• 系統編號	RC8803-0011
• 計畫中文名稱	蛇毒蛋白 Triflavin 抑制血小板引起去內皮血管收縮反應及抑制腫瘤細胞移動之機轉探討
• 計畫英文名稱	Mechanism Involved in the Inhibits Platelet-Induced Contraction of Deendothelialized Blood Vessels and Tumor Cell Migration of Triflavin, an RGD-Containing Peptide
• 主管機關	行政院國家科學委員會
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• 研究人員	許準榕 Sheu, Jone-Ron
• 中文關鍵字	蛇毒蛋白；腫瘤細胞移動；RGD 作用區；醣蛋白 IIb/IIa 受體；血管收縮
• 英文關鍵字	Triflavin；Tumor cell migration；RGD motife；Glycoprotein IIb/IIa receptor；Vasoconstriction
• 中文摘要	Triflavin 爲一含 RGD 具有 7.5-kD/sub a/分子量的蛇毒蛋白,亦稱爲 Disintegrin。在本實驗中,凝集的人類血小板懸浮液會依劑量-相關性引起去內皮老鼠的胸主動脈收縮反應。相對的,其他含 RGD 的 Peptide 如 Trigramin 或者合成的 Peptide 如 GRGDS、GRGDSPK 以及 GRGDF 則無此作用。另一方面 Triflavin 亦可明顯抑制血小板凝集時所釋放的 Serotonin 和 Thromboxane A/sub 2/;反之,其他含 RGD 的 Peptide 亦不具明顯的抑制作用(Trigramin、GRGDS、GRGDSPK、GRGDF)。在掃描式電子顯微鏡下可明顯的看到血小板附著到去內皮的血管上;當投與 Triflavin (2.mu.M)後,其附著到血管內皮下層的血小板數目明顯的減少。再者,Triflavin 和其他含 RGD 的 Peptide(包括 Trigramin 和其他合成的 Peptide 可明顯的抑制血小板附著到細胞外基質蛋白(如 Fibronectin、Vitronectin 及 von Willebrand factor)。因此,我們認爲 Triflavin 可以明顯的抑制血小板引起去內皮血管的收縮反應,而其他含 RGD 的 Peptide 卻不行,其原因至少是因 Triflavin 可明顯的抑制血小板活化;因此導致血小板釋放 Serotonin 和 Thromboxane A/sub 2/的量明顯減少。而 Serotonin 和 Thromboxane A/sub 2/都是血管收縮物質;Serotonin 和 Thromboxane A/sub 2/的減少會因此減少去內皮血管的收縮反應。
• 英文摘要	Triflavin, a 7.5-kDa polypeptide purified from snake venom, belongs to a family of (RGD) containing peptides, termed disintegrins. In this study, aggregating human platelets dose-dependently induced vasoconstriction in de-endothelialized isolated rat thoracic aorta. At 5*10/sup 7/ cells/ml, platelets induced a peak tension averaging 65.plmin.7.2% of the tension induced by phenylephrine (10.mu.M). The relative effectiveness of RGD-containing peptides [including venom peptides triflavin and trigramin, small RGD synthetic peptides (GRGDS, GRGDF and GRGDSPK)] was

examined, by testing the inhibitory effect on aggregating platelet-induced vasoconstriction in de-endothelialized aorta. Triflavin (1.mu.M) significantly inhibited the platelet-induced vasoconstriction, whereas neither trigramin (10.mu.M) nor small RGD-peptides (2mM) (i.e., GRGDS, GRGDF as well as GRGDSPK) showed any significant effect. The release of serotonin and the formation of thromboxane A/sub 2/ from aggregating platelets were both significantly inhibited by triflavin (2.mu.M), whereas, trigramin and small RGD-containing peptides showed no significant effect. On scanning electron micrographs of de-endothelialized aorta, aggregating platelets adhered to the subendothelium, with loss of their discoid shape, to form irregular spheres with pseudopod extension. Triflavin (2.mu.M) markedly reduced the adhesion of platelets to the subendothelium in the same aorta. Furthermore, RGD-containing peptides (including triflavin, trigramin and small RGD-containing peptides) inhibited the adhesion of collagen (10.mu.g/ml)-activated platelets to extracellular matrices (i.e., fibronectin, vitronectin and von Willebrand factor). It is concluded that the marked ability of triflavin to inhibit aggregating platelet-induced vasoconstriction in de-endothelialized aorta, may be due at least partly, to triflavin efficiently preventing the activation of platelets subsequent to inhibition of serotonin release and thromboxane A/sub 2/ formation. However, the different abilities of triflavin, as compared with other RGD-containing peptides, was not related to the ability to inhibit the adhesion of platelets to extracellular matrices.