

Naringenin relieves Paclitaxel-induced pain via inhibiting CGRP production and DRG neuron sensitization and enhances Paclitaxel's anti-tumor action

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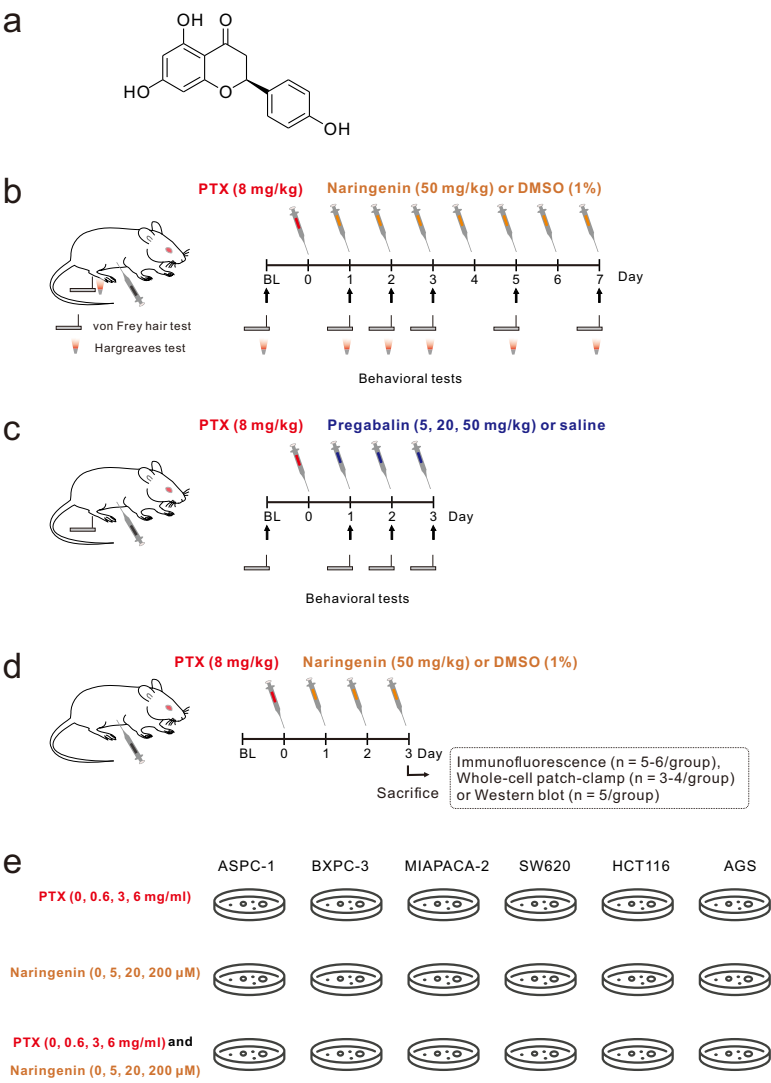
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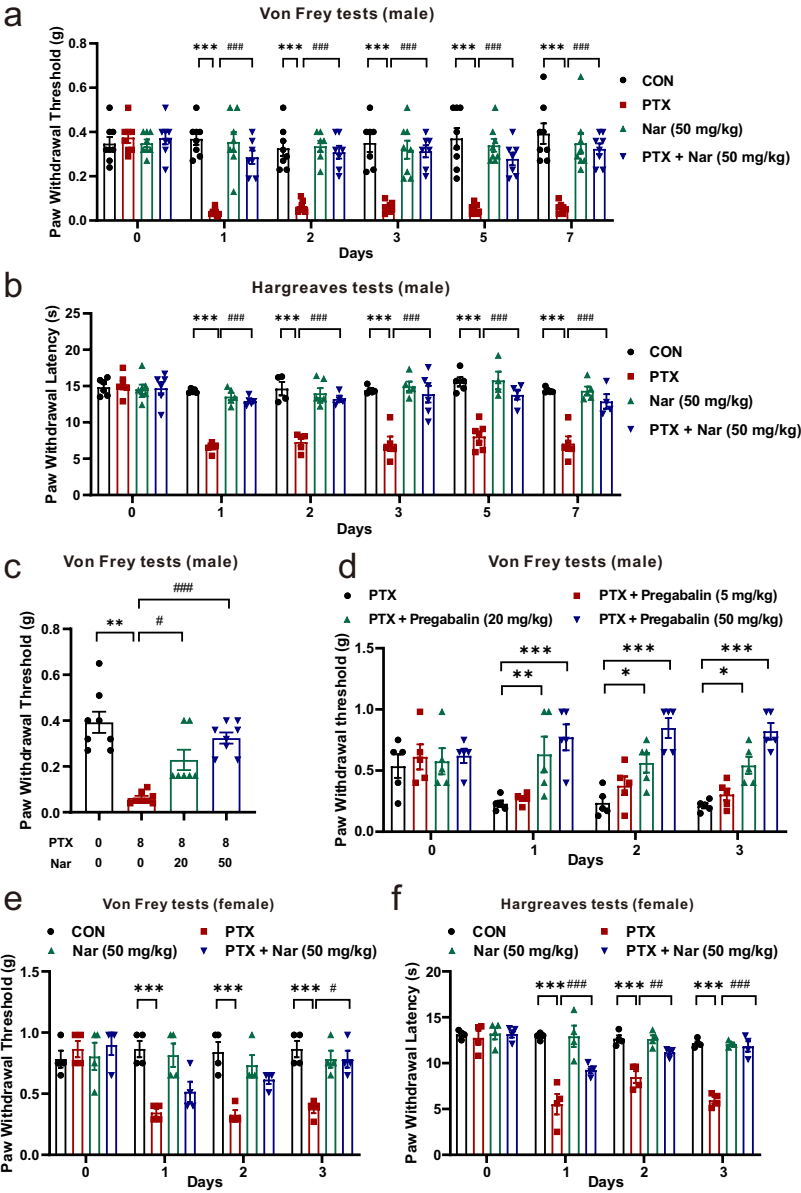
Abstract

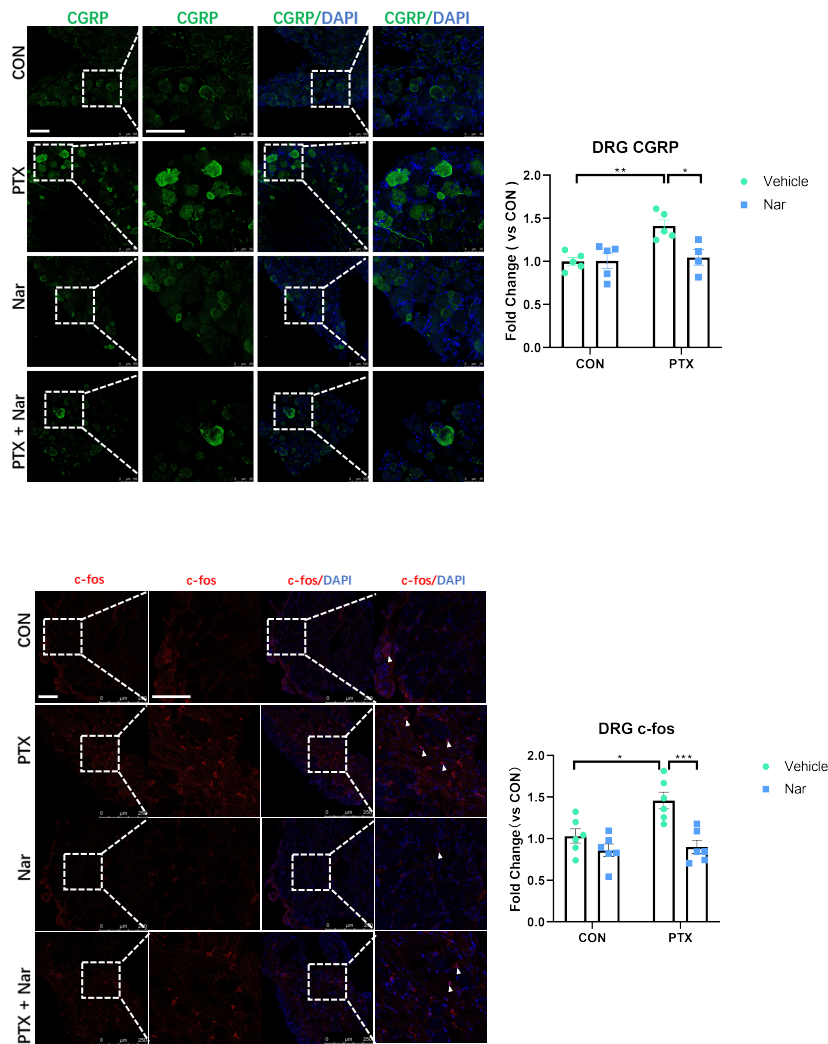
Background and Purposes: Chemotherapy-induced peripheral neuropathy commonly causes neuropathic pain. The pathogenesis of CIPN is unclear, and effective therapies are also lacking. Naringenin, a dihydroflavonoid compound in Rutaceae plants and citrus fruits, has anti-inflammatory, antioxidant, and anti-tumor activities. However, its effect on chemotherapy-induced pain has not been investigated. **Experimental Approach:** We used Paclitaxel (PTX) to establish a mouse model of chemotherapy-induced pain. Mechanical and thermal pain thresholds, glial activation, calcitonin gene-related peptide (CGRP) expression, c-fos expression, phosphorylation of nuclear factor κ B (NF- κ B), dorsal root ganglion (DRG) neuron excitability, and cell survival of pancreatic, colorectal, and gastric cancer cell lines were measured. **Key Results:** Systemic application of Naringenin reduced the mechanical and thermal pain hypersensitivity induced by PTX. Naringenin reduced the activation of glial cells in both DRGs and the spinal dorsal horn of PTX-treated mice. Naringenin decreased the PTX-enhanced CGRP expression in DRG and spinal neurons. Naringenin reversed the PTX-enhanced c-fos expression and excitability of DRG neurons. Naringenin downregulated PTX-elevated NF- κ B phosphorylation in the spinal cord. Additionally, co-administration of Naringenin with PTX enhanced the inhibitory effect of PTX on pancreatic and colorectal cancer cell growth, whereas the application of Naringenin alone inhibited the survival of pancreatic cancer cells. **Conclusion and Implications:** Naringenin alleviates PTX-induced pain and may facilitate PTX's anti-tumor effect. The mechanism involves the inhibition of glial activation, CGRP production, and neuronal sensitization in PTX-treated mice. Our study suggests the multiple beneficial actions of Naringenin in chemotherapy by mitigating side effects and inhibiting tumor growth.

