Title: Human Placental Extract (HPE) Reduces Cartilage Damage After Traumatic Joint Injury

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*Presenter

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Background: Persistence of the inflammatory cascade initiated at knee injury and exacerbated by surgical repair leads to cartilage degradation and may preclude optimal functional recovery despite excellent surgical results. The post knee injury challenge is simultaneously arresting the joint inflammation and augmenting natural processes that restore articular cartilage. Current intra-articular osteoarthritis (OA) treatments (e.g. hyaluronic acid, steroids, and platelet-rich plasma) are ineffective and have either negative long-term impacts, limited efficacy, or inconsistent formulations. None of these treatments repair cartilage. None are used at the time of injury to mitigate the injury induced inflammation that drives cartilage damage, perturbs bone remodeling, and enhances pain signaling cascades. HPE is an acellular product derived from donated post-delivery, term pregnancy placental discs which contain the placental chemokine milieu and excludes the inflammatory chemokines synthesized by the amniotic membrane. Previously, HPE has demonstrated anti-inflammatory, proliferative, and heterochronic properties in vitro in chondrocytes and cartilage explants.

Hypothesis: An intra-articular treatment, like HPE, which interrupts several pathways of joint inflammation and invigorates and sustains proliferative mechanisms of articular cartilage, would overcome the inflammation cascade initiated at joint injury and protect and initiate innate healing mechanisms, thus maximizing functional outcomes with or without eventual surgical reconstruction.

Methods: OA was induced in skeletally mature Lewis rats via transection of the anterior cruciate and medial collateral ligaments, and medial meniscus rarefication (SoBran, Maryland). Treatment groups were either 1) normal saline, 2) 7.7 mg protein/mL or 3) 38.5 mg protein/mL of HPE in normal saline administered via a single intra-articular injection at injury. Four weeks post-injury, joints were decalcified, sectioned, and stained with toluidine blue and cartilage degradation was scored per OARSI guidelines by a histologist blinded to treatment.

Results: Cartilage damage was reduced with both lower and higher doses of HPE compared to saline treated joints. Cartilage lesions in both low dose and high-dose HPE groups were significantly decreased compared to the saline-treated controls **(Fig. 1)**.

Conclusions: HPE, currently in cGMP development, results in a shelf stable, crystalline powder that can be reconstituted at the point of care. Plakous has demonstrated preclinical bioactivity of HPE and its effectiveness to increase chondrocyte proliferation, decrease catabolic enzymes, and decrease articular cartilage degradation to help protect against the development of post traumatic OA.

