細胞因子信號傳遞抑制體 3(SOCS-3)在脊髓經損傷、甲基去氫氧化可體松(MP)、或紅血球生成素(EPO)投予後的表現

The expression of suppressor of cytokine signaling-3 (SOCS-3) in spinal cord following injury, MP or EPO treatment

中文摘要

脊髓損傷(Spinal cord injury)是目前醫界所面臨極大的難題，病人往往有相當嚴重的後遺症，造成社會家庭嚴重的經濟負擔與精神損失，然而醫學界目前並無任何積極有效的治療方法。甲基去氫氧化可體松(Methylprednisolone)是目前唯一經美國食品藥物檢驗局所核准用來治療急性脊髓損傷的藥物，然而其詳細的機制不明，療效也似乎相當有限。

紅血球生成素 (erythropoietin, EPO)對於神經保護的研究已被廣泛的報告與驗證，其機制似乎是透過 Bcl-XL，STAT-5 及 NFkB 等抗細胞凋亡(anti-apoptotic)的路徑所達成，然而其對脊髓損傷的詳細保護機制依然不明。藉由 cDNA microarray 的技術，我們的初步研究發現在脊髓損傷的動物中，有一些特殊的基因被活化，其中包括 SOCS-3，過去有報告指出：剔除 SOCS-3 基因的老鼠在經過脊髓損傷之後，受損的行動能力有明顯地改善。因此本研究即在找出 SOCS-3 在脊髓損傷中所扮演的角色，並探討對脊髓損傷有保護作用的 MP 及 EPO 是否會影響 SOCS-3 在受傷脊髓的展現。

我們選用大鼠的動物脊髓損傷模式，分成兩個實驗：第一個實驗探討脊髓損傷及 MP 是否會影響受傷脊髓 SOCS-3 蛋白質的展現；第二個實驗探討 EPO 是否會影響受傷脊髓 SOCS-3 蛋白質的展現。我們的研究結果發現，在脊髓損傷後，SOCS-3 蛋白質在受傷的脊髓顯著的增加，在投予 MP 或 EPO 之後，SOCS-3 蛋白質在受傷脊髓的表現量減少。因爲 MP 或 EPO 過去被認定對脊髓損傷有保護的作用，且去除 SOCS-3 基因已被證實可改善脊髓損傷動物的後肢行動能力。根據我們的研究結果，我們推測：MP 或 EPO 對脊髓損傷的保護作用至少有一部分是透過降低 SOCS-3 蛋白質的表現量來達成的。如果此理論可行，未來 Anti-SOCS-3 antibody 或 SOCS-3 siRNA 的應用將對脊髓損傷病患帶來新的治療契機。

英文摘要

Spinal cord injury (SCI) is an important and serious medical issue. SCI results in significant dysfunction and disability of patients. It affects not only the SCI patients, but also their caring family members and society. It makes tremendous economic costs and gives caregiver huge burden and stress.

There is no aggressive treatment for SCI. High dosage of Methylprednisolone (MP) is the only therapeutic regimen approved by FDA for acute spinal cord injury. Its definite mechanism for neuro-protection remains unclear.

Erythropoietin (EPO) also has protective effects on SCI. It seems to protect cells through JAK2, STAT5, Ras, PI3K, MAPK, AKT/PKB, and NF-kB pathway. Its definite mechanism for protection of spinal cord is still unknown.

From the result of cDNA microarray, we find several genes up-regulated after spinal cord injury, including SOCS-3. A study has reported a significant improvement in functional recovery in SOCS-3 knock out mice, suggesting that SOCS-3 plays a detrimental role in spinal cord injury.

Our study aimed to investigate if SCI induces the expression of SOCS-3 in the injured spinal cords and if MP or EPO affects the expression of SOCS-3 in injured spinal cord.

Our results showed that SCI led to a significant increase of SOCS-3 protein expression in the injured spinal cord. Application of MP or EPO attenuated the SCI-induced expression of SOCS-3. Because deletion of SOCS-3 gene promotes functional recovery after SCI, our findings strongly suggest that MP or EPO may exert its neuroprotective effect on SCI via inhibition of SOCS-3 protein.