Supplementary Information

Circadian regulation of chemotherapy-induced peripheral neuropathic pain and the underlying transcriptomic landscape

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Supplementary Information for the above manuscript contains seven supplementary figures (Fig. S1-S7) and ten supplementary tables (Table S1-S10).
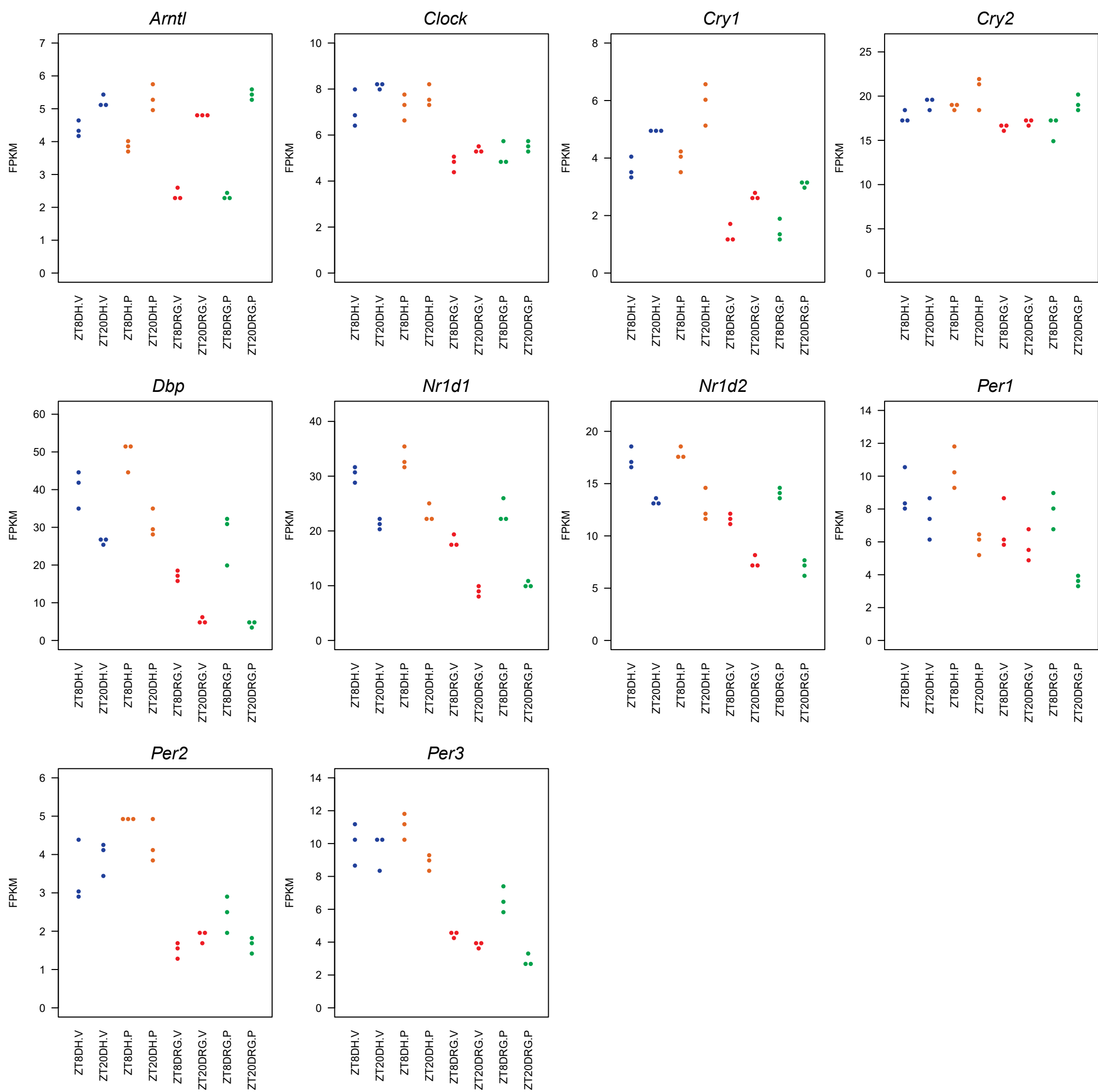
Fig. S1. Expression of core clock genes in the DH and the DRG.
