FACULTAD DE CIENCIAS DE LA SALUD

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Resumen. La respuesta inflamatoria es probablemente uno de los principales eventos destructivos que ocurren después de una lesión de la médula espinal (LME). Su progresión depende en gran medida de la respuesta autoinmune desarrollada contra los componentes neuronales. Por lo tanto, la modulación o la inhibición de esta respuesta autorreactiva podrían ayudar a reducir la destrucción del tejido. La desviación inmune asociada a la cámara anterior (ACAID, por sus siglas en inglés) es un fenómeno que induce la tolerancia inmunológica a antígenos inyectados en la cámara anterior del ojo, lo que provoca la reducción de dicha respuesta inmune. A la luz de esta noción, la inducción de la ACAID a los componentes neuronales podría utilizarse como una terapia profiláctica potencial para promover la neuroprotección. Para evaluar este enfoque, se llevaron a cabo tres experimentos. En el primero se evaluó la capacidad de inducir la ACAID del extracto de médula espinal (EME) y de la proteína básica de mielina (PBM). Utilizando la prueba de hipersensibilidad retardada (PHR), demostramos que tanto el EME como la PBM fueron capaces de inducir la ACAID. En el segundo experimento, se evaluó el efecto de la ACAID inducida por el EME en la recuperación neurológica y morfológica después de la LME. En los resultados, hubo una mejora significativa de recuperación motora, hipersensibilidad nociceptiva y supervivencia de motoneuronas en ratas con ACAID inducida por el EME. Además, la ACAID también propició la sobrerregulación de la expresión de los genes que codifican las citocinas antiinflamatorias y el FoxP3, pero produjo la infrarregulación de aquellos que codifican las citocinas proinflamatorias. Finalmente, en el tercer experimento se evaluó el efecto de una estrategia más simple y práctica: la ACAID inducida por la PBM. También encontramos resultados neurológicos y morfológicos significativos. En este

estudio demostramos que la inducción de la ACAID contra antígenos neuronales en ratas promueve la neuroprotección después de la LME.

Abstract. The inflammatory response is probably one of the main destructive events occurring after spinal cord injury (SCI). Its progression depends mostly on the autoimmune response developed against neural constituents. Therefore, modulation or inhibition of this self-reactive reaction could help to reduce tissue destruction. Anterior chamber associated immune deviation (ACAID) is a phenomenon that induces immune-tolerance to antigens injected into the eye´s anterior chamber, provoking the reduction of such immune response. In the light of this notion, induction of ACAID to neural constituents could be used as a potential prophylactic therapy to promo Abstract The inflammatory response is probably one of the main destructive events occurring after spinal cord injury (SCI). Its progression depends mostly on the autoimmune response developed against neural constituents. Therefore, modulation or inhibition of this self-reactive reaction could help to reduce tissue destruction. Anterior chamber associated immune deviation (ACAID) is a phenomenon that induces immune-tolerance to antigens injected into the eye´s anterior chamber, provoking the reduction of such immune response. In the light of this notion, induction of ACAID to neural constituents could be used as a potential prophylactic therapy to promote neuroprotection. In order to evaluate this approach, three experiments were performed. In the first one, the capability to induce ACAID of the spinal cord extract (SCE) and the myelin basic protein (MBP) was evaluated. Using the delayed type hypersensibility assay (DTH) we demonstrated that both, SCE and MBP were capable of inducing ACAID. In the second experiment we evaluated the effect of SCE-induced ACAID on neurological and morphological recovery after SCI. In the results, there was a significant improvement of motor recovery, nociceptive hypersensitivity and motoneuron survival in rats with SCE-induced ACAID. Moreover, ACAID also up-regulated the expression of genes encoding for anti-inflammatory cytokines and FoxP3 but down-regulated those for pro-inflamatory cytokines. Finally, in the third experiment, the effect of a more simple and practical strategy was evaluated: MBP-induced ACAID, we also found significant neurological and

morphological outcomes. In the present study we demonstrate that the induction of ACAID against neural antigens in rats, promotes neuroprotection after SCI. te neuroprotection. In order to evaluate this approach, three experiments were performed. In the first one, the capability to induce ACAID of the spinal cord extract (SCE) and the myelin basic protein (MBP) was evaluated. Using the delayed type hypersensibility assay (DTH) we demonstrated that both, SCE and MBP were capable of inducing ACAID. In the second experiment we evaluated the effect of SCE-induced ACAID on neurological and morphological recovery after SCI. In the results, there was a significant improvement of motor recovery, nociceptive hypersensitivity and motoneuron survival in rats with SCE-induced ACAID. Moreover, ACAID also up-regulated the expression of genes encoding for anti-inflammatory cytokines and FoxP3 but down-regulated those for pro-inflamatory cytokines. Finally, in the third experiment, the effect of a more simple and practical strategy was evaluated: MBP-induced ACAID, we also found significant neurological and morphological outcomes. In the present study we demonstrate that the induction of ACAID against neural antigens in rats, promotes neuroprotection after SCI.