HMGB1:a critical mediator for oxidized-low density lipoproteins induced atherosclerosis

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Dear Editor:

We have recently read with great interest the report by Mollace V and colleges [1] concerning "Oxidized LDL attenuates protective autophagy and induces apoptotic cell death of endothelial cells: Role of oxidative stress and LOX-1 receptor expression." They indicate that oxidized-low density lipoproteins leads to impaired NO generation and apoptotic cell death in endothelial cells. This effect occurs via the overexpression of LOX-1 and subsequent attenuation of protective autophagic response thereby contributing to the pathophysiology of oxidized-low density lipoproteins-induced endothelial dysfunction which characterizes early stages of atherosclerotic process.

In this paper, the authors find that impaired NO generation induced by oxidized-low density lipoproteins is a critical contribution to atherosclerosis. Based on our own study, we think HMGB1 must take an important role in this process. The reasons are as follows:

First, the importance of HMGB1 in the development of atherosclerosis has been demonstrated in apolipoprotein E deficient mice fed with a high-fat diet. The administration of neutralizing monoclonal antibodies against HMGB1 attenuated atherosclerosis by 55% [2]. Furthermore, Haraba et al. observed that HMGB1 serum levels were increased in golden Syrian hamsters with induced hyperlipidemia, and HMGB1 release was increased in cultures of U937-cells exposed to hyperlipemic sera [3]. In addition, oxidized-low density lipoproteins have been confirmed that it can induce HMGB1 release from cells [4].

Second, in our previous work, we have demonstrated HMGB1 can increase TLR4/Caveolin-1 expression in endothelial cells, and then induce high permeability of endothelial cells [5]. So it is possible that oxidized-low density lipoproteins can increase the endothelial cell permeability through increased HMGB1, which obviously contribute to the process of atherosclerosis.

Third, the authors have indicated the underlying mechanism is the decreased NO level via the overexpression of LOX-1 and subsequent

attenuation of protective autophagic response. However, in our opinion, the impaired NO production can also be caused by increased HMGB1 level through TLR4/Caveolin-1 pathway activation. Because caveolin-1 has been known as a negative modulator of eNOS activity [6,7]

As we have discussed above, HMGB1 can be induced by oxidized-low density lipoproteins, which can in further decrease NO production, impair endothelial cells function and eventually lead to atherosclerosis.

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Conflict of interest

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

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