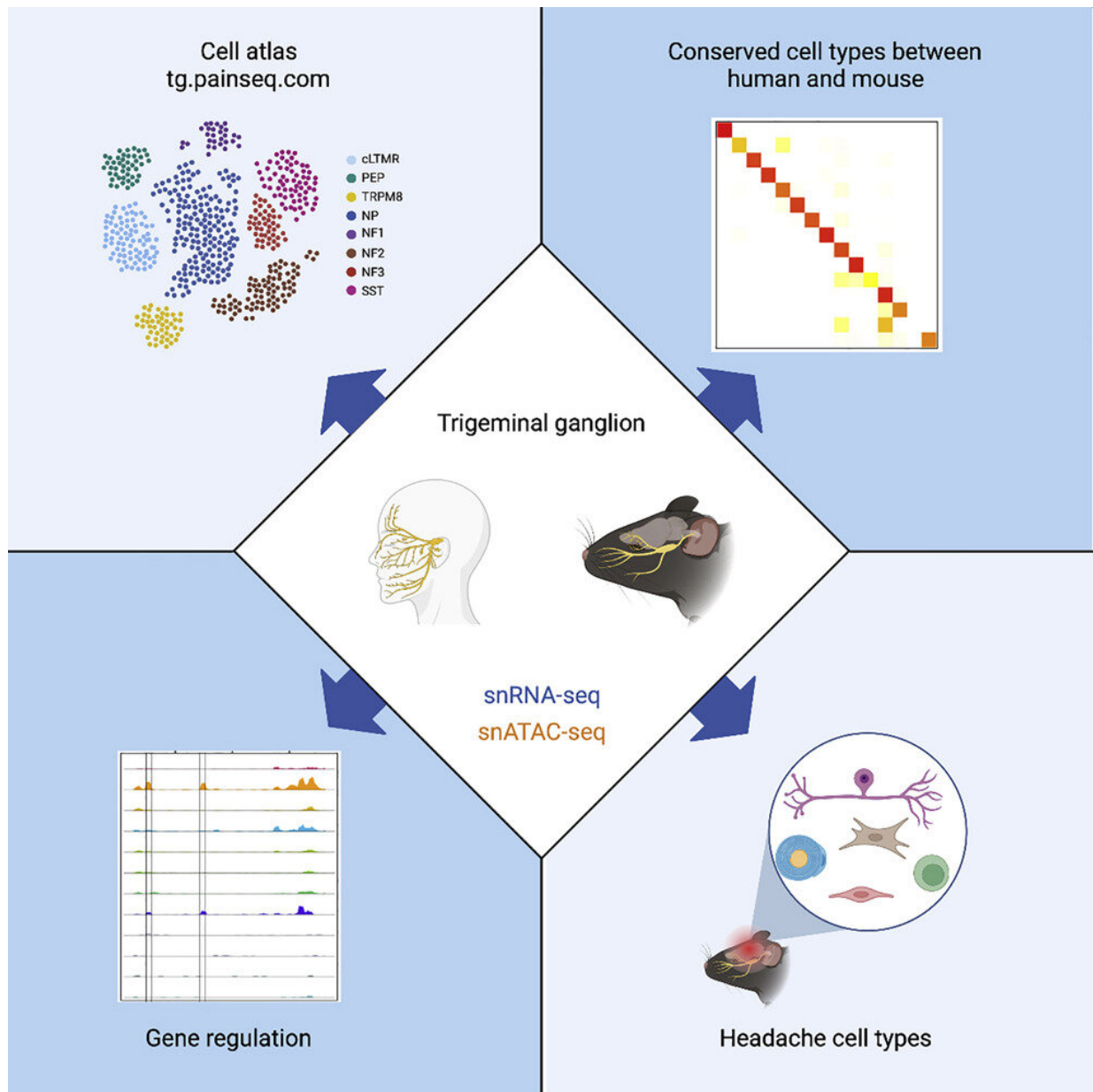


# Atlas of migraine cell types sheds light on new therapeutic targets

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Graphical abstract. Credit: *Neuron* (2022). DOI: 10.1016/j.neuron.2022.03.003.

Headaches such as migraine are among the leading causes of morbidity worldwide, but most treatments provide only partial relief. While scientists know that migraine and related headaches are caused by activity in a part of the nervous system known as the trigeminal ganglion (TG), it remains unclear which genes and cell types of the TG are involved. By analyzing both human and mouse TG, investigators from Brigham and Women's Hospital and Massachusetts General Hospital profiled, at single-cell resolution, the genes expressed in each TG cell type. Their research, published in *Neuron*, will allow researchers to design more effective treatments for pain by selectively targeting certain genes and cells.

"Very few pain therapeutics have made it to the clinic, despite strong efficacy in animal models, so our goal was to analyze [human tissue](#) to look for new targets for headache and facial pain treatment," said William Renthal, MD, Ph.D., of the Department of Neurology at the Brigham. "We now have an atlas of the genes that are expressed in each of the cell types in the TG, the key relay center for migraine and facial pain, and we are now using this tool to identify potential therapeutic targets that are selectively expressed in cell types that drive head pain. We believe this will lead to more precise medicines without as many side effects."

In addition to analyzing the TG of four human donors, the researchers studied two mouse models of headache. Importantly, they found that while [cell types](#) between mice and human are largely conserved, some of the genes known to be involved in pain are expressed in different subsets of cells in mice versus humans. This gave the researchers new ideas about which cells to study further.

"A major value of this study is that it wasn't limited to one specific cell-type or branch of the trigeminal ganglion," said Jochen K. Lennerz, MD, Ph.D., of the Center for Integrated Diagnostics in the Department of Pathology at MGH. Lennerz's lab performed the complex tissue-harvesting procedures required to extract the TG, which is located inside the cranium but has neurons that enervate the teeth, eyes, and other facial structures. "We included all of the cells that make up the TG," he said. "This was a very [holistic approach](#) which has resulted in an amazing compendium that researchers can look at from all perspectives and specialties. It may not only be neurons we are looking for when identifying biomolecules as therapeutic targets."

The information from the researchers' atlas, which is available publicly online, could prompt new investigations into the molecular basis of different varieties of pain, such as tooth pain. It may also shed light on how to treat head pain beyond migraine, including post-concussive headaches or cluster headaches.

Going forward, the researchers plan to improve the current atlas by sequencing additional human tissues. They hope that the atlas can help researchers develop more selective [pain](#) therapeutics by targeting, through gene therapies, the specific cells they've identified.

"We have a resource now that allows an individual to go online, look up a gene of interest, find out where it's expressed and how it's regulated, and then use this information to inspire new experiments," Renthal said. "This atlas is only a first draft, and we need to expand the number of donors to build a more complete one. That's a current limitation but also a future direction for our work."

**More information:** William Renthal, Human and mouse trigeminal ganglia cell atlas implicates multiple cell types in migraine, *Neuron* (2022). [DOI: 10.1016/j.neuron.2022.03.003](https://doi.org/10.1016/j.neuron.2022.03.003).

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