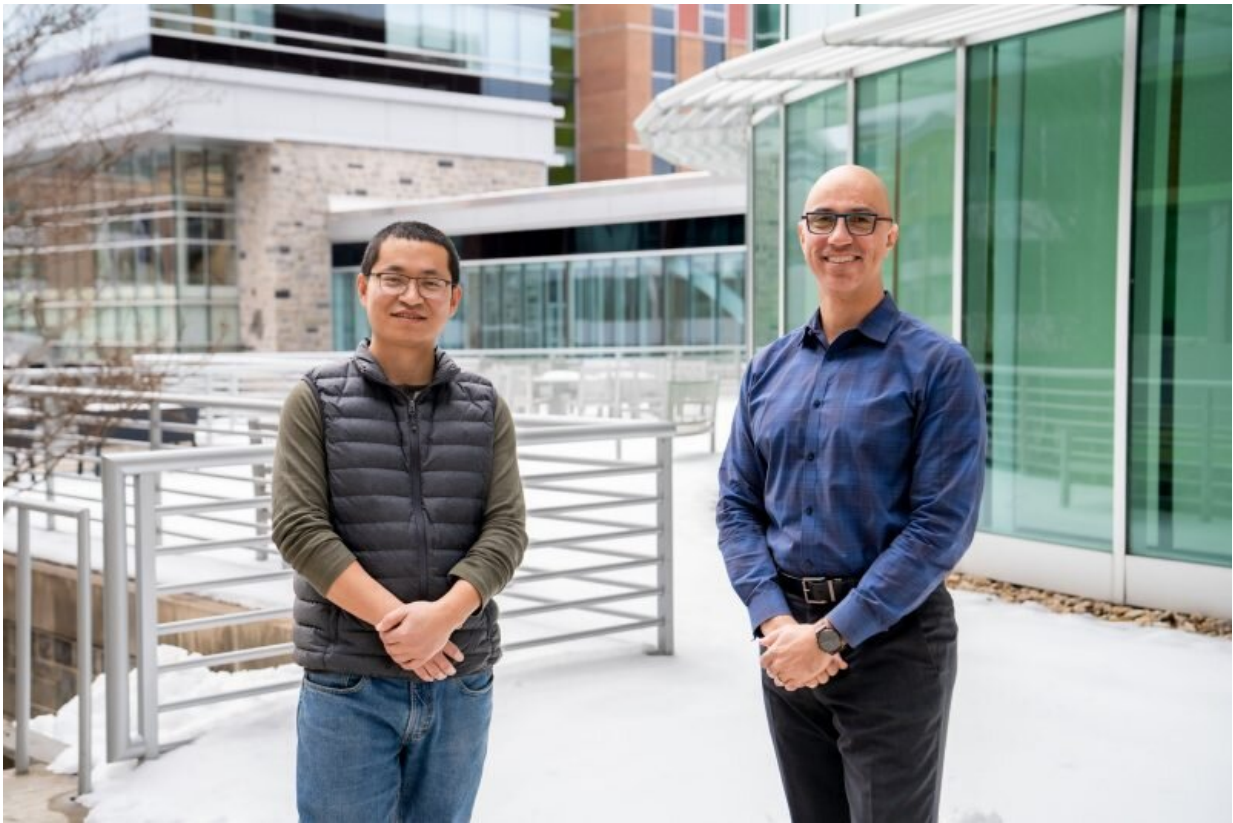


Deadly arrhythmia trifecta: Salt, swelling, and leaky sodium channels

May 25 2022, by Whitney Slightham



Xiaobo Wu, the study's first author and a graduate student in Virginia Tech's Translational Biology, Medicine, and Health Program, was mentored by Steven Poelzing, the study's principal investigator and an associate professor at the Fralin Biomedical Research Institute. Credit: Clayton Metz / Virginia Tech

Less than 1% of the population has been diagnosed with Long QT

syndrome—a rare heart condition that can cause chaotic, sometimes fatal, heart rhythms.

Now, Virginia Tech researchers at the Fralin Biomedical Research Institute at VTC have identified two core factors that may put patients with Long QT syndrome Type 3 at significantly higher risk of sudden cardiac death. Their findings were recently published in the *American Journal of Physiology—Heart and Circulatory Physiology*.

The researchers found that heart inflammation and elevated blood [sodium](#) levels together elevate the risk of dangerous arrhythmias and sudden cardiac death in [guinea pigs](#) with faulty intercellular sodium channels—a condition modeling a form of the Long QT syndrome.

"Monitoring salt intake is a simple, inexpensive intervention, but our new findings demonstrate that controlling blood sodium could help Long QT patients prevent dangerous arrhythmias," said Steven Poelzing, the study's lead author and associate professor at the Fralin Biomedical Research Institute.

Some Long QT syndrome patients are born with the disease, while others develop it as a result of natural aging, certain medications, tissue swelling, or heart disease.

The syndrome remodels the heart's sodium channels to become hyperactive and leaky, which disrupts the heart's normal electrical pathways. Long QT is diagnosed when the length of time it takes for a heartbeat to drop from its peak to baseline, the QT interval, is extended on an electrocardiogram reading.

"Some patients with Long QT live long, healthy, and event-free lives, while others suddenly die. We've examined cellular activity to better understand which factors exacerbate the disease," Poelzing said.

Poelzing's laboratory was the first to examine the impacts of heart tissue swelling and blood chemistry in relation to the syndrome. The research team injected wild type guinea pigs with a toxin derived from [sea anemones](#) that makes the heart's sodium channels leaky.

The scientists observed that while the anemone toxin mildly prolonged QT intervals, it didn't trigger arrhythmias on its own. Next, they increased sodium levels in the blood.

"Combined, leaky sodium channels and elevated blood sodium levels slightly altered the [heart rhythms](#), but it didn't cause sudden cardiac death," said Poelzing, who is also an associate professor in the Virginia Tech College of Engineering's Department of Biomedical Engineering and Mechanics, and co-director of the Translational Biology, Medicine, and Health (TBMH) Graduate Program.

Finally, Poelzing's research team added mannitol, a drug that causes swelling by drawing water into the spaces called the perinexus between heart cells. This "trifecta" was enough to prompt sudden cardiac death.

"Our data suggests that the combination of tissue edema, elevated blood sodium, and faulty sodium channels trigger deadly heart arrhythmias," Poelzing said.

Poelzing believes these findings could help Long QT patients, as well as the general population. As humans naturally age, heart muscle cells grow and require more calcium to contract. To sustain elevated calcium levels, heart muscle cells also need more sodium. As a result, the aging human [heart](#) naturally adapts "leaky" sodium channels, allowing more sodium to enter the cell.

"While Long QT is a rare disorder, anyone could acquire similar sodium channel dysfunction with age, ischemia, or other [heart disease](#)," Poelzing

said.

Sylvia Priori, who was not involved in the study, is one of the world's leading scientists in the field of Long QT syndrome.

"This is a thought-provoking study," said Priori, professor of cardiology at the University of Pavia and Scientific Director of the ICS Maugeri.

"Bringing the concept closer to the [clinical setting](#) will require teaching cardiologists on how parameters related to perinatal expansion and extracellular sodium levels may be monitored in a clinical environment."

More information: Xiaobo Wu et al, Hyponatremia and intercalated disc edema synergistically exacerbate long-QT syndrome type 3 phenotype, *American Journal of Physiology-Heart and Circulatory Physiology* (2021). [DOI: 10.1152/ajpheart.00366.2021](https://doi.org/10.1152/ajpheart.00366.2021)

Provided by Virginia Tech

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