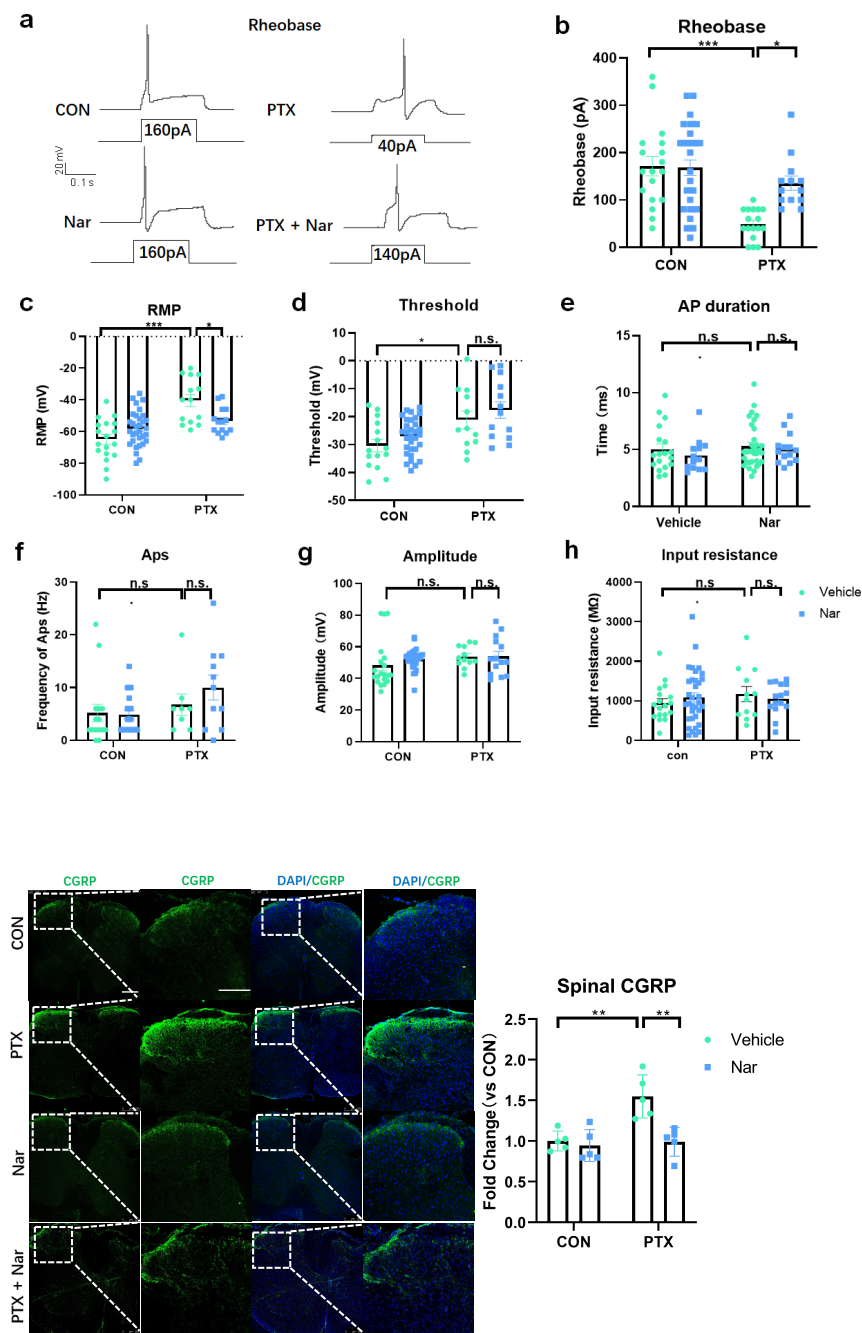
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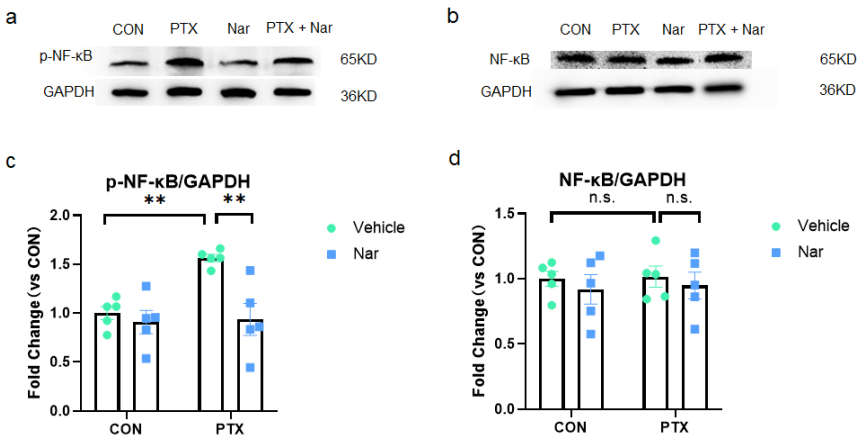
