How to mend a broken heart

Dr Mirana Ramialison and her colleagues are trying to determine what makes a stem cell a stem cell. It is a quest that might unlock solutions to congenital heart disease.

Mirana heads up the Developmental Systems Biology Laboratory at the Australian Regenerative Medicine Institute (ARMI) at Monash University, which comprises a multidisciplinary team of computational and molecular biologists. They are united in what she describes as "a bioinformatics application to cardiac development and disease".

"What we're trying to understand is why a particular stem cell is *that* particular stem cell," she says. "What is the genomic information within the cell that makes it what it is?"

It is a question that drove her to undertake her PhD at the European Molecular Biology Laboratory in Germany, and then take a role as an investigator at the Victor Chang Cardiac Research Institute in Sydney before joining ARMI in 2014. It is also a question with much more than blue-sky import.

"If we can understand how a particular stem cell is made, then we can reverse-engineer it to become the cell we want it to be," she explains.

To this end, she and her colleagues combine biology and computer science, custom-making software to explore the genomics of stem cells.

In 2019, this research resulted in a program called 3D-Cardiomics, which takes heart gene sets and produces true-to-life three-dimensional representations that depict gene expression in each part of the organ. The program, hosted at Monash University in Melbourne in collaboration with Prof. Jose Polo's lab, can be accessed via a simple browser interface.

"We can now look at each region and know exactly which genes are expressed there," says Mirana.

3D-Cardiomics is proving especially valuable to one of Mirana's colleagues, Dr Ekaterina Salimova, a research fellow at the lab.

Ekaterina says her research career is focussed on a single question: "How can we mend a broken heart?"

"I was always fascinated by the heart," she says. "It is the most intriguing organ, but it has almost no regenerative capacity."

Her work, therefore, involves studying the genetic and regulatory factors that condition a stem cell to turn into a heart cell. She is looking to manipulate the epigenetic landscape of cardiac cells to boost their ability to regenerate.

"One in 100 babies in Australia is born with a heart defect," explains Mirana, "which means something went wrong in their development."

Ekaterina, Mirana and others at the developmental systems biology lab have a very specific endpoint for their research: a cure for congenital heart disease.