**Growing Heart Cells For Epilepsy Patients?**

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**Editor's Note:**

*While on-site at the American Epilepsy Society's 68th Annual Meeting in Seattle, Washington, Medscape correspondent Andrew N. Wilner, MD, spoke with Chad R. Frasier, PhD, a Postdoctoral Fellow in the Department of Pharmacology at the University of Michigan about exciting new research in sudden unexpected death in epilepsy (SUDEP).*

**Dr Wilner:**We just had a press conference on SUDEP, a topic of great concern. Several posters at this meeting address new research in SUDEP, including one of yours.[1] Can you tell me what your poster is about?

**Dr Frasier:**We have taken skin biopsies from patients with Dravet syndrome, a very severe form of epilepsy that presents early in life. Using the induced stem cell method, we have taken the skin biopsies and turned them into pluripotent stem cells, so now these stem cells are just like embryonic stem cells that can then be differentiated into cardiomyocytes or neurons for the brain. You can do anything with them. Other people have made pancreatic beta cells. It is very exciting because it eliminates the ethical considerations that you have with the embryonic stem cells, because you are only using a skin biopsy from a patient.

Another great thing is that you have the genetic background of the patient, so in these cardiomyocytes, you have the actual patient genetic background as well as the patient mutation.

We have taken these cardiomyocytes and grown them in cell culture.

**Dr Wilner:**You have taken a skin biopsy from a patient with Dravet syndrome, and then you have turned some of those cells into pluripotent stem cells and then some of those into cardiac myocytes. Now they are sitting in a dish in the laboratory, these cardiac myocytes that originated in a patient with Dravet syndrome. The DNA of those cardiac myocytes is the same as the DNA of the original patient?

**Dr Frasier:**Yes, which is great. It is a diverse genetic background because we have four different patients and each patient has a mutation in SCN1A, but they might have mutations in completely different genes as well. Depending on the genetic background and everything else, there are thousands of mutations, so each patient might have a completely different background. We are seeing very similar things between patients when we go for the factors we just looked at.

We have these heart cells in a dish, and they actually beat by themselves. What we found in the cells from patients with Dravet syndrome is that they are beating about twice as fast. Helen Zhang (a research assistant at the University of Michigan Medical School) has found this, and we haven't figured out the best way to quantify it yet, but they are actually also beating very irregularly. The human heart typically beats about 80 times per minute and it is very regular, but we see that in these Dravet patients lines, they will beat five or six times and then pause.

**Dr Wilner:**So they have a resting tachycardia and an arrhythmia?

**Dr Frasier:**We can't call it an arrhythmia because it is still in a dish. There is not a good term for it yet because this is such a new field. The method for making the pluripotent stem cells has only been around since 2006, and differentiation into the heart cells has been around even less time because they had to figure out how to make the pluripotent stem cells, and then after that, figure out how to take those into the heart cells.

**Dr Wilner:** The normal human heart has sympathetic and parasympathetic innervation that helps control the heart rate, but these are not efferented, right? These are just cells. They don't have any connections to anything.

**Dr Frasier:**Correct. They are just heart cells so there is no autonomic innervation. There is an intrinsic defect in the heart cells of these patients. That is what is really cool. There is probably an autonomic component that predisposes the heart to go into a cardiac arrhythmia in patients if there is some sort of autonomic event and the heart is already susceptible. You can see why you might have a perfect storm where you have something in your brain going on and something in the heart that is already wrong, and this leads to SUDEP.

**Dr Wilner:** Are patients with Dravet syndrome more likely to develop SUDEP than other people with epilepsy?

**Dr Frasier:**One of the tragic things is that patients with Dravet syndrome are more likely to have SUDEP than the general epilepsy population.

**Dr Wilner:** What are you going to do next?

**Dr Frasier:** We have seen an increase in sodium current density, so we have some electrophysiologic differences in these cells, on top of seeing the tachycardia. We want to get the patients with this phenotype in their myocytes to see a cardiologist and have a Holter monitor ECG to find out whether we see something similar in the patients. We have completed only one workup in a patient so far, so it is very preliminary, but it seems that the patient does have the baseline tachycardia as well. It is really cool seeing something translate from the dish to guiding the work of the cardiologist—and hopefully to preventing SUDEP in patients who might be at risk.