NerVesicle

Engineered Extracellular Vesicles as a Novel Treatment Option for Peripheral Nerve Injury

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Projektbeschreibung

Injuries to the peripheral nerves often have devastating impact on the patients. The gold standard for treatment of nerve injuries is the surgical reconstruction of segmental nerve defects with an autologous nerve transplant. This may lead to lifting morbidities such as sensitivity deficits and scarring. Another difficulty is the limitation of the resources available. Alternatively, possibilities are being sought to improve peripheral nerve regeneration (molecular biological, cell-based, through electrical or mechanical stimulation, etc.). A promising approach is the use of extracellular vesicles (EVs). As a transport vehicle for various cell components such as proteins, growth factors, mRNA and microRNA, they play an important role in the exchange of information between cells and are therefore an ideal therapeutic agent for peripheral nerve injuries. The positive influence of EVs on the nervous system and the regeneration of the nerves have been highlighted in several papers. Extracellular vesicles induce the neural differentiation of stem cells and are able to prevent the degeneration of peripheral nerves to some extent. Furthermore, they have a direct effect on injured nerves and accelerate their regeneration by influencing the differentiation of Schwann cells, the glial cells of the peripheral nervous system, into specific repair Schwann cells.
We hypothesize that specifically modified extracellular vesicles can independently reach a peripheral nerve defect after intravenous administration and have a positive effect on nerve regeneration upon uptake by Schwann cells.
The present project investigates extracellular vesicles (EVs), with targeted mutation in a EV-specific transmembrane protein to provide an increased binding affinity to laminin, a glycoprotein on the basement membrane of Schwann cells. For this purpose, laminin-binding EVs are produced in immortalized Wharton’s Jelly mesenchymal stem cells and their binding and absorption by Schwann cells is assessed in vitro. The EVs with the best uptake profile are then used in vivo in a rat median nerve model to analyze their homing, the specific attachment of EVs in the nerve defect, and their proregenerative effectiveness. For this purpose a 7 mm long segment of the median nerve on the right is resected at the level of the upper arm and reconstructed using an autologous nerve transplant or a muscle-vein conduit. The extracellular vesicles described are administered intravenously via the tail veins. The accumulation of the extracellular vesicles within the animal model is then examined and analyzed. We assume that by successfully modifying the surface proteins of the EVs, they explicitly target the neural injuries and have a positive effect on regeneration.
We are convinced that a successful targeted modification of the extracellular vesicles represents a new technology, not only

for the therapy of nerve injuries, but also in other areas of tissue regeneration and degenerative diseases.

Projektpartner

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