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Title: Cardiometabolic diseases: is the Inflammasome A Key and innovative pharmacological target?

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The role of a low-grade, chronic inflammatory response in promoting cardiometabolic diseases (CMD) is well known. However, despite the recent publication of several documents and papers suggesting clinical and social interventions to prevent and benefit subjects afflicted with these comorbidities, the identification of common mechanisms of disease and related innovative pharmacological strategies are far from clear. Most recent evidences suggest a substantial role for the NLRP3 inflammasome, a large multimeric danger-sensing platform that promotes autocatalytic activation of the cysteine protease caspase-1 and mediates the cleavage of inactive pro-IL-1beta, among other proteins, into its active form. In the last few years, our research team has significantly contributed to elucidate the effects of pharmacological modulation of NLRP3 inflammasome to reverse the detrimental consequences of the cardiometabolic inflammation. We have recently demonstrated that a fructose-enriched diet evokes upregulation of renal NLRP3 expression, which significantly contributes to the development of the diet-related renal dysfunction. Similarly, we documented a key role of NLRP3 inflammasome activation in hepatic lipotoxicity evoked by microparticles produced following hepatic cell exposure to high concentration of saturated fatty acid. We also demonstrated that chronic mice feeding with an high-fat high-fructose diet induces an up-regulation of Nlrp3 inflammasome complex within the heart and its expression was exacerbated by an ischemic event. Our results will be discussed in keeping with most recent literature data for a better understanding of the potential role of NLRP3 inflammasome as innovative pharmacological target for CMD.