

Application of ultrahigh frequency transcutaneous electrical nerve stimulation for alleviation of neuropathic pain and neuroinflammation modulation in rat sciatic nerve chronic constriction injury

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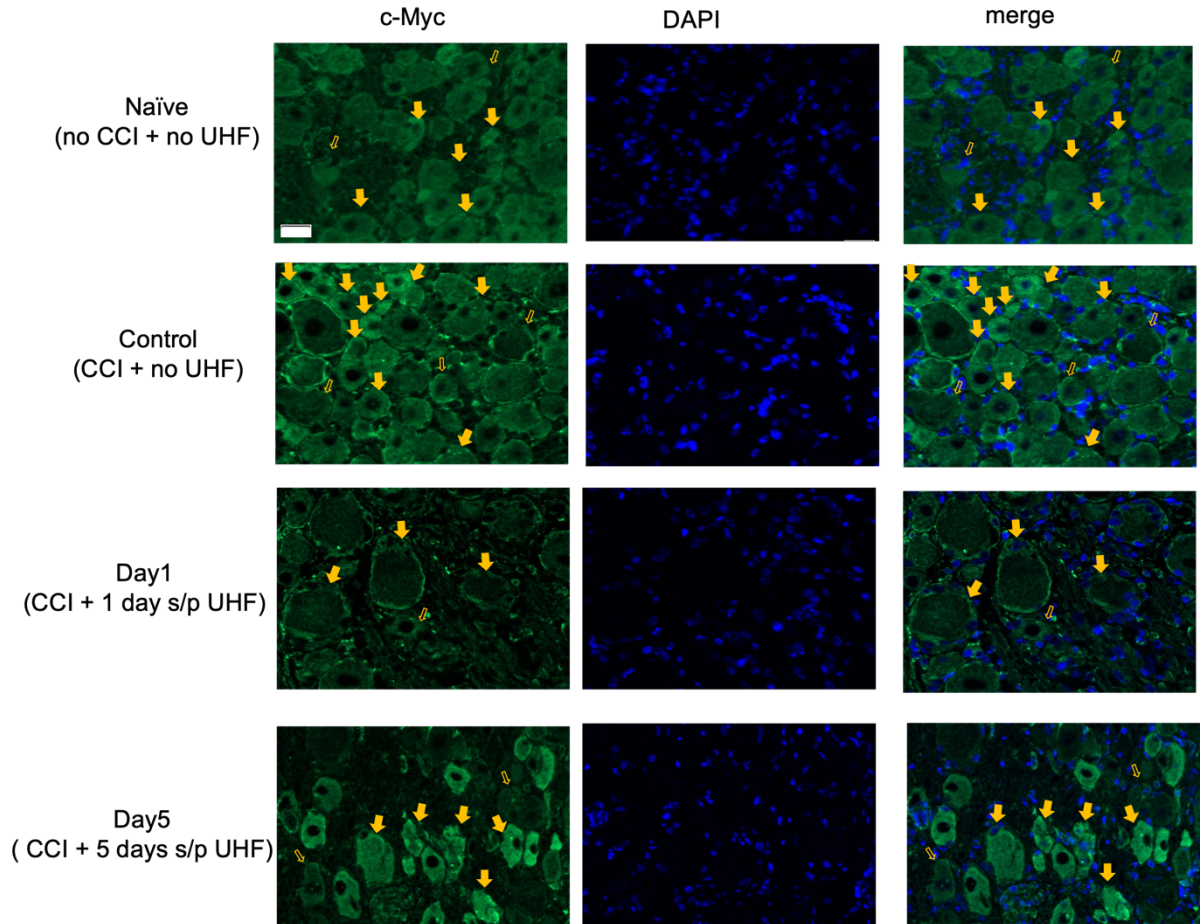
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Yuan-Yu Hsueh

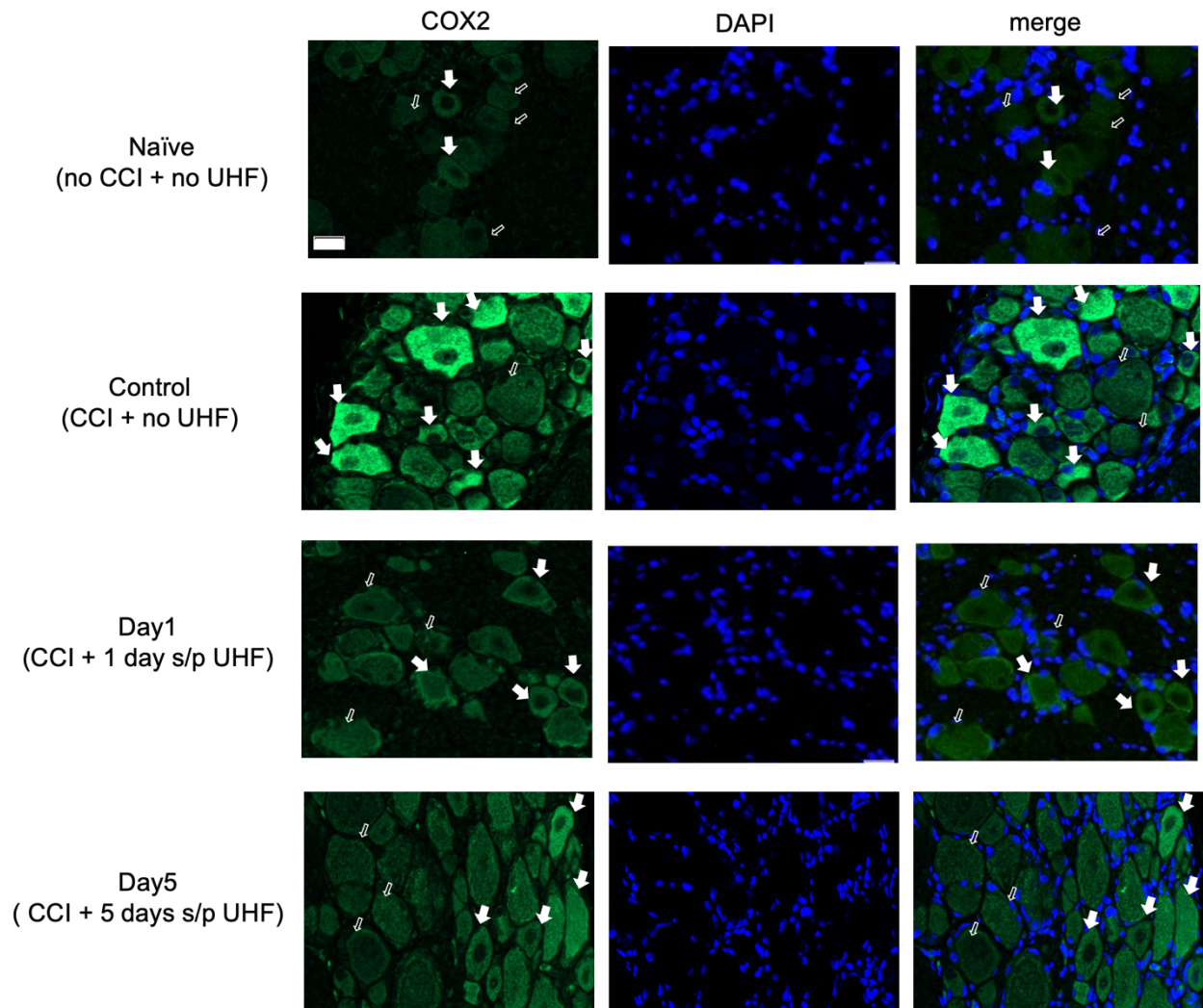
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Supplementary Material

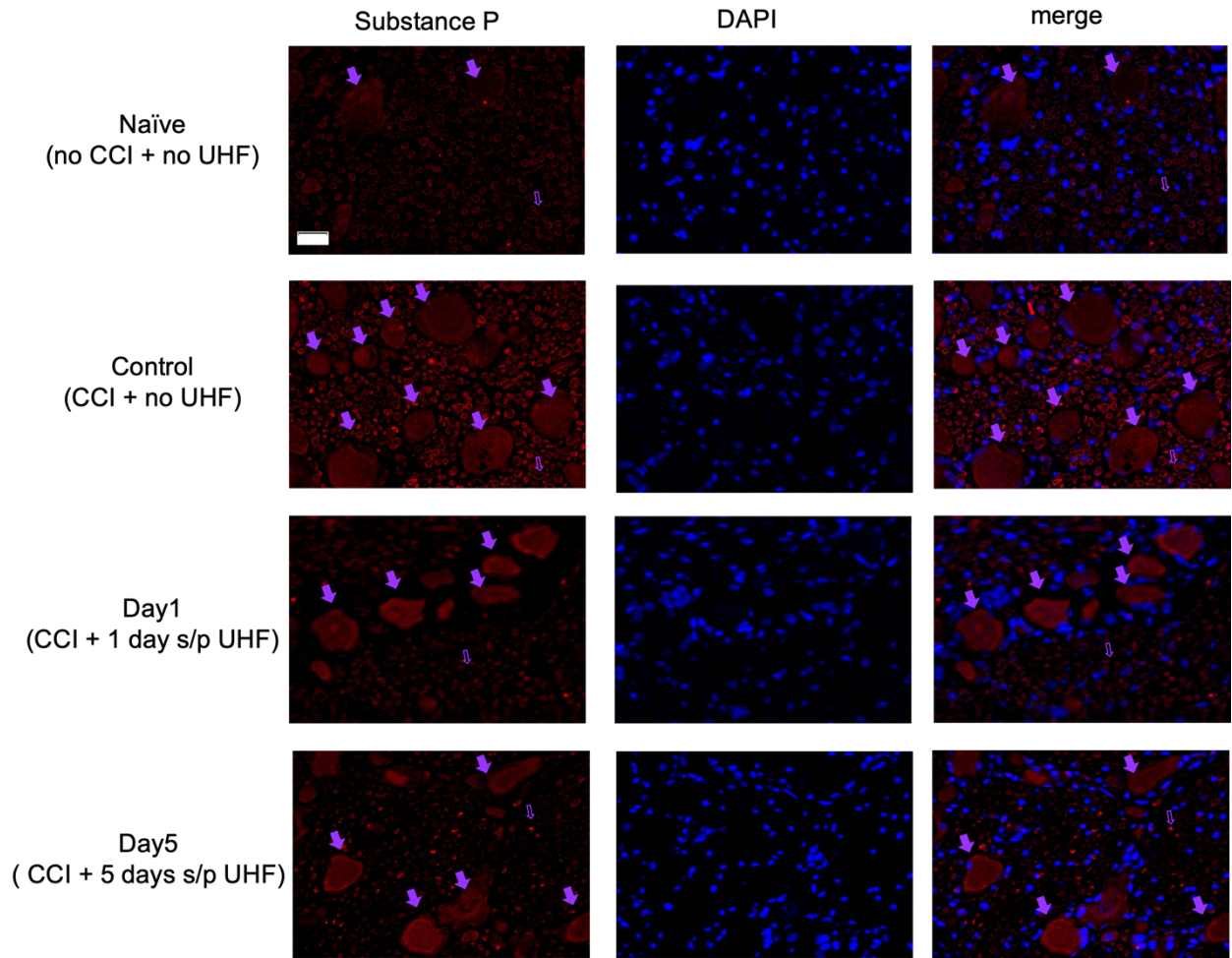
1.1 Supplementary Figures



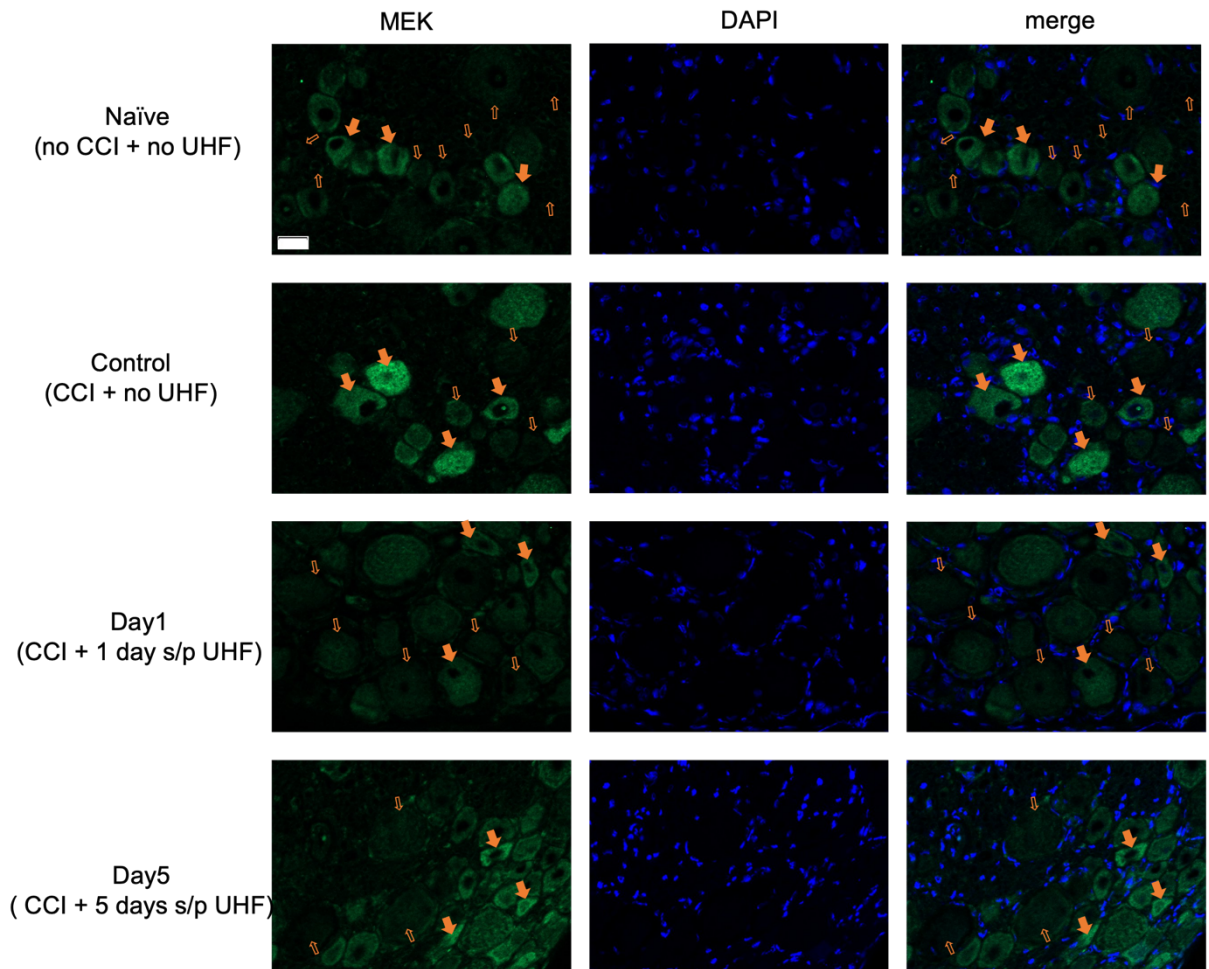
