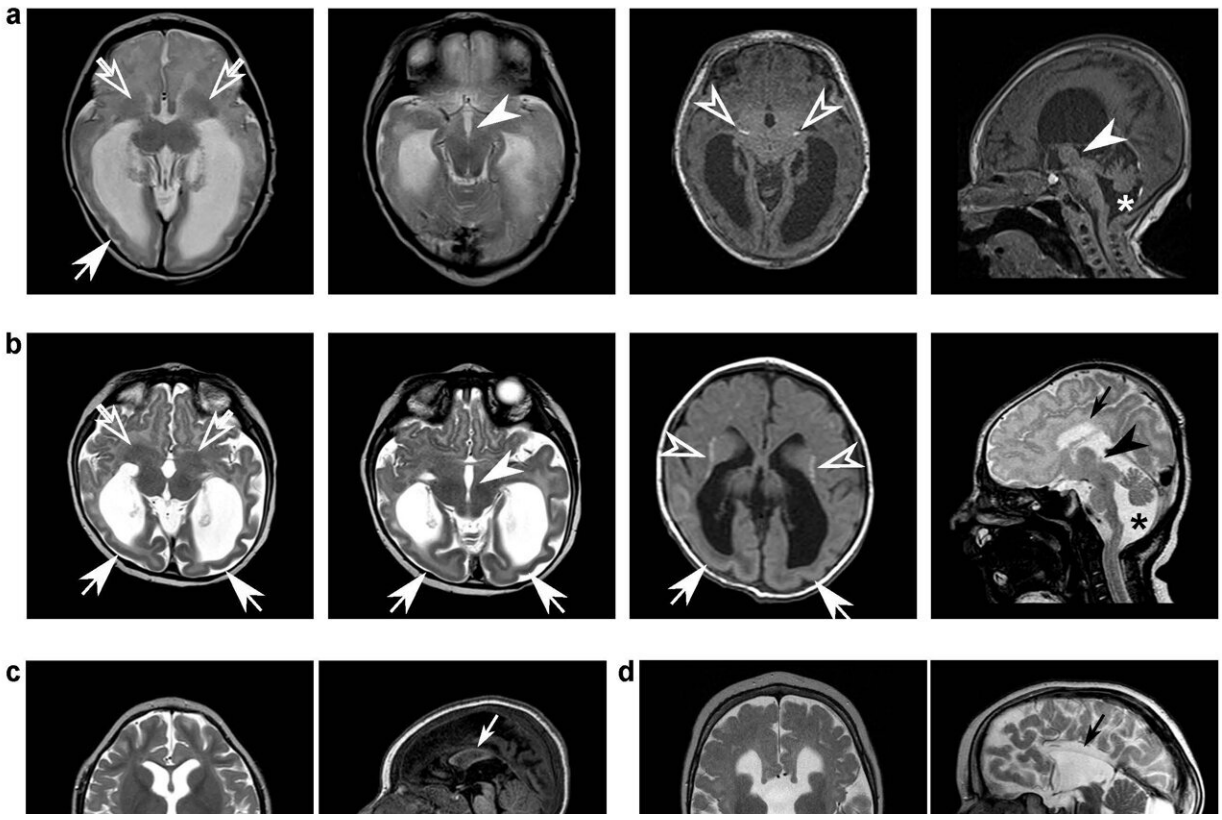
Discovery gives answers to parents of children with rare neurological gene mutation

August 27 2024, by Shawn Hayward



MRI images of people with epileptic encephalopathy. Credit: The Neuro

Shortly after Kelly Cervantes's daughter Adelaide was born, she started having terrible seizures. Doctors were unable to give her a solution, or

even a cause.

"We never had an overarching diagnosis for her, which was extraordinarily frustrating and isolating," she says. "If we did, we could join groups or talk to people who had various symptoms in common. We also had no idea what her prognosis looked like, or if we could have other children."

Over time, her condition worsened and sadly she died five days before her fourth birthday.

