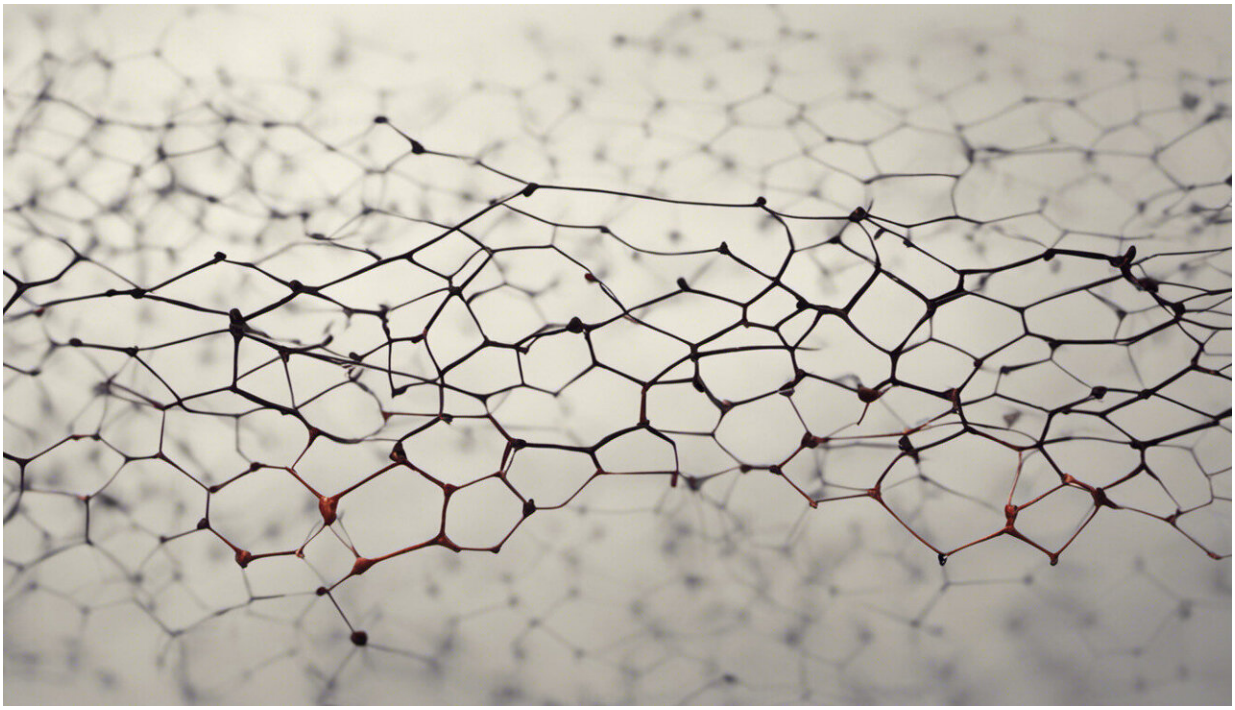
Mutant protein takes babies' breath away

November 24 2014, by Kim Krieger



Credit: AI-generated image (disclaimer)

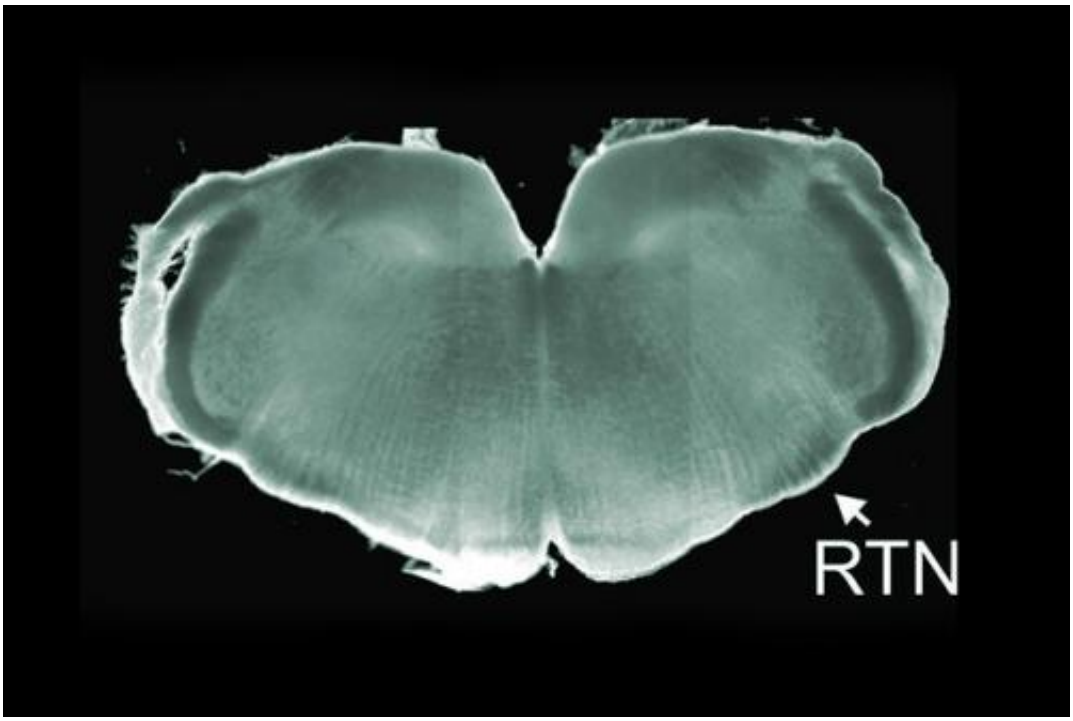
Babies start breathing in the womb, inhaling and exhaling irregularly at first, and then gradually more and more, until the day when they're born and have to do it all the time. But premature babies sometimes have trouble. They stop breathing periodically, sometimes for 20 or 30 seconds at a time. Sometimes they're fine, and sometimes they're not, and doctors struggle to help them. That may soon change, however, thanks to a two-month-old patient at UConn Health with a rare connexin

mutation, and his doctor's willingness to call for help.

