

NLRP3 Inflammasome Activation and Inflammation : Effect of Ouabain-Induced Potassium Efflux in Macrophages

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Summary

Background: Inflammation plays a crucial role in the pathophysiology of cardiovascular disease and life-related disease. Recent evidence indicates that the inflammation is mediated through an intracellular multi-protein complex, termed as NLRP3 inflammasome. In the present study, we investigated the role of potassium in activation of the NLRP3 inflammasome.

Methods and Results: Treatment with nigericin (a potassium ionophore) induced potassium efflux and interleukin (IL)-1 β production in low-dose lipopolysaccharide (LPS)-primed J774 macrophages. Treatment with ouabain (a Na-K pump inhibitor) also induced pro-IL-1 β processing and subsequent IL-1 β production in LPS-primed J774 and murine primary macrophages, and this production was almost completely inhibited in the macrophages derived from NLRP3-knockout (KO) mice. The processing of pro-IL-1 β , determined by western blot analysis, was confirmed in the cells treated with ouabain. *In vivo* experiments showed that ouabain treatment induced cardiac dysfunction in LPS-pretreated wild-type mice, but not in NLRP3-KO mice.

Conclusion: Our findings demonstrate that ouabain induces NLRP3 inflammasome activation and IL-1 β production through potassium efflux, leading to inflammatory responses, which are involved in cardiac dysfunction.