Glutathione (GSH), antioxidant enzymes and alkaline phosphatase (AP) activities and duodenal superoxide anion (O_2^-) were also determined. The weight gain, body mass index, waist circumference and serum triglycerides were significantly higher in FRU rats compared to those from the control rats. These parameters were normalized with NA treatment. The intestinal Ca^{2+} absorption as the Ca^{2+} uptake and AP activity decreased in FRU rats in comparison with those from controls. These effects were avoided with NA. FRU rats decreased the GSH content, whereas FRU + NA rats increased GSH content above the control values. FRU rats showed lower SOD and CAT activities than those from the controls, and NA avoided these effects. The levels of O_2^- increased in the FRU rats and NA prevented this increase. To conclude, MS produced by supplying FRU inhibits the intestinal Ca^{2+} absorption due, at least in part, by oxidative stress triggering. Since NA has the ability to stimulate the GSH synthesis and to improve intestinal redox state, it can protect against the inhibitory effect of the cation absorption caused by FRU ingestion.

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Código 10
Naringin: A possible bone protector for experimental type I diabetes mellitus

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There is a relationship between Diabetes mellitus (D.m.) and low bone remodeling that cannot be improved by insulin administration. As D.m. also produces oxidative stress, our hypothesis is that bone alterations may be associated with redox changes and if so, this could be avoided by an antioxidant therapy like naringin. Adult male Wistar rats were used: 1) controls, 2) diabetic rats treated with 60 mg/kg/bw of streptozotocin (STZ), 3–4) STZ rats treated with 40 or 80 mg/kg/bw/day of naringin for 30 days. Histomorphometry, bone mineral density (BMD) and content (BMC) and microcomputarized tomography were analyzed (μCT). We also determined vitamin D status and other systemic parameters of calcium metabolism. Bone marrow was studied for glutathione content (GSH), catalase activity (CAT), while adipocyte and osteoclast (OC) numbers were counted from histological sections. Calcitriol and osteocalcin levels were reduced by STZ. Naringin returned osteocalcin values to control ones. STZ rats presented low BMD and BMC in distal femur and proximal tibiae, and the highest dose of naringin avoided this effect. STZ group presented reduced bone volume, thickness, trabecular number and intertrabecular spaces. All these changes were overcome with naringin-80. Diabetic rats had increased adipocytes and OC numbers and low GSH concentration and high CAT activity. All these changes were prevented with naringin. In summary, our results suggest that naringin protects the bone osteolytic effects triggered by insulin deficiency. Osteocalcin normalization and the reduction in the number of adipocytes and OC suggest that naringin acts as an anabolic agent for the diabetic bone.

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Código: 11
Effect of different doses of zoledronate on bone growth in rats

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Zoledronate (Z) is a potent antiresorptive drug used in children with bone diseases. The lack of information about their safety in these patients raises some concerns. The aim of this work was to study the effect of Z on bone growth. A 4 × 2 factorial design was used to study the dose of Z (D) and the time of treatment (T) at different levels (**D**: 0–2.5–12.5–25 μg Z/kg bw/s.c. weekly; **T**: 15–30days). Sprague-Dawley rats (n = 24) of 21 days were assigned to a different level combination of each factor. Bone morphometric, histomorphometric, connectivity and biomechanical studies were performed. Data were expressed as mean ± SD. To evaluate the significance of factors and interactions, two-way ANOVA and Bonferroni post-test were used. Different letters indicate significant differences ($p < 0.05$). Significant interaction was found in femur length with lower growth (mm) at D25T30 (D0T15 = 23.7 ± 0.06[a], D2.5T15 = 23.6 ± 0.5[a], D12.5T15 = 23.6 ± 0.6[a], D25T15 = 23.8 ± 0.1[a], D0T30 = 28.4 ± 0.9[b], D2.5T30 =28.7 ± 0.3[b], D12.5T30 = 28.3 ± 0.5[b], D25T30 = 27.6 ± 0.3[c]). Total sectional area, cortical area and cortical thickness increased with T. Histomorphometric and connectivity variables significantly increased with D. Cortical bone strength increased with T independently of D. Biomechanical parameters of trabecular bone, fracture load (FL) and stiffness, showed significant interaction with greater effect at high D and T (FL: D0T15 = 2.5 ± 5.9[a] N, D2.5T15 = 37.6 ± 35.1[a], D12.5T15 = 53.5 ± 22.9[a], D25T15 = 37.8 ± 25.5[a], D0T30 = 35.8 ± 7.9[a], D2.5T30 =107 ± 35.1[b], D12.5T30 = 111 ± 34.1[b], D25T30 = 126 ± 33.6[b]). All the variables analyzed were modified as expected according to the growth. Only a negative effect on linear growth at the highest D was found. Careful risk/benefit analysis suggests that the administration of Z would not adversely affect the properties of growing bone in rats.

