

Targeting cannabinoid 1 and delta opioid receptor heteromers alleviates chemotherapy-induced neuropathic pain

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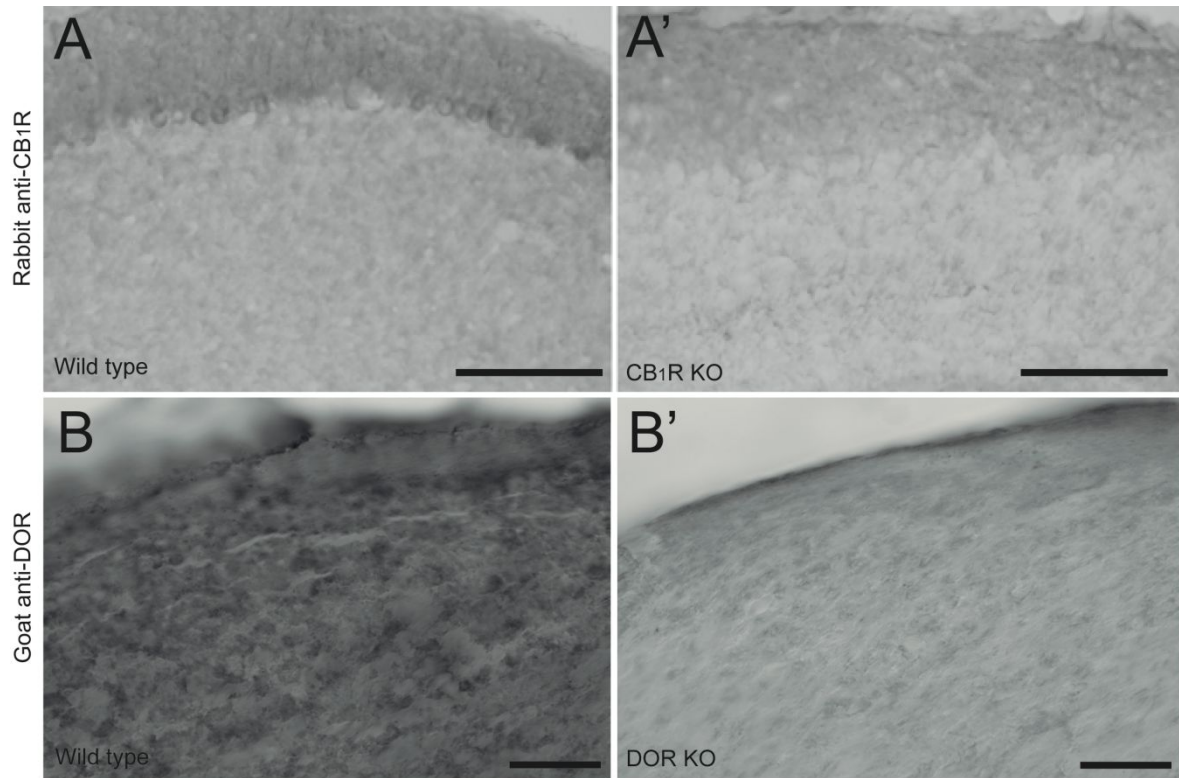
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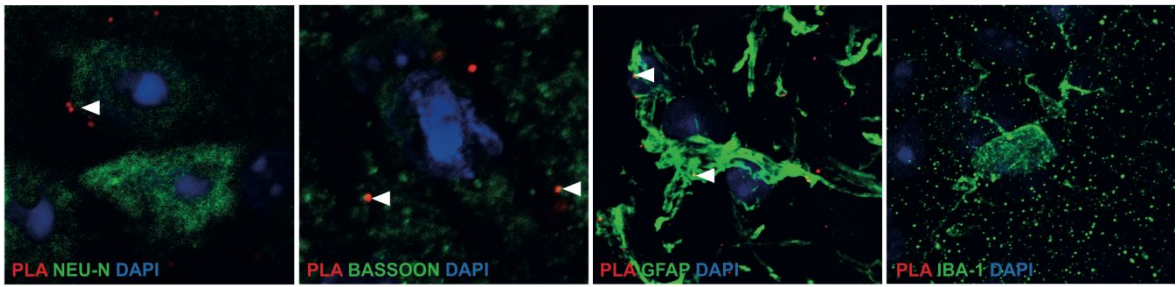
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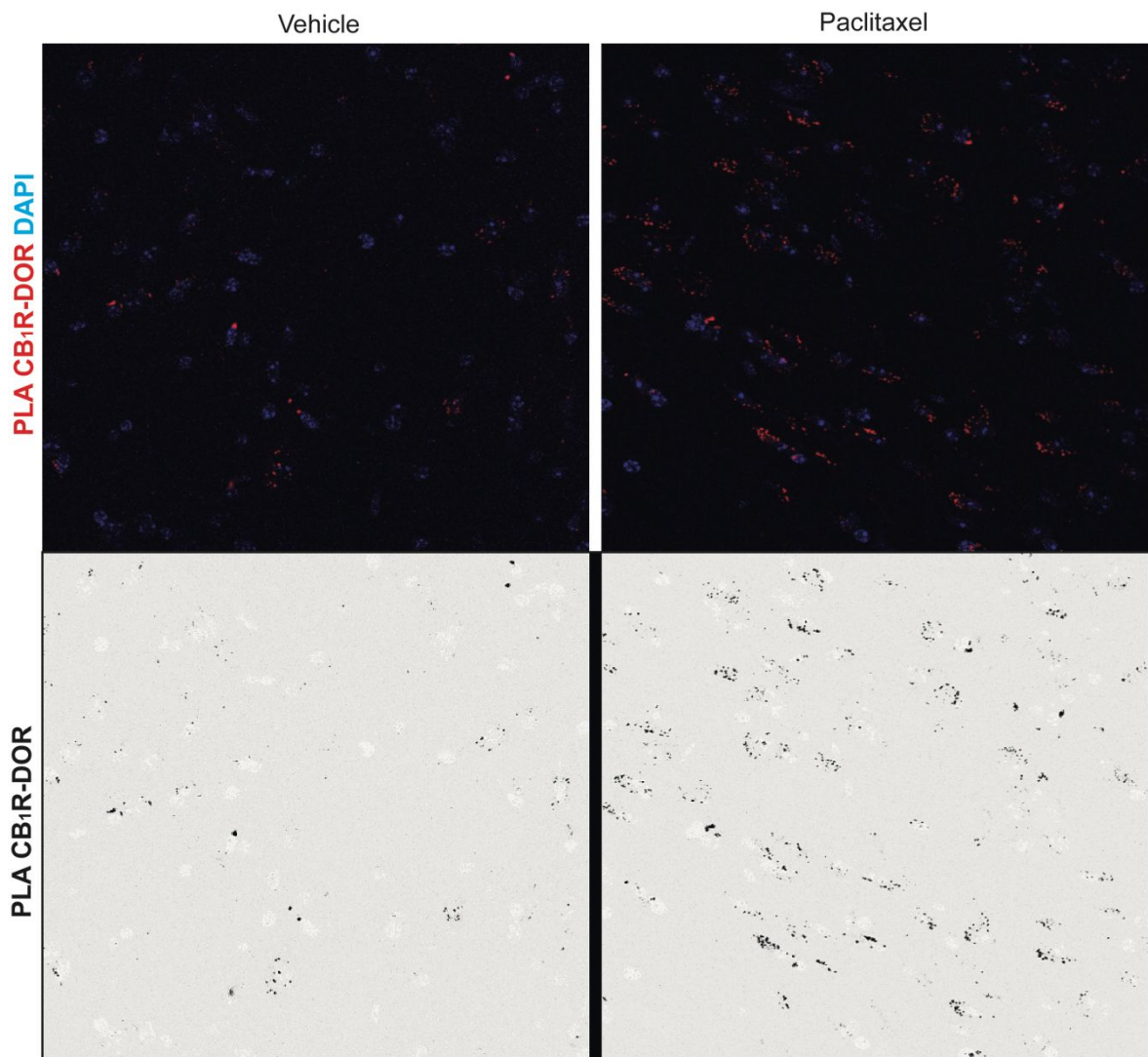
Suppl. Fig.1

