

Simultaneous activation of mu and delta opioid receptors reduces allodynia and astrocytic connexin 43 in an animal model of neuropathic pain

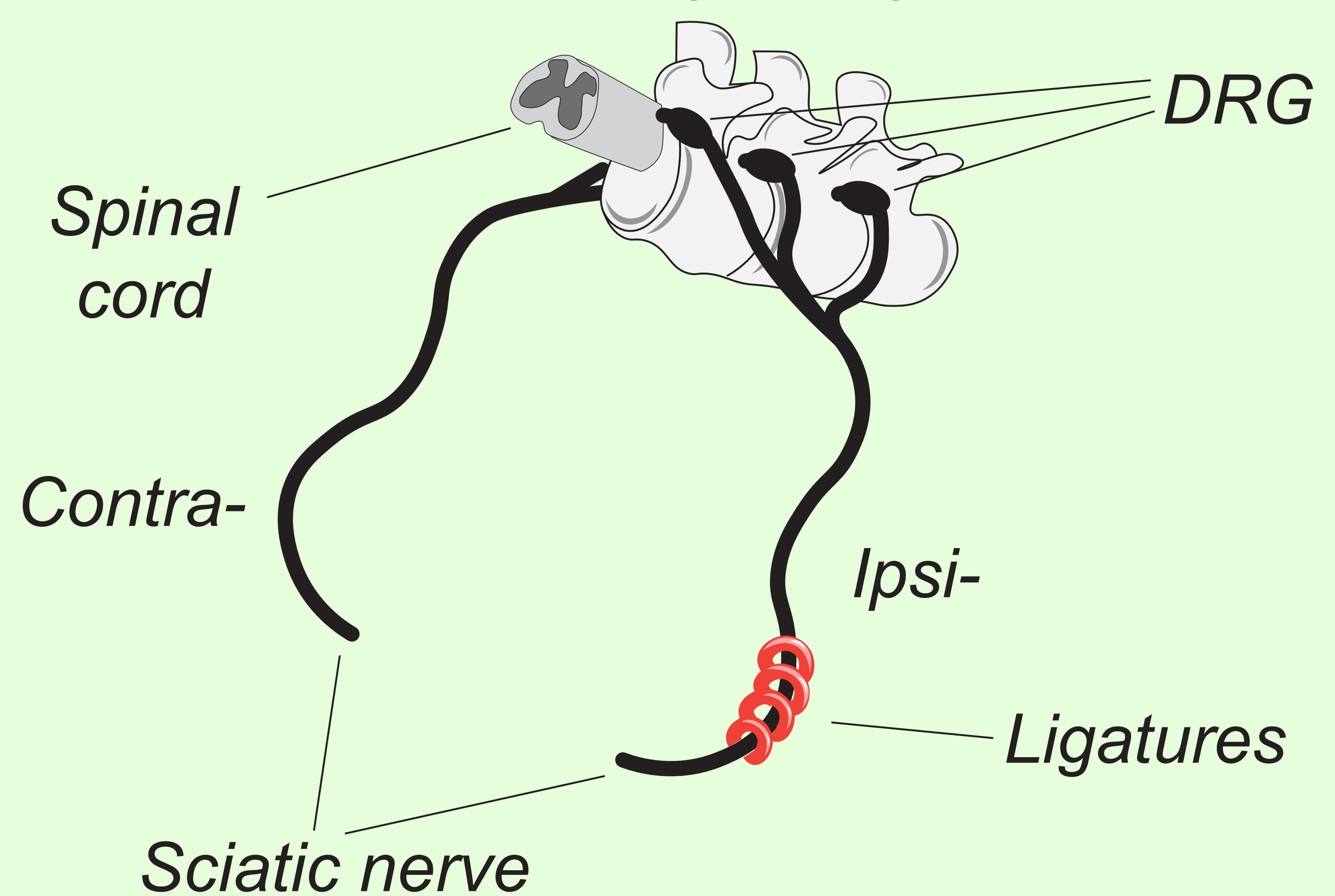
Nunzio Vicario¹, Lorella Pasquinucci², Federica M. Spitale¹, Santina Chiechio^{3,4}, Rita Turnaturi², Filippo Caraci^{3,4}, Daniele Tibullo⁵, Roberto Avola⁵, Rosario Gulino¹, Rosalba Parenti¹, Carmela Parenti³.

