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Cardiac pericyte is promising target for ischemic heart diseases: Role of Notch3

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Keywords

Notch3; Pericyte; Cardiac fibrosis; Myocardial infarction

We thank Dr. Jiang and colleagues for their interest in our work and appreciate their comments. We agree that targeting Notch3 to reduce cardiac fibrosis and improve mitochondrial function is a promising therapeutic approach for the treatment of ischemic heart disease. While we are intrigued by the potential contribution of Notch3 to cardiac fibrosis and mitochondrial dysfunction in the MI mice [1,2], our study was not designed to address these questions. We believe the studies by Zhang et al. would not detract from overall role of Notch3 in cardiac vascular remodeling in MI.

Recent studies have highlighted the critical roles of pericytes in the regulation of normal cerebrovascular blood flow and ischemia/reperfusion (I/R)-induced no-reflow [3]. Although pericytes are the second most common cell type in the heart after endothelial cells (ECs), their role in myocardial ischemia/reperfusion (I/R)-induced no-reflow and myocardial infarction has not been well defined [3]. Accumulating evidence suggests that pericytes detach from the capillary and migrate into the perivascular interstitium to differentiate into myofibroblasts. This process leads to increased vascular permeability, inflammation, and ultimately, tissue fibrosis and capillary rarefaction [4]. Our previous study found that disruption of HIF-2α/Notch3 signaling pathway caused pericyte detachment and microvascular dysfunction in LPS treated mice [5]. Taken together, these findings suggest a reduction of Notch3 may disrupt EC/pericyte communications that causes pericyte detachment and promotes its differentiation into myofibroblasts during I/R or MI. Therefore, Notch3 maybe a novel therapeutic target for cardiac pericyte-myofibroblast transition and coronary no-reflow after myocardial infarction or I/R.

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Conflict of interest

None declared.

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