CARDY-28

THE ROLE OF A NOVEL ADHESION MOLECULE, SCUBE1, IN PATIENTS WITH ACUTE CORONARY SYNDROME AND ISCHEMIC STROKE

J-J Chen[1], D-F Dai[2], R-B Yang[3]

Department of Internal Medicine, [1]National Taiwan University Hospital, [2]Taoyuan General Hospital, [3]Institute of Biomedical Sciences, Academic Sinica, Taipei, Taiwan

BACKGROUND/AIMS: Platelet activation plays a crucial role in both acute coronary syndrome (ACS) and acute ischemic stroke (AIS). SCUBE1 (**s**ignal peptide-**CUB**-**E**GF-like domain containing protein **1**), a novel secreted protein selectively expressed in platelets and vascular endothelial cells, is externalized upon platelet activation. Here, we investigate whether SCUBE1 is involved in platelet activation associated with ACS as well as AIS.

METHODS: Plasma SCUBE1 concentrations from 40 controls, 80 chronic coronary artery disease (CAD) patients, 40 ACS patients, and 40 AIS patients were compared by ELISA.

RESULTS: After adjustment for covariates, plasma SCUBE1 concentrations were significantly higher in ACS and AIS patients (391±98 and 282±97 ng/ml, respectively, versus undetectable in controls, $p<0.001$), but not in CAD patients. Plasma SCUBE1 was detectable as early as 6 hours after the onset of symptoms, but no later than 84 hours. Western-blot analysis revealed the presence of smaller SCUBE1 fragments from ACS plasma samples, similar to those proteolytic products generated by a serum-associated protease *in vitro*. While the matrix-bound SCUBE1 fragments containing the EGF-like repeats promote platelet adhesion, soluble SCUBE1 fragments enhance ristocetin-induced platelet aggregation.

DISCUSSION/CONCLUSIONS: Plasma SCUBE1 was elevated in patients with ACS and large atherothrombotic stroke. Matrix-bound and cell-tethered SCUBE1 may function as a novel platelet adhesion molecule that can mediate “matrix-platelet,” or “platelet-platelet” interactions via its amino-terminal EGF-like repeats. Our findings provide new insights into the mechanisms of platelet activation and possible development of novel therapeutic agents for thrombotic diseases.

Key words: SCUBE1, Acute coronary syndrome, Acute ischemic stroke