• 系統編號 RC8703-0415

- •計畫中文名稱 腸胃黏膜細胞的癒合,適應與成熟(III)
- 計畫英文名稱 The Healing, Adaptation and Maturation of Rat Gastrointestinal Mucosal Cell. (III)

• 主管機關 行政院國家科學委員會

- 執行機構 台北醫學院細胞及分子生物研究所
- •本期期間 8508 ~ 8607
- 報告頁數
 0頁

• 中文摘要

使用語言 英文

NSC86-2314-B038-022

計書編號

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• 中文關鍵字 腸胃黏膜細胞;癒合;Bcl-2蛋白;多元胺;細胞凋亡;消化性潰瘍;轉穀氨醯胺?;腐胺

• 英文關鍵字 Gastrointestinal mucosa; Healing; Bcl-2 protein; Polyamine; Apoptosis; Peptic ulcer; Transglutaminase; Putrescine

動物細胞內有一種組織性轉麩胺?,在鈣離子的促進下使蛋白質分子內之 Glutamine 和另一蛋白質之 Lysine 間產生共價交聯,而形成.epsilon.-(.gamma.-glutamyl)-lysine isopeptide bond,或使多胺素的兩端氨基與兩蛋白質分子之 Glutamine residues 間形成交聯。據報導腸胃黏膜在糜爛的康復過程中,轉麩胺?之活性升高,但此?活性受抑制時糜爛的康復也因而延緩。同時本實驗室又發現一種細胞質內的類轉 数胺?,此?不需鈣作其輔因子即可使多胺素嵌入蛋白質結構上。因而我們觀研了這兩種酵素在因心理壓力引發的腸胃黏膜糜爛與康復過程中其活性的變化,以期歸結出這些酵素在腸胃糜爛與復原過程中可能扮演的角色。實驗結果顯示,需鈣與不需鈣的轉麩胺?之活性在Stress 引發糜爛後之康復初期有顯著的活化現象。 很多文獻指出在細胞開始凋亡(Apoptosis)時需鈣的組織性轉麩胺?有活性驟增的現象。因而我們猜測十二指腸黏膜糜爛時,那些受損細胞必先凋亡,才有空間讓健康的黏膜細胞移位,再促使隱窩內黏膜原細胞增生,進而修復 組織。為了觀研此假設是否成立,我們以轉麩胺?之抗體,以免疫組織染色法來為轉麩胺?在十二指腸黏膜之所在處訂位。同時也以 Turnel 的方法來測試十二指腸組織是否有 DNA 斷裂的現象。結果顯示,在修護初期轉麩胺?的免疫染色增強與其活性增高的數據吻合。同時 Turnel method 及 DNA analysis 的結果表現了十二指腸黏膜確有 DNA 斷裂的現象。 所得結果與我們的假設相符合。在修復初期,十二指腸黏膜細胞確實有規則性 DNA 碎斷的現象,顯示細胞有凋亡的傾向。轉麩胺?之活性在黏膜康復過程中也增高了。其活化也許與受傷細胞之凋亡有關。另外,不需鈣的轉麩胺?在十二指腸黏膜糜爛和修復過程中可能扮演的角色有待更進一步探研。

• 英文摘要 Trasglutaminases (TGase) are a family of calcium-dependent enzymes. They catalyze the formation of .epsilon.-(.gamma.-glutamyl)-lysine isopeptide bond between the glutamyl and lysyl residues of two polypeptides/proteins. TGase also promotes protein crosslinking through the

interaction between the terminal amino groups of polyamine and glutamyl residues of two molecules of polypeptide/protein, using the back bone of polyamine as crossing bridge. TGase activity increased during the healing of duodenal mucosa from stress-induced erosion. The healing delayed when rats were treated with monodansylcadaverine to inhibit duodenal TGase activity, indicating that TGase may play a role in the healing process. In this laboratory, a calcium-independent transglutaminase-like enzyme has been identified. It is capable of incorporating [/sup 3/H] -putrescine into proteins in the absence of calcium. Therefore, it is intended to investigate the possible role(s) of both TGase in the course of duodenal mucosal erosion and healing. The data obtained from this study show that both calcium-dependent and independent TGases were stimulated during the early phase of duodenal mucosal healing from stress-induced erosion. The data need to be further substantiated. On the other hand, numerous data have documented that the activity of calcium-dependent TGase increased during apoptosis. It is, thus, speculated that the apoptosis of mucosal cells damaged by stress is essential for the healthy cells to migrate into the vacant space followed by proliferation of cryptic cells. To test this speculation, TGase antibody has been used to localize TGase along the cryptic-villus axis of rat duodenal mucosa during the course of stress-induced erosion and subsequent healing using immuno-histochemical staining method. In addition, turnel method and agarose gel analysis of extracted cellular DNA were also employed to determine whether apoptosis occurred. Data from the above studies demonstrated that the increased TGase staining is correlated with the increased staining by turnel method as well as the appearance of typical DNA ladder in agarose gel. Finally, the calcium-dependent and independent transglutaminase activities are stimulated during the course of stress-induced erosion and healing. The increase in calcium-dependent activity is correlated with the increased staining for the number of DNA ends and TGase molecules, as well as the appearance of DNA ladders. It is, thus, concluded that apoptosis is associated with the process of duodenal mucosal erosion and the early phase of healing.