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Expanded human meniscus-derived cells in 3-D polymer–hyaluronan scaffolds for meniscus repair

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ABSTRACT

Treatment options for lesions of the avascular region of the meniscus using regenerative medicine approaches based on resorbable scaffolds are rare. Recent approaches using scaffold-based techniques for tissue regeneration known from cartilage repair may be a promising treatment option for meniscal tears. The aim of the study was the investigation of meniscus matrix formation of in vitro expanded human meniscus-derived cells in a three-dimensional (3-D) bioresorbable polymer graft for meniscal repair approaches. Cultivation of the human meniscus cells was performed in a resorbable scaffold material made of polyglycolic acid (PGA) and hyaluronic acid, stabilized with fibrin glue. Cell viability and distribution of human meniscus cells in PGA–hyaluronan scaffolds were evaluated by fluorescein diacetate and propidium iodide staining. Verification of typical meniscal extracellular matrix molecules like type I and type III collagen was performed histologically, immunohistochemically and by gene expression analysis. In results, 3-D scaffold-based meniscus cultures showed high cell viability over an observational period of 21 days in PGA–hyaluronan scaffolds. On the protein level, type I collagen and proteoglycans were evident. Gene expression analysis confirmed the re-expression of meniscus-specific markers in PGA–hyaluronan scaffolds. This study demonstrated that in vitro expanded human meniscus cells allow for formation of meniscal matrix components when cultured in 3-D PGA–hyaluronan scaffolds stabilized with fibrin. These results encourage scaffold-based approaches for the treatment of meniscal lesions.

1. Introduction

The meniscus of the knee joint was initially considered to be functionless, but it is now known to have important functions in shock absorption, joint lubrication, stability of the knee joint and power transmission from the upper to the lower leg [1–5]. The function of the meniscus is reflected by its cellular and biochemical composition [6].

The wedge-shaped knee meniscus tissue contains mainly water (72%) and collagens (22%) [6]. Particularly in the avascular inner region of the meniscus, the phenotype of the tissue is fibro-cartilage-like, whereas the vascular peripheral zone shows a fibrous phenotype [7]. The matrix of the meniscus is composed mainly of collagen type I (over 90%), but also a number of minor collagens (e.g. types II–VI), and extracellular proteins like aggrecan (ACAN) and glycosaminoglycans (GAG) are also present in small quantities. The collagen type I is arranged in bundles for strong tensile stress absorption and maintains the structural integrity of the meniscus during load bearing [5,7–10].

A decrease in the amount of meniscus tissue can lead to cartilage degeneration, an increase in pain and a loss of joint function. Meniscus lesions are frequently occurring injuries and pose a complex problem in orthopedic practice. After meniscus injury, a partial or total resection is often necessary. Only injuries in the outer vascularized part of the meniscus may heal spontaneously or upon suturing, while the inner avascular region shows a low capacity for self-regeneration. Due to the notoriously limited self-healing capacity of the meniscus fibro-cartilage-tissue, meniscectomy often leads to the degeneration of the articular cartilage of the knee joint and the later development of osteoarthritis in the knee [11–13].

Current repair techniques are effective in the peripheral vascularized meniscus, but their success in the avascularized region is not reliable. Tissue engineering, combining cell culture techniques and scaffold materials for tissue repair, offers new treatment options for meniscus repair of the avascular region and even enables whole meniscus replacement by an in vitro engineered construct [14].

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