¹Department of Biomedical and Biotechnological Sciences, Section of Physiology, University of Catania, 95123 Catania, Italy; ²Department of Drug Sciences, Section of Medicinal Chemistry, University of Catania, 95125 Catania, Italy; ³Department of Drug Sciences, Section of Pharmacology and Toxicology, University of Catania, 95125 Catania, Italy; ⁴Oasi Research Institute—IRCCS, 94018 Troina, Italy; ⁵Department of Biomedical and Biotechnological Sciences, Section of Biochemistry, University of Catania, 95123 Catania, Italy

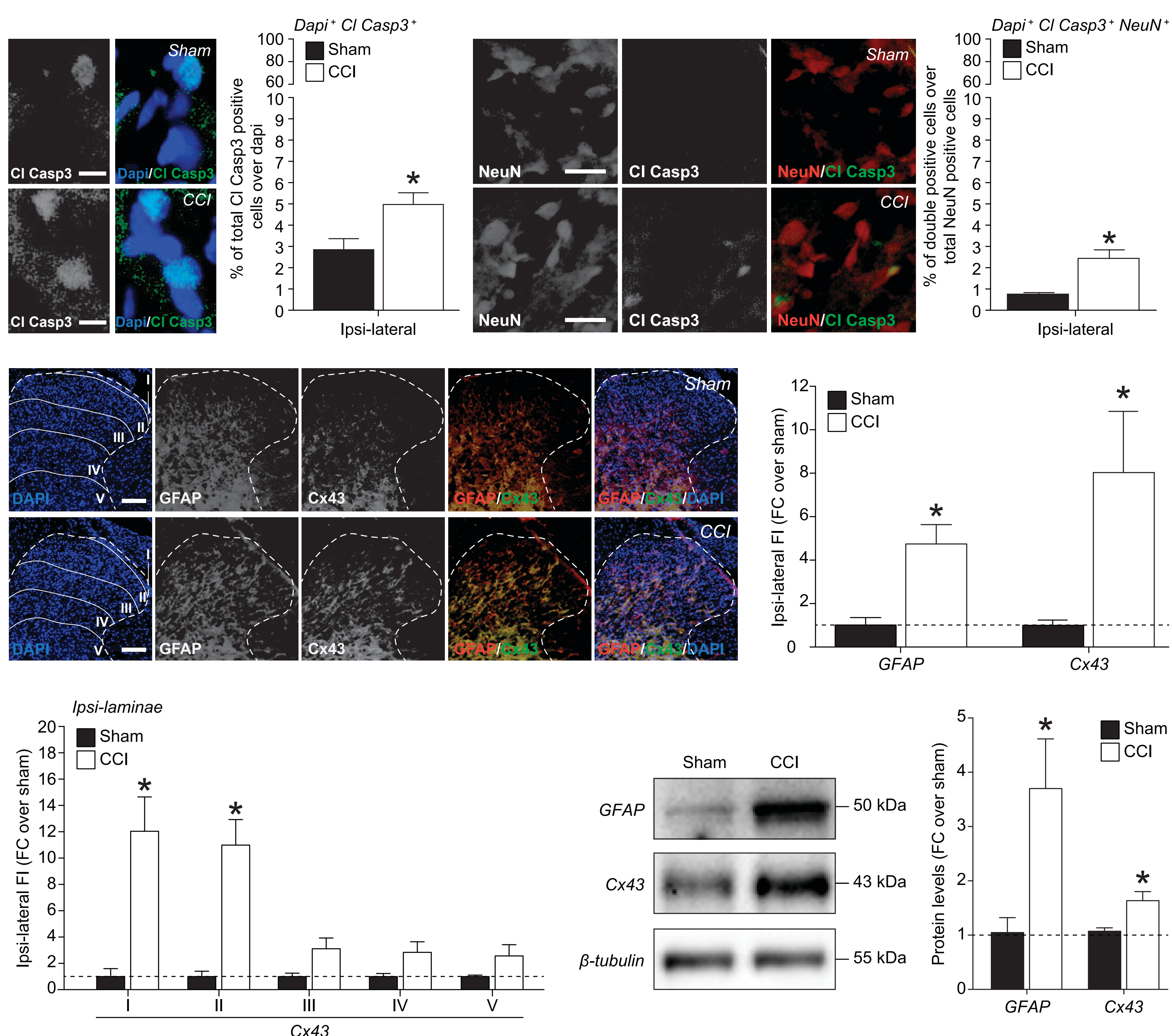
Neuropathic pain is a chronic condition triggered by lesions to the somatosensory nervous system. Mu opioid receptor (MOR) is a master regulator of moderate to severe pain, but during chronic conditions the role of MOR is controversial.

