



Letter to the Editor

IL-18 might be a novel therapeutic target in the treatment of aortic valve calcification

Bo Wang^{*}, Huiqing Lin, Zhangfan Mao

Department of Thoracic Surgery, Renmin Hospital of Wuhan University, Wuhan, China

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Recently, we have read with great interest DR. Zhou and colleague's research to entitled "Interleukin 18 promotes myofibroblast activation of valvular interstitial cells." that published in International Journal of Cardiology [1]. In their paper, DR. Zhou draws a conclusion that Interleukin-18 (IL-18) promotes the myofibroblast differentiation of valvular interstitial cells (VICs) and accelerates calcification in the presence of conditioning medium via the NF- κ B pathway.

IL-18 is a member of the IL-1 family of cytokines and plays an important role in the pathogenesis of atherosclerosis [2]. Atherosclerosis has the similar pathological process with aortic valve calcification. IL-18 administration initiates inflammatory cascade by binding with IL-18 Ra via NF- κ B which is involved in progression and destabilization of atherosclerotic plaques in ApoE^{-/-} mice. Blocks IL-18 signaling through down-regulation of IL-18, IL-18 Ra, CD36, and MMP-9, thus reducing inflammation and restoring plaque instability via upregulation of LXR-a [3]. Moreover, IL18, IL1b, or TNF-a can indirectly stimulate osteoclast formation through up regulation of RANKL production from T cells [4]. Our previous study also demonstrated that IL-18 and HMGB1 are more highly expressed in nonrheumatic human stenotic aortic valves and HMGB1 mediated IL-18-induced VIC myofibroblastic transition [5]. Therefore, IL-18 might be a novel therapeutic target in the treatment of aortic valve calcification.

As to the underlying mechanisms that by which IL-18 participates aortic valve calcification are somewhat unclear yet. Some very likely mechanisms might be via Toll-like receptor 4 pathway, MAPKs and STAT3 dependent manner, NLRP inflammasome pathway, ROS and HMGB1 and so on.

In summary, the majority of studies suggest that IL-18 play an important role in aortic valve calcification. However, further studies

should be carried out to better understand the more effect of IL-18 in aortic valve calcification and related underlying mechanisms.

Conflict of interest

The authors report no relationships that could be construed as a conflict of interest.

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^{*} Corresponding author.

E-mail address: bowang027@163.com (B. Wang).