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EDITORIAL COMMENT

High-throughput technologies and bioinformatic tools to clarify the molecular mechanisms behind sepsis-induced cardiomyopathy

Tecnologias de alto rendimento e ferramentas bioinformáticas para clarificar os mecanismos moleculares por detrás da miocardiopatia induzida pela sepsis

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The noteworthy progress over the last decade in molecular technologies and bioinformatic tools has led to the generation and integration of significant amounts of Big data, including DNA, RNA, protein and metabolite levels of a wide range of tissue samples and patients. These have improved our knowledge of health and disease and consequently enabled the leverage of precision medicine for several diseases.

Worldwide, sepsis is an ongoing challenge for physicians and health-care administrators due to its high incidence, mortality and its huge burden on public health resources in developed countries. It is the leading cause of intensive care unit related deaths.[1]

Sepsis-induced cardiomyopathy (SICM) or sepsis-induced myocardial dysfunction (SIMD) is a form of transient cardiac dysfunction in sepsis patients and presents a challenging diagnosis. It is one of the major causes of death among sepsis patients.[2] It is important to stress that in sepsis-induced cardiomyopathy, the myocardium is functionally and structurally injured by inflammatory cytokines and mitochondrial dysfunction. Nevertheless, knowledge of the pathophysiology of this condition remains elusive.[3]

The analysis and integration of large volumes of data obtained using high-throughput technologies require bioinformatic and computational tools to reveal the complex biological processes and the molecular mechanisms behind diseases, increasing our understanding of the course of diseases and opening up new possibilities for drug development.

Considering this technological progress and the increasing in our knowledge of SICM, several potential therapies are under investigation in animal models of septic cardiomyopathy, such as statins, dexmedetomidine, hydrocortisone, alpha-2 blockers, yohimbine, Chinese yam, erythropoietin,

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vitamin c, and sulfur dioxide (see references in L'Heureux et al.[2]).

In the current issue of the Journal, Chen et al.[4] conducted bioinformatic analysis on the myocardial transcription spectrum of sepsis chips from the GEO database, which revealed 601 genes significantly enriched in the following biological processes, cellular components and molecular functions: generation of ribosomal protein complexes, ribose RNA-related metabolism, myeloplast migration, phagocytic vesicles, membrane rafts, binding of Toll-like receptor and amide binding. These 601 genes are mostly involved in NF-κB signaling pathway, autophagy, mitochondrial autophagy, proteasome, RNA transport, TGF-beta signaling pathway and JAK-STAT signaling pathways.

After a detailed analysis of these results, the authors concluded that *TLR1* seems to influence the survival of cardiomyocytes by interacting with the NF-κB signaling pathway. So, the authors hypothesized that curcumin could have a therapeutic role through down regulating *TLR1* to mediate apoptosis of myocardial cells in septic myocardial injury.

Lipopolysaccharide (LPS) was used to construct a rat model of sepsis, where the results demonstrated that curcumin decreased the expression of pro-inflammatory factors TNF-α and IL-6, up-regulated the expression of anti-inflammatory factors IL-10, and down-regulated the expression levels of BNP, cTnI, CK and CK-MB.

Additionally, using a model of myocardial injury induced by LPS through *in vitro* cell experiments, the authors showed that curcumin can not only inhibit the expression levels of TLR1 mRNA and NF-κB mRNA, but also the protein expression of TLR1 and p-NF-κB was down-regulated. Curcumin seems to improve the survival rate of cells and inhibit apoptosis after LPS treatment in a dose-dependent manner.

This work conducted biological function experiments after an *in silico* analysis of microarray gene expression from the Gene Expression Omnibus database to prove the effect of curcumin on LPS-induced cardiomyocytes and also explored the molecular mechanism of curcumin on *TLR1* through molecular docking experiments, which points to curcumin being a potential inhibitor of *TLR1*.

In 2022, Rattis et al.[5] demonstrated that treatment with curcumin and nanocurcumin in a mice model promoted a cardioprotective response that could be linked to the modulation of the mTOR pathway.

Curcumin, extracted from the dried rhizomes of Curcuma longa (or turmeric), presents antioxidant, anti-apoptotic, and anti-inflammatory activities that seems to be related to its modulatory effects on AMPK, Nrf2, JAK/STAT, NF-κB, PI3k/Akt, MAPK, Notch, mTOR, PPARs, arachidonic signaling pathways and toll-like receptors, histone acetylation and deacetylation, and the renin angiotensin system.[6]

Further studies are warranted to clarify the mechanisms of sepsis-induced myocardial injury and to validate the therapeutic potential of curcumin.

Most research on the mechanism of SICM is only based on a single omic technology.[7] Therefore, considering technological progress together with the decreased costs and turnaround times a fast use of high-throughput techniques is expected and consequently an increase in the molecular omics-based data to unravel the complex biological networks underlying SICM, opening the pathway for new therapeutic target development.

Conflicts of interest

The author has no conflicts of interest to declare.

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