FEATURES

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Interactions Between Muscle Tissues and Bone Metabolism

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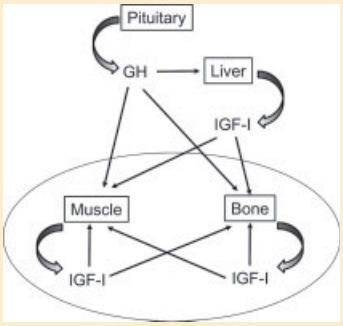
Sarcopenia and osteoporosis have recently been noted for relationship with locomotive syndrome and increased number of older people. Sarcopenia is defined by decreased muscle mass and impaired muscle function, which may be associated with frailty. Several clinical data have indicated that increased muscle mass is related to increased bone mass and reduced fracture risk. Genetic, endocrine and mechanical factors as well as inflammatory and nutritional states concurrently affect muscle tissues and bone metabolism. Several genes, including myostatin and α-actinin 3, have been shown in a genome-wide association study (GWAS) to be associated with both sarcopenia and osteoporosis. Vitamin D, growth hormone and testosterone as well as pathological disorders, such as an excess in glucocorticoid and diabetes, affect both muscle and bone. Basic and clinical research of bone metabolism and muscle biology suggests that bone interacts with skeletal muscle via signaling from local and humoral factors in addition to their musculoskeletal function. However, the physiological and pathological mechanisms related to muscle and bone interactions remain unclear. The authors found that Tmem119 may play a critical role in the commitment of myoprogenitor cells to the osteoblast lineage. They also reported that osteoglycin and FAM5C might be muscle-derived humoral osteogenic factors. Other factors, including myostatin, osteonectin, insulin-like growth factor I, irisin and osteocalcin, may be associated with the interactions between muscle tissues and bone metabolism.



Quantitative Superresolution Microscopy Reveals Differences in Nuclear DNA Organization of Multiple Myeloma and Monoclonal Gammopathy of Undetermined Significance

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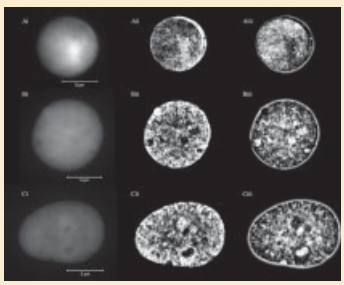
The mammalian nucleus has a distinct substructure that cannot be visualized directly by conventional microscopy. In the following study, the organization of the DNA within the nucleus of multiple myeloma (MM) cells, the precursor cells (monoclonal gammopathy of undetermined significance; MGUS) and control lymphocytes of the representative patients is visualized and quantified by superresolution microscopy. Three-dimensional structured illumination microscopy (3D-SIM) increases the spatial resolution beyond the limits of conventional widefield fluorescence microscopy. 3D-SIM reveals new insights into the nuclear architecture of cancer as shown for the first time that it resolves organizational differences in intranuclear DNA organization of myeloma cells in MGUS and in MM patients. In addition, a significant increase in nuclear submicron DNA structure and structure of the DNA-free space in myeloma nuclei compared to normal lymphocyte nuclei is reported. The study provides previously unknown details of the nanoscopic DNA architecture of interphase nuclei of the normal lymphocytes, MGUS and MM cells.



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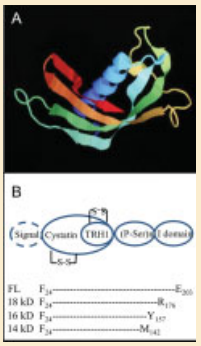
The following study found that the C-terminus of Spp24 is labile to proteolysis by furin, kallikrein, lactoferrin, and trypsin, indicating that both extracellular and intracellular proteolytic events could account for the generation of biologically-active Spp18, Spp16, and Spp14. The authors determined the effects of the truncation products on kinase-mediated signal transduction, gene expression, and osteoblastic differentiation in W-20–17 bone marrow stromal cells cultured in basal or pro-osteogenic media. After culturing for five days, all forms inhibited BMP-2-stimulated osteoblastic differentiation, assessed as induction of alkaline phosphatase activity, in basal, but not pro-osteogenic media. After 10 days, they also inhibited BMP-2-stimulated mineral deposition in pro-osteogenic media. Spp24 had no effect on Erk1/2 phosphorylation, but Spp18 stimulated short-term Erk1/2, MEK 1/2, and p38 phosphorylation. Pertussis toxin and a MEK1/2 inhibitor ablated Spp18-stimulated Erk 1/2 phosphorylation, indicating a role for G_i proteins and MEK1/2 in the Spp18-stimulated Erk1/2 phosphorylation cascade. Truncation products, but not full-length Spp24, stimulated RUNX2, ATF4, and CSF1 transcription. It is suggested that Spp24 truncation products have effects on osteoblastic differentiation mediated by kinase pathways that are independent of exogenous BMP/TGF-β cytokines.



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In the following study, second-generation RNA sequencing was performed to examine the transcriptomes of long non-coding RNAs (lncRNAs) in atrial fibrillation (AF) and non-AF canine cardiac fat pads. A total of 61,616 putative lncRNAs were yielded, in which 166 were downregulated and 410 were upregulated with more than twofold change. Bioinformatics analysis showed that the aberrantly expressed genes were associated with neural development, migration and neurodegenerative disorders. On the basis of a series of filtering pipelines, two new lncRNAs, namely, TCONS_00032546 and TCONS_00026102, were selected. Silencing of TCONS_00032546 or TCONS_00026102 with lentiviruses in vivo could significantly shorten or prolong the atrial effective refractory period thereby increasing or preventing AF inducibility by promoting or inhibiting the neurogenesis. Besides, the expression of CCND1-FGF19-FGF4-FGF3 gene cluster and SLC25A4, the nearby genes of TCONS_00032546 and TCONS_00026102, were negatively correlated with that of lncRNAs. Furthermore, combining bioinformatics analysis with literature review, TCONS_00032546 and TCONS_00026102 may induce effects by increasing the CCND1-FGF19-FGF3-FGF4 gene cluster and SLC25A4 via complex mechanisms during neural remodeling. Taken together, dysregulated lncRNAs may play regulatory roles in AF neural remodeling, which may further provide potential therapeutic targets for prophylaxis and treatment of AF.