



## CHALLENGE

Understand the biological pathways underlying chronic pain in hopes of identifying new therapeutic targets.

## SOLUTION

JMP Genomics supports next-generation sequencing and a variety of other types of genomic analysis, including exon, SNP and microarray.

## RESULTS

Researchers have identified a particular mouse gene that appears to play a role in reducing the effectiveness of morphine to control pain. The next step will be to identify target genes downstream from this “Gene X” and see how morphine affects them.

## MORE INFORMATION

Learn more about JMP Genomics at [www.jmp.com/genomics](http://www.jmp.com/genomics)

For more information about SAS, please visit [www.sas.com](http://www.sas.com)

# Seeking clues to the causes of chronic pain – and a cure

Neuroscientist likes the flexibility and power of analysis with JMP® Genomics

An HIV diagnosis used to be a death sentence. But today, thanks to advances in medical science, the virus that causes AIDS often can be controlled with antiretroviral drug regimens that allow patients to lead long and productive lives.

However, there’s a cruel irony: although virus levels may be controlled by medication, treatment frequently causes debilitating chronic pain.

Susan G. Dorsey, PhD, is trying to address this conundrum on behalf of chronic pain sufferers, who number 75 million in the United States alone. In her quest to comprehend the root causes of this pain, this nurse-turned-neuroscientist at the University of Maryland Baltimore is using JMP Genomics from SAS, the customized JMP software package that brings dynamic interactivity to the desktop for biostatisticians and researchers around the world.

## A persistent epidemic

Chronic pain – defined as discomfort that persists longer than one year – has reached epidemic proportions in the United States, afflicting one adult in 10. For HIV/AIDS patients – as well as people suffering from cancer, diabetes, fibromyalgia, chronic fatigue syndrome and arthritis, to name just a few – the very drugs that are extending patients’ lives are also causing persistent pain. Unfortunately, stopping a treatment does not always stop the pain, as a drug may cause temporary or permanent peripheral neuropathy that even morphine can’t control. In fact, 35 percent of HIV patients taking highly active antiretroviral therapy develop chronic pain, which never resolves in 10 percent of those cases.

“You might cure the disease, but patients often have to come off the therapy prematurely because of the pain,” Dorsey explains. “So these are critical, critical problems.” Some patients won’t even report the pain, she adds, for fear that they might be taken off the treatments that are keeping them alive.

**STATISTICAL  
DISCOVERY.™  
FROM SAS.**

“You don’t have to be a whiz-bang programmer to get your answers. It’s very visual but also very statistically accurate.”

Susan Dorsey

Using JMP Genomics, Dorsey and her team at the University of Maryland Baltimore are working to understand the biological pathways underlying chronic pain in hopes of identifying new therapeutic targets. “Mechanisms affecting the development and persistence of chronic pain are not well understood,” she said.

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### Investigating ‘Gene X’

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With a grant from the National Institutes of Health, Dorsey has worked for several years with a network of collaborators, including Greenebaum Cancer Center, the National Institute of Nursing Research (part of NIH) and doctors, nurses and dentists from the University of Maryland Medical Center. Using inbred strains of genetically identical mice, researchers apply a stimulus and examine the drug’s effect on the expression levels of various genes. Dorsey and her team have employed microarray technology to identify a particular mouse gene – she calls it Gene X for now – that appears to play a role in reducing the effectiveness of morphine to control pain.

The next step will be to identify target genes downstream from Gene X and see how morphine affects them. Dorsey works with mice because of their remarkable genetic similarities to humans.

But she’s also exploring other causes of pain. Peripheral neuropathy is not confined to users of high-powered medications. People who have suffered back injuries, undergone amputations or had nerves injured during surgery also sometimes suffer, as do people with inflammatory tissue problems associated with arthritis, multiple sclerosis or other conditions. Dorsey is also examining links between inflammation and long-term pain, seeking to identify genes in the spinal cord that regulate pain persistence.

“It’s not so much the inflammation, per se; it’s potentially the damage those nerve endings undergo that can send signals to the spinal cord to promote chronic pain,” she observes.

The correlation matrix, box plot and principal components analysis are features of JMP Genomics that help Dorsey spot trends and outliers in her data immediately. “It’s the most flexible and powerful genomics software available,” she says. “I can upload raw data from a variety of Affymetrix platforms, including gene-level data from whole-genome expression arrays, gene and exon-level expression data from exon arrays and SNP data from a 500K array.”

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### Genetic sequencing: a new frontier

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JMP Genomics now allows her to go even further – into the new scientific realm of next-generation sequencing. The range of analysis capabilities in JMP Genomics is exceptional, she says: “I can’t think of another software package that can do all this analysis, that can go from your genome array to summarized information derived from your sequencing data and be able to do analysis on it all.”

Genetic sequencing technology greatly multiplies the amount of genomic information that can be obtained from a patient, Dorsey explains. She began her research analyzing 3’ gene arrays, which record 45,000 transcripts of the mouse genome. “What the 3’ gene arrays are capturing is information summarized at the transcript level,” she explains.

With Affymetrix exon arrays, she can use JMP Genomics to examine 1.2 million known and predicted exons. Within a transcript, exons may combine in multiple different ways to create alternative splice isoforms (similar, but not identical, messenger RNAs). But sequencing goes further still. “If we do sequencing ... we’ll be able to see everything that cell is making – all the transcripts. I might find novel transcripts that I couldn’t have found with the exon arrays.”



Dorsey discovered JMP Genomics while seeking a replacement for another, more limited, genomics software package. She knew that the University of Maryland had a SAS license, so she asked for a demonstration of JMP Genomics, which combines the data visualization capabilities of JMP statistical analysis with the power of SAS analytics to deliver the unique capabilities required by biostatisticians and biologists. Dorsey now uses JMP Genomics for a variety of analyses, including exon, SNP and microarray. She likes its comprehensiveness, versatility and ease of use.

“You don’t have to be a whiz-bang programmer to get your answers,” she says. “It’s very visual but also very statistically accurate.”

She also likes the feeling of partnership between her lab and the genomics experts at SAS. “That’s the other beautiful part. It’s not like you’ve got this piece of software and there’s nobody else around. The people there will work with us, which is, I think, unique and nice.”

Dorsey says her studies involving mice have yielded promising results. “I think now we’re poised to do more translational research.” That research, she hopes, will bring Dorsey closer to her ultimate goal: taking the pain out of the cure.

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SAS Institute Inc. World Headquarters +1 919 677 8000 To contact your local JMP office, please visit [www.jmp.com](http://www.jmp.com)

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