Selective Nanovector Mediated Treatment of Activated Proinflammatory Microglia/ Macrophages in Spinal Cord Injury

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ABSTRACT

Much evidence shows that acute and chronic inflammation in spinal cord injury (SCI), characterized by immune cell infiltration and release of inflammatory mediators, is implicated in development of the secondary injury phase that occurs after spinal cord trauma and in the worsening of damage. Activation of microglia/macrophages and the associated inflammatory response appears to be a self-propelling mechanism that leads to progressive neurodegeneration and development of persisting pain state. Recent advances in polymer science have provided a huge amount of innovations leading to increased interest for polymeric nanoparticles (NPs) as drug delivery tools to treat SCI. In this study, we tested and evaluated *in vitro* and *in vivo* a new drug delivery nanocarrier: minocycline loaded in NPs composed by a polymer based on poly-ε-caprolactone and polyethylene glycol. These NPs are able to selectively target and modulate, specifically, the activated proinflammatory microglia/macrophages in subacute progression of the secondary injury in SCI mouse model. After minocycline-NPs treatment, we demonstrate a reduced activation and proliferation of microglia/macrophages around the lesion site and a reduction of cells with round shape phagocytic-like phenotype in favor of a more arborized resting-like phenotype with low CD68 staining. Treatment here proposed limits, up to 15 days tested, the proinflammatory stimulus associated with microglia/macrophage activation. This was demonstrated by reduced expression of proinflammatory cytokine IL-6 and persistent reduced expression of CD68 in traumatized site. The nanocarrier drug delivery tool developed here shows potential advantages over the conventionally administered anti-inflammatory therapy, maximizing therapeutic efficiency and reducing side effects.