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« Collagen VI: a key extracellular regulator of muscle homeostasis and regeneration »

Collagen VI (COL6) is an extracellular matrix protein with a unique structural organization and playing a remarkably broad range of functions in several tissues, including skeletal muscle (Cescon et al., 2015). Although COL6 expression in muscles is mainly provided by interstitial fibroblasts, its proper deposition is critical for myofiber homeostasis, and mutations of COL6 genes are causative for human congenital myopathies such as Bethlem myopathy and Ullrich congenital muscular dystrophy. In the last two decades, a number of studies in COL6 null (Col6a1−/−) mice allowed shedding light into the pathophysiological mechanisms of COL6-related disorders. COL6 deficiency affects key intracellular pathways, leading to defective regulation of autophagy, accumulation of dysfunctional organelles and spontaneous apoptosis (Irwin et al., 2003; Grumati et al., 2010).

Based on the close contact of COL6 microfibrillar network with myofiber sarcolemma and its distinctive deposition in muscle endomysium, further studies revealed that this matrix molecule plays a pivotal role for satellite cells. Indeed, COL6 is a component of the satellite cell niche, which is expressed by quiescent satellite cells in a regulated manner and is required for the proper self-renewal of satellite cells both in physiological conditions and during muscle regeneration. In vivo and in vitro studies in Col6a1−/− mice demonstrated that COL6 is involved in the fine regulation of the biomechanical properties of skeletal muscle, and this is one mechanisms through which COL6 influences the maintenance of satellite cell stemness (Urciuolo et al., 2013). In unpublished work with myoblast and satellite cell cultures, we found that treatment with soluble COL6 is able to counteract myogenic differentiation and increase the incidence of Pax7-positive cells differentiation, pointing at a biochemical effect on signaling pathways. Altogether, these data indicate that COL6 has a dual function for satellite cells: on the one hand, COL6 is critical for the regulation of the mechanical properties of muscle, and on the other hand it transduces specific signals with satellite cells.

Separate work revealed that COL6 regulates macrophage recruitment and polarization (Chen et al., 2015). In unpublished studies, we found that COL6 ablation impairs macrophage recruitment and polarization after muscle injury, pointing at a further independent role of this matrix protein in muscle regeneration. These findings strengthen the concept that COL6 plays multiple functions for skeletal muscles, and besides influencing myofiber homeostasis and regulating satellite cell activities, it also plays a critical role in the inflammatory process and tissue repair during muscle regeneration.

Cited literature