RNA binding metabolic enzymes orchestrate gene transcript organisations and functions

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Heart disease is a leading cause of death in Australia, understanding gene expression regulation in the heart will lead to discovery of effective cures for heart diseases.

Gene expression in the heart is regulated at multiple steps, genetic information is encoded in double-stranded DNA in the cell nucleus, this information is then copied to mobile RNA, which is the template to make functional proteins outside the cell nucleus. RNAs do not function alone, rather they are accompanied by a variety of specialized binders. This project uses "mRNA interactome capture" and "RBDmap" approaches, coupled with quantitative proteomics approach to identify proteome-wide RNA-binding proteins, and the intricate mode of RNA-protein interactions.

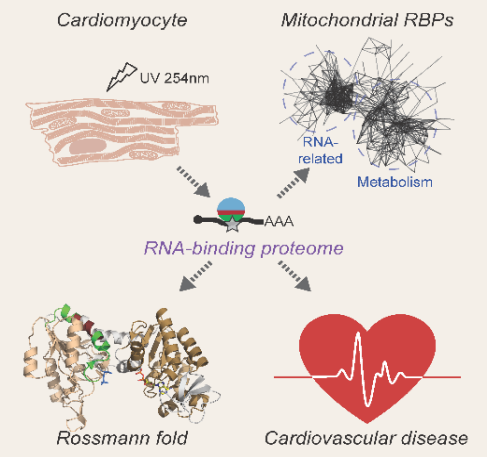

Figure 1. Cardiomyocyte RNA-binding proteome.

The main findings (summarized in Figure 1) are:

1. 1148 proteins are identified as RNA-binding proteins in beating HL-1 cardiomyocytes (termed as cardiomyocyte RNA-binding proteome). 393 are unique to cardiomyocyte.
2. 82 cardiomyocyte RNA-binding proteins have links to heart disease. Our result opens novel revenue to study functional of these proteins from an angle of RNA regulation.
3. 187 cardiomyocyte RNA-binding proteins have mitochondrial localization, heavily represent two groups: known mitochondrial RNA regulators and mitochondrial intermediary metabolism machinery.
4. 73 metabolic enzymes bind RNA in cardiomyocyte. These enzymes are mostly involved in energy production pathways. RNA binding on these enzymes frequently involves an ancient protein secondary structure Rossmann fold. Mutual exclusivity of, or compatibility between, RNA-binding and enzymatic function could occur according to structural analyses.

Our findings raise the prospect of previously hidden RNA-mediated regulatory interactions between cardiomyocyte gene expression, physiology and metabolism