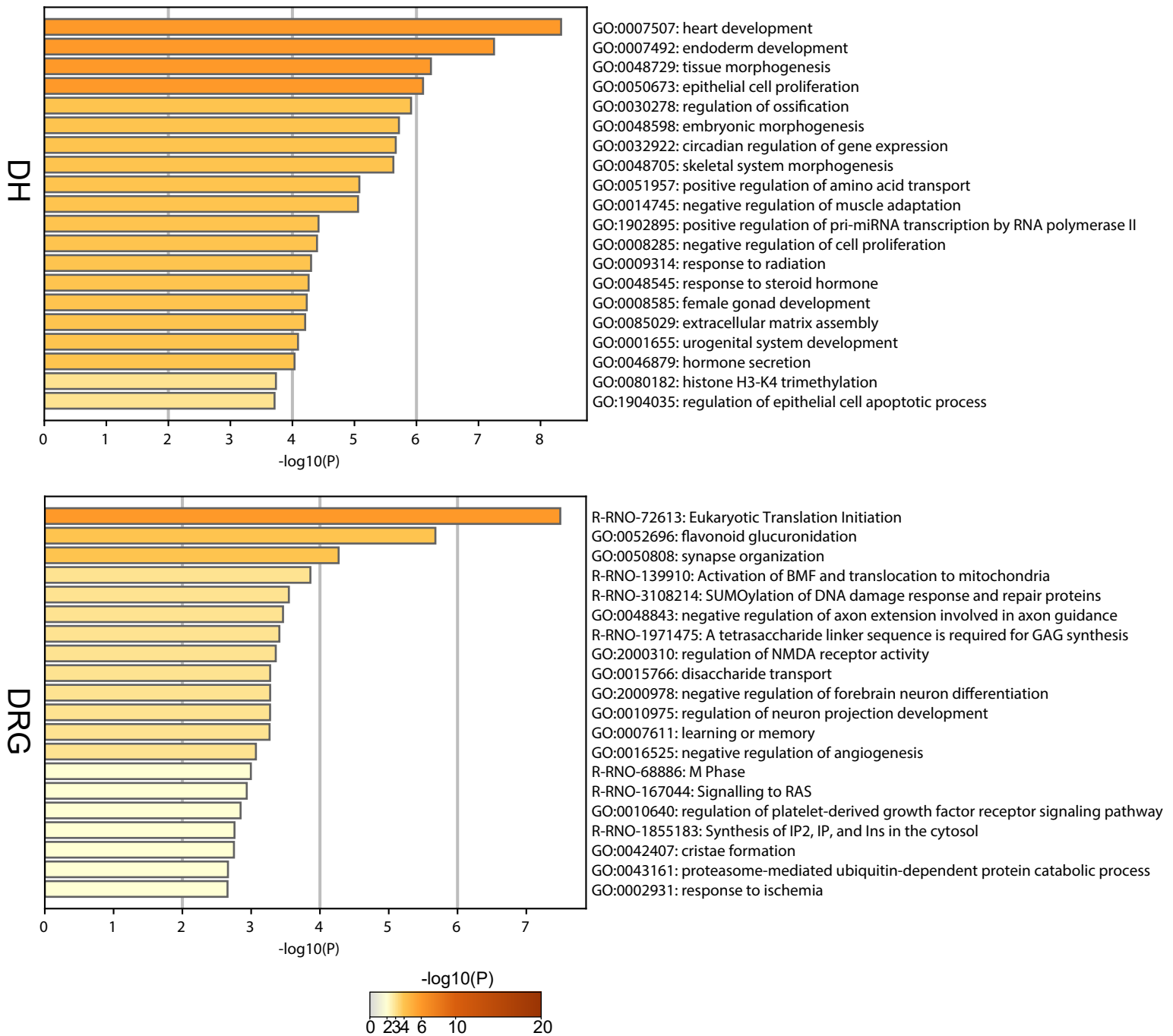
Fig. S2. Heat map showing the top enrichment clusters by Metascape analysis using paclitaxel-induced de novo diurnal DEGs in the DH and the DRG.
