Combining Self-assembly and Phage Display to Develop a Targeted Nanodelivery System for Cartilage Therapies

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The present work focuses on a specific challenge of great clinical importance: targeted therapy for osteoarthritis (OA). The identification of molecules expressed exclusively, or at elevated levels, by cartilage cells (chondrocytes) in OA conditions might provide a strategy for targeted OA therapy by enhancing drug specificity. Towards this goal, we report the identification of peptide ligands, that bind selectively and with affinity to OA chondrocytes, using phage display, a technology in which a library of phage particles expressing a wide diversity of peptides is screened to identify those that bind the desired target. A random 12-mer peptide library, displayed on the surface of a filamentous phage (M13), was screened by biopanning against the surface of OA chondrocytes to identify peptide ligands specific for these cells. Healthy and OA chondrocytes for the panning experiments were isolated from cartilage samples obtained in local hospitals under pre-established agreement and from patients after informed consent. Isolation and expansion of chondrocytes was performed according to published procedures and their phenotype was characterized by FACS (CD44, CD26, CD10 and CD95), RT-PCR (aggrecan, collagen I, II and X and Sox9), immunohistochemistry (collagen I, II and X), SDS-PAGE and western blot analyses. The identified peptide sequences are being integrated into nanocarrier systems formed by self-assembling approaches and the potential of these targeted delivery systems is currently being tested *in vitro.* This approach, if successful, will yield important insights into the regenerative mechanisms of cartilage and could be applied for developing more efficient and less invasive therapies for treating OA.

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Abstracts

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