

## Reveal New Spatial Insights in the Neurobiology of Pain with RNAscope™ ISH Assays

### Your Genes. Your Way.

Easily interrogate just the genes you want in the combinations you need to achieve your research goals.

Select from a list of proven probes for cell type identification and add any additional RNA markers from an online catalog of 1000's of pre-designed neural probes. If we don't have the target you need, you can easily design a new custom probe using ACD expert probe design.

### Your Success.

- Uncover molecular mechanisms of pain to identify new drug targets and advance therapeutic development.
- Spatially interrogate and quantify RNA expression in pain-associated dorsal root ganglia (DRGs).
- Identify and delineate the involvement of Ion channels and receptors in the neurobiology of pain.
- Easily visualize GPCR targets with high specificity.

## RNAscope Probes for Mouse Neuronal Cell Types

Mouse Neurons		
Cell Type	Top Probes	Reference RNAscope Probe Publications
Mature neurons	<i>Map2, Rbfox3, Tubb3</i>	<ul style="list-style-type: none"> <li>• Meneghello et al., Neuroscience, 2015.</li> <li>• Nakazato et al., Sec. Multiple Sclerosis and Neuroimmunology, 2020.</li> <li>• Lorsch et al., Nature neuroscience, 2019.</li> </ul>
Cholinergic neurons	<i>Ache, Chat, Slc18a3</i>	<ul style="list-style-type: none"> <li>• Steinkellner, Thomas et al., eNeuro, 2019.</li> <li>• Skirzewski, M. et al., Nature Communications, 2022.</li> <li>• Francis, T. Chase et al., Neuron, 2019.</li> </ul>
Dopaminergic neurons	<i>Slc6a3, Slc17a6, Th</i>	<ul style="list-style-type: none"> <li>• Buck, Silas A et al., The Journal of neuroscience, 2021.</li> <li>• Venkataraman, A. et al., Neuropsychopharmacology, 2021.</li> <li>• Chefer, Vladimir I et al., Neuropsychopharmacology, 2013.</li> </ul>
GABAergic neurons	<i>Gad1, Slc6a1, Slc32a1</i>	<ul style="list-style-type: none"> <li>• Wang, Lei et al., Neuropharmacology, 2016.</li> <li>• Rizzi, Giorgio, and Kelly R Tan. Cell reports , 2019.</li> <li>• Szlaga, Agata et al., Neuropharmacology, 2022.</li> </ul>
Glutamatergic neurons	<i>Gls, Slc17a6, Slc17a7</i>	<ul style="list-style-type: none"> <li>• Maldonado et al., Current biology, 2021.</li> <li>• Kroeger et al., Sleep, 2022.</li> </ul>
Serotonergic neurons	<i>Pet-1, Slc6a4, Tph</i>	<ul style="list-style-type: none"> <li>• Xiao, Xing et al., Nature communications, 2021.</li> <li>• Kast, Ryan J et al., ACS chemical neuroscience, 2017.</li> </ul>

## Mouse Glial, Oligodendrocytes, and Immune Cells

Mouse Glial, Oligodendrocytes, and Immune Cells		
Cell Type	Top Probes	Reference RNAscope Probe Publications
Astrocytes	<i>Aldh1l1, Aqp4, Gfap</i>	<ul style="list-style-type: none"> <li>Boulay et al., Cell discovery, 2017.</li> <li>Mazumder et al., iScience, 2022.</li> <li>Becker-Krail et al., Biological psychiatry, 2022.</li> </ul>
Brain microvascular endothelial cells	<i>Cd31, Cldn5, Vwf</i>	<ul style="list-style-type: none"> <li>Chen, Michelle B et al., Cell reports, 2020.</li> <li>Dudek, Katarzyna A et al., PNAS United States of America, 2020.</li> <li>Liu, CC. et al., Nature Neuroscience, 2022.</li> </ul>
Ependymal cells	<i>Cd24, Foxj1, Mia</i>	<ul style="list-style-type: none"> <li>MacDonald, Adam et al., Frontiers in cellular neuroscience, 2021.</li> <li>Rodrigo A., Aida et al., Developmental cell, 2023.</li> </ul>
Microglia	<i>Aif1, Cd68, Tmem119</i>	<ul style="list-style-type: none"> <li>Lovatt et al., Communications biology, 2022.</li> <li>He, Baixuan et al., FASEB journal, 2020.</li> <li>Liu, Yu-Yan et al., Neural regeneration research, 2023.</li> </ul>
Oligodendrocytes	<i>Mbp, Mog, Olig2</i>	<ul style="list-style-type: none"> <li>Barak et al., Nature neuroscience, 2019.</li> <li>Flygt et al., Journal of neurotrauma, 2018.</li> <li>Losurdo et al., Brain sciences, 2020.</li> </ul>
Pericytes	<i>Asma, Pdgfra, Rgs5</i>	<ul style="list-style-type: none"> <li>Smyth, L.C.D. et al., Communications Biology, 2022.</li> <li>Ayloo, Swathi et al. Neuron, 2022.</li> <li>Chasseigneaux, S. et al., Scientific Reports, 2018.</li> </ul>
T cells	<i>Cd3, Cd4, Cd8</i>	<ul style="list-style-type: none"> <li>Lee, S.H. et al., Cell Rep, 2021.</li> </ul>
Schwann cells	<i>Gap43, Mpz, S100</i>	<ul style="list-style-type: none"> <li>Renthall et al., Neuron, 2020.</li> <li>Shadrach et al., iScience, 2021.</li> <li>Matson et al., Nature Communications, 2022.</li> </ul>

