Macrophages-derived, LRG1-enriched extracellular vesicles exacerbate aristolochic acid nephropathy via a TGFβR1-dependent manner

Wenjuan Jiang[1], Jiahui Dong[1], Changlin Du[1], Songbing Xu[1], Rui Feng[1], Cheng Huang[1], and Taotao Ma[1]

[1]Anhui Medical University

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Abstract

Background and Purpose: Aristolochic acid nephropathy (AAN) is a progressive kidney disease caused by some herbal medicines, but treatment remains ineffective. We previously found NADPH oxidases 4 (NOX4), which regulates oxidative stress, play an important role in kidney injury model. However, its regulatory mechanism of action in AAN is still obscure. Experimental Approach: In this study, we established AAN model in vivo, a co-culture system of macrophage and TEC, and macrophage/TEC conditioned media culture model in vitro respectively. Key Results: We found macrophages infiltration promoted injury,oxidative stress and apoptosis of TEC. Furthermore, the role of macrophage in AAN was dependent on macrophages-derived EV. Importantly, we found that macrophages-derived, Leucine-rich α-2-glycoprotein 1(LRG1)-enriched EV induced TEC injury and apoptosis of via a TGFβR1-dependent process. Mechanistically, macrophages-derived, LRG1-enriched EV mediating TECs injury by upregulating NOX4 in AAN model. Conclusion and Implications: We identified EV as a potential link between macrophage-mediated inflammation and AAI-induced TEC oxidative stress and apoptosis. This study may help design a better therapeutic strategy to treat AAN patients.

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