Supplementary Figure 1. Immunohistochemical staining of c-Myc in the injured side of dorsal root ganglion under UHF-TENS treatment. A significant increase in signal intensity was induced by nerve constriction injury in the control group compared to naïve nerve as the baseline. After UHF stimulation, the signal intensity of c-Myc decreased significantly on Day 1 and returned to baseline level on Day 5. (n=3-4 per group; 20 μ m; positive neuron: yellow solid arrowhead; negative neuron: yellow hollow arrowhead).



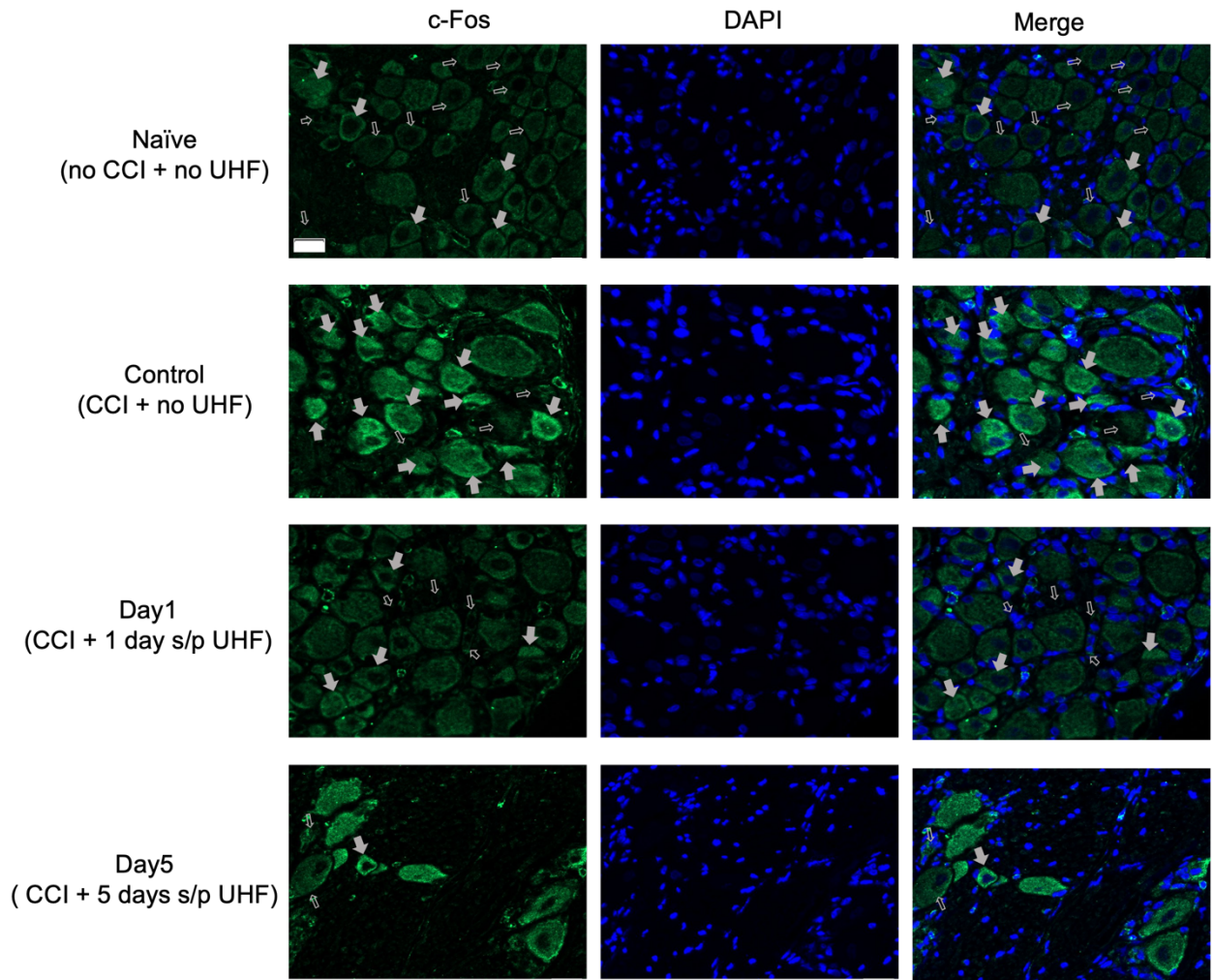
