Accepted Manuscript

A hyaluronic acid binding peptide-polymer system for treating osteoarthritis

Heather J. Faust, Sven D. Sommerfeld, Sona Rathod, Andrew Rittenbach, Sangeeta Ray, Benjamin M.W. Tsui, Martin Pomper, Mario L. Amzel, Anirudha Singh, Jennifer Elisseeff

PII: S0142-9612(18)30605-7

DOI: 10.1016/j.biomaterials.2018.08.045

Reference: JBMT 18851

To appear in: *Biomaterials*

Received Date: 4 June 2018

Revised Date: 13 August 2018

Accepted Date: 20 August 2018

Please cite this article as: Faust HJ, Sommerfeld SD, Rathod S, Rittenbach A, Ray S, Tsui BMW, Pomper M, Amzel ML, Singh A, Elisseeff J, A hyaluronic acid binding peptide-polymer system for treating osteoarthritis, *Biomaterials* (2018), doi: 10.1016/j.biomaterials.2018.08.045.

A HYALURONIC ACID BINDING PEPTIDE-POLYMER SYSTEM FOR TREATING OSTEOARTHRITIS

Heather J. Faust[1], Sven D. Sommerfeld[1], Sona Rathod[1], Andrew Rittenbach[2], Sangeeta Ray[3], Benjamin M. W. Tsui[3], Martin Pomper[3], Mario L. Amzel[4], Anirudha Singh[1,5,6], and Jennifer Elisseeff[1*].

[1]Translational Tissue Engineering Center, Wilmer Eye Institute and Department of Biomedical Engineering, Johns Hopkins University, Baltimore, MD 21287, USA.
[2]University of Southern California, Information Sciences Institute, CA
[3]Department of Radiology, Johns Hopkins University, Baltimore, MD 21218, USA
[4]Department of Biophysics and Biophysical chemistry, Johns Hopkins University, Baltimore, MD-21218
[5]Department of Urology, The James Buchanan Brady Urological Institute, The Johns Hopkins School of Medicine, Baltimore, MD-21287
[6]Department of Chemical and Biomolecular Engineering, Johns Hopkins University, Baltimore, MD-21218
*Corresponding author. Tel.: 410-614-6837; fax: 410-614-6840

Abstract

Hyaluronic acid (HA) is found naturally in synovial fluid and is utilized therapeutically to treat osteoarthritis (OA). Here, we employed a peptide-polymer cartilage coating platform to localize HA to the cartilage surface for the purpose of treating post traumatic osteoarthritis. The objective of this study was to increase efficacy of the peptide-polymer platform in reducing OA progression in a mouse model of post-traumatic OA without exogenous HA supplementation. The peptide-polymer is composed of an HA-binding peptide (HABP) conjugated to a heterobifunctional poly (ethylene glycol) (PEG) chain and a collagen binding peptide (COLBP). We created a library of different peptide-polymers and characterized their HA binding properties *in vitro* using quartz crystal microbalance (QCM-D) and isothermal calorimetry (ITC). The peptide polymers were further tested *in vivo* in an anterior cruciate ligament transection (ACLT) murine model of post traumatic OA. The peptide-polymer with the highest affinity to HA as tested by QCM-D (~4-fold greater binding compared to other peptides tested) and by ITC (~3.8-fold) was HABP2-8-arm PEG-COLBP. Biotin tagging demonstrated that HABP2-8-arm PEG-COLBP localizes to both cartilage defects and synovium. *In vivo*, HABP2-8-arm PEG-COLBP treatment and the clinical HA comparator Orthovisc lowered levels of inflammatory genes including IL-6, IL-1B, and MMP13 compared to saline treated animals and increased aggrecan expression in young mice. HABP2-8-arm PEG-COLBP and Orthovisc also reduced pain as measured by incapacitance and hotplate testing. Cartilage degeneration as measured by OASRI scoring was also reduced by HABP2-8-arm PEG-COLBP and Orthovisc. In aged mice, HABP2-8-arm PEG-COLBP therapeutic efficacy was similar to its efficacy in young mice, but Orthovisc was less efficacious and did not significantly improve OARSI scoring. These results demonstrate that HABP2-8-arm PEG-COLBP is effective at reducing PTOA progression.