Lauren G. Guillot
L2
LSU Health Sciences Center, New Orleans, LA

Dr. Luis Marrero, PhD:
LSUHSC, Department of Orthopaedic Surgery

"Transcriptional Analysis of Articularis Genu Sarcopenia in Osteoarthritis"

Knee osteoarthritis (kOA) causes atrophy and changes in myofiber distribution in regional musculature, including the *Quadriceps femoris* (QF) complex and the *Articularis genu* (AG), a mono-articular muscle that retracts the suprapatellar bursa during extension. The AG shares similar myofiber structure and innervation to the QF and can be easily sampled during total knee arthroplasty (TKA) for kOA, allowing its potential use in developing a diagnostics platform for management of peri-articuar muscle health. The differential expression of myosin heavy chains (MHC) in type (T) T1 slow oxidative (MHC7), T2a fast glycolytic (MHC2), T2a/x hybrids (co-expression of MHC2 and MHC1), and T2x super-fast twitch (MHC1) fibers can be co-detected by immunohistochemistry of QF and AG histological sections. Notably, a higher occurrence of T2x and T2a/x hybrid fibers has been linked to sedentary behavior in studies involving the *Vastus lateralis* of the kOA QF. Consistent with those findings, we have measured a higher incidence of T2a/x hybrids in AGs from kOA patients with poor active range of motion (ROM) compared to cohorts with better ROM. Also similar to evidence from the kOA QF, we have measured the most elevated collagen deposition in the AG endomysium in patients with poor ROM and that collagen deposition in the AG is associated with severity of fibrosis in the neighboring synovium. To strengthen these results, we aim to measure the expression of genes related to these processes in the kOA AG. We predict the expression of transcripts specific to muscular atrophy, hypertrophy, and fibrosis to be dysregulated in the kOA AG in agreement with the significant histological changes that we have previously measured in a ROM-dependent manner.

KOA cohorts were grouped by active ROM within full arc (135º maximum) measured pre-operatively as good (≥115º), fair (90º to 114º), and poor (≤89º). AG samples were collected during TKA, snap-frozen in liquid nitrogen, and stored at the LSU Integrated Musculoskeletal Biobank (LIMB). Cryopreserved AGs (n=24) were homogenized for RNA isolation followed by cDNA synthesis and qPCR. Primer pairs for genes related to atrophy (*Fbxo32, Trim63*), MHC expression (*Myh1, 2, 7*), myofiber type switching (*Nos2, Ppargc*), hypertrophy (*Igf11, Mef2c*), and fibrosis (*Tgfb1, Ctgf,* and *Acta2*) were assayed, normalized against housekeeping *Hprt1 and Actb,* and values determined using the comparative CT method and log scaled. One way ANOVA was used to compare differences between groups and Spearman's rho (r) applied to test associations. Alpha was set to 0.05.

In agreement with our data on kOA AG morphometry, myofiber distribution, and collagen deposition, we expect that the RNA isolated from the AGs of patients with worse ROM will display elevated transcription of genes related to atrophy, expression of MHC1 (T2x and T2a/x hybrids), and pro-fibrotic factors. These results will contribute to determining if the AG can be used as a surrogate for muscle wasting and fibrosis of the QF during kOA. Our overarching goal is to develop a diagnostic platform for kOA QF status based on phenotyping the AG and related genes that may translate to secreted biomarkers of sarcopenia into the synovial fluid and/or blood serum. Since the QF cannot be routinely sampled during TKA, an effort to indirectly evaluate its status

through histology and RNA analytics of the AG relative to local and systemic biomarkers of sarcopenia would help guide individualized peri-operative pain management and refine post-operative strength rehabilitation of kOA patients.