

Genome Maps Solve Medical Mystery For Calif. Twins

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Courtesy of Baylor College of Medicine
The Beery family in 2010 on a visit to Baylor.

Ever since scientists began to sequence the entire genomes of individuals—beginning with those of Nobelist [James Watson](#) and scientific entrepreneur [J. Craig Venter](#) in 2007—skeptics have wondered just how useful this elegant and expensive trick would become.

A pair of 14-year-old twins, [Alexis and Noah Beery](#), now provide a compelling answer, even if it's not yet clear how generalizable their case is to others with genetic disorders.

Whole-genome sequencing has enabled doctors to provide the Beery twins with a simple, highly effective treatment for a rare condition called [DRD](#), or

[dopa-responsive dystonia](#). The tale of their cure [appears](#) in this week's issue of the journal *Science Translational Medicine*.

The twins were diagnosed with cerebral palsy at age two. But their mother, Retta Beery, didn't think that was correct. For one thing, Alexis's contorted posture and jerky movements always seemed to be better in the morning and increased as the day went on.

Turns out DRD is known for these diurnal variations, as Retta found out through dogged research. That led to a diagnosis of DRD when the twins were five. Since DRD was thought to be a deficiency of the neurotransmitter [dopamine](#), low doses of a drug called L-dopa (also used for Parkinson's disease) rather miraculously made the twins' "cerebral palsy" go away within days.

But other symptoms persisted and worsened. At age 14, Noah had hand tremors, awkwardness and attentional problems. More alarmingly, Alexis had breathing problems due to spasms in her larynx. But when doctors probed for an explanation of these symptoms, the twins tested negative for known mutations of two genes known to be involved in DRD.

As it happens, the twins' father, Joe Beery, works for a [California biotech company](#) that makes DNA sequencing machines. So the parents wondered if a deep dive into their twins' DNA might explain the nature of their particular genetic defect.

Scientists at Baylor College of Medicine, a [pioneer](#) in whole-genome sequencing of individuals, thought it was worth a go. They sequenced the genomes of the twins, their older brother, their parents and their grandparents.

Comparing the results, the researchers found that the twins both inherited a gene variant from each parent that, together, led them to have low levels of not just

dopamine but two other neurotransmitters, [serotonin](#) and [noradrenalin](#).

The twins' neurologist, [Jennifer Friedman](#) of Rady Children's Hospital in San Diego, suggested giving the teenagers a supplement called 5-HTP that's a precursor for serotonin.

Together with the L-dopa, the additional supplement has improved Alexis's breathing point to the point that she's now running track again. Noah's handwriting and athletic performance have improved, and he's better able to focus in school.

And there's an intriguing bonus. Scientists think the gene mutation that the Beery twins inherited from their mother may be responsible for a pattern of a neuromuscular disease called [fibromyalgia](#) in her family. Fibromyalgia sometimes responds to anti-depressants called SSRIs that raise serotonin levels.

If that hypothesis pans out, it would suggest that rare genetic disorders such as DRD are just the most dramatic manifestation – in people who inherit a double dose of certain gene variants – of much more common disorders such as fibromyalgia among people who have a single copy of the mutation.

Study authors say the Beerys' case shows how genomics will ultimately revolutionize medicine by making diagnosis more precise and pointing toward life-changing treatments. Other cases are beginning to pop up, such as a [Wisconsin boy](#) whose rare disease was diagnosed by whole-genome sequencing and subsequently treated with a bone marrow transplant. (His story appeared in a Pulitzer Prize-winning series by the *Milwaukee Journal-Sentinel*.)

Cost is still a big obstacle. At the time the Beery family's genomes were sequenced, it cost around \$100,000 per person. [Dr. Richard Gibbs](#) of Baylor says now, less than two years later, it would cost about half as much – less than \$10,000 for the actual sequencing, plus the cost of computer processing of the results and validation.

The skeptics also point out that not all genetic insights from sequencing will lead to such cheap, simple and effective treatments as the Beery twins got.

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