Naringenin relieves Paclitaxel-induced pain via inhibiting CGRP production and DRG neuron sensitization available at <https://authorea.com/users/630029/articles/649953-naringenin-relieves-paclitaxel-induced-pain-via-inhibiting-cgrp-production-and-drg-neuron-sensitization-and-enhances-paclitaxel-s-anti-tumor-action>

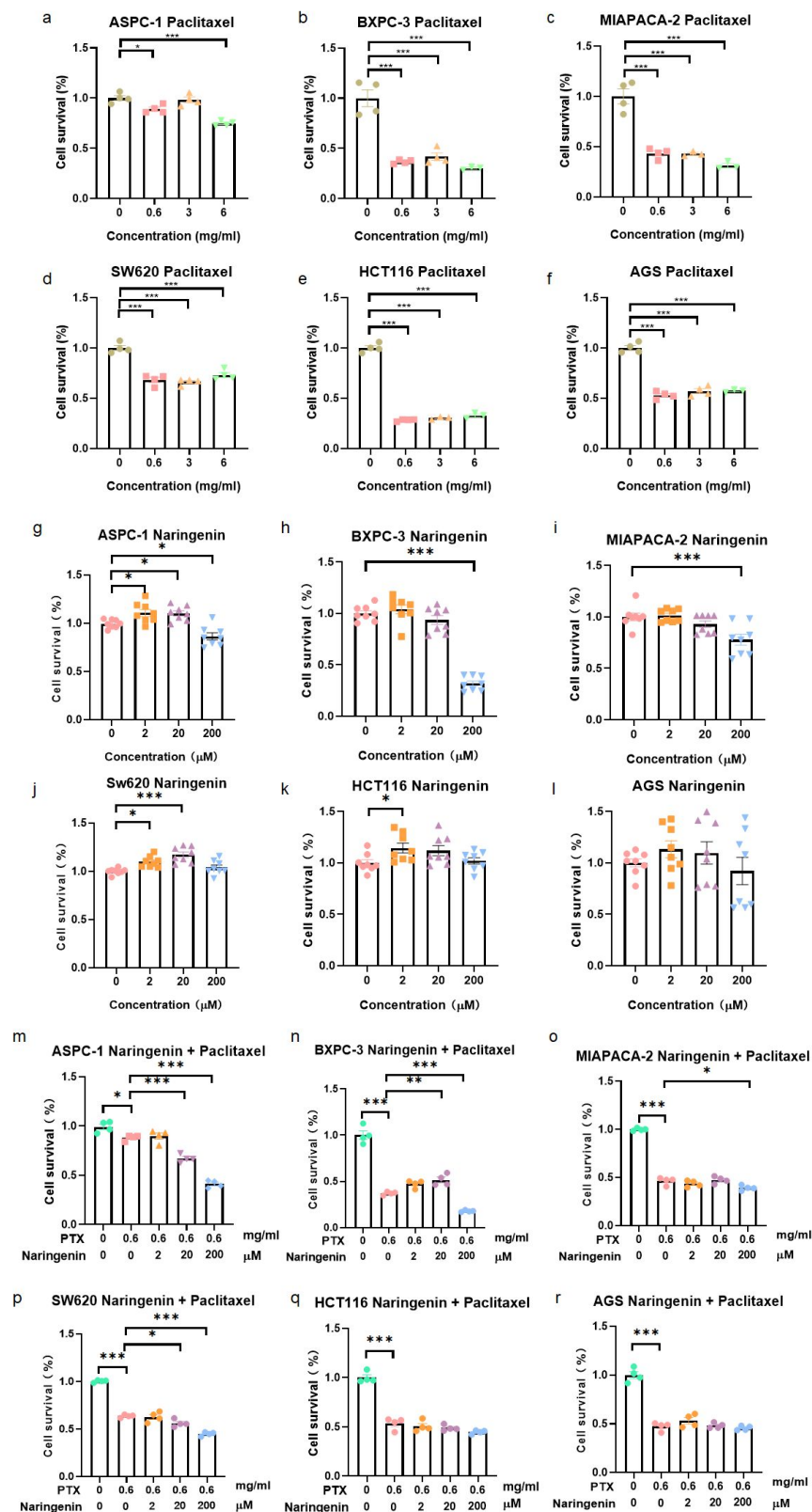


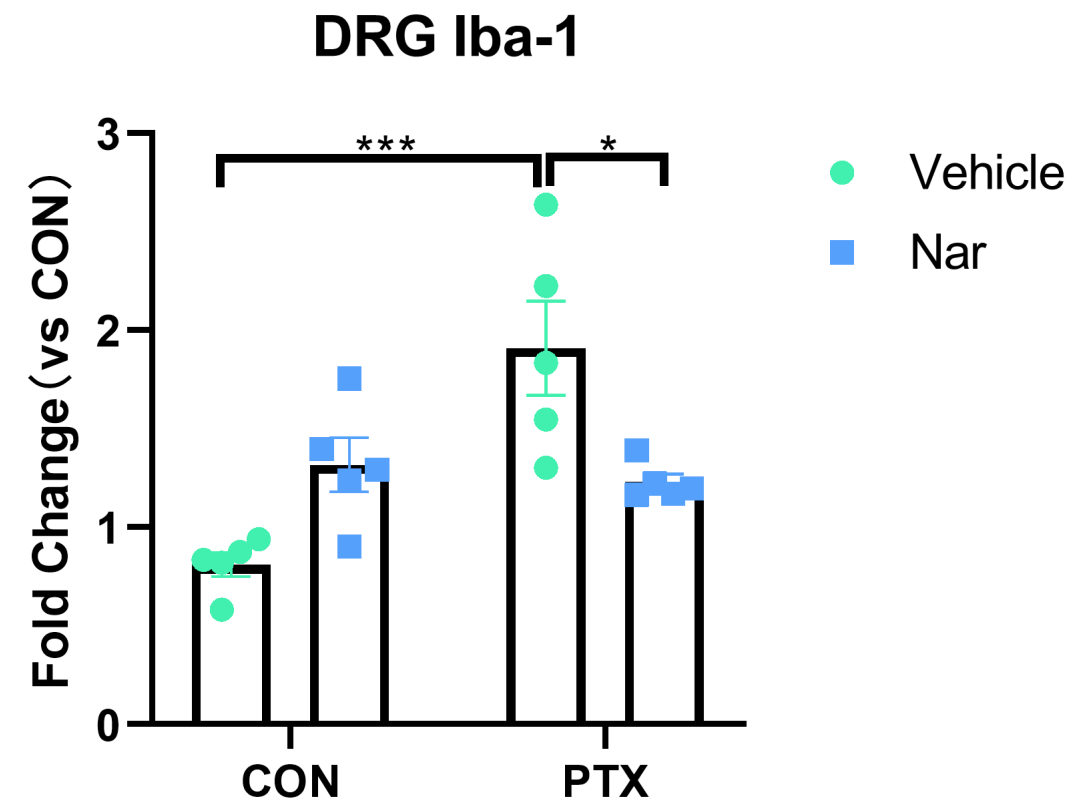
