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Candidate Gene Culprits for Chronic Pain Discovered

Chronic pain severely limits patients' quality of life and is among the cost drivers in U.S. health care. Patients can suffer pain without an apparent cause and often fail to respond to available treatments. Mayo Clinic researchers and collaborators now report that chronic pain may be caused by the inadvertent reprogramming of more than 2,000 genes in the peripheral nervous system.

The research findings appear in the current issue of the journal *Genome Research*.

The research might ultimately lead to "transcription therapy," the researchers speculate, which would employ drugs that kill pain by correcting the activity of specific genes.

The researchers focused on nerve cells suspected to be involved in pain: dorsal root ganglion neurons of the peripheral nervous system in rodent models. They performed high-throughput sequencing of hundreds of millions of mRNA molecules, the messengers of gene activity.

Powerful computer science was required to sort through the many pieces of information (50 base-pair long mRNA sequence "reads") assembling the complicated genomic puzzle. The resulting picture revealed a number of surprises, among them 10,464 novel exons (sections of the genome involved in creating proteins) and some 400 gene candidates described for the first time in the study. Furthermore, detailed building plans for thousands of spliced mRNA were mapped.

"Using this new approach offers greater sensitivity, dynamic range and more efficient unbiased genetic mapping compared to the previous microarray-based methods and may be an efficient new approach to a wide array of problems in neuroscience research," says Andreas Beutler, M.D., Mayo Clinic Onco­logist and Corresponding Author on the study.

Chronic pain affects 50 million Americans and costs \$100 billion in health costs, lost work time and other economic impacts, according to the National Institutes of Health.

Others involved in the study were Michaela Banck, M.D., and Ronny Amberg, both of Mayo Clinic; Paul Hammer, Gabriele Petznick, and Peter Beyerlein, Ph.D. all of the University of Applied Sciences, Wildau, Germany; Cheng Wang, M.D., Mount Sinai School of Medicine; and Shujun Luo, Ph.D., Irina Khrebtukova, Ph.D., and Gary P. Schroth, Ph.D. all of Illumina Inc., Hayward, Calif.

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