

# Tissues, Pathology, and Diagnostic Microscopy

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### Effects of growth hormone and/or resistance exercise on the myotendinous junction of the plantaris muscle in hind-limb unloaded rats.

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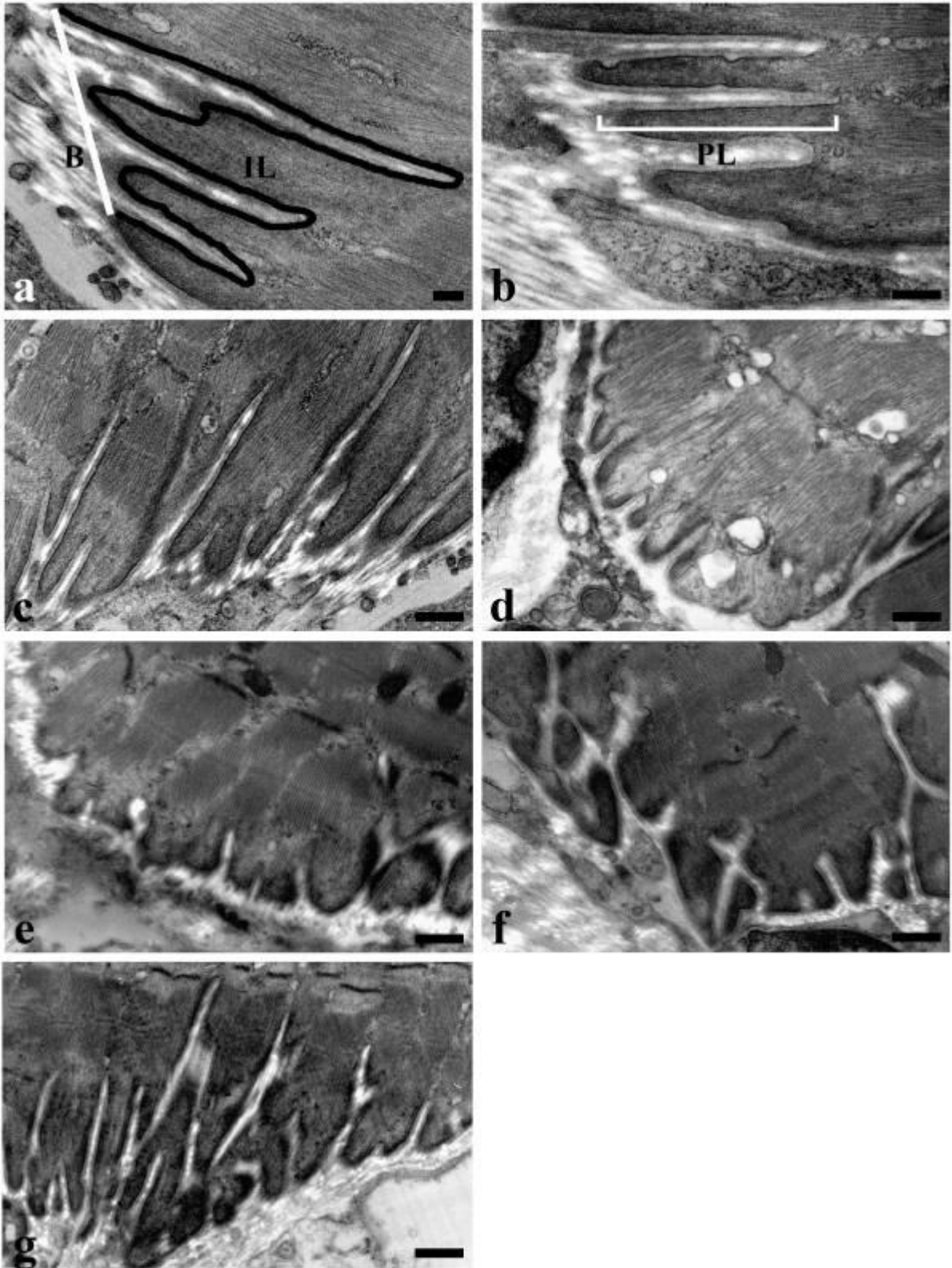
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The myotendinous junction (MTJ) is the site where muscle contractile force is transmitted from the myofibrils across the plasma membrane to the extracellular matrix (ECM), therefore it is a key structure for the locomotor system [1]. At ultrastructural level, the interface between muscle cell membrane and ECM is highly folded and interdigitated [2]. We recently demonstrated that changes at MTJ level occur as an adaptation to exercise-induced tension increase. In particular, branching of finger-like processes increases, so enlarging the whole tendon-muscle surface area and, consequently, allowing a better tension resistance [3].

In this ultrastructural study, we analyze MTJ behavior in the atrophic condition and during particular prevention protocols. Twenty, hypophysectomized, Sprague-Dawley rats were assigned to one of five groups: control (CTRL), hind-limb suspended (HS), hind-limb suspended and exercised (EX), hind-limb suspended and growth hormone injected (GH) and hind-limb suspended, GH injected and exercised (GH+EX). After sacrifice, MTJs of plantaris muscles were processed for electron microscopy [4]. The contact between muscle and tendon was evaluated with IL/B ratio, where "B" is the base and "IL" is the interface length of tendon finger-like processes at MTJ level (Figure 1a) [5]. After 10 days of suspension the IL/B ratio decreases from 6.39 in CTRL to 3.92 in HS. After unloading, the prevention treatments increase IL/B ratio to 4.18 in GH, 5.25 in EX and 7.3 in GH+EX, respectively. For investigating the causes of the decrease in IL/B ratio in HS and the effects of prevention protocols, we measured the finger-like process extension (Figure 1b), the percentage of branched primary processes and their bifurcation means. In the HS group, there was a lower number of muscle-tendon interdigitations compared to the CTRL group. Finger-like processes were frequently absent and, where present, appeared small and irregular (Figure 1c-d). Growth hormone treatment appears not to stimulate the healing of MTJ but it has a partially effect on the muscle, that seem to slightly recover some CTRL features (Figure 1e). The resistance exercise protocol, as well as GH treatment, was not capable of maintaining the contact surface between tissues, but an interesting observation in both exercised groups was the higher number of bifurcated interdigitations than in the CTRL group (Figure 1f). The combination of GH treatment and exercise protocol prevent any significant adverse effects of chronic unloading on the MTJ interface (Figure 1g).

In conclusion, ultrastructural changes occur at MTJ organization level in HS, as an adaptation to muscle unloading. Differently, MTJ structure is partially maintained by resistance exercise protocol or GH treatment, while the exercise with simultaneous somatropin administration showed a greater effect.

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**Figure 1.** Plantaris muscle MTJs. a) MTJ from CTRL group, the base (B) and the interface length (IL) of junction are highlighted. b) Measure of the primary finger-like process extension (PL). c) Long and numerous tendon interdigitations in the CTRL group. d) Short and rare finger-like processes in the HS group. e) In the GH group, changes appear similar to HS group, but occurring to a lesser extent. f) In the EX group, the length of the finger-like processes was similar to control and a large number of branched interdigitations were observed. g) In the GH+EX group, the tendon interdigitations increase their length and start to branch. A, B Bar 0.25  $\mu\text{m}$ ; C, D, E, F, G Bar 0.5  $\mu\text{m}$ .