REGENERATION OF AGING SKELETAL MUSCLE IS ASSOCIATED WITH IMPAIRED INFLAMMATION AND INCREASED ADIPOGENESIS

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Sarcopenia is the age-related loss of skeletal muscle mass and strength leading to physical frailty, loss of independent daily living, increased lifestyle-related disease, and high health care costs. One concern is that the incidence of sarcopenia is increasing in the world. There is a great deal of interest in strategies to prevent or reverse sarcopenia in our aging population.

Aging muscle consists of fewer myofibers compared to adult muscle and these myofibers show signs of atrophy and increased muscle adiposity. Adiposity in skeletal muscle has been widely recognized as one of the hallmarks of sarcopenia. Adult skeletal muscle has a remarkable regenerative capacity, largely mediated by myogenic stem cells, termed satellite cells (SCs). SCs are located in the plasma membrane of myofibers beneath the basement membrane and are mitotically quiescent in adult muscle. During muscle regeneration, satellite cells are activated, giving rise to myoblasts that proliferate, differentiate and fuse together or fuse to pre-existing muscle fibers to produce fully mature muscle fibers. However, skeletal muscle regeneration is markedly impaired with age. Recently we demonstrated that the number of activated, proliferated, and differentiated SCs was lower in old rats compared with young rats after muscle damage. In addition, old rats exhibited impaired muscle regeneration and increased intermuscular adipocytes post-injury. Our data suggest that impaired regeneration of old skeletal muscle might be attributed to changes in several functions of SCs. We indicated that rat SCs are multipotent cells that can undergo not only myogenic, but also adipogenic differentiation in vitro and in vivo, and their adipogenic responses increase as a function of age.

Inflammation is an obligatory event in skeletal muscle injury. Recovery of skeletal muscle injuries requires severely injured myofibers to be degraded, phagocytized, and replaced via the migration and maturation of SCs. It is well established that macrophages are the dominant inflammatory cell type during early muscle injury and may contribute to skeletal muscle regeneration by facilitating myofiber repair via the production of inflammatory cytokines, chemokines, and growth factors. Recently we demonstrated that the number of activated macrophages within skeletal muscle was lower in old rats compared with young rats after muscle damage. In addition, our DNA chip data has indicated that the expression of genes including inflammatory cytokines, chemokines, and growth factors was attenuated during the regeneration of aged skeletal muscle. These data suggest that the impaired inflammatory response to muscle damage that occurs with aging may contribute to the impaired muscle regenerative capacity and to increased muscle adiposity, both characteristic of aged muscle. These factors may be underlying causes of sarcopenia.

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