Recently, the simultaneous MOR and delta opioid receptor (DOR) targeting has become an attractive target for the treatment of pain conditions, reducing side effects that limit opioids use. Interestingly, coexpression of DOR/MOR could be the cellular basis for inter-modulatory interactions of molecules, such as LP2, which act as MOR/DOR agonists exerting significant long-lasting antinociceptive effects.

Chronic constriction injury (CCI) model of neuropathic pain



CCI model of neuropathic pain - Astrocytes and connexin43





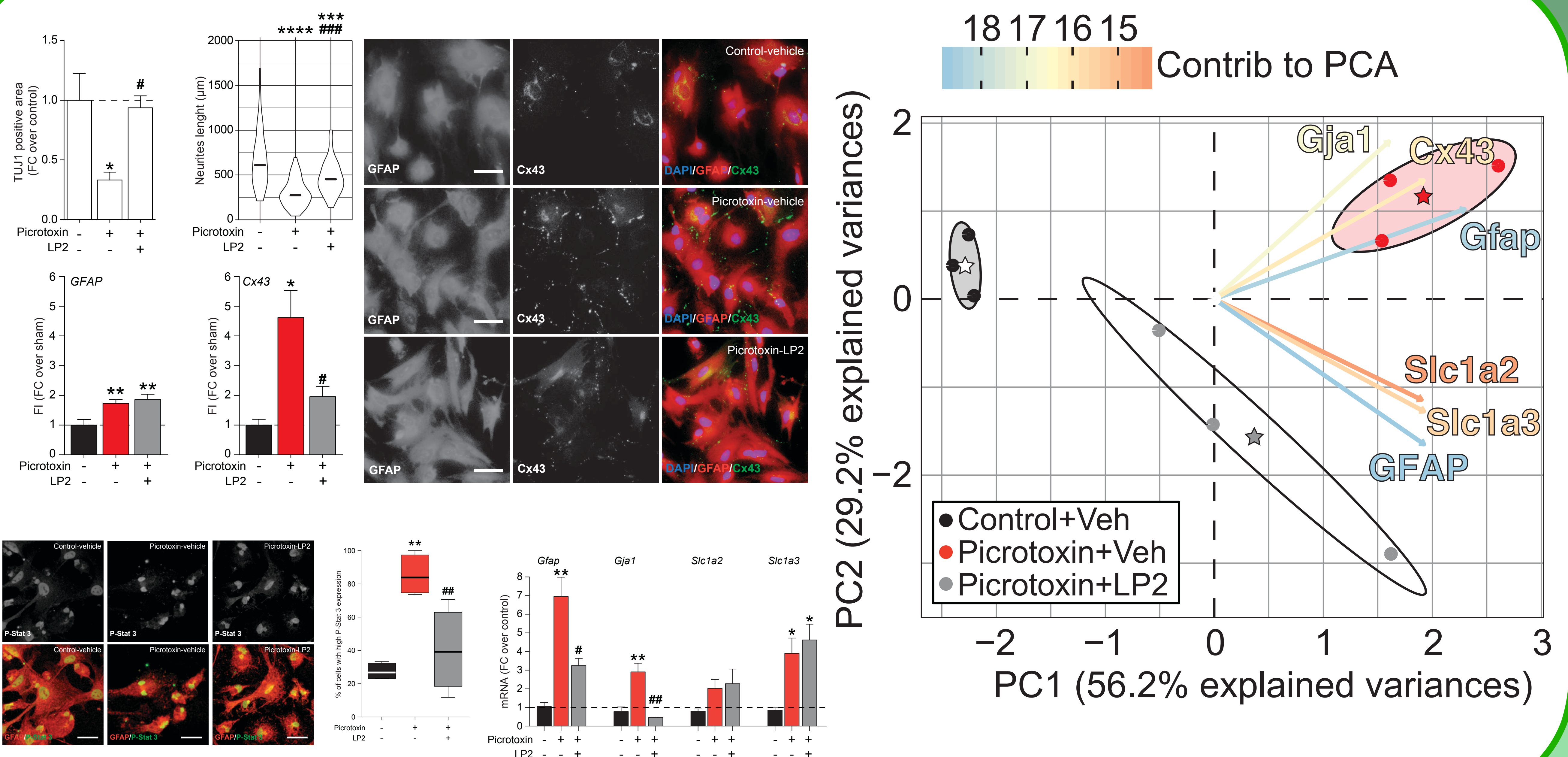
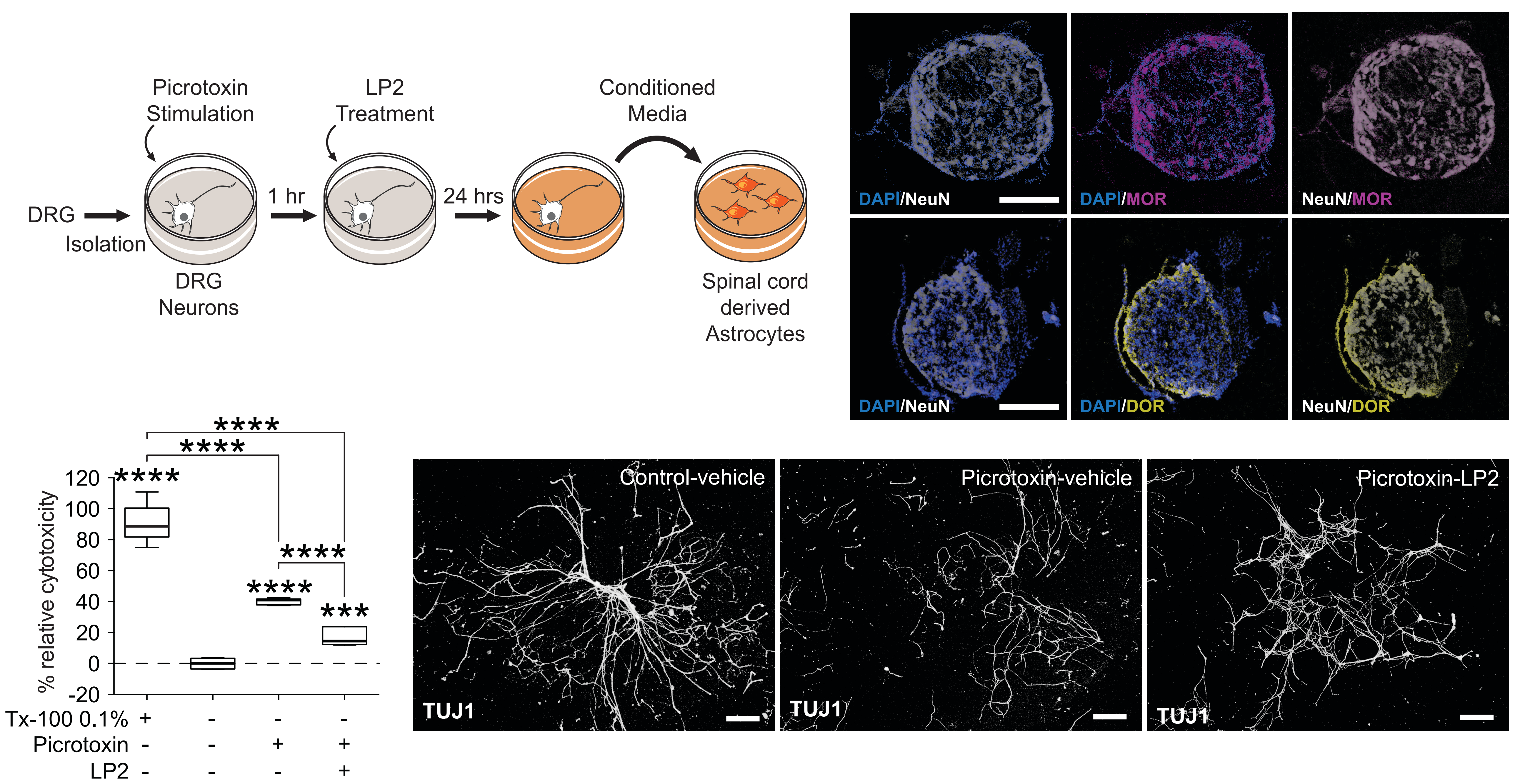
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In vitro model of excitotoxic pulse

