INTRODUCTION: Optimal healing of rotator cuff injuries involves reinsertion of the tendon into bone at the original site of attachment. A lack of tendon fiber reinsertion into bone at the repair site can potentially lead to limited function and an increased chance for re-injury. Studies have reported a relatively high incidence of failure regarding rotator cuff repair, as observed on MRI and ultrasound [1,2], which has been suggested to result from poor tendon tissue quality and tendon to bone healing. Addition of growth factors at the time of surgery may augment tendon to bone healing of these injuries, thereby reducing the incidence of re-tears. Platelet-derived growth factor-BB (PDGF-BB) is a well characterized wound healing protein known to be chemotactic and mitogenic for cells of mesenchymal origin, including bone (osteoblast) and tendon (tenoblast/tenocyte) cells. Additionally, PDGF-BB has been shown to improve healing when applied to animal models of tendon injury [3-4]. We hypothesized that the application of rhPDGF-BB combined with a type I bovine collagen matrix as an interpositional graft at the site of tendon repair would augment and improve tendon reattachment as evaluated biomechanically and histologically.

METHODS: Treatment Groups: Five treatment groups (n=12/group) were used for rotator cuff repair in this study: (1) suture only, (2) suture+collagen, (3) suture+collagen+75µg rhPDGF-BB, (4) suture+collagen+150µg rhPDGF-BB, and (5) suture+collagen+500µg rhPDGF-BB. Surgical Procedure: The infraspinatus tendon of 60 skeletally mature ewes (3.5+ years) was surgically exposed and sharply detached from the humeral head [5,6]. The tendon footprint was decorticated and three perforations were made into the bone to induce bleeding. The test articles were placed as an interpositional graft between the tendon and the bone. Two sutures were passed through the tendon using a Mason-Allen technique and the tendon was secured to the humeral head through a single-row repair consisting of 3 bone tunnels. The surgical site was closed using standard procedure and the sheep were allowed to ambulate normally. Animals were sacrificed 12 weeks after surgery. Biomechanical Testing: Specimens (n=9/group) were cleaned and potted using high strength polymethylmethacrylate and mounted in a custom-designed testing fixture that was rigidly attached to the materials testing system loading frame (MTS MiniBionix). A custom-designed clamp designed to preserve the natural cross section of the infraspinatus tendon was used to apply uniaxial traction forces to the construct at an angle of approximately 135° to the potted humerus to model the physiological force vector of the tendon. Preconditioning was performed by applying an initial preload of 10 N, followed by cyclic loading (in load-control) from 10 to 50 N at 0.25 Hz for 60 cycles. Preconditioning was followed by a quasi-static load-to-failure ramp at 1 mm/s. From this load-to-failure test, the quasi-static stiffness, ultimate load-to-failure, elongation at failure, and failure mode were determined. Histology: Histologic specimens (n=3/group) were decalcified, processed, embedded, and sections were taken from the central region of the infraspinatus-humerus repair site. Sections were stained with hematoxylin and eosin and evaluated using a semi-quantitative scoring system assessing the quality of the reparative/healing tissue, the tendon-bone interface, vascularization, inflammation, collagen orientation/fiber alignment, and presence of Sharpey’s fibers at the insertion site. Statistical Analysis: A One-Way ANOVA and post-hoc Fisher’s LSD test were performed using SigmaStat 3.1 to identify significant differences in continuous biomechanical parameters between treatment groups. Significance was set at p<0.05. Data are shown as mean ± SEM.

RESULTS: Animal Observations: All animals survived the 12 week in-life study and no adverse gross findings were observed. Biomechanical Testing: The ultimate load at failure (Figure 1) was significantly increased in the 75µg rhPDGF-BB (63.7%, p=0.029) and 150µg rhPDGF-BB (63.3%, p=0.013) groups relative to the suture only control and the 500µg rhPDGF-BB group (120%, p=0.023 and 119.3%, p=0.023, respectively). There were no significant differences in the quasi-static stiffness between groups (p>0.234). The 75µg rhPDGF-BB and 150µg rhPDGF-BB groups also exhibited a significant increase in elongation at failure compared to the suture only (p=0.018 and 0.024, respectively) and compared to the suture+collagen group (p=0.015 and 0.011, respectively). No significant differences in elongation were observed between the three groups containing rhPDGF-BB. Sample failure occurred in the repair tissue for all specimens in the suture only, suture+collagen, and suture+collagen+500µg rhPDGF-BB groups. A majority of the specimens in the suture+collagen+75µg rhPDGF-BB (6/9) and suture+collagen+150µg rhPDGF-BB (5/9) groups exhibited some degree of bony avulsion at failure. Histology: Specimens exhibited varying degrees of new bone formation, inflammation, vascularity, and Sharpey’s fiber’s inserting the tendon to the bone at the insertion site. No differences were noted in the suture only, suture+collagen, and suture+collagen+500µg groups in the assessment of tendon retraction, inflammation that the vascularization, or Sharpey’s fibers. Histologic sections of the suture+collagen+75µg and suture+collagen+150µg groups displayed increased tendon repair and interdigitation of tendon collagen with that of bone at the fibrocartilage interface (Figure 2).

DISCUSSION: A type I bovine collagen matrix saturated with rhPDGF-BB significantly enhanced repair, in a dose responsive manner, as compared to standard of treatment (suture only). Biomechanical strength of the repair tissue was significantly enhanced in the low and mid dose groups; whereas, the high dose group did not result in enhanced biomechanical strength of the repair tissue. Additionally, the measured ultimate force in low and mid dose treated groups compares favorably to other studies using a biological or matrix augmentation of rotator cuff repair in this ovine model [5,6]. Histology outcomes (including Sharpey’s fibers insertion from tendon into bone) were consistent with observed biomechanical properties. The combination of a type I collagen matrix and rhPDGF-BB may have promise as a therapeutic treatment for the augmentation of rotator cuff repair procedures in humans.