



Letter to the Editor

Response to Letter of Stephenson et al.: Nardilysin: A potential biomarker for the early diagnosis of acute coronary syndrome

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Dear Dr. Stephenson:

Thank you for your valuable comments and interest in our study [1]. As you mentioned in your Letter, we have recently demonstrated that nardilysin is one of mediators of turbulence-induced production of platelets from human-induced pluripotent cells (hiPSCs)-derived megakaryocytes [2]. First, secretion of nardilysin from megakaryocytes is strongly stimulated by turbulent flow. Second, addition of recombinant nardilysin, but not the enzymatic-inactive protein, increased platelet production in fluidic system. Third, gene knockdown of endogenous nardilysin in hiPSCs-derived megakaryocytes diminished platelet generation. These results indicate that nardilysin in the extracellular space contributes platelet production through its metalloendopeptidase activity. Moreover, the intracellular nardilysin might cooperate with HDAC6 to control tubulin remodeling in megakaryocytes *via* deacetylation, which is an important step for platelet production. Future studies should clarify roles of nardilysin and its enzymatic activity in platelet biogenesis *in vivo*.

Platelets play major roles in thrombosis and vascular inflammation, which are critically involved in the pathogenesis of acute coronary syndrome (ACS) [3]. Indeed, antiplatelet therapy is beneficial for primary and secondary prevention of ACS. Several reports have shown that higher platelet counts are associated with poorer prognosis of ACS [4,5]. Considering the rapid elevation of serum nardilysin after the onset of ACS, nardilysin might contribute to the regulation of platelet number and atherothrombosis process in ACS. It would be interesting to investigate the correlation between nardilysin and platelet count in clinical studies.

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