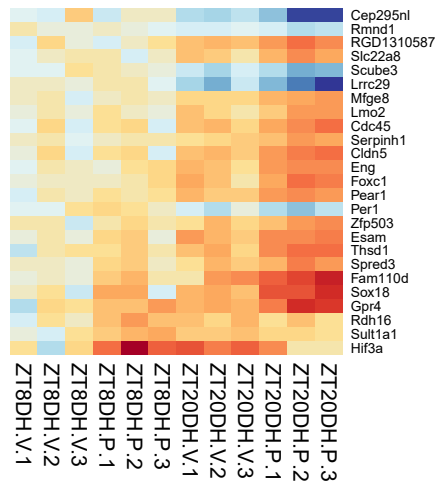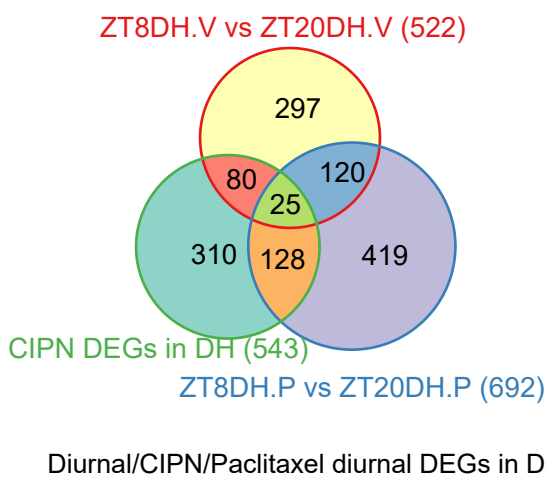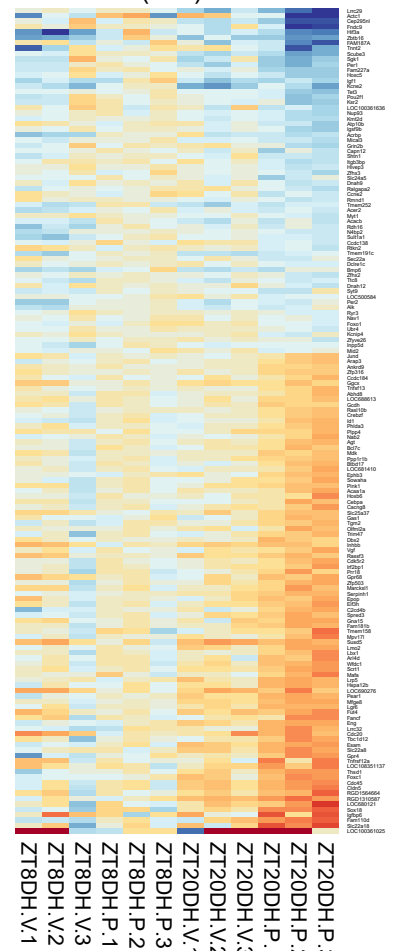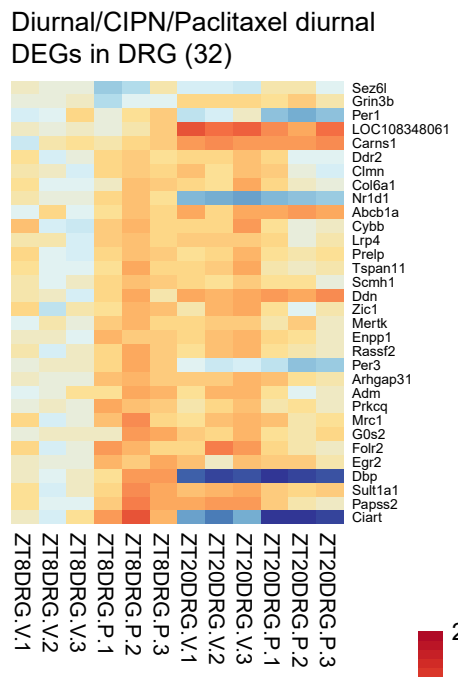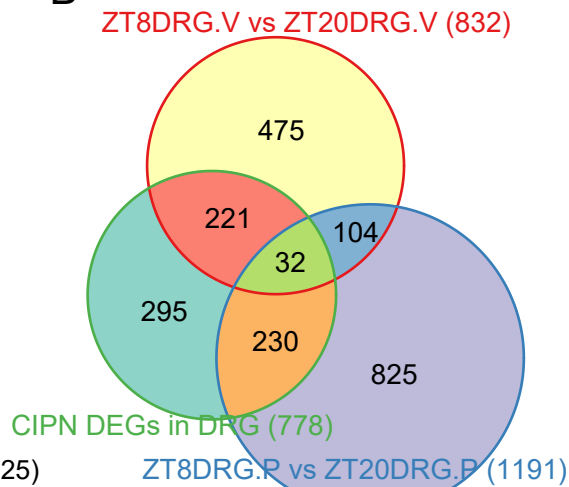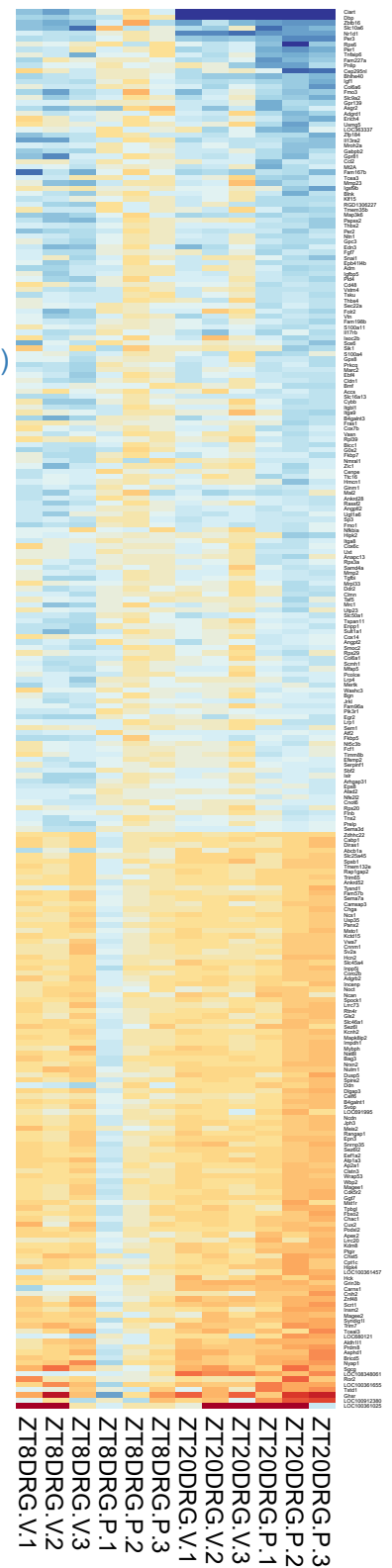
Fig. S3. Venn diagrams of diurnal, CIPN, and paclitaxel-induced diurnal DEGs in the DH (A) and the DRG (B). Heat maps indicate DEGs at the intersections of diurnal genes, CIPN, and paclitaxel-induced diurnal DEGs in the DH and the DRG. Each gene is represented as a horizontal line ordered vertically by log2 fold change in expression level at ZT20 with vehicle treatment relative to ZT8.
