You've Got to Have Heart

By Regan Smithers

"Always listen to your heart, because even though it is on the left side, it is always right."

The heart is so complex – and no, I am not referring to its designated role in romanticism and relationships, but rather its imperative function as a powerhouse organ. Without a functional heart, the body begins to break down resulting in many devastating disorders and diseases. For instance, cardiovascular disease (CVD) claims nearly 18 million lives annually across the globe [1]. In the U.S. 1 in 3 adults suffer from CVD [1]. Imagine! That is over 500,000 people in Sacramento County alone suffering at the hands of CVD!

What if I told you there was a way to restore vitality in a failing heart ... a way to help your loved ones suffering from the detrimental effects of a heart attack – would you listen?

Is that your heart beating out of your chest in excitement that I hear?! Excellent! Stay tuned!

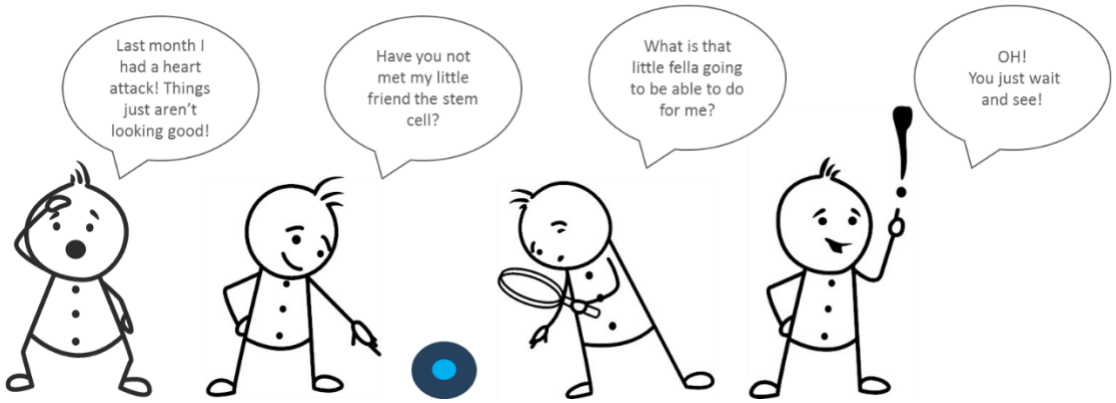

Figure 1

The heart is composed of cells known as cardiomyocytes that can be grouped into three major categories: atrial, ventricular, and nodal. The atrial and ventricular subtypes are charged with contraction, while the nodal subtype is responsible for generating the electrical conduction that controls the heart rate [2]. After a cardiac injury, cardiomyocytes can become damaged or undergo cell death—and our body does not have a way to replace damaged or dead heart cells [3]. When these cells are destroyed or fail to do their job correctly, the heart begins to malfunction. This can cause an arrhythmia (irregular heartbeat), heart attack, stroke, and many more harmful and deadly conditions.

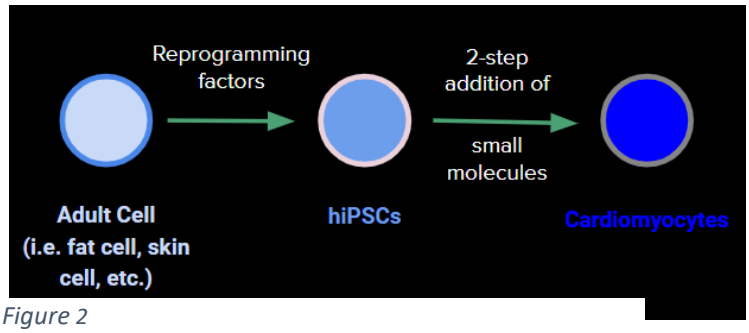

Figure 2

To target these heart conditions, researchers have turned to human induced pluripotent stem cells (hiPSCs). HiPSCs are created by taking adult cells such as skin cells or fat cells, and reprogramming them into a state where they have the potential to become any cell type in the body [4]. After reprogramming, hiPSCs can then be directed to form cardiomyocytes (Figure 2). Researches are currently able to take hiPSCs and generate beating cardiomyocytes in a dish in the lab (Figure 3). Amazing, right?! Well, despite this unbelievable accomplishment, we are still shy of developing functional cardiomyocytes that can be used for regenerative medicine in humans.

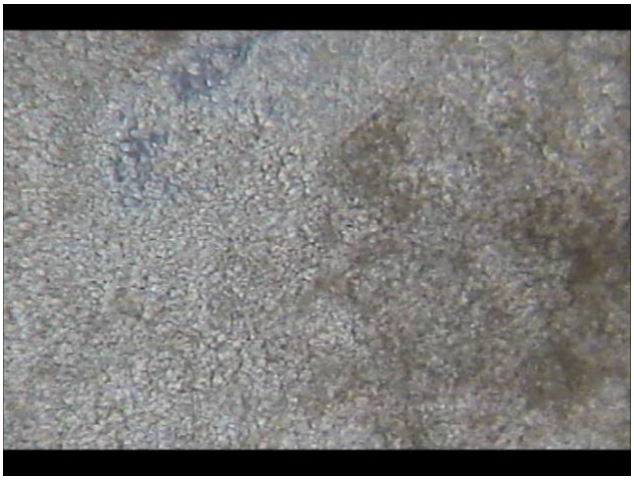

Figure 3. Courtesy of Dr. Deborah Lieu's Lab at the UC Davis Institute of Regenerative Cures

The goal of our lab is to develop pacemaking cardiomyocytes for engineering biopacemakers, as well as contractile cardiomyocytes for cell replacement therapy after a heart attack. To accomplish this, we must be able to develop homogenous (only one cardiomyocyte subtype) populations of heart cells. Unfortunately, we are only able to generate heterogeneous (a mixture of atrial, ventricular, and nodal) populations. This is dangerous! For instance, injecting a heterogeneous population of cells into the heart would inevitably cause haywire! You would have cells contracting at the wrong time and likely in the wrong place. Goodbye sinus rhythm (normal heart rate), hello arrhythmia!!

So, how do we fix this issue? Imagine making a homemade smoothie for the first time. You go to the store and buy juice, fruit, ice, and sherbet. You throw a mixture of ingredients into the blender and try it out. Woah! Yuck! You had read a recipe on Pinterest, but it doesn't taste right, you wanted something sweeter. So you throw in a few more strawberries, add a little more juice, and try it again. Yum! Guess what?! That's science! As researchers, just like you turn to recipes on Pinterest, we turn to published journals and articles to get an idea of the work that has already been done in our field. We know that we can generate a population of beating cardiomyocytes in the lab, but it's just not right – we have a heterogeneous population when we want a homogenous population. So we add in combination of small molecules that influence important pathways involved in the transformation of hiPSCs to cardiomyocytes (Figure 2) with hopes of generating a high yield of homogenous cardiomyocytes that can be used for treating CVD. We have to keep altering the addition of small molecules until we get it just right!!

This type of research is just a small subset of the work being done in the field of stem cell biology to generate treatments for detrimental diseases and disorders. Stem cell research offers great promise for not just the future of cardiovascular medicine, but public health as a whole! Researchers are hard at work to find cures for diseases that we never thought were possible!

References

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