Dr Li Qian, Assistant Professor at the University of North Carolina School of Medicine has been fascinated by the heart since her undergraduate days. Now, her innovative technique for reprogramming resident cardiac fibroblasts in the damaged heart into functional cardiomyocytes could lead to a new treatment for heart disease, one of the Western world’s biggest killers.

Heart failure – the inability of the heart to pump blood effectively around the body – is one of the leading causes of disease and death in the Western world, affecting an estimated 5.7 million people in the US alone.

Heart failure occurs when healthy heart muscle cells, known as ‘cardiomyocytes’, die – for instance, during a heart attack – and are replaced by scar tissue comprising a different type of cell, cardiac ‘fibroblasts’. Normal fibroblasts are an important structural component of a healthy heart, but following an injury, they are produced in too great a quantity in the wrong parts of the heart – what Dr Qian terms as ‘bad’ fibroblasts.

The body cannot naturally regenerate lost cardiomyocytes so this change is generally considered to be irreversible. If only there were a way to convert fibroblasts back into cardiomyocytes – the award-winning Dr Qian and her coworkers are exploring a way to do just that.

REPAIR THROUGH REPROGRAMMING

In 2012, Dr Qian published ground-breaking research showing that cardiac fibroblasts in living mice could be reprogrammed to become functional, contracting cardiomyocytes, when treated with the right ‘cocktail’ of proteins. The three proteins – ‘Gata4’, ‘Mef2c’, and ‘Tbx5’ – are all types of ‘transcription factors’, molecules that can switch genes on and off, thus controlling a cell’s function. Unlike previous cell regeneration studies, Dr Qian found that, using her cocktail, cardiac fibroblasts did not need to first be converted to stem cells in order to be reprogrammed into cardiomyocytes.

In mice with induced heart attacks, treatment with the cocktail caused heart function to improve after eight weeks, and continue recovering for over three months. Dr Qian’s team showed that this was due to the conversion of cardiac fibroblasts into cardiomyocytes, which successfully integrated with the healthy heart tissue, while reducing scar size. Essentially, the once ‘irreversible’ damage caused by heart attacks could be reversed and healthy heart tissue regenerated – a potential game changer for the millions of people who suffer heart attacks each year.

These findings – which were ranked second in the American Heart Association’s ‘Top 10 Advances in Heart Disease and Stroke Research’ in 2012 – together with her own laboratory’s recent work identifying molecular barriers of reprogramming, gained Dr Qian many awards, including the prestigious 2016 BoyaLife, Science and Science Translational Medicine Award in Stem Cell and Regenerative Medicine.

Born and educated in China, Dr Qian moved to the US as a PhD student, to pursue her dream of carrying out basic science with real-world applications. She hopes that her discovery will eventually lead to a novel treatment for human heart disease patients, which she believes could be in
how the fundamental mechanisms of heart function and disease are regulated. To achieve this, her team is using an interdisciplinary approach, combining biology, biochemistry, and engineering techniques to develop new tools and methods for heart repair.

Q&A

How did you first get into science? And how did you end up where you are now?

The "onion cell" experiment in middle school was when I got so interested in science. I was immensely excited when I first saw a cell from a prepubescent mouse made by myself. I want to use "POP" to describe the moment I ended up where I am now. Passion, Optimism, and Perseverance. I am also very fortunate to have had support from my mentors throughout my career especially my PhD mentor Dr Rolf Bodnar and postdoc mentor Dr Deepak Srivastava, with which I would not be where I am now.

What is so novel and exciting about this method of reprogramming cells?

It takes advantage of the endogenous existing "bad" cells (fibroblasts becoming the scar) to turn them into healthy heart muscles.

What do you hope to achieve during the current project, looking at the molecular mechanisms underlying cell reprogramming?

The successful completion of the current project will define the molecular components and determine the optimal condition for iCM reprogramming.

How do we think we will be treating heart disease in twenty years’ time?

Personalised treatment without open heart surgery and/or heart transplantation.

And how did you end up where you are now?

I ended up where I am now. Optimism, and Perseverance. I am myself. I want to use "POP" to describe the moment I ended up where I am now. Passion, Optimism, and Perseverance. I am also very fortunate to have had support from my mentors throughout my career, especially my PhD mentor Dr Rolf Bodnar and postdoc mentor Dr Deepak Srivastava, with which I would not be where I am now.

This will give a basic science foundation to pre-clinical trials, and beyond. Can science help repair a broken heart? With Dr Qian’s help, it can.