中文題目: 運用人類細胞激素蛋白微陣列發現人類鹼性成纖維細胞生長因子是內皮細胞受層流剪力壓所產生的條件培養液中針對腫瘤壞死因子α所造成內皮功能失能的主要保護因子

英文題目：Identification of basic fibroblast growth factor as the dominant protector of laminar Shear Medium in Tumor Necrosis Factor-α induced endothelial dysfunctions by Human Cytokine Antibody Array

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Background: Endothelial dysfunction is the harbinger of majority of cardiovascular disease. The straight part of an artery is protected from atherosclerosis owing to its laminar blood flow and high shear stress. This study investigated the cytoprotective effects of the new laminar shear medium (LSM) derived from a modified cone-and-plate shear device and identified human aortic endothelial cells (HAECs) secreted basic fibroblast growth factor (bFGF) as the dominant protector of LSM.

Methods: Based on the modified cone-and-plate shear device system, laminar shear (15 dynes/cm2) and static exposed to HAECs for 24 h to produce the new supernatant LSM and static medium (SM). Evaluation of the protective effects of LSM and SM on TNF-α (10 ng/ml) induced endothelial dysfunctions by reactive oxygen species (ROS) inductions, inflammatory monocyte adhesion and tissue factor activity assays. Determination of the ROS induction, inflammation and thrombosis related genes and proteins expressions by Q-PCR and western blots. In order to identify the critical cytokine responded for the cytoprotection of LSM, we carried out the human cytokine antibody arrays and selected high abundance marker cytokine, bFGF to validate different cytoprotective effects by recombinant bFGF (rbFGF) and neutralization by monoclonal antibody (rbFGF+Ab) co-treatments. The aortic and lung tissues from different groups of C57BL/6J mice were examined by immunohistochemistry staining. The SB203580 (specific inhibitor of p38) and BIX 02189 (specific inhibitor of MEK5) were used to identify the cytoprotection effects of bFGF via p38/MAPK and MEK5-KLF2 pathways.

Results: Compared with traditional LSM, the new LSM not only significantly decreased the TNF-α–induced intracellular adhesion molecule 1 and plasminogen activator inhibitor type 1 but

also significantly increased heme oxygenase 1 gene expression. The new LSM and bFGF were demonstrated to attenuate the TNF-α induced ROS inductions, inflammation and tissue factor activity and inhibit the inflammatory and thrombosis related gene/protein expressions in both of *in vitro* and *in vivo* experiments. Mechanistically, the cytoprotective pathway of bFGF was mediated via p38/MAPK and MEK5-KLF2 pathways.

Conclusion: The bFGF was identified as the dominant protector of LSM derives from the modified laminar shear system.