conferenceseries.com

J Proteomics Bioinform 2016, 9:11(Suppl)
http://dx.doi.org/10.4172/0974-276X.C1.092

Discover the underlying mechanism in diabetic cardiac dysfunction by integrating knowledge from genomic and genetic studies

Zhengyuan Xia, Zipeng Liu and Junwen Wang
University of Hong Kong, Hong Kong

Myocardial infarction (MI) is a major cause of sudden death and one of the most common perioperative complications prevalent in diabetes mellitus. The underlying biological process is different from that in non-diabetes partially due to increased oxidative stress in diabetes. Cardioprotective interventions that are effective in non-diabetic patients lose their effectiveness in diabetic patients, which exacerbates the susceptibility of diabetic hearts to myocardial ischemia reperfusion injury (IRI). However, the mechanism is still largely unclear. The rapid evolution of genomic and genetic approaches, such as microarray and genome-wide association study (GWAS), provides additional insights into complex disease studies. Here, by combining gene co-expression network analysis from a set of microarray profiling and MI/type 2 diabetes (T2D) associated gene sets from GWAS, we built a transcription factor (TF) based regulatory network to explore the pathological behavior. The resulting network using this combination method was validated by high enrichment in several well-documented pathways of diabetic cardiac pathology (e.g. PI3K/Akt and Jak/Stat3 signaling pathway) and was also significantly improved than that using only genomic or genetic data individually. This TF-based network also revealed numbers of previously unreported protein interactions linking distinct pathways, among which we verified a relation between Stat3 and Hif-1α in diabetic myocardial IRI model. Thus, our study showed potency of combining knowledge from genomic and genetic studies in discovering the hidden mechanism in diabetic cardiac dysfunction.

Zyxia@hku.hk

Studying mtDNA replication using *in vitro* reconstituted systems

Jay P Uhler
University of Gothenburg, Sweden

Mitochondria are essential for the production of cellular energy and contain their own genomes (mtDNA) that encode 13 subunits of the respiratory chain, 22 tRNAs and 2 rRNAs. The remaining >1500 mitochondrial proteins are nuclear encoded including those required for mtDNA maintenance. The human mitochondrial genome is an approximately 16.5kb circular molecule; mutations in which can lead to mitochondrial disease. mtDNA is replicated by a dedicated mitochondrial replication machinery that includes the replicative DNA polymerase POLγ, the TWINKLE helicase and mitochondrial single stranded DNA binding protein. However, many other DNA replication factors remain to be identified and studied. Moreover, the regulation of mtDNA replication initiation, elongation and termination are not yet fully understood. To help address these unresolved questions, our research group reconstituted a minimal mitochondrial replisome *in vitro* over 10 years ago. This *in vitro* mtDNA replication system is based on purified recombinant proteins and specifically designed DNA templates. Based on this approach, many basic mechanisms have been addressed such as leading/lagging strand replication and RNA priming/removal. The system also enables *in vitro* modeling of mitochondrial diseases by using disease-based mutant proteins or by reconstituting aberrant replication processes. Most recently, the system has been useful in performing screens to uncover the effects of various drug compounds on mtDNA replication.

jennifer.uhler@medkem.gu.se