Title: Novel Targeting Nanotherapeutics to Improve Functional Recovery and Reduce Side Effects after Acute Spinal Cord Injury

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Abstract:

INTRODUCTION: Spinal cord injury (SCI) is a catastrophic medical problem that leads to loss of sensory, motor, and autonomic functions. To date, no therapy has been proven to be efficacious in fully restoring neurological functions post SCI. Systemic high-dose methylprednisolone (MP) treatment improves neurological recovery after acute SCI in both animal and human. The utility of high-dose systemic MP in acute SCI remains controversial due to its modest effect on functional recovery and the accompanying adverse effects.

PURPOSE: To overcome the limitation of MP therapy, we have developed a *N*-(2-hydroxypropyl) methacrylamide copolymer-based MP prodrug nanomedicine (Nano-MP) that can selectively deliver MP to the inflamed SCI site when administered systemically in a rat model of acute SCI, aiming to improve the therapeutic efficacy of MP while minimizing unwanted distribution to and actions on other tissues, thereby, reducing untoward side effects.

METHODS: Nano-MP was synthesized. Both complete spinal cord transection and moderate contusion SCI models were used. Immediately after SCI, a single dose of Nano-MP was administered to the SCI rats via intravenous (i.v.) injection. Unconjugated MP and vehicle were subjected to a bolus i.v. injection and followed by 24-h infusion with the Bracken protocol.

RESULTS: After a single i.v injection, Nano-MP preferentially accumulated to the SCI injury site, sequestered and retained mainly by $CD11^+$ infiltrating inflammatory cells. The Nano-MP significantly inhibited lipid peroxidation and inflammation of the injured spinal cord, resulting in reduced neuronal damage and enhanced neuroprotection after acute SCI. Compared to conventional i.v delivery of free MP, Nano-MP administration provided better functional improvement after acute SCI in rats and had far fewer systemic adverse side effects—that is, reduced muscle atrophy, bone loss, and less carbohydrate intolerance.

CONCLUSION: Nano-MP is a promising drug candidate that is more effective and safer than standard MP therapy and it may be translated as a new treatment for SCI patients to improve functional recovery, social independence, and quality of life.

Biography:

Dr. Qin is a professor at the Icahn School of Medicine at Mount Sinai & James J. Peters Veteran Affairs Medical Center, based in New York City. Dr. Qin received his M.D. degree from Fujian Medical University, China, and his Ph.D. degree from Kanazawa University, Japan. Dr. Qin is a recognized authority on studying neuromusculoskeletal disorders after spinal cord injury (SCI). Since 2007, Dr. Qin has evaluated mechanisms of bone loss after SCI and has developed pharmacological interventions to block bone loss or restore bone mass after SCI. More recently, Dr. Qin has developed a novel cutting-edge nanomedicine approach for drug-targeted delivery as more efficacious and safer method to provide neuroprotection and functional recovery in acute SCI. Dr. Qin recently also discovered a novel mechanism of muscle-bone crosstalk in maintaining homeostasis of the local musculoskeletal environment through osteocytes by the generation and release of microRNAs from extracellular microvesicle-exosomes.