Letter to Editor

Letter by Mezzaroma, et al Regarding Article, “NLRP3 Inflammasome as a Therapeutic Target in Myocardial Infarction”

To the Editor:

We read with great interest the review article by Takahashi on the role of the NLRP3 inflammasome in acute myocardial infarction (AMI). The author reviewed the recent literature evaluating the role of the NLRP3 inflammasome in an animal model of AMI pointing out that the inflammatory response in which the NLRP3 inflammasome takes part is an essential part of the tissue response to injury. The NLRP3 inflammasome is activated by several stimuli produced during tissue injury or stress and, following the interaction with the ASC and the pro-inflammatory enzyme caspase-1, induces production of the mature forms of the pro-inflammatory cytokines IL-1β and IL-18. As evidenced in this review, the investigation on the role of the single components of the inflammasome has generated contradictory data, however, the consensus is that the blockade of the NLRP3 inflammasome may be a valuable therapeutic target. Therefore, NLRP3 may be acting through two different mechanisms of inflammasome-mediated and inflammasome-independent myocardial damage.

Several pre-clinical studies have provided evidence that targeted IL-1 signaling blockade (with one exception) is a strategy to reduce ischemic injury to the heart. Clinical evidence is now emerging, strengthening confidence concerning the valuable use of IL-1 blockade in AMI. Pre-clinical and clinical data show that IL-18 is a second product of the inflammasome potentially involved in myocardial injury. However, the evidence on beneficial effects of IL-18 blockade following AMI is nowadays limited to a single study. As pointed out in the review, the NLRP3 inflammasome is not only involved in the production of cytokines, but may directly participate in cardiomyocyte cell death through the activation of caspase-1. We agree with the author that NLRP3 is a potentially valuable target for a therapeutic intervention. We want to report that we have recently developed a novel NLRP3 inhibitor effective both in vitro and in vivo. The NLRP3 inhibitor reduced ischemia reperfusion injury by reducing infarct size and by preventing caspase-1 activation, thus confirming in a preclinical animal model that NLRP3 inhibition represents a therapeutic strategy to reduce the effects of NLRP3 in the ischemic myocardium. Whether the NLRP3 inhibitor blocks both the inflammasome-dependent and independent effects, however, remains to be tested in future studies.

REFERENCES


Eleonora Mezzaroma, PhD
Department of Pharmacotherapy and Outcome and Victoria Jonson Research Center, Virginia Commonwealth University, Richmond, Virginia, USA
Carlo Marchetti, MS Pauley Heart Center and Victoria Jonson Research Center, Virginia Commonwealth University, Richmond, Virginia, USA
Stefano Toldo, PhD Pauley Heart Center and Victoria Jonson Research Center, Virginia Commonwealth University, Richmond, Virginia, USA
E-mail: stoldo2@vcu.edu