Dad1 inhibits cardiomyocyte death by promoting cell adhesion

Mori Shota[1], Rumi Kimura[1], Shota Fuchigami[1], Kotaro Matsumoto[1], Makiko Maeda[2], Masanori Obana[1], Yasushi Fujio[1,2]

[1]Laboratory of Clinical Science and Biomedicine, Grad. Sch. Pharm., Osaka Univ., [2]Project Laboratory of Clinical Pharmacology, Grad. Sch. Pharm., Osaka Univ.

[Background] Cardiomyocyte (CM) death causes the loss of CMs, resulting in heart failure. Therefore, the prevention of CM death could be a therapeutic strategy against heart failure. Defender against cell death 1 (Dad1) was reported to play anti-apoptotic roles in neural cells. Though Dad1 is highly expressed in heart, the functional roles of Dad1 remain to be elucidated. Previously, we reported that the knockdown of Dad1 induced CM death. The aim of this study is to elucidate the cytoprotective mechanism of Dad1 in CMs.

[Methods/Results] CMs were prepared from neonatal rats. The expression of Dad1 was suppressed by using siRNA. Immunofluorescent microscopic analyses demonstrated that the Dad1 knock-down CMs exhibited a round shape. Immunoblot analyses showed that the expression of N-Cadherin, a cell adhesion protein, was reduced in Dad1 knock-down CMs. Moreover, the expression of phosphorylated focal adhesion kinase (pFAK) expression, which is reported to regulate cell adhesion, was downregulated by the knockdown of Dad1, but not FAK protein. Importantly, a cell adhesion enhancer, adhesamine, prevented CM death caused by suppression of Dad1.

[Conclusion] Dad1 could protect CMs from cell death by regulating cell adhesion. Dad1 may be a novel target to prevent CM death in heart failure.