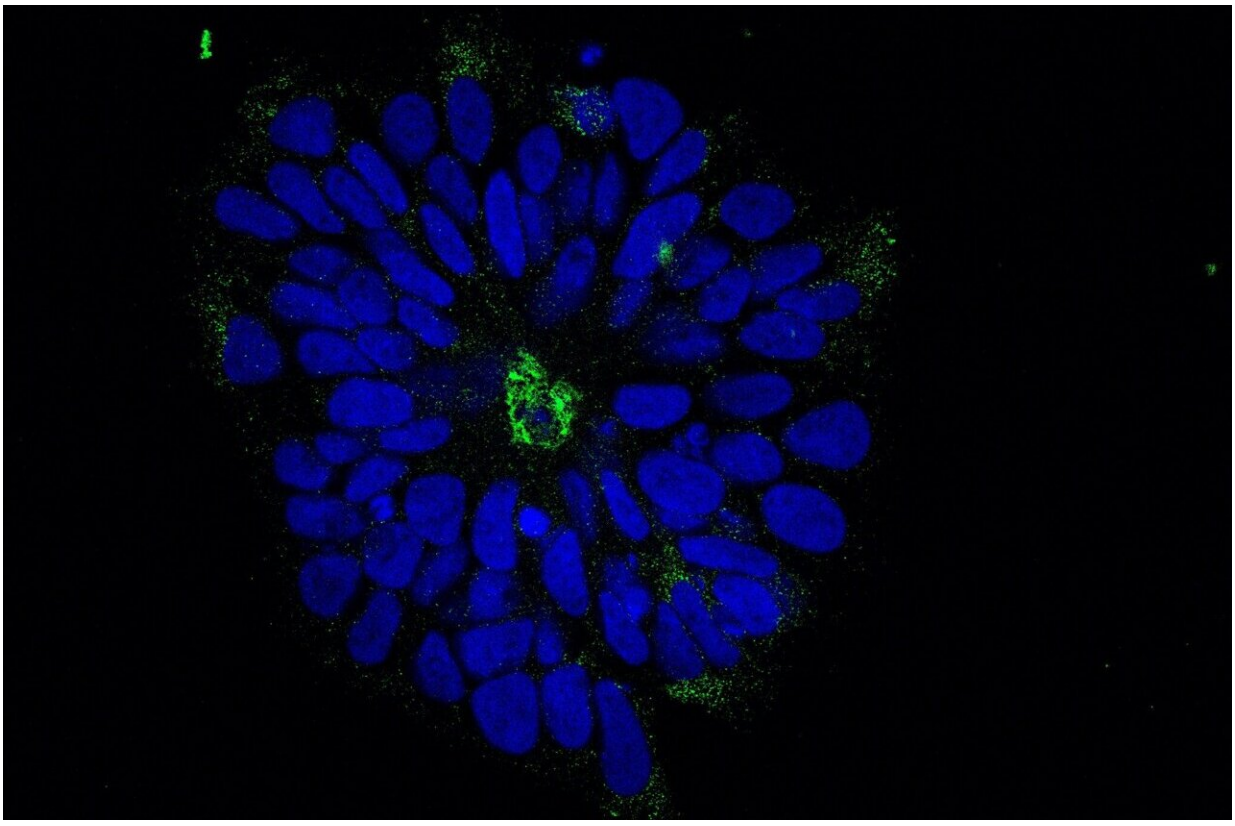
"She never really progressed past about a three-to-six-month physical development, and we're not entirely sure where she was intellectually. She was incredible but her life was really challenging and really hard,"

Cervantes had enrolled her daughter in a research program for people with undiagnosed illnesses. After her daughter's death, she got a call asking if she'd like to participate in a study being conducted at The Neuro. Now the results of that study have been published published in the journal *Nature Communications*.

The scientists analyzed samples from Adeliade and 21 other people with the condition. By growing stem cells in a dish using the participants' genetic code, the scientists found that mutations in a gene called DENND5A create dysfunction, and this dysfunction stops brain cells from dividing properly during development. The result is a developing brain with fewer stem cells, shortening the crucial time period that the brain forms as an embryo.

The finding provides answers for families of people with this rare condition. It also allowed family members to be tested for the mutations so they can make informed choices about family planning. For example, for aspiring parents who carry the mutation, genetic counselors can

recommend genetic testing for their partners and give the odds of passing on the condition.



Rosettes that show PALS1 staining, which the study identified as a new binding partner to DENND5A. Credit: The Neuro

With advancements in gene editing technology, one day the mutation might be corrected with the knowledge this study provides. While such a step is years away at best, Cervantes says it would provide comfort knowing her daughter contributed to a cure.

"Maybe someday down the road, the next Adelaide will have a treatment, and there will be an answer for that family. And how

incredible is that to think that my baby girl had a hand in that?"

More information: Emily Banks et al, Loss of symmetric cell division of apical neural progenitors drives DENND5A-related developmental and epileptic encephalopathy, *Nature Communications* (2024). DOI: 10.1038/s41467-024-51310-z

Provided by McGill University