Targeted Drug Delivery for Spinal Cord Injury Using Retrograde Transport of a Nanoconjugate

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Respiratory problems such as pneumonia, septicemia, and pulmonary emboli are the leading causes of death in humans after spinal cord injury (SCI). Persistent respiratory recovery in rats can be achieved by multiple administrations of theophylline class of drugs. This suggests that chronic drug administration induces functional plasticity in the respiratory circuitry. It was determined that while theophylline worked in humans in a similar manner as in rats, most SCI patients could not tolerate theophylline when the drug was delivered systemically at standard therapeutic dose levels.[1] To directly address the problem of the side effects following systemic drug therapy in cervical SCI patients being treated for respiratory muscle weakness, we developed a novel approach that combines nanotechnology with proven neurobiological principles to selectively target the lower motor and premotor neurons responsible for diaphragm function.[2,3] Our nanotherapeutic design consists of a targeting transporter protein, wheat germ agglutinin conjugated to horseradish peroxidase (WGA-HRP), chemically conjugated to a gold nanoparticle (AuNP), which in turn is chemically conjugated to a pro-drug, pro-theophylline or pro-DPCPX. Our targeted drug administration can induce recovery of the hemidiaphragm in SCI rats by using a fraction of the systemic dose necessary to induce the same recovery. For comparison, the systemic dose of theophylline in rats is 15 mg/kg, while the theophylline content in the nanoconjugate is only 0.12 mg/kg. The systemic dose of DPCPX in rats is 0.1 mg/kg, while the DPCPX content in the nanoconjugate is 0.15 μg/kg, ~ 0.1% of the systemic dose. In addition, the nanoconjugate is capable of inducing persistent recovery after only one injection. Our effort is part of an accelerating trend to translate basic nanoscience discoveries into nanotherapeutic products.

References:

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