## Hear what customers are saying about RNAscope

“ In our projects, we mainly use multiplex fluorescent assays combined with confocal microscopy on sectioned mouse brains. We are extremely pleased with the high resolution and the quality of the images we obtained. We compared RNAscope to other similar products developed recently and found that RNAscope’s sensitivity is much higher, the background is much lower, and assays are much easier to perform. ACD’s service and technical team is another important asset. They are fast to answer our purchasing and technical questions via email and are always attentive to our requests. I highly recommend ACD’s RNAscope Assay for any kind of multiplex ISH assay.”

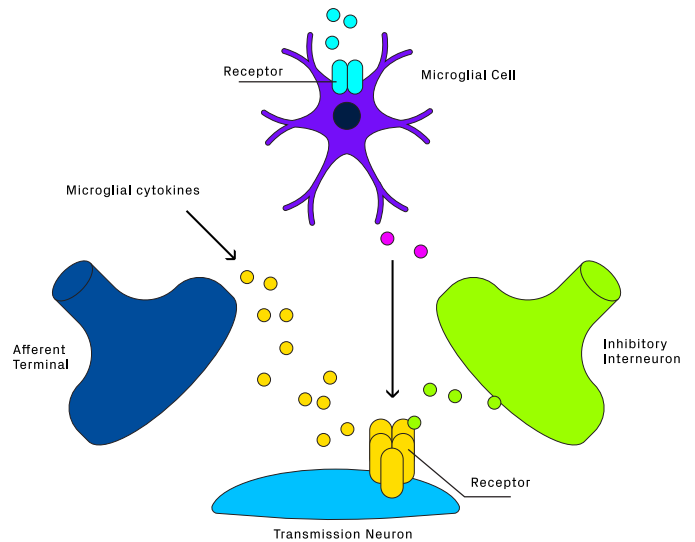
- Assistant Professor, Children’s Hospital Los Angeles

## Mouse Pain Biomarkers

Pain is a protective evolutionary function that involves unpleasant sensory and emotional experiences associated with or resembling that associated with actual or potential tissue damage. Many physiological and psychological factors influence pain, and measuring pain biomarkers provides an opportunity to identify objective markers of peripheral nerve damage and other contributing pathology.

The schematic depicts the neuropathic pain triad involving the neurons, immune cell recruitment and activation of spinal microglia. . Direct modulation of dorsal horn neuron activity by these cytokines may be involved in the development of neuropathic pain.

Common pain biomarkers used in conjugation with cell-type markers are listed below.

