**P429 Simulated hypergravity induces changes in human tendon-derived cells: from cell morphology to gene expression**

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Gravity influences physical and biological processes, having an impact on development, as well as homeostasis of living systems. The musculoskeletal system is comprised of several mechano-responsive tissues and altered gravitational forces are known to influence distinct properties, including bone mineral density and skeletal muscle mass. This is particularly relevant in a near-weightlessness (microgravity) environment, which is found during spaceflight and, not less importantly, during bed resting. Over the years, several studies have been conducted under simulated conditions of altered gravity owing to the advances on ground-based facilities, such as bioreactors for microgravity / hypo-gravity (<1g) research and centrifuges for hypergravity (>1g) studies. Interestingly, microgravity-induced alterations are comparable to tissue degeneration caused by disuse and ageing. In turn, exposing musculoskeletal tissues to hypergravity may constitute a way of simulating (over)loading or, eventually, to be used as a measure to rescue cell phenotype after exposure to near-weightlessness conditions. Different studies have focused on bone, cartilage and skeletal muscle, but effects on tendons and ligaments have been underappreciated. Therefore, we evaluated the influence of increasing g-levels (5g, 10g, 15g and 20g) and different hypergravity exposure periods (4 and 16 h) on the behaviour of human tendon-derived cells (hTDCs). For this purpose, hTDCs were exposed to simulated hypergravity conditions using the Large Diameter Centrifuge (LDC) from the European Space Research and Technology Centre (ESTEC, ESA, The Netherlands). Human TDCs cultured under standard conditions (1g, normogravity, Earth gravity force) were used as controls. The effects of hypergravity on the viability of hTDCs, as well as on the expression of tendon related markers at the gene level were evaluated.

Simulated hypergravity resulted in a reduced cell content after 16 h independently of g-level, as determined by DNA quantification. Additionally, the different g-levels studied led to changes in cell and cytoskeleton morphology. Strikingly, a 16-hour period of exposure resulted in alterations of gene expression profiles. Overall, gene expression of tendon-related markers, including collagen types I (*col1a1*) and III (*col3a1*), scleraxis (*scx*), tenomodulin (*tnmd*), decorin (*dcn*) and tenascin (*tnc*), seemed to be increased upon hypergravity stimulation and in comparison to cells cultured under control conditions.

Altogether, these results highlight that altered gravity, particularly simulated hypergravity, has an influence on the phenotype of tendon cells, opening new avenues for research focused on using altered gravity as a model for overloading-induced tendon tissue injury or as measure to rescue the phenotype of degenerated tendon cells.

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