Supl Fig 1. Validation of antibodies. CB₁R and DOR staining is present in the cerebellar cortex or pontine gray of wild-type but not in CB₁R or DOR knock-out mice respectively. Tissue sections were stained using a goat rabbit anti-CB₁R or anti-DOR receptor antibody followed by HRP-conjugated anti-species IgG secondary antibodies, and reaction with diaminobenzidine.



Suppl. Fig. 2

Supl Fig 2 Detection of CB₁R-DOR heteromers in the dorsal region of the lumbar spinal cord of paclitaxel-treated mice using PLA. CB₁R-DOR heteromers are located in neurons (somatodendritic and presynaptic location) and astrocytes, but not in microglia.



Suppl. Fig. 3

Supl Fig 3. CB₁R-DOR heteromers are increased in the basolateral amygdala of paclitaxel-treated mice. CB₁R-DOR heteromers (red dots in color panels, black dots in inverted color panels) are detected in the basolateral amygdala of control and paclitaxel-induced chemotherapy mice.

Table S1. Summary information of control and patients with chemotherapy-induced peripheral neuropathy (CIPN)

| Control group | | | |
|----------------------|--------------------|---------------------------|----------------------------|
| sex | age (years) | cause of death | PLA (CB1R-DOR) dots |
| female | 68 | cardiac arrest | 364 |
| female | 30 | cardiorespiratory failure | 127 |
| female | 72 | cardiac arrest | 110 |
| male | 42 | surgery complication | 313 |
| male | 57 | cardiac arrest | 122 |
| male | 34 | septic shock | 147 |
| male | 38 | cardiac arrest | 257 |
| male | 50 | multiorgan failure | 164 |
| male | 64 | procedure complication | 218 |
| male | 56 | cardiac arrest | 358 |

| CIPN group | | | | |
|-------------------|--------------------|-------------------|-------------------------|----------------------------|
| sex | age (years) | disease | drugs | PLA (CB1R-DOR) dots |
| female | 49 | pharynx carcinoma | paclitaxel, carboplatin | 284 |
| female | 51 | breast cancer | paclitaxel, carboplatin | 721 |
| female | 51 | multiple myeloma | cisplatin | 370 |
| male | 48 | larynx cancer | paclitaxel, oxaliplatin | 362 |
| male | 75 | larynx cancer | paclitaxel | 426 |
| male | 70 | lung cancer | paclitaxel | 588 |
| male | 65 | B-cell lymphoma | oxaliplatin | 420 |
| male | 51 | breast cancer | paclitaxel | 728 |
| male | 73 | tongue cancer | cisplatin | 631 |