• 系統編號	RC9112-0038
• 計畫中文名稱	氣球擴張術引起老鼠動脈血管內膜增生的研究---比較 Triflavin 和抗 AVB3 單源抗體的相對作用機轉及活性(II)
• 計畫英文名稱	Study of Neointimal Hyperplasia of Balloon Injured Rat Carotid Arteries---Comparison of the Mechanism
• 主管機關	行政院國家科學委員會
• 計畫編號	NSC90-2320-B038-023
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• 研究人員	許準榕 Sheu, Joen-Rong
• 中文關鍵字	血管內膜增生；氣球撐開受傷；頸動脈；內皮細胞；三黃素
• 英文關鍵字	Vascular neointimal hyperplasia；Balloon injury；Carotid artery；Endothelial cell；Triflavin；Abciximab
• 中文摘要	在病人施行冠狀動脈血管造形術(Percutaneous transluminal coronary angioplasty)後，根據統計約有 40-50%的病患常會發生手術血管發生再窄化(Restenosis)的現象；意即進行手術的部位其血管管腔減小，而使心肌的缺血現象產生最後導致心肌梗塞。一般而言，血管再窄化的發生約可分爲 3 個主要步驟，依序爲(1)血管內的彈性回縮作用(Elastic recoil)；(2)血栓的形成(包括血小板的附著、凝集及釋放生長因子)與發炎細胞的侵入；(3)血管中層平滑肌細胞的增生和移動以及細胞外基質蛋白(Extracellular matrix)的擴張。目前有許多的動物實驗利用各種不同的藥物來試圖減少血管再窄化的發生；包括使用抗血小板凝集藥物(如 Aspirin、Ticlopidine)，抗凝血藥、鈣離子通道阻斷劑，降血脂藥物等等；但大多藥物經臨床試驗後發現效果卻不理想。Triflavin 爲一種由出血性的蛇毒(Trimeresurus flavoviridis)中所分離的強效抗血小板凝集蛋白；它本身爲單鍵含有 70 amino acids；在靠近 C 端位置含有 Arg-Gly-Asp(RGD) 這三個 Amino acid 在 Triflavin 抑制血小板凝集過程中扮演了決定性的角色。Triflavin 的作用機轉爲競爭性的抑制 Fibrinogen 和血小板 αIIbβ3 integrin 的結合作用，爲一種專一性的 αIIbβ3 integrin 拮抗劑；因此在活體內亦能有效的防止血栓產生。在之前的研究中發現 Triflavin 於手術一週及二週後可明顯抑制血栓的生成及血管內膜增生；同時，Triflavin 亦可抑制因氣球擴張術所引起的 Thromboxane B2 的增加。αIIbβ3 integrin 本身爲 β3 integrin 的一員，屬於一種附著蛋白受體；它在體內參與了發育(Development)、發炎(Inflammation)與血栓(Thrombosis)等等。在血管再窄化的過程中，有關血管平滑肌的附著和移動；內皮細胞與細胞外基質蛋白的結合，此 αIIbβ3 integrin 都扮演了相當重要的角色。因此本計畫的主要目的，在探討 Abciximab (Anti-αIIbβ3 integrin 單源抗體)對於氣球擴張術後引起大白鼠頸動脈血管內膜增生的抑制作用以及其作用機轉的探討。
• 英文摘要	Recent large-scale trials of percutaneous transluminal coronary angioplasty (PTCA) have emphasized the frequency of stenosis recurrence about

40-50% of patients with percutaneous treatment. Restenosis is the decrease of the vessel lumen at the site of the procedure, thereby leading to induce ischemia. The major steps in the development of restenosis are: (1) elastic recoil; (2) subclinical development of thrombosis (platelet adhesion, aggregation, and release of growth factors) with inflammatory cell infiltration, and (3) medial smooth muscle cell proliferation and migration, followed by extracellular matrix expansion. There are numerous agents have been tested in animal models, such as antiplatelet drugs (aspirin, ticlopidine); antithrombotic drugs (hirudin, heparin); calcium-channel blockers; immunosuppresive agents, hypolipidemic agents; until recently none has translated into benefit in large-scale clinical trials. Triflavin, a potent platelet aggregation inhibitor, was purified from the venom of Trimeresurus flavoviridis. Its sequence contains the Arg-Gly-Asp (RGD) in the carboxyl terminal domain. The RGD sequence of triflavin plays an important role in mediating the binding of triflavin towards glycoprotein IIb/IIIa complex (αIIbβ3 integrin). Triflavin inhibits platelet aggregation by interfering with the interaction of fibrinogen with the αIIbβ3 integrin. It is an effective agent in the prevention of thromboembolism. In our previously described, triflavin significantly inhibited neointimal hyperplasia and lowering the increased of thromboxane A2 formation after balloon angioplasty in rat carotide arteries. αIIbβ3 belongs a β3 integrin family, involves in cell development, inflammation and thrombosis. The αIIbβ3 integrin is thought to play a major role in the adhesion and migration of smooth muscle cells and endothelial cells on extracellular matrices. The present project was designed to determine the inhibitory mechanisms of abciximab (anti-αIIbβ3 integrin monoclonal antibody) in neointimal hyperplasia of balloon injured rat carotid arteries angioplasty.