



Oxidative Stress-Responsive Apoptosis Inducing Protein (ORAIP) Plays a Critical Role in the Cardiac Injury in Patients with Heart Failure

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Short Communication

Although oxidative stress has been implicated in the pathogenesis of heart failure (HF), the precise mechanism of myocardial injury involved has been unclear. We previously identified an apoptosis-inducing humoral factor secreted from cells subjected to oxidative stresses. We named this novel post-translationally modified secreted form of eukaryotic translation initiation factor 5A (eIF5A), Oxidative stress-Responsive Apoptosis Inducing Protein (ORAIP) [1]. ORAIP is rapidly secreted from cells in response to oxidative stresses and induces apoptosis of the cells in an autocrine fashion. To investigate the role of ORAIP in the mechanism of oxidative stress-induced myocardial injury in HF, we analyzed plasma levels of ORAIP, cardiac troponin T (cTnT), and brain natriuretic peptide (BNP) in 110 patients (male/female: 83/27; age 71.67±0.98 [mean±SE] years) with HF of various etiology including atrial fibrillation, ischemic heart disease, aortic stenosis, chronic kidney disease, and diabetes mellitus. Plasma ORAIP levels were analyzed by the sandwich enzyme-linked immunosorbent assay [1]. Figure 1A shows the correlation between plasma levels of ORAIP and cTnT in 85 patients with HF. Plasma levels of ORAIP (81.71 ±5.00 ng/ml; normal range <10.0 ng/ml) [2,3] and cTnT (53.24 ± 5.51 pg/ml; normal range < 14 pg/ml) in 85 patients with HF (male/female: 60/25; age 71.89 ±1.10 years) were markedly increased. There was a significant positive correlation ($r=0.372$, $p=0.00046$) between them. Plasma levels of ORAIP (73.15 ±4.66 ng/ml) and BNP (140.13 ± 15.10 pg/ml; normal range <18.4) in 103 (male/female: 76/27; age 71.67 ± 0.98 years) were also markedly increased. There was a tendency of positive correlation (but not significant, $r=0.168$, $p=0.0904$) between them (Figure 1B). A significant positive correlation between plasma levels of ORAIP and cTnT in patients with HF, strongly suggested that ORAIP plays a critical role in myocardial injury, which in turn contributes to the pathogenesis of HF. This was supported by a tendency for positive correlation (but not significant) between plasma levels of ORAIP and BNP. Thus, plasma ORAIP levels can be a novel biomarker and a therapeutic target for the oxidative stress-induced myocardial injury involved in HF. Our findings offer a possible anti-ORAIP therapy with neutralizing monoclonal antibodies against ORAIP to protect from cardiovascular injury in patients with HF at least partly induced by oxidative stresses.

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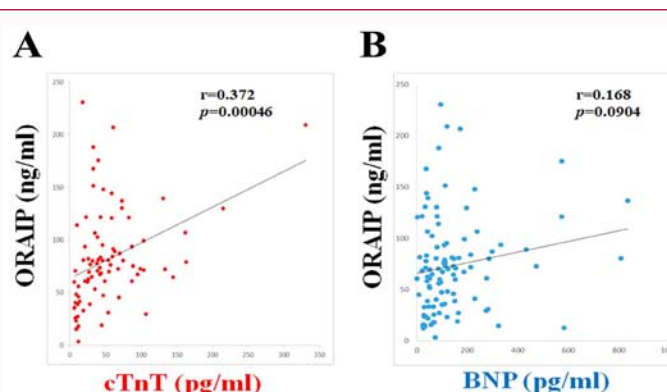


Figure 1:

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