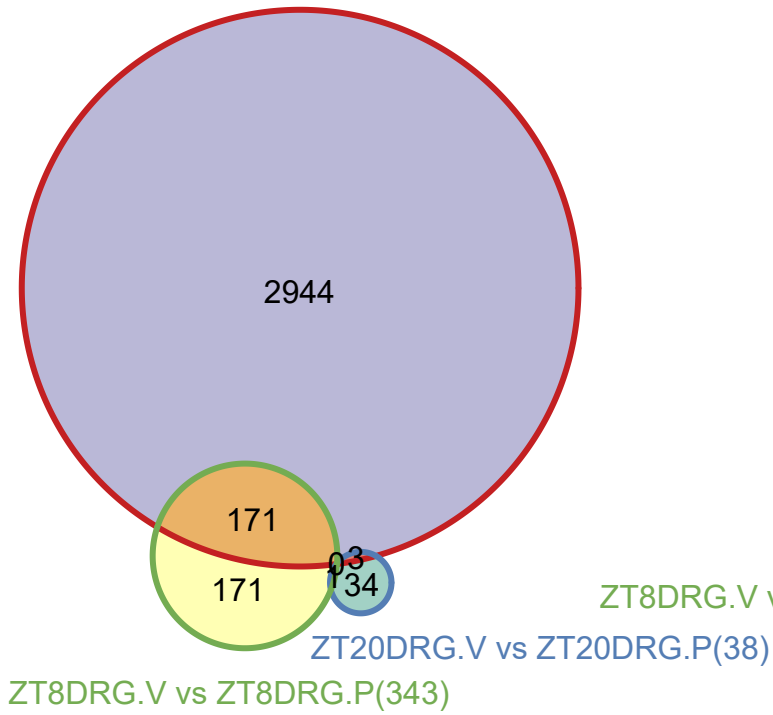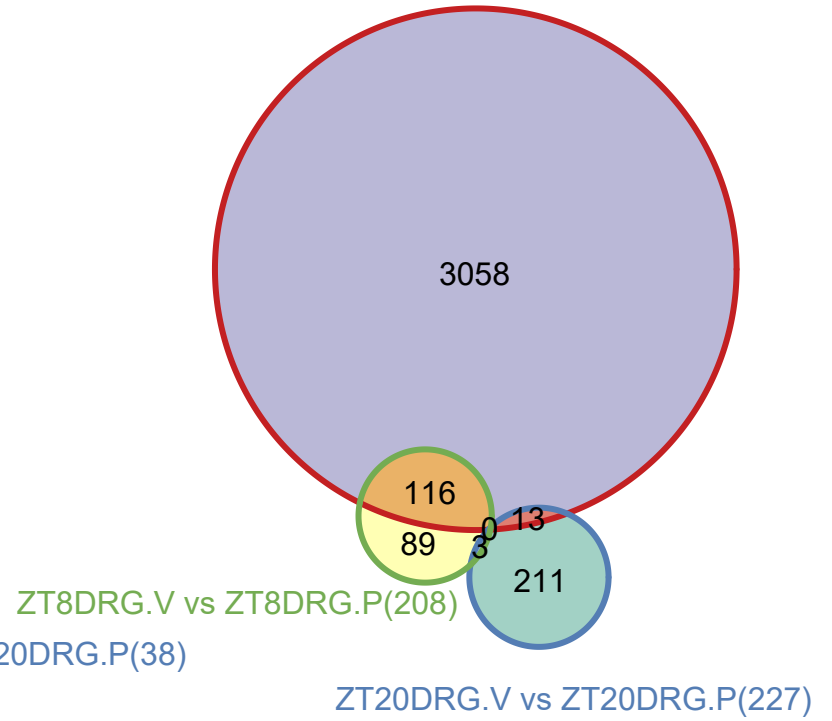
Fig. S4. Venn diagrams of DEGs of SNL and CIPN. (A) Up-regulated genes from both SNL and paclitaxel CIPN models. (B) Down-regulated genes from both SNL and paclitaxel CIPN models.