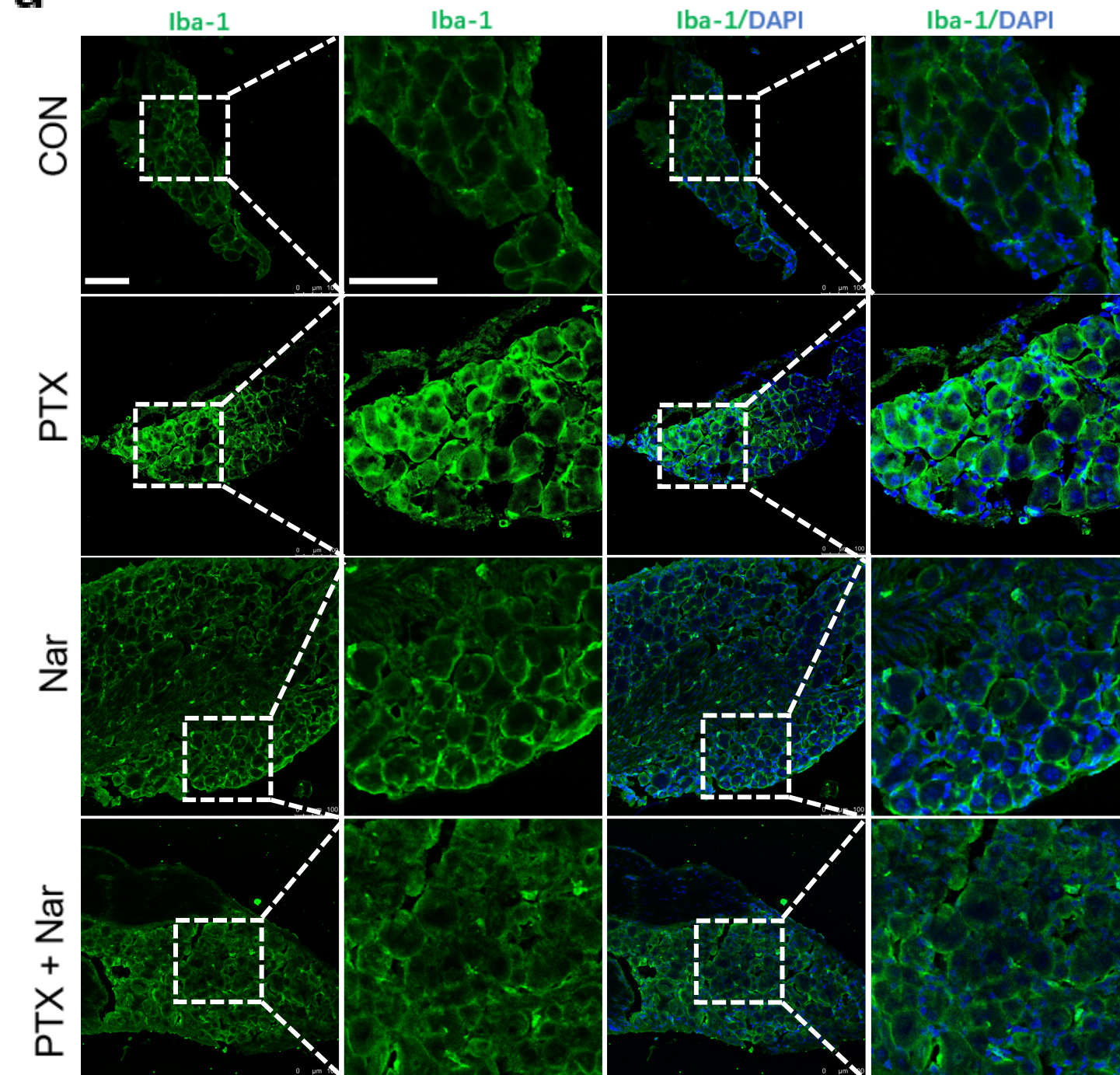




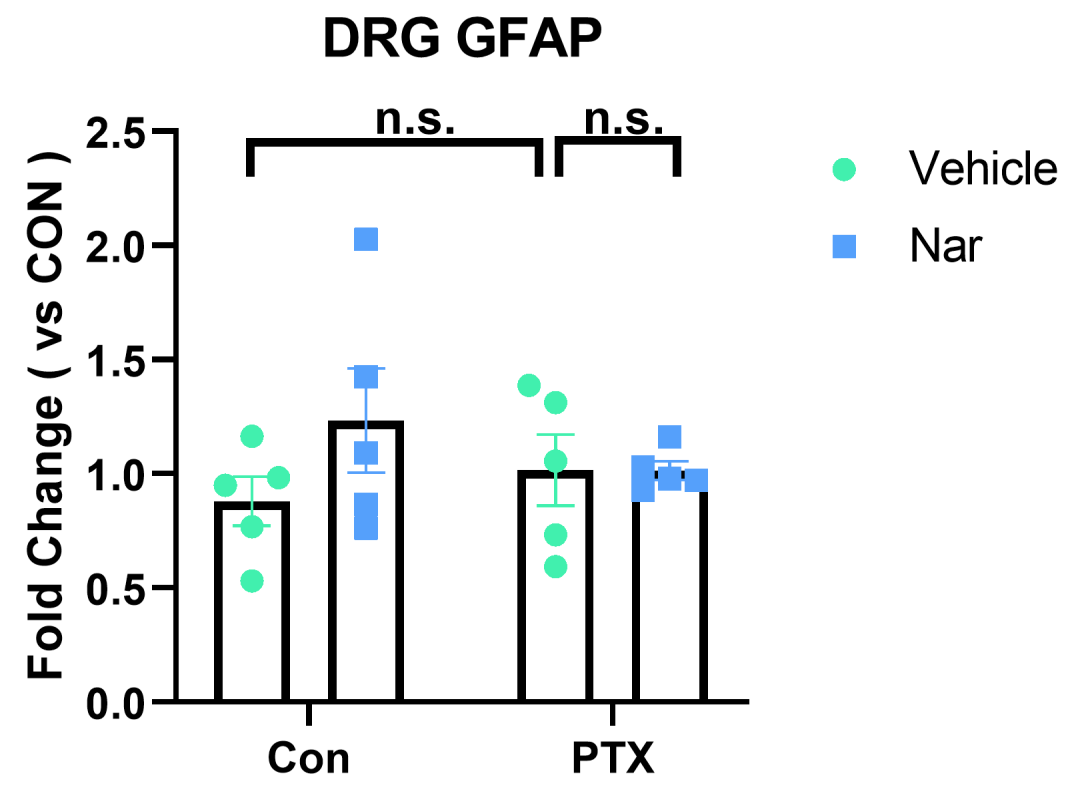
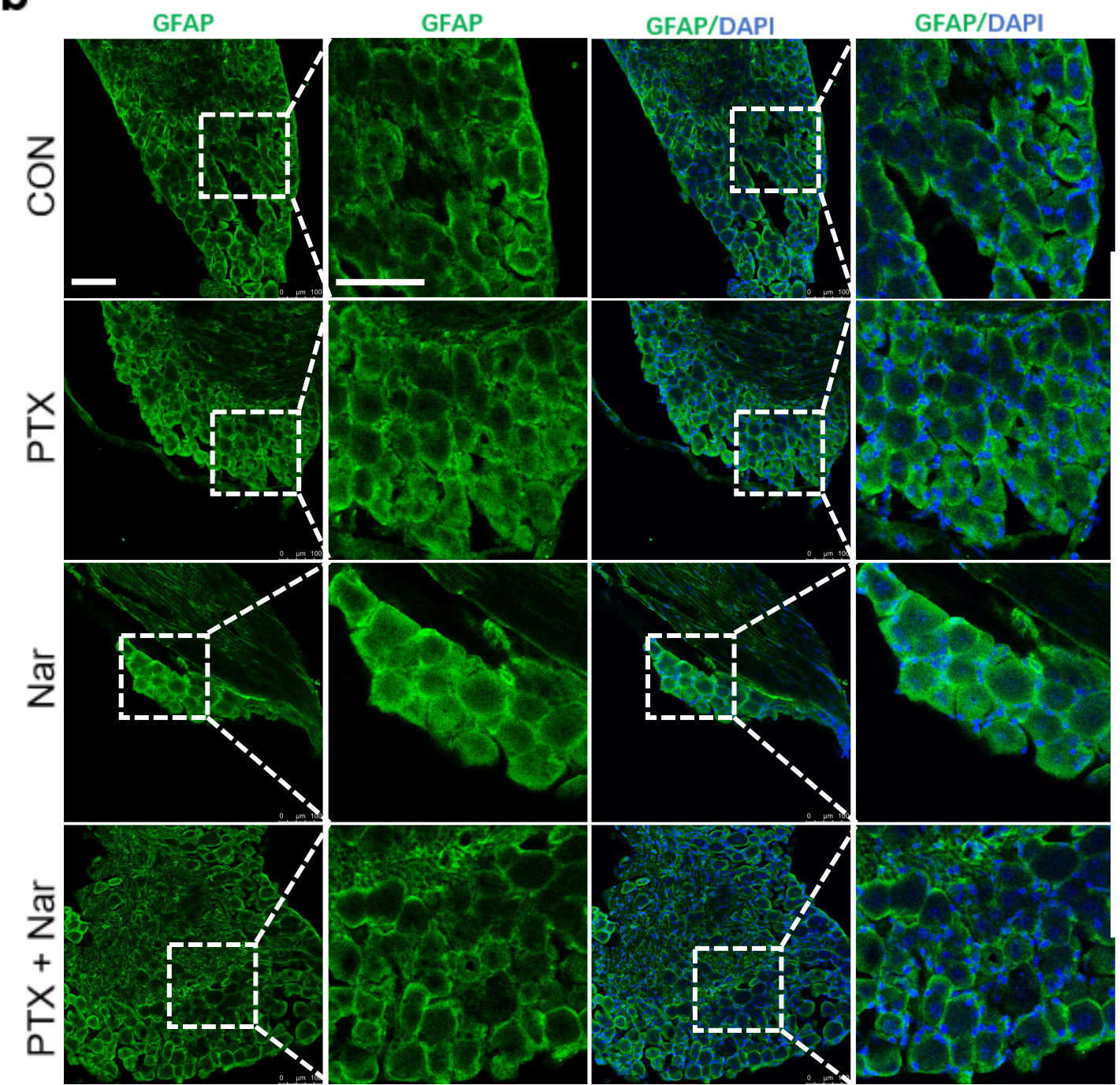