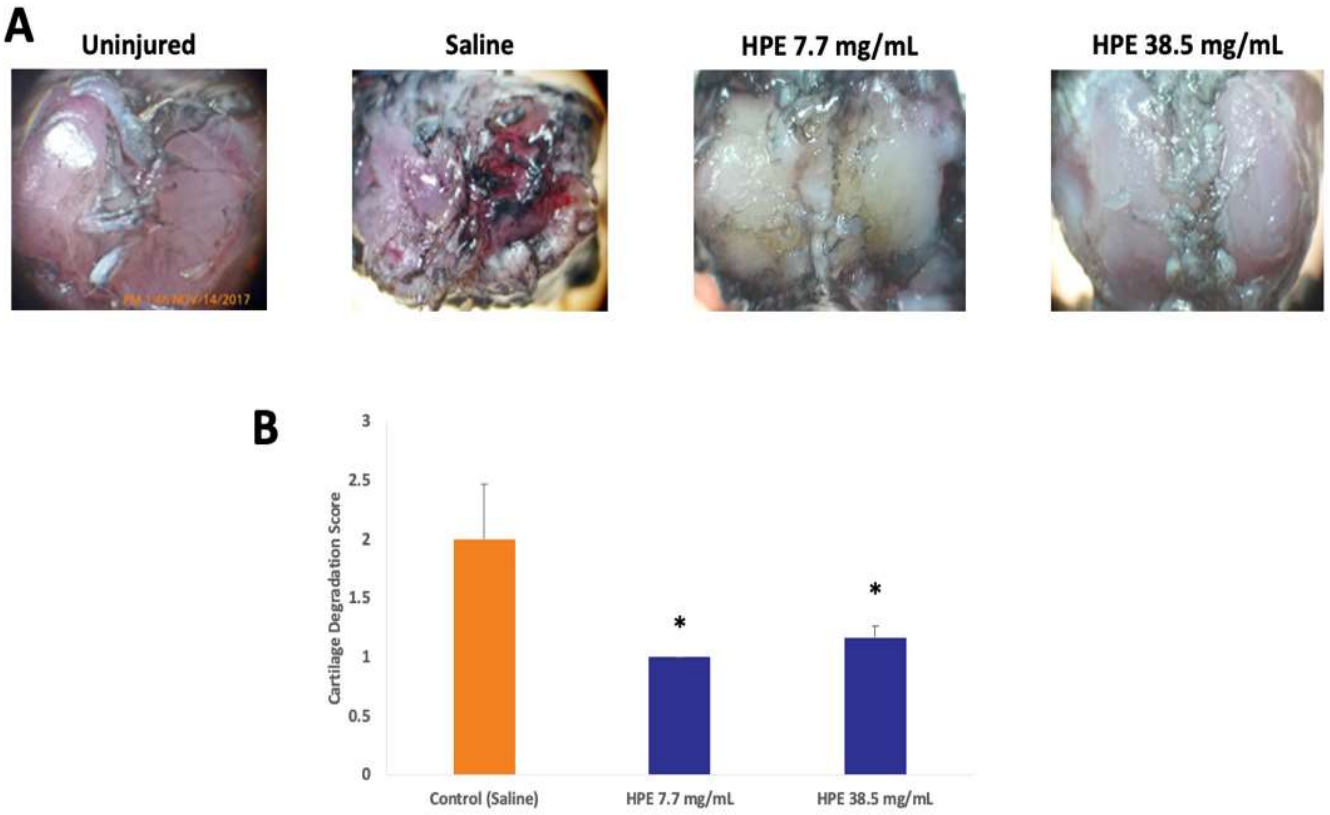

*Figure 1 HPE prevents post-injury knee damage and arthritis in a rat model of Post Traumatic OA. (A) India-ink-stained gross morphology (Meachim) of uninjured knee and injured knee treated with single injections of saline control and low- and high- dose HPE (n=5). (B) Articular cartilage scoring as part of OARSI standards on frontal sections (n=5), *p<0.05.*

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Significance

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Preliminary Results

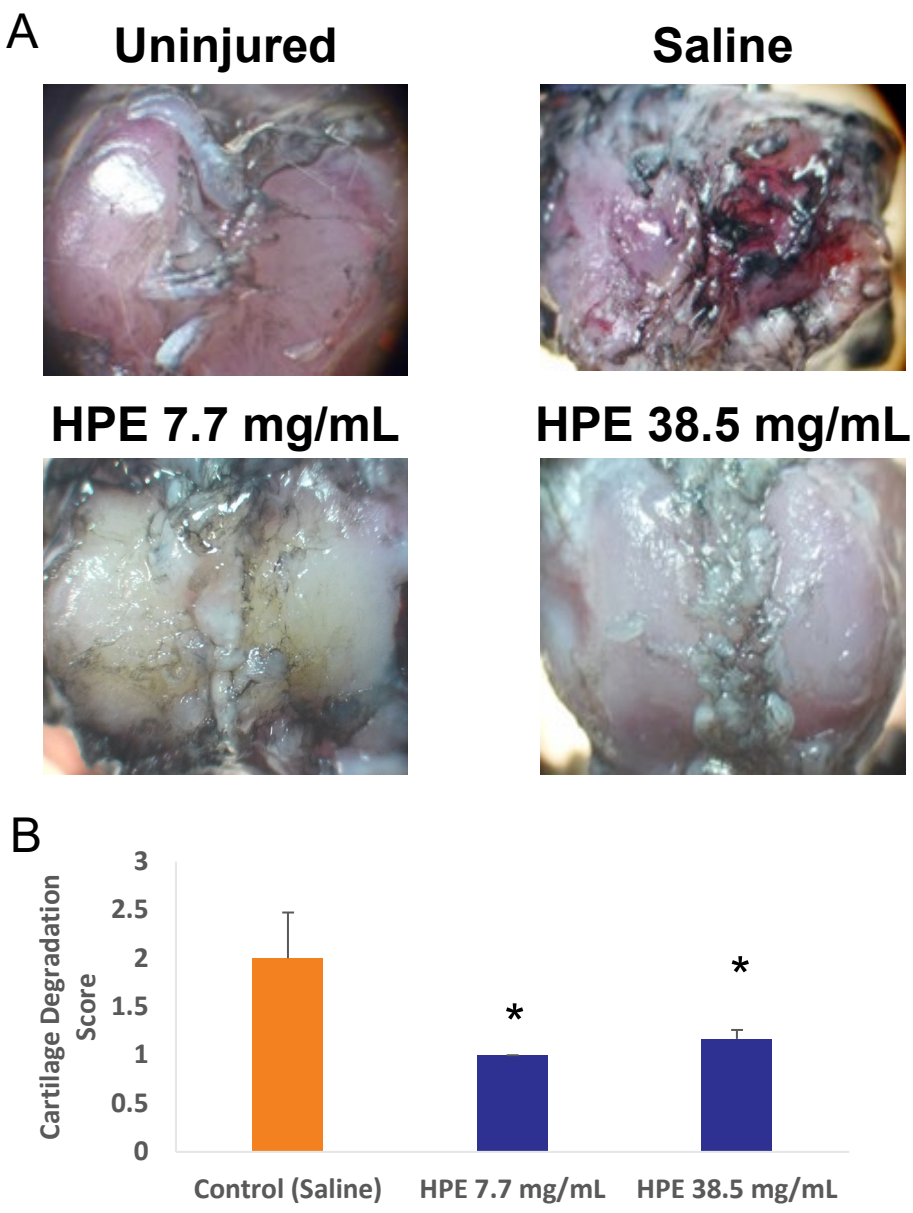

Figure 1. HPE prevents post-injury knee damage and arthritis in a rat model of Post Traumatic OA. (A) India-ink-stained gross morphology (Meachim) of uninjured knee and injured knee treated with single injections of saline control and low- and high- dose HPE (n=5). (B) Articular cartilage scoring as part of OARSI standards on frontal sections (n=5), *p<0.05.

Conclusions

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Acknowledgements

We thank SoBran Biosciences, Inc of Baltimore, MD for the assistance in performing the animal studies in this project. Wake Forest University Comprehensive Cancer Center and Dept of Radiation Oncology Internal Funds (J. Willey) provided partial support for scoring of cartilage degradation.