Does Enhancing Cartilage Endplate Permeability Improve Nucleus Pulposus Cell Function?
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Purpose
Low back pain is the leading cause of disability and is closely linked to disc degeneration. Intradiscal biologic therapy is a promising strategy for managing disc degeneration. However, biologic therapies place increased demands on the limited nutrient supply inside the avascular disc. With NASS support in 2016-2017, we demonstrated for the first time that nutrient diffusion through the cartilage endplate (CEP) is insufficient to meet the metabolic demands of the disc cells when CEP permeability is less than a critical value; consequently, individuals with low CEP permeability may be poor candidates for biologic therapies. Those findings led to an NIH R01 to develop diagnostic tools for non-invasively assessing whether CEP permeability is adequate to support biologic therapies. But what's to be done if CEP permeability is inadequate? We now ask if two novel treatment approaches that enhance CEP permeability can improve nutrient transport and disc cell function, and we propose studies to optimize treatment parameters and assess translational potential.

Hypothesis
Based on our discovery in Year 1 that CEPs with low matrix porosity and high mineral content impede nutrient transport and impair disc cell viability, we hypothesize that treatments which increase porosity and reduce mineralization will significantly improve CEP permeability and disc cell function, and that optimal treatment parameters constitute a tradeoff between maximizing permeability and minimizing strength loss.

Method of Research
To test these hypotheses, we developed two approaches for enhancing matrix porosity and nutrient transport. The first approach (“enzymatic”) involves treatment with the human collagenase MMP-8 to liberate matrix and increase porosity. The second approach (“structural”) uses an infrared laser to focally ablate collagen and mineral and thereby remove the impediments to fluid flow. Our first goal is to identify optimal treatment parameters by characterizing their effects on CEP matrix composition/porosity, permeability, and biomechanical behavior. Next, we’ll assess translational potential by determining whether these treatments improve solute transport and disc cell function without appreciably compromising CEP biomechanical behavior.

Expected Results
Together, the proposed studies will exert a broad impact by: 1) defining relationships between permeability enhancement, solute transport, and disc cell function that can serve as benchmarks for new strategies; 2) identifying optimal treatment parameters and assessing translational potential for two innovative strategies aimed at enhancing CEP permeability; and 3) establishing the relevance of any tradeoffs between CEP permeability and strength.