The resulting collaboration between physicians and researchers at the University of Connecticut and the University of Warwick demonstrated that astrocytes with that same connexin mutation cannot bind to carbon dioxide. Astrocytes are the most abundant cells in the brain and do many things, including signaling to neurons. If astrocytes in the area of the brain stem that controls breathing had this mutation, they would be oblivious to dangerously high carbon dioxide levels. Doctors believe this explained the baby's disordered breathing. It was also the first time a direct link between the connexin channel, carbon dioxide, and respiration had been shown in humans. The results will be published on 24 November in the journal *eLife*.

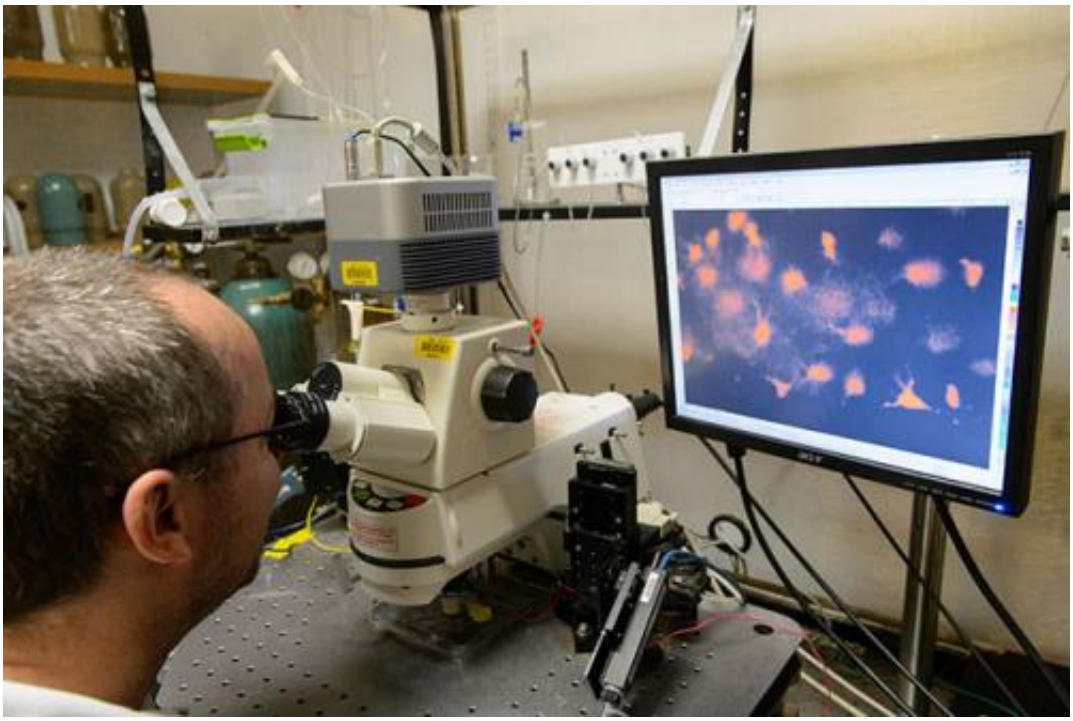
While neurophysiologists were looking at the mutation's effect on human cells, the baby's doctor, UConn Health neonatologist Naveed Hussain, began to review recordings of the breathing patterns of his patient, trying to see if there was anything that could give advance warning of a bad breathing episode. There's not much in the medical literature about the breathing patterns of newborn infants, and Hussain and his colleagues began to wonder if they were even looking at the right things. He invited University of Connecticut physiologist Dan Mulkey and Xinnian Chen, a UConn assistant professor of physiology and neurobiology who specializes in biosignal processing, to examine the recordings.

"They pointed out things we at the hospital hadn't paid any attention to. We invited them to speak at one of our conferences, and that led to a discussion with fellows, and faculty questioning if we maybe could do more with breathing patterns in babies" to help them, Hussain says.



Carbon dioxide-sensing astrocytes are found in the retrotrapezoid nucleus (RTN) area on the brainstem. These astrocytes help trigger breathing when blood levels of carbon dioxide rise too high. Credit: Daniel Mulkey/UConn Image

Chen began carefully sifting the data, looking at records of normal breathing, of bad breathing, and most importantly at the recordings taken minutes before the start of a bad breathing episode. She was searching for subtle differences that could serve as warning signs.



Daniel Mulkey, associate professor of physiology and neurobiology, looks at tissue under a microscope at his lab. Credit: Peter Morenus/UConn Photo

What she has found so far has been suggestive. It looks like healthy breathing rhythms are similar to healthy heartbeats. Both of them have slight blips and variations here and there. Heart rhythms have been studied extensively, and cardiologists know that if a heart starts to beat too simplistically regularly, a heart attack is likely in the coming hours. With Hussain's help, the team is gathering recordings of many more premature infants and developing an algorithm that should eventually be able to pinpoint when a baby's breathing pattern goes south.

Provided by University of Connecticut