Fig. S5. Heat map showing the top 50 enrichment clusters by Metascape analysis using paclitaxel-induced DEGs in the DH at two circadian time points (ZT8 and ZT20).
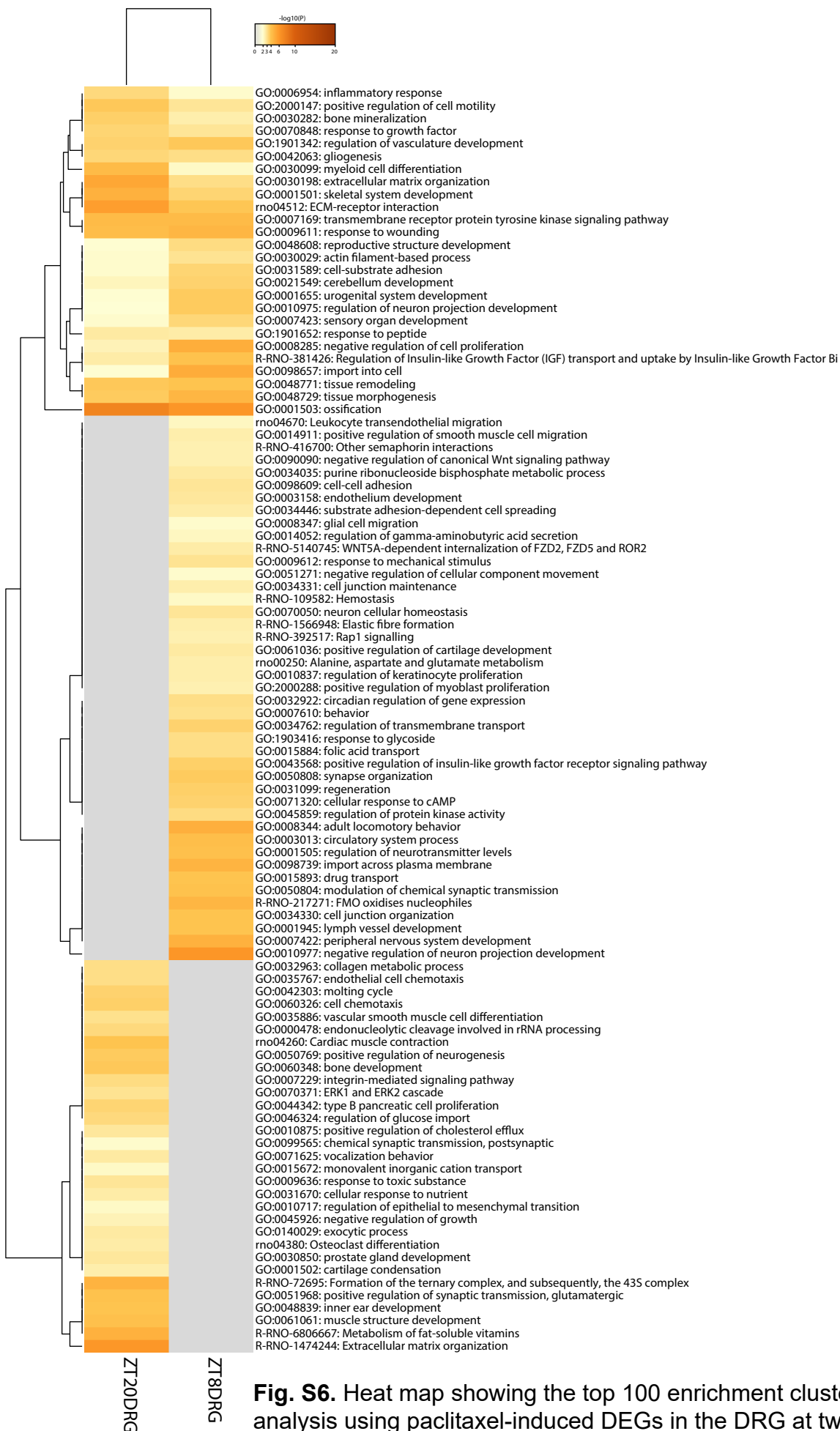
Fig. S6. Heat map showing the top 100 enrichment clusters by Metascape analysis using paclitaxel-induced DEGs in the DRG at two circadian time points (ZT8 and ZT20).

