Priority Statement Title: Defining Skeletal Muscle-Extracellular Matrix Communication

Priority Statement Code: CJ4D

Domain: Cellular and Tissue

Priority Statement

Background and Relevance

Since passive joint mechanics are "felt" by the clinician and since they affect function, it is important to understand the structural basis of extracellular matrix (ECM) properties and to establish the "rules" of communication between muscle and ECM. Skeletal muscle exerts its effect via the connective tissue matrix to move the skeleton. Indeed, muscles cells are embedded in an ECM that beautifully converges on a tendon that exits the muscle and inserts into bone. Skeletal muscles and tendons demonstrate remarkable ability to adapt to changes by the other tissue even compensating for altered function when needed. Mechanical properties of the ECM seem to dominate the passive mechanical properties of muscle and do not scale with muscle fiber length in spite of the fact that fiber length largely determines active mechanical properties. Also, a resident mesenchymal stem cell (MSC) population exists in muscle and ECM that is capable of regenerating these tissues. Clearly muscle exerts a powerful influence on ECM and *vice versa* which is clearly seen when muscles become fibrotic after disease or injury. In order to develop rational therapies for such problems it is necessary to define the structure and function of the muscle ECM as well as the nature of communication between muscle cells and the ECM.

One of the major barriers in this area results from the fact that individuals studying skeletal muscle are typically resident in Physiology or Biology Departments while those studying connective tissues are often in Bioengineering and Orthopaedic Surgery Departments. In addition, there is not a single professional Society in which cross-fertilization between these two disciplines occur. Finally, the two fields are highly specialized already and the idea of combining the disciplines is daunting.

Objectives

1. To define the structural properties of skeletal muscle ECM and its variation throughout various muscles with various functions (*e.g.*, fast- and slow-contracting muscles and anti-gravity muscles and their antagonists).
2. To define the mechanical properties of the skeletal muscle ECM and its relationship to whole muscle passive mechanical properties.
3. To determine the relationship (if any) between whole muscle passive mechanical properties and skeletal muscle architecture.
4. To define the nature of the biological interaction between muscle and ECM and how this interaction changes in response to ECM perturbations (*e.g.*, aging, disuse, myopathy and training)

Recommended Actions

1. Issue an RFA for proposals that investigate "Skeletal Muscle-Connective Tissue Interaction."
2. Contact the ASB Executive Board and request a special student competition in this topic area with a prize to the best paper on this topic.
3. Send a representative of the ASB to the appropriate connective tissue meeting (not the Orthopaedic Research Society) in order to make this need known to the connective tissue scientific community.