• 系統編號	RN9701-3395
• 計畫中文名稱	提昇私校研發能專案計畫---探討氧化態低密脂蛋白在中風疾病過程所扮演的病角色---子計畫一:氧化態低密脂蛋白調控腦內皮細胞 LOX-1 受體表現之分子機制研究(III)
• 計畫英文名稱	Molecular Mechanism of LOX-1 Gene Regulation by Oxidized LDL in Cerebral Endothelial Cells (III)
• 主管機關	行政院國家科學委員會
• 計畫編號	NSC95-2745-B038-001-URD
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• 中文關鍵字	--
• 英文關鍵字	Cerebral endothelial cell; Oxidized LDL; Apoptosis; Bax translocation; Mitochondrial dysfunction; Cytochrome c release; Caspase activation
• 中文摘要	查無中文摘要
• 英文摘要	Cerebral endothelial cells (CECs) are crucial components of the blood-brain barrier. Oxidized low-density lipoprotein (oxLDL) can induce cell injuries. In this study, we attempted to evaluate the effects of oxLDL on mouse CECs and its possible mechanisms. Mouse CECs were isolated from brain tissues and identified by immunocytochemical staining of vimentin and Factor VIII. oxLDL was prepared from LDL oxidation by copper sulfate. Exposure of mouse CECs to oxLDL decreased cell viability in concentration- and time-dependent manners. oxLDL time-dependently caused shrinkage of cell morphologies. Administration of oxLDL to CECs induced DNA fragmentation in concentration- and time-dependent manners. Analysis of the cell cycle revealed that oxLDL concentration- and time-dependently increased the proportion of CECs which underwent apoptosis. Analysis of confocal microscopy and immunoblot revealed that oxLDL significantly increased cellular and mitochondrial Bax levels as well as the translocation of this proapoptotic protein from the cytoplasm to mitochondria. In parallel with the increase in the levels and translocation of Bax, oxLDL time-dependently decreased the mitochondrial membrane potential. Exposure of mouse CECs to oxLDL decreased the amounts of mitochondrial cytochrome c, but enhanced cytosolic ocytochrome c levels. The amounts of intracellular reactive oxygen species were significantly augmented after oxLDL administration. Sequentially, oxLDL increased activities of caspase-9, -3, and -6 in time-dependent manners. Pretreatment with Z-VEID-FMK, an inhibitor of caspase-6, significantly decreased caspase-6 activity and the oxLDL-induced DNA fragmentation and cell

apoptosis. This study showed that oxLDL induces apoptotic insults to CECs via signal-transducing events, including enhancing Bax translocation, mitochondrial dysfunction, cytochrome c release, increases in intracellular reactive oxygen species, and cascade activation of caspase-9, -3, and -6. Therefore, oxLDL can damage the blood-brain barrier through induction of CEC apoptosis via a Bax-mitochondria-caspase protease pathway.