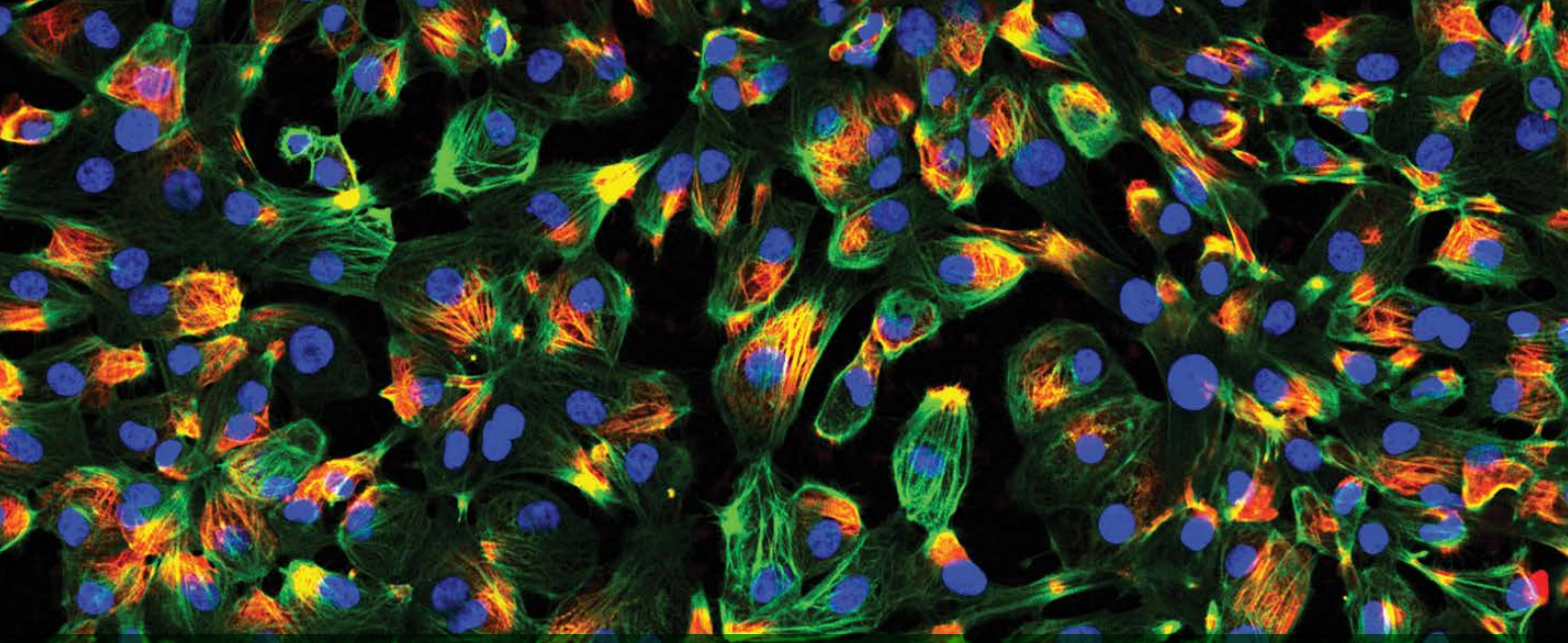

Studying heart development one cell at a time

Examining how individual heart cells develop is revealing how they make decisions to form a working heart.

Once an adult heart is damaged, it has no ability to heal itself. Dr Nathan Palpant at the Institute for Molecular Bioscience at the University of Queensland and Associate Professor Joseph Powell at the Garvan Institute of Medical Research and the University of New South Wales are trying to understand how that might be changed by tracking individual stem cells along their journey to becoming heart cells.

"We think the answers to heart repair are likely to lie in understanding heart development."

"Heart development is a difficult and complicated process, but we think the answers to heart repair are likely to lie in understanding heart development," Nathan says. "So we are using stem cells to model development as it occurs in our bodies."

The development of a stem cell into a heart cell requires a series of complex changes, and changes in one cell affect the activity of others. By looking at individual cells along the path of development, researchers can learn how different types of cells are made as they work together to build the heart. This, in turn, can reveal what goes wrong in conditions such as heart disease.

The standard sequencing experiments for studying genetic material use tissue samples from multiple cells for analysis. This means rare cells can't be studied and variations between cells might go unnoticed.

Single-cell sequencing, however, analyses how genes function in an individual cell. It can reveal rare cell populations, uncover how genes might switch each other on and off, and track the development of distinct "families" of cells.

"When we began this project in 2016 we were the only lab in Australia, and the third in the world, to have a high-throughput single-cell sequencing machine," says Joseph.

Nathan and Joseph believe that research collaborations like theirs are vital and valuable.

"My lab focusses on stem cell biology and cardiovascular disease development; Joseph works on statistical genetics and single-cell sequencing. Neither of us could do this research alone," says Nathan.

Joseph agrees. "We can now address questions that were inaccessible before."

In 2018 the pair found that a gene called HOPX plays a crucial role in controlling heart growth. Their next step is to zoom in even further on cellular development, to study the genetic activity that happens in the nuclei of individual cells.

"This is a resolution of information we've never seen before," says Nathan. "The questions we could answer are almost limitless."