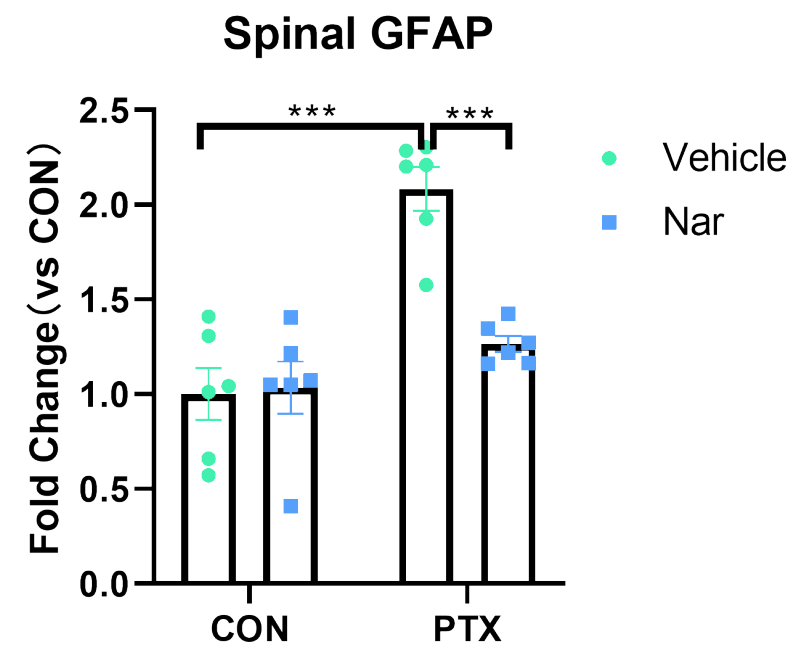
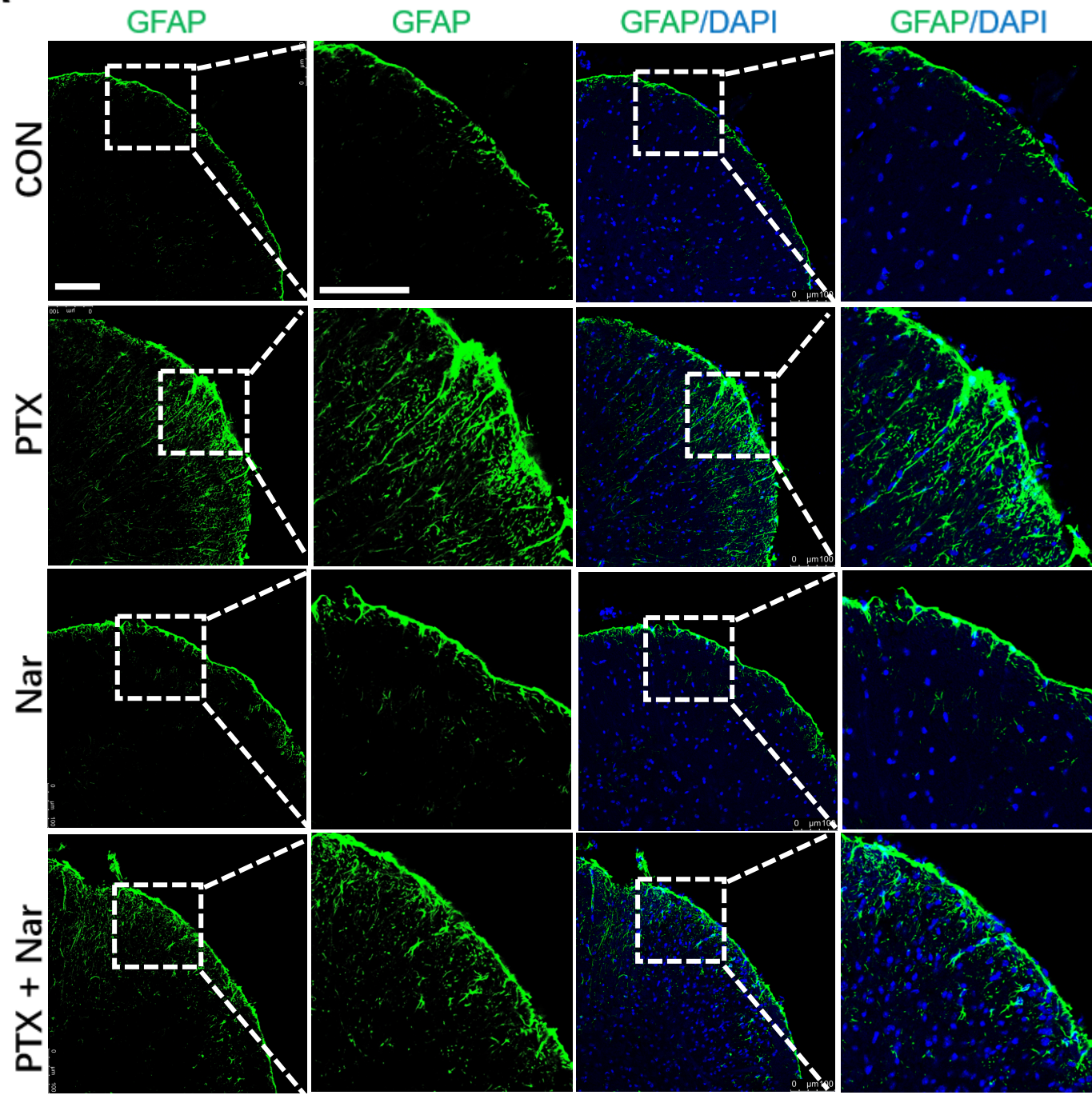


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