The heat map color scale shows -log10(P) with values 0, 2, 3, 4, 6, 10, 20.

Row labels (top to bottom):
- GO:0006954: inflammatory response
- GO:2000147: positive regulation of cell motility
- GO:0030282: bone mineralization
- GO:0070848: response to growth factor
- GO:1901342: regulation of vasculature development
- GO:0042063: gliogenesis
- GO:0030099: myeloid cell differentiation
- GO:0030198: extracellular matrix organization
- GO:0001501: skeletal system development
- rno04512: ECM-receptor interaction
- GO:0007169: transmembrane receptor protein tyrosine kinase signaling pathway
- GO:0009611: response to wounding
- GO:0048608: reproductive structure development
- GO:0030029: actin filament-based process
- GO:0031589: cell-substrate adhesion
- GO:0021549: cerebellum development
- GO:0001655: urogenital system development
- GO:0010975: regulation of neuron projection development
- GO:0007423: sensory organ development
- GO:1901652: response to peptide
- GO:0008285: negative regulation of cell proliferation
- R-RNO-381426: Regulation of Insulin-like Growth Factor (IGF) transport and uptake by Insulin-like Growth Factor Bi
- GO:0098657: import into cell
- GO:0048771: tissue remodeling
- GO:0048729: tissue morphogenesis
- GO:0001503: ossification
- rno04670: Leukocyte transendothelial migration
- GO:0014911: positive regulation of smooth muscle cell migration
- R-RNO-416700: Other semaphorin interactions
- GO:0090090: negative regulation of canonical Wnt signaling pathway
- GO:0034035: purine ribonucleoside bisphosphate metabolic process
- GO:0098609: cell-cell adhesion
- GO:0003158: endothelium development
- GO:0034446: substrate adhesion-dependent cell spreading
- GO:0008347: glial cell migration
- GO:0014052: regulation of gamma-aminobutyric acid secretion
- R-RNO-5140745: WNT5A-dependent internalization of FZD2, FZD5 and ROR2
- GO:0009612: response to mechanical stimulus
- GO:0051271: negative regulation of cellular component movement
- GO:0034331: cell junction maintenance
- R-RNO-109582: Hemostasis
- GO:0070050: neuron cellular homeostasis
- R-RNO-1566948: Elastic fibre formation
- R-RNO-392517: Rap1 signalling
- GO:0061036: positive regulation of cartilage development
- rno00250: Alanine, aspartate and glutamate metabolism
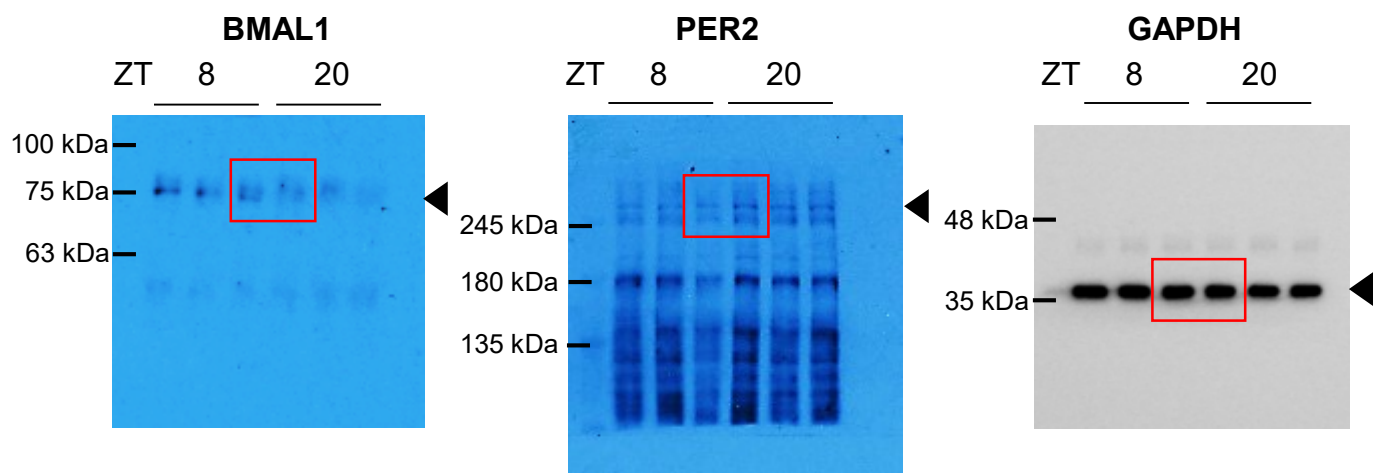- GO:0010837: regulation of keratinocyte proliferation
- GO:2000288: positive regulation of myoblast proliferation
- GO:0032922: circadian regulation of gene expression