Effects of neuronal MOR/DOR targeting on astrocytes

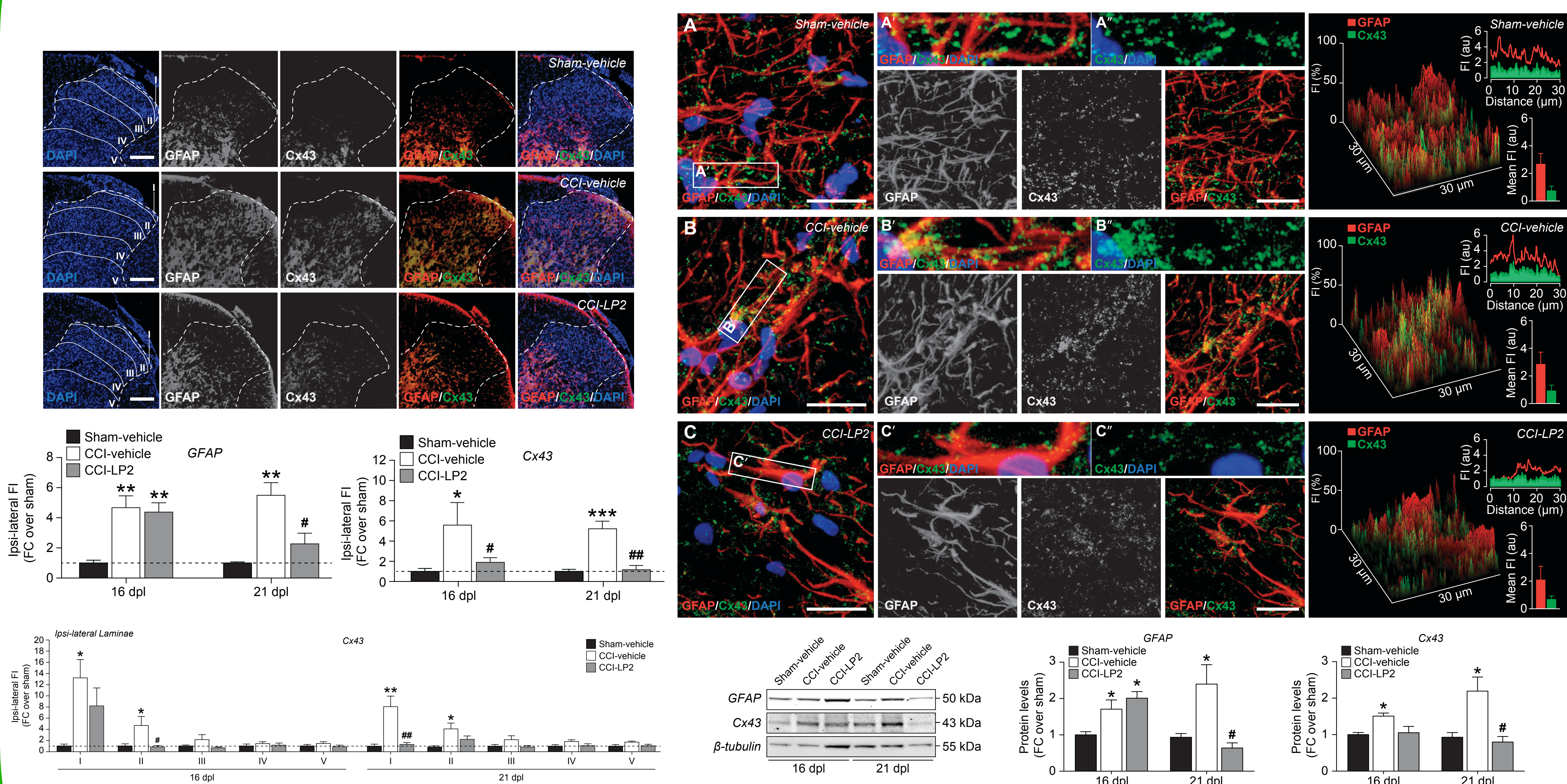
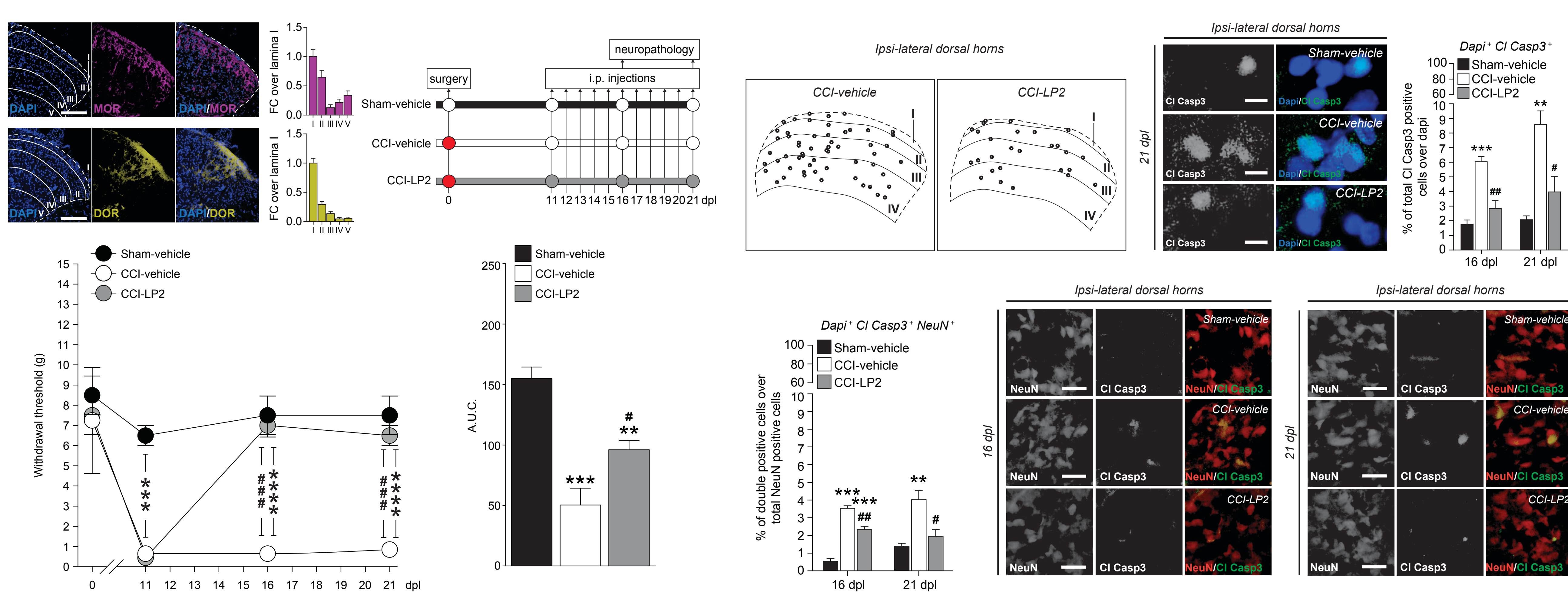


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CCI model of neuropathic pain - Astrocytes and connexin43



CONCLUSIONS and PERSPECTIVES

- Neuropathic pain induces significant increase of reactive astrocytes and Cx43-mediated coupling;
- MOR and DOR exert a reduction of Cx43 levels coupled with a significant reduction of pro-apoptotic signalling in ipsi-lateral dorsal horn;
- MOR and DOR activation in CCI injured rats restores astrocytes and neurons homeostasis.