Nanotechnology applied to Spinal Cord Injury Treatments
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Abstract

The Nanotechnology research project has demonstrated delivery of drugs only to the phrenic nerve cells that induce spinal cord functional recovery. This is accomplished by synthesizing gold nanoparticles that link drugs with a transporter protein targeting the phrenic nerve cells.

A spinal cord injury interrupts the axons necessary for breathing that connect the nerve cells in a brainstem (medulla) center and the phrenic motor neurons, and this causes paralysis of the diaphragm making breathing difficult. A transporter protein, wheat germ agglutinin conjugated to horseradish peroxidase (WGA-HRP), was discovered by our collaborator, Dr. Harry Goshgarian, to be taken up by the phrenic axons in the diaphragm and transported back to the phrenic motor neurons in the spinal cord. Theophylline represents a major class of drugs to treat patients with spinal cord injury by stimulating phrenic nerve cells and contraction of the paralyzed diaphragm. However, there are deleterious side effects of the drug in humans including stomach pains, insomnia, and nausea. These effects are not caused by stimulating the respiratory centers, but rather by stimulating several other central nervous system centers after the drug is injected systemically. Thus, the problem confronting us is not with the drug, but rather how to apply the drug so that ONLY the respiratory centers would be exposed to the drug.

We have demonstrated a breakthrough technology that specifically delivers drugs to ONLY the phrenic nerve cells and the nerve cells that stimulate them to induce recovery. Dr. Mao’s laboratory has synthesized three-part nanoconjugate comprising of 1) WGA-HRP, 2) gold nanoparticles, and 3) a form of theophylline, pro-theophylline. The WGA-HRP is known as the “transporter”, the gold nanoparticles are the “coupler”, and the pro-theophylline is the “recovery inducing drug”. The nanoconjugate was injected into the paralyzed diaphragm of rat models to induce recovery. The WGA-HRP component of the nanoconjugate selectively transports the conjugate to the phrenic nerve cells (and nowhere else). The amount of drug delivered to the respiratory centers exclusively is less than 0.4% of the total free drug necessary to induce recovery in rats after systemic injection. The idea is the small amount of drug used should reduce or completely eliminate the side effects of drug administration suffered by humans. Our ongoing research is aimed at optimizing this technique so that it may be developed for clinical/human use. We have filed a patent based on this technology. We are the only lab in the world that has successfully demonstrated a nanotechnology solution for functional recovery of breathing in spinal cord injury, which no cures currently exist.