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BDNF gene therapy vectorized by neuron-targeted nanoparticles is neuroprotective in the context of nerve injury

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The application of biomaterials in neurosciences has given so far a substantial contribute to the development of implantable and interfaceable devices dedicated to the restoration of a number of neural functions. But the use of biomaterials in the context of nervous system regenerative medicine is still in its infancy. We have been dedicated to using nano-enabled solutions to the design of new therapeutic approaches towards the enhancement of the process of nerve regeneration.

In this presentation we put forward a novel non-viral biomaterial-based nanoparticle for neuron-targeted retrograde gene delivery based on a thiol trimethylated chitosan (TMCSH). The nanoparticles were grafted with the non-toxic carboxylic fragment of the tetanus neurotoxin (HC) to allow neuron targeting, which has been confirmed by molecular recognition force spectroscopy [1]. Using a microfluidic platform we have shown the capacity of these nanoparticles to be retrogradely transported to the cell body of dorsal root ganglia neurons after a peripheral administration. Finally, the performance of this targeted nanoformulation to deliver therapeutic genes to peripheral neurons and rescue them from degeneration was explored *in vivo,* in a peripheral nerve crush injury animal model, using as therapeutic transgene a plasmid DNA encoding for the brain-derived neurotrophic factor (BDNF). Using this animal model, in which nerve degeneration and regeneration occurs in a well-established cascade of events, we were able to establish the effect of the proposed nanoparticles in protecting peripheral nerves from degeneration, enhancing the speed of nerve regeneration and functional recovery.

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