Development of Nanoparticle and Nanowire Technologies to Treat Spinal Cord Injury

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Introduction

The zebrafish model, which has been used for neural degeneration/regeneration research [1], is of potentially great value because of its relative simplicity, transparency and regenerative capabilities. The transparency of the zebrafish CNS and the identifiable brainstem and spinal neurones make this an ideal preparation to evaluate regenerative delivery (Figures 1 & 2) of nano-therapeutics and subsequent enhancement of substantive animal regeneration using gene therapy. Such evaluations are deemed critical to the development of new therapeutic approaches for treating spinal cord injury and other neurological disorders.

Goal: Delivery and expression of therapeutic genes specifically to damaged descending neurones.

Proposed Methodology:
1. Rely on bulk uptake of particles by patent openings of severed axons [4]
2. Evaluate uptake of gold nanoparticles (NP) and utility of stabilizing agents
3. Evaluate particle-agglomeration, size optimization and plasmid transport
4. Use fluorescent proteins to visualize efficacy of gene delivery and expression to neuronal cell bodies of injured axons

Results & Conclusion

Applications of Nanoparticle Arrays to Neuronal Networks Include:
- Vertically arranged nanoelectrode array
- High spatial & temporal resolution
- Capability to stimulate and record from several different sites on a neuron
- Study of live neuronal activity at the subcellular level in single neurons & neuronal networks

Results & Conclusion

We evaluated whether either gold NPs would be feasible in regards to:
1) visualization inside the spinal cord of intrathecal using optical microscopy
2) neuronal delivery via bulk injections into the spinal cord of larval zebrafish
3) regenerative transport from the spinal injury site to neuronal cell bodies in brainstem

Schematic of Gold Nanoparticles and Transport Characterization

Results of Gold Nanoparticles

Linear Relationship: Increase in current results in an increase in voltage. Net Resistance calculated from the slope of the line is 80 kΩ.

Growth of Primary Hippocampal Cultures on Nanoparticle Arrays

Calcium Imaging to Measure Neuronal Activity

Synaptic Connectivity of Neuronal Cells

Calcium Imaging to Measure Neuronal Activity

Calcium imaging of neurons using either nanowires or nanoparticle arrays can be used to track synaptic activity. This can be achieved by staining either the neuron or the nanowire array with calcium-sensitive dyes or by using optogenetics.

Development of Nanoparticle Devices should help us to:
- Understand the information processing capabilities of both single nerve cells and systems of nerve cells
- Advance our understanding of how specific patterns of neural activity associated with learning and memory are created
- Comprehend the mechanisms of plasticity within neuronal networks

Literature Cited


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