Functional impairment in tendons, such as those which control movement in the heel, elbow and shoulder, represent a major health care problem. The long-term goal of my laboratory is to determine whether the altered cell responses and extracellular matrix (ECM) disruption that are the hallmark of tendinopathies, can be modified towards healing using biologic and/or biomechanical therapies. In this seminar, a novel in vivo model of TGFβ1-induced murine Achilles tendinopathy will be described; the model produces biomechanical and biochemical alterations in the tendon which closely mimic those of the human pathologic condition. Specifically, tendinopathic tissues exhibited pronounced loss of mechanical properties (relative to uninjured tendons) and accumulated chondroid deposits within the ECM. Consistent with clinical studies which describe beneficial effects of eccentric exercise, mechanical stimulation promoted restoration of mechanical properties and resolution of the chondroid deposits. Conversely, induction of tendinopathy in mice lacking ADAMTS5 (A Disintegrin and Metalloproteinase with Thrombospondin Motifs 5) followed by mechanical stimulation resulted in enhanced chondrogenic responses and continued loss of mechanical properties. The latter findings are consistent with the generalized deficiency of fibrogenic repair responses in this knockout mouse, due to impairment of fibroblastic collagen synthesis and contraction. These results constitute key findings which will facilitate the development of therapeutic mechanobiologic strategies to treat human tendinopathies.