## Porcine Urinary Bladder Matrix as an Inductive Template for Temporomandibular Joint Meniscus Reconstruction

Bryan N. Brown<sup>1,2</sup>, Scott A. Johnson<sup>2</sup>, Mark W. Ochs<sup>3</sup>, William L. Chung<sup>3</sup>, Alan J. Russell<sup>1,2,4,5</sup>, and <u>Stephen F. Badylak<sup>1,2,5</sup></u> 1. Department of Bioengineering, 2. McGowan Institute for Regenerative Medicine,

3. Department of Oral and Maxillofacial Surgery, 4. Department of Chemical Engineering 5. Department of Surgery

University of Pittsburgh, Pittsburgh, PA

Statement of Purpose: Temporomandibular joint (TMJ) disorders are common and typically involve either a spatial dislocation or a structural defect of the enclosed cartilaginous meniscus. A variety of procedures, including minimally invasive surgical techniques, have been attempted in an effort to treat this condition. Meniscectomy is indicated in cases where the TMJ meniscus is irreparably damaged or if the meniscal disc prohibits smooth movement of the condyle. Complications arising from meniscectomy without replacement include heterotopic bone formation and joint ankylosis. Alloplastic materials such as Silastic, silicone, and Proplast-Teflon, have been used to replace the TMJ meniscus following meniscectomy, but results have been less than satisfactory. Autograft tissues have been used as replacement materials following meniscectomy and as interpositional materials in the treatment of joint ankylosis. Tissue sources such as the temporalis muscle flap, auricular cartilage and dermis have proven better options than their alloplastic counterparts; however, the morbidity associated with the donor site represents a disadvantage of this approach. Furthermore, fibrosis or necrosis and devitalization of autogenous tissue grafts has been shown. An ideal graft material for the replacement of the TMJ meniscus would provide a substrate for tissue in-growth, prevent degenerative changes of the condyle and the fossa, and be readily implanted and attached to the peripheral tissues without the associated morbidity of autogenous tissue harvest.

A device consisting of particulate Methods: extracellular matrix (ECM) derived from porcine urinary bladder (urinary bladder matrix; UBM) was encased within sheets of UBM to provide an inductive and resorbable "pillow" of interpositional material and an anchoring site while mimicking the shape and size of the native canine TMJ meniscus. The device was implanted in canine models of unilateral and bilateral TMJ meniscectomy and the remodeling of the devices was assessed at time points of 3 weeks, 1, 2, 3 and 6 months post-implantation. The unilateral model included meniscectomy followed by replacement with a UBM The bilateral model included meniscectomy device. followed by replacement of the disc on one side with a UBM device, leaving the contralateral side devoid of a meniscal substitute. Assessment was performed using morphologic gross examination, histologic and immunohistochemical methods, and mechanical testing.

**Results:** Gross morphologic examination showed that the UBM test article remodeled over time and was replaced by a structure that resembled the native TMJ disc at the 6-month time point. There were no obvious pathologic changes in the articulating surfaces of the fossa or the

condyle at any time point following placement of the UBM device. Further, there were no signs of synovitis, or excess fluid in the joint space. Histologic examination showed that the UBM device promoted the deposition of predominantly collagen type I and a small amount of collagen type III, the organization and density of which increased with time. Additionally, growth of the native musculature into the device was observed at the peripheral attachment sites. No histopathologic changes of the articulating surfaces were present following the implantation of the UBM device. Immunohistochemistry indicated that the device was initially infiltrated by a large number of mononuclear macrophages, the presence of which decreased with time. By 3 months postimplantation, mononuclear macrophages were no longer observed, and the device was populated by a small number of spindle shaped cells resembling those found in the native meniscus. Immunohistochemical staining further showed that there were a large number of blood vessels within the remodeling UBM device at early time points. Both the number and size of the vessels within the remodeling device decreased with time and resembled those found in the native meniscus by 6 months postimplantation. The majority of the vessels observed within the remodeling device were found near the peripheral attachment sites. Unconfined compression testing showed that the maximum stress, equilibrium stress and tangent modulus of the UBM device were at least 2-3 times higher than observed for the native meniscus, while the percent relaxation for the native meniscus and the UBM device were found to be similar. The mechanical properties of the implanted ECM device changed during the remodeling process and were more similar to those found in the native TMJ by 6 months post-implantation.

**Conclusions:** The remodeling process of the UBM device in the TMJ location can be characterized as a dense cellular infiltration of predominantly mononuclear macrophages at early time points changing with time to a sparse population of spindle shaped cells that resemble those found in the native TMJ by 6 months post-The device was shown to promote the implantation. deposition of both collagen type I and small amounts of collagen type III with a density and organization that increased with time. The device was found to be well integrated with native tissue at the peripheral attachment sites. At the six month time point, the morphology of the remodeled site highly resembled that of the native TMJ meniscus in terms of its shape, size, and the organization and the composition of the cellular population. We conclude that the UBM device represents an effective tissue engineered scaffold for the reconstruction of the TMJ meniscus following meniscectomy.