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Código: 14
1alpha,25(OH)2-vitamin D3 effects in cellular cycle of Rhabdomyosarcoma cells

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Our research group has recently opened a new investigation line about 1α,25$(OH)_2$-vitamin D_3 (1,25D) hormone actions in rhabdomyosarcoma cells. Rhabdomyosarcoma is one of soft tissue cancers that affects skeletal muscle and bone, predominantly in kids and older people. Treatments employed to fight this pathology did not advance in the last 30 years. In this work we use the cellular line of human rhabdomyosarcoma, RD, and we evidence that the hormone promotes interesting changes in the cellular cycle. Our data indicate that 1 nM of 1,25D significantly diminishes the amount of live cells at 72 h of treatment (respect its control). When we analyzed the phases of cellular cycle by flow cytometry, we observed that the hormone reduces the number of cells into S phase (at 48 and 72 h of treatment) with a concomitant augment of cells into G0/G1 phase. These results reveal that 1,25D controls rhabdomyosarcoma cells proliferation. To go in deep with these results, we studied the behavior of cellular cycle key proteins by Western blot assays. We determinate that cells treated for 72 h with 1,25D showed an increase in the cyclin D1 and cyclin D3 expression. Of relevance, we evidenced that the hormone augments the protein levels of cyclin dependent kinase inhibitors. Our results indicate that the hormone regulates the cellular cycle of rhabdomyosarcoma cells. Altogether these outcomes open doors to investigate in deep the modulation of different signaling cascades involved in the inhibition of proliferation of these cancer cells exerted by 1,25D.

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Código: 15
Role of intestinal alkaline phosphatase in calcium absorption

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Intestinal alkaline phosphatase (iAP) is an enzyme related to calcium (Ca) absorption regulation. Previously, we found higher Ca absorption as a function of absorption surface in duodenal alkaline phosphatase deficient ($Akp3^{-/-}$; [KO-mice]) mice. Bone from KO-mice showed greater fracture load than controls in the femoral neck fracture test. In the current study we evaluated bone mineral density (BMD) and bone histomorphometric parameters in C57BL/6 female KO-mice (n = 10) and controls (WT, n = 6) mice. The percentage of trabecular bone (BV/TV), trabecular thickness (Tb.Th, mm) and trabecular number (Tb.N, 1/mm) and trabecular connectivity index (ICI and NDX) and the ratio node-termini (R) were analyzed on digital images (100×) of histological sections (Image J 1.40). BMD (mg/cm^2) of the tibia was determined using X-ray simultaneously with a pattern of known Ca concentrations. BMD was measured at the same site where histomophometry were evaluated. Results: no significant differences were observed in bone length, cortical thickness or BMD (WT = 10.47 ± 3.04; KO = 13.30 ± 1.54). While BV/TV showed no significant difference (WT = 9.29 ± 1.25; KO = 14.58 ± 2.59) we observed an increase in an increased in Tb.Th without changes in Tb.N in KO-mice. The node-termini ratio was significantly higher in KO-mice. Similarly, although not reaching statistical significance due to the dispersion of data, NDX and ICI were higher in KO-