OVERVIEW

iPSCs are cells generated from adult cells such as human skin or blood, and can potentially differentiate into any kind of human cell. They are a promising new field of research yielding novel insights into molecular mechanisms of disease, which is hoped to lead to new and better treatments.

Dr Elena Matsa is a cell biologist and iPSC specialist at Stanford University in California, USA. She is in charge of ongoing studies on Dilated Cardiomyopathy (DCM), a fatal heart disease.

DCM has various causes, one of which is mutations in genes involved in sarcomeric proteins in the heart muscle, which make the heart muscle baggy and thin so it can no longer pump blood efficiently.

Dr. Matsa uses iPSCs for studying cardiovascular disease within a wider research remit looking at biological mechanisms of adult stem cells, embryonic stem cells and iPSCs in general.

The lab uses next generation sequencing, tissue engineering, physiological testing, and molecular imaging technologies.

Using induced Pluripotent Stem Cells (iPSCs) to study molecular mechanisms in Dilated Cardiomyopathy

TECHNICAL SITUATION

Dr Elena Matsa is using Qlucore's Omics Explorer to analyze data from studies that use iPSCs to understand molecular mechanisms in Dilated Cardiomyopathy (DCM), the third leading cause of heart failure in the US. The experiments are carried out on tissue from genetically affected DCM patients. Heart muscle cells (cardiomyocytes) are collected from these individuals if they have heart surgery. iPSCs are made from 'reprogrammed' skin or blood cells from the same patients and then turned into beating heart muscle cells for direct comparison. Since the technique for making iPSCs is relatively new, one aim of the DCM studies is to assess whether 'lab-made' heart cells are a good representation of equivalent adult human cells. A second goal is to see how both cell types respond to various drugs, such as beta-blockers, used to treat DCM. "If the two types of heart cell respond similarly, it means we can potentially do pre-clinical drug tests on iPSC cardiomyocytes confident that the results will accurately predict how the real human heart will react to a new drug before it is released on the market," explains Dr Matsa.

SOLUTION

To compare the heart cell behaviors, the lab carries out RNA sequencing and looks at differences in gene expression. Data is then uploaded into Omics Explorer.

"Right now we are performing principal component and hierarchical heat map analyses to see how the samples are clustering and we identify genes that can group together the heart tissue and cardiomyocytes from the same patient," says Dr Matsa. "We then look at the ontologies of the genes to compare similarities and differences between the two."

Using iPSCs to study molecular mechanisms in Dilated Cardiomyopathy at Stanford University

"We have a high volume of experiments and we want results promptly. The Qlucore software is definitely helping."

BENEFITS

"We have a high volume of experiments and we want results promptly. The Qlucore software is definitely helping," she says. "It means that cell biologists like myself can look at data, analyze and perform statistical analyses for a presentation or a paper without having to go through our bioinformatician."

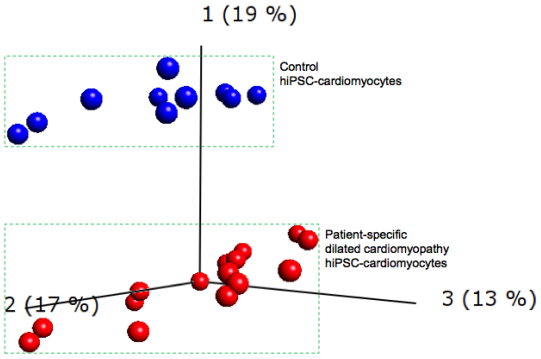

Figure 1: Principal component analysis (PCA) of RNA-sequencing data showing distinct transcriptional heterogeneity between hiPSC-cardiomyocytes derived from healthy control patients and patients carrying familial mutations associated to dilated cardiomyopathy.

She adds: "With Qlucore, you can see how things are changing in real time when you set a p-value cut-off for statistical analysis. Also it's flexible, so you can run custom R scripts if required."

Dr Matsa and her team are hoping that most analyses can eventually be done on Omics Explorer, including incorporation of different normalization strategies.

The lab is also thinking of using Qlucore more for other types of analyses such as methylome-sequencing and ChIP-sequencing looking at epigenetic modifications associated with heart disease and response to drug treatment.

"These analyses would deepen our understanding regarding the mechanisms involved in these processes, and could facilitate the discovery of novel therapies", says Dr Matsa.

For More information

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