Letter by Siracusano and Girasole Regarding Article, “Toll-like Receptor-Mediated Inflammatory Signaling Reprograms Cardiac Energy Metabolism by Repressing Peroxisome Proliferator-Activated Receptor γ Coactivator-I Signaling”

To the Editor:

We read with great interest the article by Schilling et al.1 about the role played by the suppression of peroxisome proliferator-activated receptor γ coactivator-I by the activation of toll-like receptor 4 in septic myocardial dysfunction.

The authors stress that the lipopolysaccharide-induced sequential activation of proinflammatory interleukins, toll-like receptor 4, and nuclear factor κB may be the root of the metabolic energy reprogramming and of the cardiac dysfunction in sepsis.

Recently, 2 important studies documented the accumulation of glycogen and glucose transporters (ie, glucose transporter type 4 [GLUT4] [insulin dependent] and GLUT1 [stress responsive]), activated by proinflammatory interleukins in the septic myocardium.2,3 Moreover, for the first time to our knowledge, the accumulation of lipids in the myocardiocytes has been observed in sepsis.3

The overall picture might be explained if we consider that, in sepsis, an inflammatory challenge is present and that, like other types of stress (ie, pressure or volume overload, hypoxia, and ischemia), it can induce the reactivation in the heart of the fetal gene program, leading to a shift from preferential lipid use to the use of glucose and lactate.4 This metabolic modification is useful in the short-term through a reduction in oxygen consumption and production of reactive oxygen species but may lead to failure in the long-term. The metabolic shift explains both the recruitment of glucose and glucose transporter and the reduction of the lipid accumulation because the down regulation of peroxisome proliferator-activated receptor [PPARα] and the reduction in lipid oxidation,5 in the presence of increased lipolysis in sepsis, may lead to lipotoxicity and mitochondrial and myocardial dysfunction.

We would appreciate the authoritative opinion of Schilling et al.1 about this global reconstruction of the events happening in septic myocardial dysfunction.

Disclosures

None.

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References

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