Expanding on Characterization of the "Forgotten Muscle" during Knee Osteoarthritis

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Introduction

Skeletal muscles are composed of type-I (T1), high endurance, slow-twitch myofibers, and type-II (T2), high strength, fast-twitch myofibers. The former derive energy from oxidative phosphorylation, and are rich in mitochondria. On the other hand, T2 fibers mostly rely on glycolysis for energy metabolism, and fatigue easily. T2 fibers are further classified into T2a and T2x subtypes. Myofibers can be identified by specific expression of different myosin heavy chains (MHC, MBC1, 2, and 7 specifically) and respectively expressed by T1, T2a, and T2x subtypes. Additionally, two different MHC can be processed and co-expressed by myofibers in a transitional state between subtypes, and thus termed hybrids, such as T2a/T2x.

The Quadriceps femoris (QF) complex in younger individuals is normally composed of an approximately even ratio of T1 and T2 fibers. The presence of T2x and T2a/T2x hybrids in the healthy QF is rare. Changes to T1/T2 distribution is dynamic, depending on activity type and level. For example, the ratio of T1 over T2 will shift to favor higher T1 counts in older individuals due to age-related, preferential de-nervation of T2 fibers. Moreover, because T2a/T2x fibers are required for sudden high strength contractions, and are the most fatigable, higher incidences of T2a/Tx hybrids are associated with inactivity and sedentary behavior.

The normal integrity of the QF is compromised by functional limitations caused by knee osteoarthritis (OA). Loss of OA knee mobility is clinically assessed by measuring active range of motion (ROM). In other words, higher ROM deficits relate to higher knee pain and therefore, based on studies on the OA knee intervals (VL), a higher risk of atrophy, fibrosis, and deleterious switching between myofiber subtypes to T2a and T2x/a hybrids. The Articularis genus (AG) is a small intra-articular muscle in close proximity to the synovium and continuous to the ilio-tibial bandage. The AG orientation movement of the suprapatellar fat pad itself tightens the synovial membranes to prevent impingement of the synovial folds. The AG can be sampled during total knee arthroplasty (TKA) for OA, and from non-OA donors and preserved in our biobank. Consistent with normal QF's, healthy AGs also contain a nearly equivalent T1/T2 composition and less than 0.5% T2x or T2a hybrids. Nearly a year ago, we generated evidence that similar to the OA V1, banked OA AGs from our TKA patients undergo myofiber atrophy and progressive switching of T1 to T2 fibers in association with deficits in ROM. Our data are compared to similar studies in the VL during OA (Noshen et al. 2016). Notably, our lab recently published evidence that the severity of synovial fibrosis (SF) during OA also correlates to ROM metrics. To date, we have profiled a higher incidence of T2a hybrids in the AG of OA knees in an increasing ROM deficits. Concurrent with this myofiber phenotype and also in a ROM deficit dependent fashion, we anticipate measuring higher fibrosis of the AG (AGF) in association with high SF in neighboring synovium.

Methods


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