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Title: Del-1 reduces endotoxin-induced polymorphonuclear leukocytes adhesion and mortality

Prof. Yunfeng 4632 Zhao yfzh71@126.com MD ¹, Ms. Liang 4633 Guo guoliang0925@yahoo.com.cn ², Ms. Shaoying 4634 Li shaoyinglikm@163.com ² and Prof. Xueling 4635 Wu wu_xueling@yahoo.com.cn MD ². ¹ Department of Respiratory Medicine, Pudong New Area Gongli Hospital, Shanghai, China, 200135 and ² Department of Respiratory Disease, Xinqiao Hospital, the Third Military Medical University, Chongqing, China, 400037 .

Body: To investigate the role of Del-1 in PMN adhesion in acute lung injury. Human pulmonary micro-vascular endothelium cells (HPMECs) was cocultured with polymorphonuclear leukocytes (PMNs) on HTS Transwell filter plates, then were pre-incubated in presence or absence of recombinant retroviral vector expressing human Del-1 (Retro-hDel-1) or Retro-V(free of any transgenes) before being stimulated with TNF- α (0.732 g ml⁻¹) for 24 hrs. And mice were challenged by intra-peritoneal injection of LPS (15 mg/kg) 48h after gene transfer by Retro-hDel-1 or Retro-v for survival for 7 days. In vitro studies showed the adhesion of PMNs with endothelial cells were significantly inhibited and endothelial permeability were dramatically decreased in Retro-Del-1 group HPMECs compared with that of control cells after TNF- α stimulation. The adhesion was partially inhibited by LFA-1 pathway through the RGD locus of Del-1 confirmed by site-specific mutagenesis. In vivo studies showed that Del-1 messenger RNA and protein concentration in lung were significantly increased after retrovirus-mediated gene delivery. The lung injury score were significantly decreased in Retro-Del-1 group mice compared with Retro-V group mice after LPS injection at 6 hrs, 24 hrs and 48 hrs. In addition Administration of Retro-hDel-1 significantly improved the survival of mice, relative to a control retrovirus. Up-regulation expression of Retro-hDel-1 restored the integrity of micro-vascular and also altered lung edema induced by LPS through the inhibition of adhesion of PMNs with endothelial cells.