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## Fighting Neuropathic Pain

Metabolomics: Researchers discover a metabolite associated with chronic pain from tissue injury

By [Stu Borman](#)

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### PAINFUL FINDINGS

Assistant professor of genetics Gary J. Patti of Washington University School of Medicine, St. Louis, first author of the *Nature Chemical Biology* paper on a newly discovered chemical cause of neuropathic pain, describes the group's study, which was conducted at The Scripps Research Institute. Patti was a research associate at Scripps during the study.

Credit: Filmed and edited by Aaron Rowe for C&amp;EN



The overproduction of a previously unknown endogenous metabolite called *N,N*-dimethylsphingosine (DMS) in injured tissues may be a key cause of a condition called neuropathic pain, according to a *Nature*

*Chemical Biology* report (DOI: 10.1038/nchembio.767). The findings, which identify DMS production as a potential novel target to which inhibitors might be directed, could lead to more effective drugs to treat the condition.

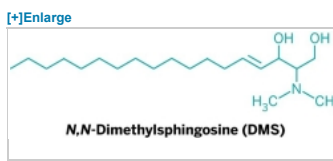
Neuropathic pain is a chronic disorder associated with tissue injury. The condition is characterized by periodic or constant "pin-and-needle" sensations; stabbing, burning, or electric-shock-like pains; or feelings of tingling or numbness. Current medications have adverse side effects such as addiction and fatigue and only rarely alleviate pain completely.

Biochemist [Gary J. Patti](#) of Washington University in St. Louis; therapeutics expert [Marianne Manchester](#) of the University of California, San Diego; metabolomics specialist [Gary Siuzdak](#) of Scripps Research Institute; and

coworkers detected the DMS surge via systematic metabolite analysis, known as metabolomics. They used liquid chromatography/mass spectrometry to survey metabolites in tissues from rats experiencing pain from a cut nerve. They found that DMS is produced at abnormally high levels in the rats' spinal cords and causes pain when injected. The results suggest that inhibition of endogenous DMS production, with a methyltransferase or ceramidase inhibitor, for example, may be an attractive therapy, the researchers write.

"In this groundbreaking study, the authors have used metabolomics not only to provide new insights into the pathogenesis of chronic pain, but also to uncover a potential new therapeutic target for a condition that is extremely difficult to treat," comments cellular stress response specialist [Albert Fornace Jr.](#) of Georgetown University.

"This is an exciting discovery," says metabolite profiling expert [Alan Saghatelian](#) of Harvard University. If future studies confirm that DMS is involved in a new and unique pain pathway, "it will be a very important finding," he says.

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