FXYD2 基因在脊髓損傷所扮演角色之探討

Investigation of the role of FXYD2 gene in functional recovery of mice with spinal cord injury

中文摘要

嚴重的脊髓損傷會造成患者四肢或下肢癱瘓、行動不良，除了對患者在經濟上造成重大負擔外，更嚴重的影響病人及照顧家人的生活品質。甲基去氫氧化可體松(methylprednisolone, MP)是目前唯一經美國藥物暨食品檢驗局所核准用來治療急性脊髓損傷的藥物，然而 MP 對脊髓損傷的保護機制到目前爲止卻仍不清楚。本實驗室的初步研究指出脊髓損傷於 4 小時後造成 FXYD2 基因的展現增加，然而在脊髓損傷後十分鐘內給予 MP 治療， FXYD2 的基因展現於 4 小時後便回復到正常範圍。因此，本研究論文想要探討 FXYD2 基因在脊髓損傷上所扮演的角色。我們使用成年剔除 FXYD2 基因的基因轉殖小鼠及同胎的正常小鼠做爲實驗對象，我們使用 IH Impactor 以 60 K 達因的力量在小鼠的第十二節胸椎的脊髓處造成脊髓損傷，我們於手術前及手術後的第 1、4、7、10、14、21、28、35 及 42 天觀察其後肢行動能力恢復之情形，並在脊髓損傷後的第 42 天將小鼠犧牲取出脊髓檢查脊髓損傷之情形。我們的研究結果顯示，剔除 FXYD2 基因的小鼠於脊髓損傷後，從第 14 天開始一直到第 42 天爲止，其後肢行動能力比正常小鼠來得好，且其脊髓損傷面積也比正常小鼠來得小。此外，剔除 FXYD2 基因在受傷脊髓處似乎保留更多的髓磷脂(myelin)。我們的研究結果證明剔除 FXYD2 基因對受傷脊髓具有保護的作用。

英文摘要

Severe spinal cord injury (SCI) often causes tetraplegia or paraplegia, which dramatically decreases the quality of life of the SCI patients and their caring members. Up to now, methylprednisolone (MP) is the only FDA-approved drug for treating acute spinal cord injury. However, the neuroprotective mechanisms of MP on spinal cord injury are still poorly understood. Our preliminary data indicated that the FXYD2 gene was up-regulated 4 h after spinal cord injury and MP treatment inhibited the SCI-induced expression of FXYD2 gene. In this study, we tested the hypothesis that deletion of FXYD2 gene affects the functional recovery of SCI mice using the FXYD2 knockout mice. Spinal cord injury was induced at T12 by the force of 60 K dynes delivered by IH Impactor. The locomotor activity of animals was evaluated before and 1, 4, 7, 10, 14, 21, 28, 35, and 42 days after SCI. After the last evaluation of locomotor function, SCI mice were sacrificed and spinal cords were processed for assessment of lesion area and the preserved myelin. Our results showed that FXYD2 knockout mice displayed better locomotor recovery than the wild-type littermates.

Moreover, deletion of FXYD2 gene resulted in a smaller lesion area. Our findings demonstrate that deletion of FXYD2 gene has a beneficial effect on spinal cord injury.