蛇毒蛋白 triflavin 抑制血管平滑肌細胞 PKC 的轉移作用

Inhibitory Effect of Triflavin on Protein Kinase C Translocation in Vascular Smooth Muscle Cells

中文摘要

血管平滑肌細胞屬於貼附型細胞，在其生長過程中，細胞外基質(Extracellular matrix)扮演重要的角色。細胞生長時，經由 integrin receptor(具 a、b 兩個次單元)接受外在蛋白質如 fibronectin 的活化，產生局部附著作用(focal adhesion)，與細胞外基質結合，造成平滑肌細胞的延展(cell spreading)。在這一系列作用中，會造成 protein kinase C pathway 的活化。

本篇論文探討蛇毒蛋白 triflavin，一種含有 RGD (Arg-Gly-Asp)胜肽序列，主要功能在與血小板 GP IIb/IIIa complex 結合達到抑制血小板凝集作用的 disintegrin；將其投與入平滑肌細胞後，應會干擾 fibronectin 與平滑肌細胞之附著情形；並與抗凝血製劑 ReoPro® (Abciximab)對平滑肌細胞和 fibronectin 附著情形的影響做一比較。藉由細胞免疫染色及共軛聚焦顯微鏡技術的應用，觀察此反應中，protein kinace C family 是否受到活化及其分佈情形,證明 triflavin 與一般已知的人工 RGD 蛋白序列,對於平滑肌細胞上 integrin receptor 產生相同的抑制效果。

Fibronectin 刺激造成平滑肌細胞中 protein kinase C 產生一短暫升高並轉移到附著作用發生處，事先給予 RGD peptides 可抑制此情形。若改以 triflavin 事先投與，其對 protein kinase C 的表現也有明顯的抑制作用；且抑制功效不亞於 ReoPro® 造成的抑制成果，甚至更好。證明 triflavin 可成功結合到平滑肌細胞的 integrin 上，達到抑制平滑肌細胞生長。

英文摘要

The extracellular matrix influences the cellular spreading of vascular smooth muscle cells (VSMCs) via integrin receptors. We know that VSMCs binding to fibronectin activates the protein kinase C (PKC) pathway, causes differential intracellular PKC isoform translocation, and mediates cell spreading. On this study, VSMCs binding to poly-L-lysine was used as control. We used commercial GRGDS peptides and RGES peptides to prove that the PKCa distribution and VSMCs spreading is mediated by integrin activation. Intracellular distribution of PKC isoforms was measured by confocal microscopy. VSMCs binding to fibronectin induced focal adhesion and cell spreading within 30 minutes. Fibronectin induced a PKC isoform translocation to the cell nucleus and to focal adhesions within 30 minutes. In our previous report, triflavin could specifically bind on platelet GP IIb/IIIa receptor. It was a strong and specific disintegrin. Preincubated VSMCs with triflavin, and then measured the PKC

distribution by confocal microscope. We observed triflavin inhibit the distribution of the PKC isofroms in VSMCs. It also inhibited the spreading of VSMCs. We compared triflavin with ReoPro®. We could say that the inhibitory effect of triflavin was stronger than ReoPro®.