Supplementary Figure 2. Immunohistochemical staining of COX2 in the injured side of dorsal root ganglion under UHF-TENS treatment. A significant increase in signal intensity was induced by nerve constriction injury in the control group compared to naïve nerve as the baseline. After UHF stimulation, the signal intensity of COX2 decreased significantly on Day 1 and returned to baseline level on Day 5. (n=3-4 per group; Scale bar:20 μ m; positive neuron: white solid arrowhead; negative neuron: white hollow arrowhead).



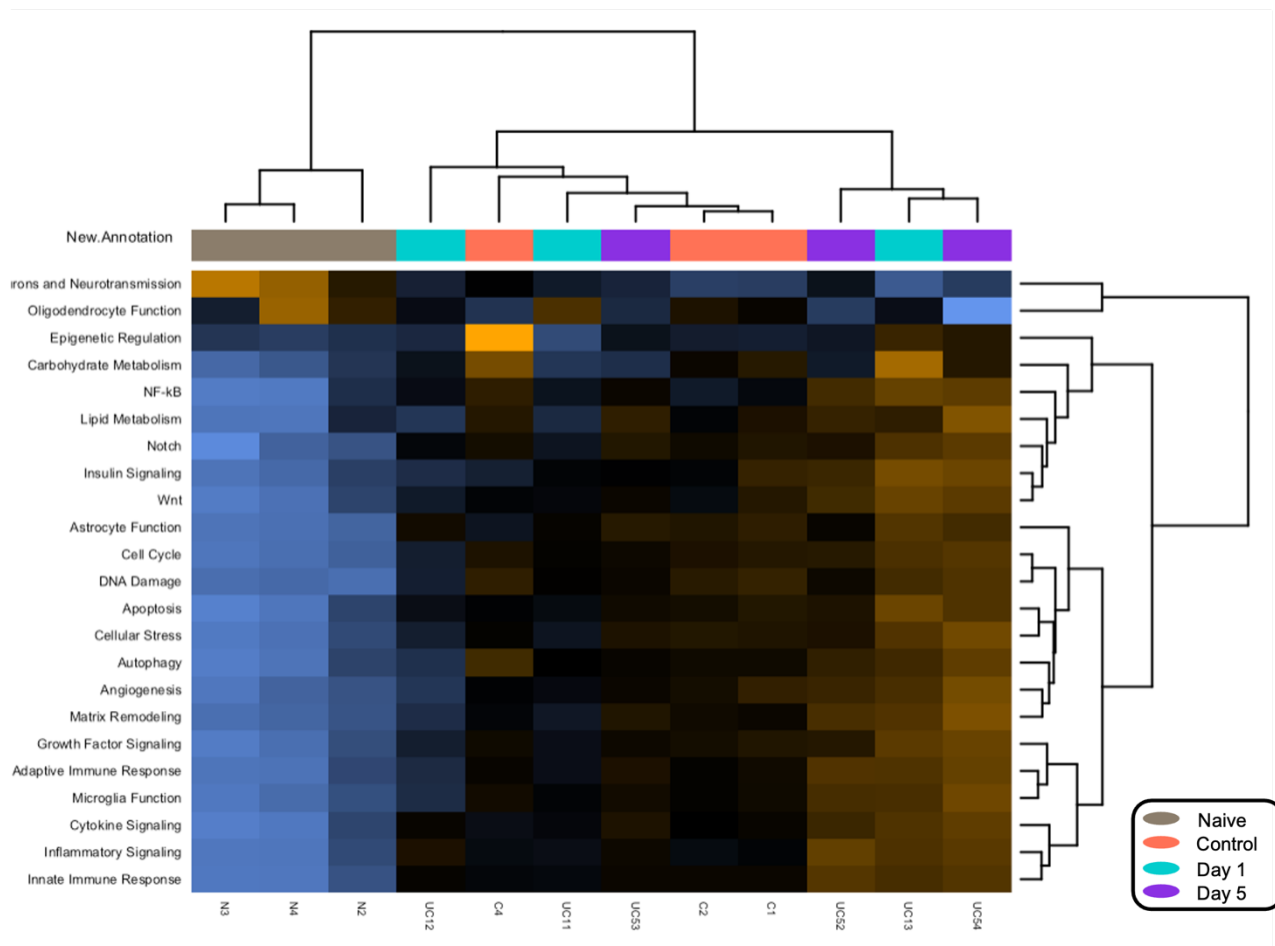
