Investigation of Macromolecular Transport Through Tunable Collagen Hyaluronic Acid Matrix

Mazin Hakim[1], Brian Jun[2], Adib Ahmedzadegan[2], Paulina Babiak[3], Qinghua Xu[3], Kevin Buno[1], Julie Liu[3], Arezoo Ardekani[2], Pavlos Vlachos[1,2], Luis Solorio[1,4]

[1] Weldon School of Biomedical Engineering, Purdue University, West Lafayette, IN, USA
[2] School of Mechanical Engineering, Purdue University, West Lafayette, IN, USA
[3] Forney School of Chemical Engineering, Purdue University, West Lafayette, IN, USA
[4] Purdue Center for Cancer Research, Purdue University, West Lafayette, IN, USA

Statement of Purpose: Hyaluronic acid (HA) is an extracellular matrix (ECM) component that is classically involved in inhibiting delivery of therapeutics due to its high viscosity and negative charge (1). For example, increased HA near subcutaneous lymphatic ducts and pancreatic tumors is responsible for decreased transport of drugs to their respective targets, however the degradation of HA via hyaluronidase has been shown to improve bioavailability (2). Though this effect has been previously studied, the parameterization of molecular transport as a function of known macromolecule and ECM properties for understanding drug/tissue interactions and preclinical drug efficacy has not yet been described.

Methods: To address this gap, we utilized a Transwell chamber with non-invasive, label-free UV spectroscopy to measure the mass recovery of macromolecules across various *in vitro* ECM barriers. Here, we show the effect of increasing HA concentration within collagen-hyaluronic acid matrices (ColHA) on the mass recovery of macromolecules – bovine serum albumin (BSA), β-Lactoglobulin (BLg), lysozyme (Lys), dextran (Dex), and bovine immunoglobulin G (IgG).

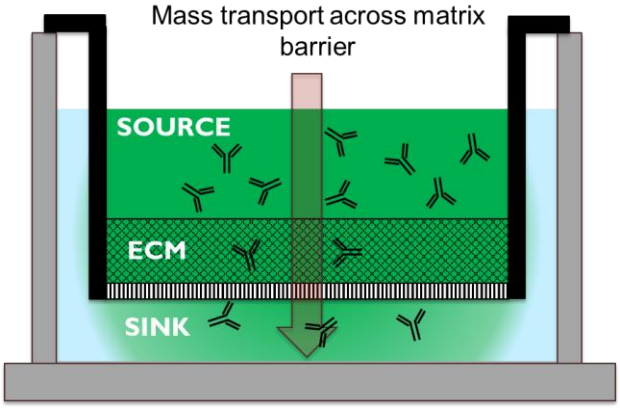

Figure 1: Transwell mass recovery of molecules through an ECM barrier.

Results: We found that as HA concentration, and subsequent viscosity and negative charge density, increased in ColHA matrices, mass recovery decreased. However, against pure HA with no collagen fiber network, the negative charge of BSA, BLg, and IgG played a large role in increasing transport compared to ColHA matrices, despite the higher viscosity. In pure HA, positively charged Lys had the lowest transport due to the highly negative matrix.

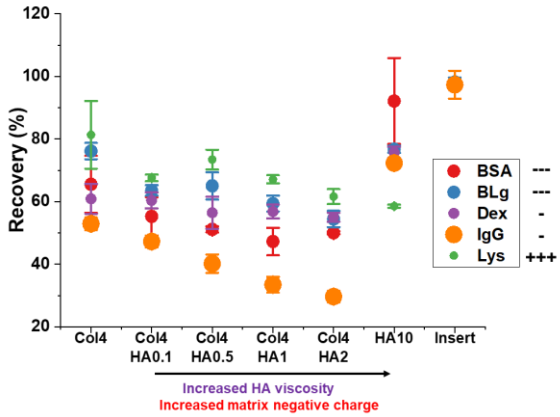

Figure 2: Primary ECM recovery results. Recovery is calculated as the ratio of mass in the sink to initial mass.

These results demonstrate that electrostatic and viscous effects from HA modulate macromolecule transport in ColHA ECMs, that HA sequesters and increases the residence time of oppositely charged macromolecules, and that the presence of collagen as a majority substituent of the ECM plays an important role.

References:

(1) Provenzano P. Cancer Cell. 2012;21;418-429.
(2) Wohlrab J. Skin Pharmacol Physiol. 2014;273:276-282.