- GO:0007610: behavior
- GO:0034762: regulation of transmembrane transport
- GO:1903416: response to glycoside
- GO:0015884: folic acid transport
- GO:0043568: positive regulation of insulin-like growth factor receptor signaling pathway
- GO:0050808: synapse organization
- GO:0031099: regeneration
- GO:0071320: cellular response to cAMP
- GO:0045859: regulation of protein kinase activity
- GO:0008344: adult locomotory behavior
- GO:0003013: circulatory system process
- GO:0001505: regulation of neurotransmitter levels
- GO:0098739: import across plasma membrane
- GO:0015893: drug transport
- GO:0050804: modulation of chemical synaptic transmission
- R-RNO-217271: FMO oxidises nucleophiles
- GO:0034330: cell junction organization
- GO:0001945: lymph vessel development
- GO:0007422: peripheral nervous system development
- GO:0010977: negative regulation of neuron projection development
- GO:0032963: collagen metabolic process
- GO:0035767: endothelial cell chemotaxis
- GO:0042303: molting cycle
- GO:0060326: cell chemotaxis
- GO:0035886: vascular smooth muscle cell differentiation
- GO:0000478: endonucleolytic cleavage involved in rRNA processing
- rno04260: Cardiac muscle contraction
- GO:0050769: positive regulation of neurogenesis
- GO:0060348: bone development
- GO:0007229: integrin-mediated signaling pathway
- GO:0070371: ERK1 and ERK2 cascade
- GO:0044342: type B pancreatic cell proliferation
- GO:0046324: regulation of glucose import
- GO:0010875: positive regulation of cholesterol efflux
- GO:0099565: chemical synaptic transmission, postsynaptic
- GO:0071625: vocalization behavior
- GO:0015672: monovalent inorganic cation transport
- GO:0009636: response to toxic substance
- GO:0031670: cellular response to nutrient
- GO:0010717: regulation of epithelial to mesenchymal transition
- GO:0045926: negative regulation of growth
- GO:0140029: exocytic process
- rno04380: Osteoclast differentiation
- GO:0030850: prostate gland development
- GO:0001502: cartilage condensation
- R-RNO-72695: Formation of the ternary complex, and subsequently, the 43S complex
- GO:0051968: positive regulation of synaptic transmission, glutamatergic
- GO:0048839: inner ear development
- GO:0061061: muscle structure development
- R-RNO-6806667: Metabolism of fat-soluble vitamins
- R-RNO-1474244: Extracellular matrix organization

Column labels: ZT20DRG, ZT8DRG

Fig. S7. Original, full-length immunoblots for Fig. 4D.