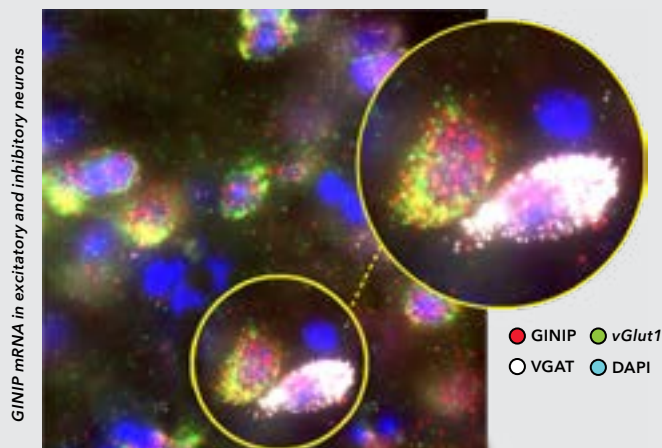


**The neuropathic pain triad:** neurons, immune cells and glia  
Scholz J, Woolf CJ., 2007, Nat Neurosci.

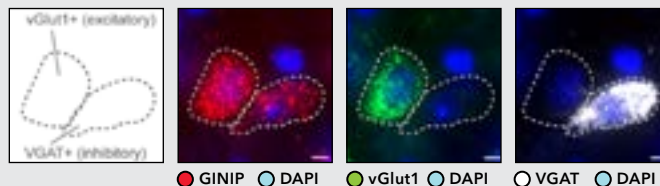
Pain Biomarkers	Marker Type	Top Probes	Reference RNAscope Probe Publications
Inflammatory Markers	Cytokine Receptors, GPCRs, Neuropeptides	<i>Il17, Tnf, Ccl2, Il1b, Il18, Cxcl10, Vip, Npff</i>	<ul style="list-style-type: none"> <li>• Luo et al., 2019, Cell Reports</li> <li>• Mifflin et al., 2021, PNAS</li> <li>• Shadrach et al., 2021, iScience</li> <li>• Guldner et al., 2020, Cell</li> <li>• Yaqubi et al., 2023, Journal of Neuroinflammation</li> <li>• Ha et al., 2017, American Journal of Pathology</li> <li>• Takesian et al., 2018, Nature Neuroscience</li> <li>• Quillet et al., 2023, Scientific Reports</li> </ul>
Nociceptive Markers	Ion Channels, Transient Receptor Potential	<i>Nav1.7 (Scn9a), Nav1.8 (Scn10a), P2rx3, Trpv1, Trpa1</i>	<ul style="list-style-type: none"> <li>• Deng et al., 2023, Neuron</li> <li>• Elias et al., 2023, Cell</li> <li>• Jung et al., 2023, Nature Communications</li> <li>• Papalampropoulou-Tsiridou et al., 2022, Brain Communications</li> <li>• Elias et al., 2023, Cell</li> </ul>
Neuropathic Markers	Acid Sensing Ion Channels	<i>Ifit3, Asic1, Asic3</i>	<ul style="list-style-type: none"> <li>• Tansley et al., 2022, Nature Communications</li> <li>• Wang et al., 2022, Endocrinology</li> <li>• Papalampropoulou-Tsiridou et al., 2022, Brain Communications</li> </ul>
Opioid Markers	Mu-Opioid Channel	<i>Oprm1, Oprd1</i>	<ul style="list-style-type: none"> <li>• Severino et al., 2018, Pain</li> <li>• Wang et al., 2018, Neuron</li> </ul>

## RNAscope Spotlight

One feature of neuropathic pain is reduced GABAergic inhibitory function. Nociceptive neurons represent a significant therapeutic site of action, as most analgesic drugs (i.e., opioids, cannabinoids, and GABA derivatives) are known to influence nociceptive terminals. However, the mechanisms behind nociceptor-mediated modulation of GABA signaling remain to be elucidated.



Park *et al.*, at University of Boston used RNAscope to visualize the spatial localization of GINIP mRNA in the neurons of the mouse cortex. This study demonstrated that GINIP was expressed in the excitatory and inhibitory neurons. Results suggest GINIP facilitates GPCR-mediated modulation of inhibitory, but not excitatory, neurotransmission in excitatory and inhibitory neurons.



**Figure 1. GINIP mRNA in excitatory and inhibitory neurons.**

Representative confocal image of GINIP mRNA expressed in excitatory and inhibitory neurons detected by RNAscope fluorescent *in situ* hybridization on mouse cortical slices of 5-month-old C57BL6 mice. GINIP, vGlut1, and VGAT mRNAs were simultaneously detected.

Park *et al.*, *Molecular Cell*, 2023

## RNAscope Technology

RNAscope is the gold-standard for RNA *in situ* hybridization, backed by over 2,000 Neuroscience peer reviewed publications from around the globe.

- **Sensitive** - Industry leading single molecule sensitivity.
- **Specific** - Unrivaled target specificity.
- **Quantitative** - Accurately measure changes in gene expression *in situ*.
- **No instrument required** - Manual and automated assays available.

## Free Project Consultation with RNAscope Specialist

We have specialists that can assist you in configuring an RNA panel that includes just the genes you want to achieve your research goals. If you are new to RNAscope, they can also assist you in selecting the best RNAscope kit for your experimental design to achieve best results.



**Request a Meeting  
with us here!**

## Getting Started is Easy

### Extensive probe catalog

Select probes to your genes of interest from an extensive online catalog with over 45,000 RNA probes in over 400 species.

### Fast and flexible custom probe design

If you we don't have the probe you need, we can easily design it for you for virtually ANY gene in ANY species for use in ANY tissue.

### Expert technical support

Our experienced technical support team has supported thousands of neuroscience researchers to deliver high impact results. We will help you get up and running quickly.

## Probe Guarantee

Backed by over 9000 peer-reviewed publications from around the world, we are confident that RNAscope probes will deliver excellent results in your study. If your target is not detectable using our probe but is detected by an orthogonal method on a serial section, Advanced Cell Diagnostics will provide either a replacement probe, an alternative probe design, or technical consultation to help you continue your research.