SCIENTIST SPOTLIGHT

ARIMA GENOMICS

CELEBRATING SCIENCE & SCIENTISTS

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RESEARCH SNAPSHOT

Research Area	Cardiology
Sample Type	Human heart tissue
Arima Product	Arima-HiC+
Application/Workflow	HiChIP

HUMAN HEART EPIGENOMES REVEAL NEW GENETIC VARIANTS RELEVANT FOR HEART DISEASE

Researchers at the Genome Institute of Singapore used control and diseased human hearts to profile enhancers and long-range chromatin interactions to map the heart epigenome. They associated 70 unique loci with heart disease and heart failure phenotypes by capturing non-coding genetic variants in enhancer elements using H3K27Ac ChIP-seq and disease-associated genes linked to these enhancers using the Arima-HiC kit. This is the first instance of the use of HiChIP on human hearts.

Tan WLW, et al. Circulation Research. 2020. doi: **10.1161/CIRCRESAHA.120.317254**

RESEARCH QUESTIONS

What non-coding variants are associated with cardiac disease?

EXPERIMENT OVERVIEW

- Human cardiac H3K27ac ChIP-seq
- Fluorescence-activated cell sorting (FACS)
- RNA-seq
- Human cardiac Hi-C (homebrew)
- Human cardiac HiChIP (using Arima-HiC Kit)
- Other - reporter assays, RT-qPCR
- hES-CM CRISPR-targeted excision and gene knockdown

HOW DID ARIMA GENOMICS MAKE A DIFFERENCE?

"When I had problems, I reached out to [Arima], and they were very helpful, especially with the mathematics. They walked the IT team through what to look for in the analysis, which was quite important because making the libraries and getting them sequenced is only just the beginning. When the data comes back, it's like a minefield, and our team was very inexperienced with dealing with that kind of Hi-C and HiChIP data sets. So, although we had expert advice from professors who wrote the algorithms to analyze Hi-C, which was really useful, we also needed the technical support from Arima because the kit is specific based on the enzymes that are used." – Dr. Roger S. Y. Foo

RESULTS AND FUTURE DIRECTIONS

Epigenetic profiling using the Arima-HiC kit and ChIP-seq identified 62 unique loci associated with heart failure (HF). Genes associated with histone-acetylation Quantitative Trait Loci (haQTL) are located within topologically associated domains (TADs) and alter transcription factor binding. These haQTLs contain many sub-threshold single nucleotide polymorphisms (SNPs) that had been previously identified through genome wide association studies (GWAS).

Foo et al. have created an enhancer map that other researchers can use to identify enhancers of genes and perform functional testing to find new ways to treat patients. Going forward, the team is looking into gene-based therapies for heart disease. Focusing on tissue-specific enhancers will allow them to develop a diagnostic tool to stratify patients and work toward precision medicine.