Letter to editor

Telocytes and sarcopenia: Possible effects of exercise training

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Dear Editor-in-Chief

Recently, telocytes (TCs) have been identified in various organs of the body, which are unique stromal cells (Manetti et al., 2019). Telopodes (very long and thin cytoplasmic projections) in TCs connect directly with other TCs and adjacent structures (including blood vessels, nerve endings, smooth muscles, glandular elements) through direct homo- and heterocellular junctions, or extracellular vesicles. Studies also show that TC damage and dysfunction is involved in the pathogenesis of inflammatory and fibrotic diseases, especially aging, and may be considered as therapeutic agents in the future (Chaitow, 2017). On the other hand, the evidence suggests that sarcopenia and fertility-related aging syndromes, due to their complex etiology, make pharmacological or nutritional prescriptions ineffective in their prevention and treatment (Kwak & Kwon, 2019). Therefore, the use of multidimensional strategies such as exercise programs with nutritional interventions may be more effective in preventing these age-related diseases (Nascimento et al., 2019; Pascual-Fernández et al., 2020). Research suggests that TCs may play a critical role in such matters as cross-talk preservation, regenerative mechanisms, and support for localized stem cell differentiation. In 2021, Ravalli et al. examined the presence of TCs in the anterior tibialis muscle of healthy rats under the endurance training protocol compared with sedentary rats. TCs in this study included CD34/CD117 and CD34/vimentin, which were identified by double-positive immunofluorescence staining technique. They showed that TCs in sedentary rats decreased significantly after 16 weeks. In contrast, trained rats showed a constant number of TCs after 16 weeks. In short, it can be stated that the protective relationship between TCs and regular sports activity may present new opportunities in the field of regenerative medicine and supports the hy-pothesis that a possible adaptative stimulus for TCs in sarcopenia and other musculoskeletal disorders is the promotion of physical activity (Ravalli et al., 2021; Rocha et al., 2021).

In order to support the repair and reconstruction of skeletal muscle, studies performed by transmission electron microscopy also show that there is a close spatial relationship between TCs and satellite cells in adult skeletal muscle. This association is probably due to the intracellular signaling mechanism of endocrine and paracrine, and although their exact function in skeletal muscle regeneration has not yet been fully understood, TCs containing vascular endothelial growth factor and platelet-derived growth factor receptor beta has been discovered in the interstitial part of skeletal muscle. In this way, TCs play an important role in promoting satellite cell self-renewal, vascular stability, facilitating angiogenesis, and preventing fibrosis (Cretoiu & Popescu, 2014; Manetti et al., 2019; Yin et al., 2013).

It is important to note that as age increases, skeletal muscle mass and potential for post-injury regeneration decrease. However, the role of intrinsic changes in satellite cells in these reductions has been controversial because studies have documented a decrease in the number of satellite cells with increasing age in mice. On the other hand, some results indicate that there is not significant reduction in this case. Moreover, evidence suggests that the potential for innate regeneration of satellite cell pools is impaired with age. Although the number of satellite cells in old muscle decreases, the inherent myogenic potential and self-renewal capacity of satellite cells remain unchanged. Factors that can play a role in the activation and differentiation of satellite cells are: paired/homeodomain box transcription factors PAX3 and PAX7 and basic helix-loop-helix myogenic regulatory factors (MRFs) such as MYF5, MRF4, MYOD (Myogenic determination gene number 1) and myogenin (Arpke et al., 2021; Mierzejewski et al., 2020).

Unlike satellite cells and fibroblasts, skeletal muscle TCs expre-

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-ss the c-kit cell surface marker. TC-specific antigenic markers are not yet fully understood; however, CD34 is currently used as the most reliable marker to detect TCs at the site of light microscopy, also known as TCs/CD34 + stromal cells (Manetti et al., 2019; Yin et al., 2013). The positive effects of regular physical activity on the number of satellite cells have been expressed, at the same time, skeletal muscle that contracts and relaxes is likely to be affected by the mechanical support of TCs during exercise (Ceccarelli et al., 2017; Kondo & Kaestner, 2019). Studies have shown evidence and conclusions about TCs, although, little research has been done on TCs in mammalian skeletal muscle tissue. At present, there is no direct experimental evidence and results that conclusively support a TCs-satellite cells morpho-functional interaction following skeletal muscle injury (Manetti et al., 2019). However, due to the beneficial role of exercise on satellite cells and TCs in the prevention of age-related muscle disorders, there are still many issues that need to be addressed, including identifying TC-specific biomarkers and their role in sarcopenia. Therefore, the role of regular physical activity on new interstitial cells such as TCs will be a new treatment for age-related diseases such as sarcopenia, which requires further investigations (Ravalli et al., 2021; Wang et al., 2016).

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