Supplementary Figure 3. Immunohistochemical staining of Substance P in the injured side of dorsal root ganglion under UHF-TENS treatment. A significant increase in signal intensity was induced by nerve constriction injury in the control group compared to naïve nerve as the baseline. After UHF stimulation, the signal intensity of Substance P decreased significantly on Day 1 through Day 5. (n=3-4 per group; Scale bar: 20 μ m; positive neuron: purple solid arrowhead; negative neuron: purple hollow arrowhead).



Supplementary Figure 4. Immunohistochemical staining of MEK in the injured side of dorsal root ganglion under UHF-TENS treatment. A significant increase in signal intensity was induced by nerve constriction injury in the control group compared to naïve nerve as the baseline. After UHF stimulation, the signal intensity of MEK decreased significantly on Day 1 through Day 5. (n=3-4 per group; Scale bar: 20 μ m; positive neuron: orange solid arrowhead; negative neuron: orange hollow arrowhead).



Supplementary Figure 5. Immunohistochemical staining of c-Fos in the injured side of dorsal root ganglion under UHF-TENS treatment. A significant increase in signal intensity was induced by nerve constriction injury in the control group compared to naïve nerve as the baseline. After UHF stimulation, the signal intensity of -Fos decreased significantly on Day 1 through Day 5. (n=3-4 per group; Scale bar: 20 μ m; positive neuron: grey solid arrowhead; negative neuron: grey hollow arrowhead).



Supplementary Figure 6. Heat map distribution of 23 neuroinflammation pathways. Upregulation of 21 inflammatory pathways was induced by nerve constriction injury in the control group compared to naïve nerve as the baseline. Among them, 18 neuroinflammation pathways were downregulated after UHF stimulation on Day 1 (n = 3 for each group).