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Peripheral nerve injuries often result in sensory and motor dysfunction in respective parts of the body. So far, peripheral nerve regeneration is often associated with poor functional recovery. Important facilitators of the regeneration process are Schwann cells (SCs), which basement membrane is chiefly comprised of laminin. Extracellular vesicles (EVs) are considered important for intercellular communication and transfer of biological information. Mesenchymal stem cell-derived EVs (MSC-EVs) have been identified as a new therapeutic option due to their function as a drug delivery system. However, the precise delivery of EVs to the site of interest upon administration remains challenging. To overcome this issue, overexpressed EV surface marker protein CD81, from the tetraspanin protein family, has been modified toward preferential binding of laminin.

This study was designed to achieve production of laminin-binding EVs derived from MSC by modification of the large extracellular loop (LEL) of CD81.

Specific CD81-LEL sequences are cloned into lentiviral vectors encoding the expression cassette for full-length CD81 proteins fused with eGFP or firefly luciferase under the control of human cytomegalovirus (CMV) promoter. Stable cell lines are obtained upon transformation of Wharton's Jelly MSCs and selected by sorting for high expressers. MSC-EVs are further isolated by ultracentrifugation and characterized by nanoparticle tracking analysis, flow cytometry and western blot.

Our results demonstrate the feasibility of production of designed laminin-binding EVs derived from MCSs. This study represents the basis for further investigation on EVs regarding their targeted binding to laminin, their internalization by SCs and their influence on peripheral nerve regeneration processes.

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DEVELOPMENT OF NEW GENERATION HYDROCOLLOID BIO-INK FOR 3D BIOPRINTING

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Bioprinting enables the production of 3-dimensional (3D) structures by combining bioinks, living cells, extracellular matrix (ECM) components, biochemical factors, proteins, drugs; and it has recently become one of the most promising techniques in the field of tissue engineering. The successful production of the 3D structure to be created by 3D bioprinting technology depends on the properties of the bio-ink to be used. Hydrogel/hydrocolloid materials used as bio-inks are developed using synthetic and natural polymers where they have the necessary rheological properties for printing, they also have biocompatibility, low toxicity and support for cell attachment. Natural hydrogels, which have the ability to mimic the extracellular matrix structure and function at a high rate, are highly preferred bioink materials for bioprinting applications. Polysaccharide-based hydrogel/hydrocolloids are one of the largest subclasses of natural polymers and are commonly used in food industry, drug release and tissue engineering applications with their gelling and biocompatibility properties. Hydrocolloids obtained from the seeds of some plants are among the promising natural materials in tissue engineering applications and the development of new generation bio-inks with their high water holding capacity, anti-inflammatory, and antioxidant properties. Here we report development of a new generation polysaccharide-based bio-ink for 3D bioprinting applications. The bioink was obtained through ''from waste to the bench-top'' approach by utilizing quince seed as a raw material. It was shown that developed bioink demonstrates desirable properties including viscoelasticity and processability, biocompatibility and non-toxicity, as well easy to obtain and cost effective as a bioink.

Keywords: 3D Bioprinting; polysaccharide bio-ink; 3D cell culture

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Abstract 1972

T CELL ACTIVATION DIRECTS ARTICULAR REPAIR OF FULL-THICKNESS OSTEOCHONDRAL DEFECTS IN RAT

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Osteochondral defects in the adult human fail to heal, resulting osteoarthritis (OA). The onset of OA has been linked to a prolonged pro-inflammatory response induced by the injury or repetitive microtrauma. This may be caused by an imbalance in the signalling cascades during the transition from the pro-inflammatory to the pro-regenerative phase.

Small (Ø: 0.15mm, SD) or large (Ø: 1.5mm, LD) full-thickness osteochondral defects were created in the trochlear groove of 10-week old wild type (T-cell+) or T cell deficient (T-cell-) female rats. Healing was characterized up to twelve weeks. Pathological evaluation confirmed that the T-cell+-SD model displayed functional healing (OARSI score 0/4), T-cell+-LD resulted in moderate fibrosis (2/4) and Tcell–SD and Tcell–LD displayed mild (1/4) and severe (3/4) fibrosis, respectively. Analysis at one week confirmed a corresponding trend between the healing potential to extracellular matrix (ECM) production, progenitor- and inflammatory cell activation. Interestingly, scRNAseq confirmed a unique inflammatory-progenitor cell population present within the defect area in the Tcell+-SD model. Injection of in vitro cartilage-activated lymphocytes, placenta derived progenitor cells (PLCs) or a 24h co-cultured combination thereof 1 week post defect creation improved the healing. But only co-cultured cells completely regenerated the Tcell–SD and LD defects based on OARSI scoring and lubricin secretion.

These results confirm the integral role of the balanced activation of lymphocytes and progenitor cells for functional osteochondral regeneration. Furthermore, the presented findings show effective, stable articular cartilage regeneration after combined treatment of cartilage-activated lymphocytes and PLCs in moderate to large osteochondral defects.

Keywords: Regeneration; Osteoarthritis; Cell therapy

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BIOFABRICATION BY MAGNETIC LEVITATIONAL ASSEMBLY OF CELLS INTO DEFINED 3D CELLULAR STRUCTURES

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