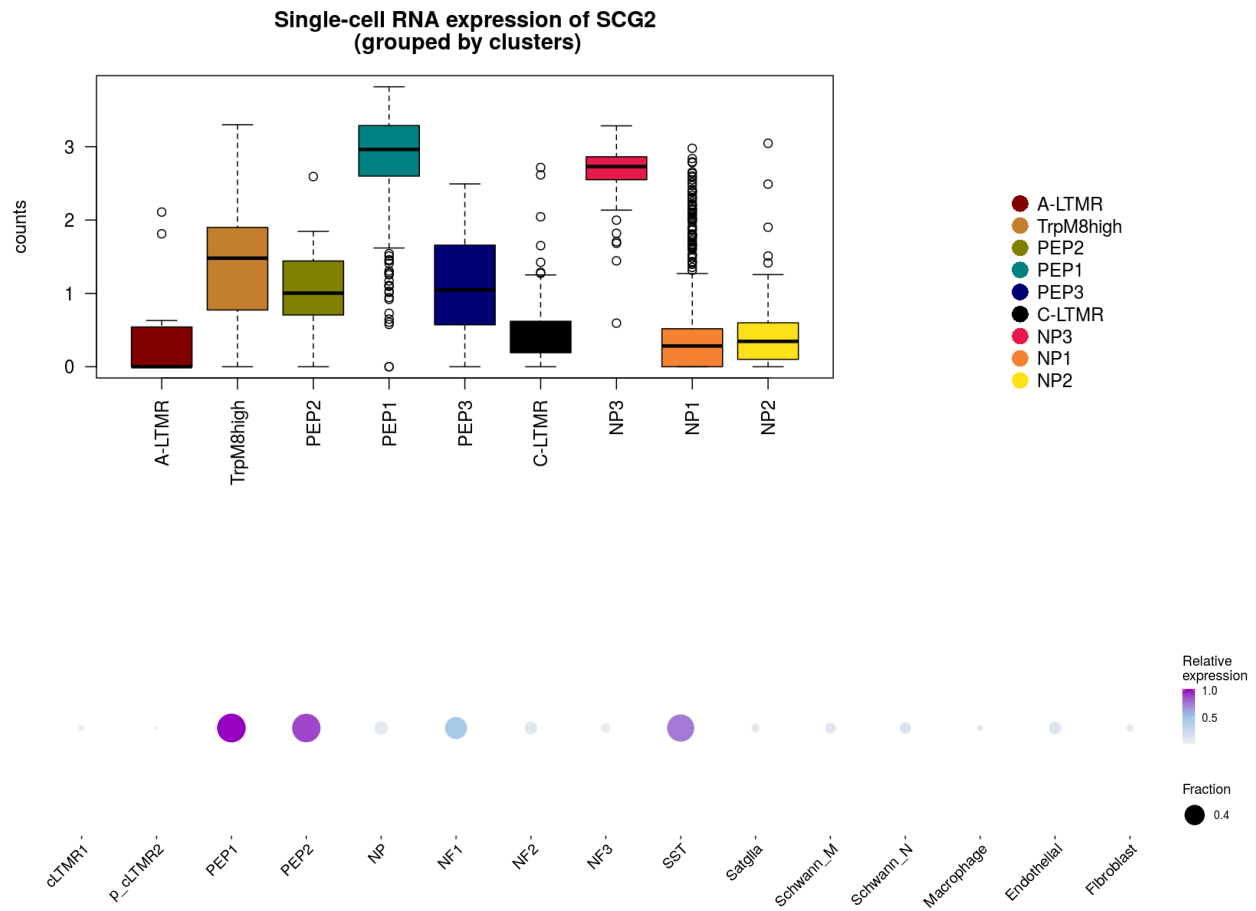


Figure S9. (top) Relative expression of SCG2 in macaque DRG obtained from (<https://ernforsgroup.shinyapps.io/macaqueDRG/>)³ and (bottom) in mouse (<https://painseq.shinyapps.io/publish/#>)⁴.

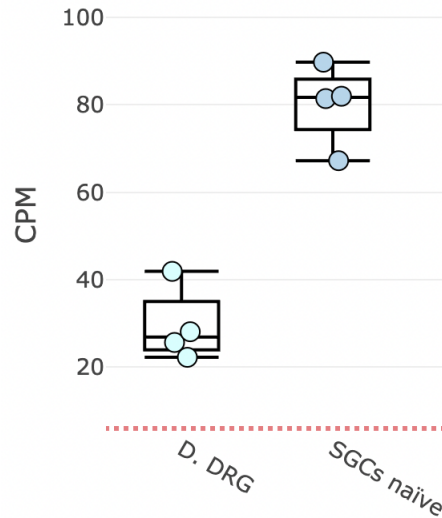


Figure S10. Expression of *GRID2* in bulk RNA-seq from human DRG as compared to sorted satellite glial cells (SCG) in mice (<http://rna-seq-browser.herokuapp.com/>)⁵.

References

1. Bakken, T. E. *et al.* Comparative cellular analysis of motor cortex in human, marmoset and mouse. *Nature* **598**, 111–119 (2021).
2. Nott, A. *et al.* Brain cell type–specific enhancer–promoter interactome maps and disease-risk association. *Science* **366**, 1134–1139 (2019).
3. Kupari, J. *et al.* Single cell transcriptomics of primate sensory neurons identifies cell types associated with chronic pain. *Nat Commun* **12**, 1510 (2021).
4. Renthal, W. *et al.* Transcriptional Reprogramming of Distinct Peripheral Sensory *Neuron* Subtypes after Axonal Injury. *Neuron* **108**, 128–144.e9 (2020).
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6. Nguyen MQ, Buchholtz LJ von, Reker AN, Ryba NJ, Davidson S. Single-nucleus transcriptomic analysis of human dorsal root ganglion neurons. *Elife* 2021;10:e71752.