Hyaluronic based hydrogel for regeneration of peripheral nervous tissue

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Resumo:
Peripheral nervous system is responsible for communication between the central nervous system and the human organism. When these nerves are damaged, communication with the associated organ is interrupted, resulting in loss of site function. The implantation of tubular prosthesis has been investigated aiming to help nerve regeneration [1]. Polymer materials has been largely studied for biomedical application since they can be modulated in order to have characteristics similar to the live tissues. In this sense, surface characteristics play a fundamental role during adsorption of proteins and substrate-cell interaction [2]. Thus, in this work, the use of a hyaluronic acid hydrogel as substrate for nervous cells growth was investigated. Hyaluronic acid is a linear polysaccharide that is present in the interior and surface of cells and in the extracellular matrix. It participates of regulation of several cellular processes, like proliferation and differentiation [3]. In addition, hydrogels are excellent substrates for cell growth since the spatial array of polymer chains are capable to locate cells and make available the flow of nutrients and metabolic residues. So, 3D matrices like hydrogels can interact with cells in all directions, with many advantages during the cell growth and tissue formation, since it induces a cell morphology closest to the in vivo morphology. So, Michael addition reaction was used to modify a 60 kDa hyaluronic acid (HA) with divinyl sulfone. The reaction product was purified by dialysis in a 0.15 M NaCl solution followed by distilled water and centrifuged to 5000 rpm for 10 minutes. Quantification of this modified HA was carried out using the Ellman's reagent, indicating that 22.75% of hydroxyl groups of HA were modified with the vinyl sulfone (HA-VS). Adhesion RGD peptide and a metalloproteinase (MMP) crosslinking agent was then added to the HA-VS generating the hydrogel. It was observed that RGD peptide improved neural crest stem cells dispersion through the hydrogel in vitro assays. Electrospun tubes–HA hydrogel systems were implanted in sciatic nerves of rats. After 14 days, cells extended 1 mm long inside the tubes, but stopped growing and dyed after 26 days.