Effect in inhibiting bone formation and enhancing TRAF6 mediated osteoclastogenesis than IL6, suggesting the role of different regulatory mechanisms governing TNFα and IL6 action on bone metabolism.

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154 PROTEOMIC ANALYSIS OF OSTEOBLASTS SECRETOME PROVIDES NEW INSIGHTS IN MECHANISMS UNDERLYING OSTEOARTHRITIS SUBCHONDRAL BONE SCROSIS
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Purpose: Osteoarthritis (OA) is characterized by cartilage degradation but also by other joint tissues modifications like subchondral bone sclerosis. In this study, we used a proteomic approach to compare secretome of osteoblast isolated from sclerotic (SC) or non sclerotic (NSC) area of OA subchondral bone.

Methods: Secretome was analyzed using differential quantitative and relative label free analysis on nanoUPLC C2 HDMS system. mRNA of the more differentially secreted proteins were then quantified by RT-PCR and the most relevant proteins identified using western blotting and immunoassays.

Results: 175 proteins were identified in NSC osteoblast secretome. Compared to NSC osteoblast secretome, 13 proteins were significantly less secreted (Osteomodulin, CSF-1, IGFBP5, VCAM-1, IG2F, 78 kDa glucose-regulated protein, versican, calumenin, IGFBP2, thrombomodulin-4, periostin, reticulocalbin 1 and osteonectin), and 12 proteins were significantly more secreted by SC osteoblasts (CHI3L1, fibulin-3, SERPIN2, IGFBP6, SHGRL3, SERPIN1, reticulocalbin1, alpha-2-HS-glycoprotein, TIMP-2, IGFBP3, TIMP-1, SERPINF1). Similar changes in periostin, osteomodulin, SERPIN1, IGFBP6, fibulin-3 and CHI3L1 mRNA levels were observed. Finally, osteomodulin and fibulin-3 specific sequences were quantified by western blot and immunoassays in serum and culture supernatants.

Conclusions: We highlighted some proteins differentially secreted by the osteoblasts coming from OA subchondral bone sclerosis. These changes contribute to explain some features observed in OA subchondral bone, like the increase of remodeling or abnormalities in bone matrix mineralization. Among identified proteins, osteomodulin was found decreased and fibulin-3 increased in serum of OA patients. These findings suggest that osteomodulin and fibulin-3 fragments could be biomarkers to monitor early changes in subchondral bone metabolism in OA.

155 EFFECT OF DENOSUMAB ON BONE FORMATION MARKER PINP

Purpose: Type I procollagen N-terminal propeptide (PINP) is considered the most sensitive bone formation marker and it is useful for monitoring osteoporosis treatment such as bone formation or anti-resorptive therapy. In our hospital, we have administered Denosumab, an anti-RANKL antibody as a treatment for osteoporosis. In addition to bone mineral determination (DXA method), PINP and serum NTx are used as osteogenic markers and bone resorption markers, respectively, for its therapeutic effect determination. In past reports it has been reported that there are many cases in which PINP falls below the standard lower limit (17.1 μg / L) in patients using bisphosphonate (BP). The purpose of this study was to investigate the state of PINP value in cases treated with denosumab.

Methods: For January 2015 - December 2016, we evaluated PINP and NTx for 30 patients with osteoporosis who administered denosumab at our hospital. For each marker, the percentage of cases below the baseline lower limit was compared.

Results: Denosumab administration resulted in PINP below the reference lower limit value in 15 cases (50%). In NTx, there were no cases below the reference lower limit. There were no cases of apparent atypical femoral fractures during the follow-up period. In 24 patients who were able to measure PINP from the first dose of denosumab, the transition of the PINP value was observed. All cases were within the reference values before the initial prescription, but 11 cases (46%) were lower than the reference lower limit value during administration of denosumab for an average of 6 months.

Conclusions: Denosumab strongly suppresses bone turnover and also decreases bone metabolism markers. When both the bone formation marker and the bone resorption marker are below the lower limit value, it is serologically in the state of inhibition of excessive bone turnover (SSBT) and may contribute to atypical fracture (Kitaori et al., 2004). In this study, PINP was lower than the lower limit in half cases in patients treated with denosumab, but it is difficult to think of all these cases as SSBT status. There are reports that there are cases in which PINP is below the lower limit in certain proportions even in BP administered patients (Eastell et al., 2011). It is difficult to use PINP as a hazard marker of SSBT in patients receiving bone resorption inhibitors including denosumab. It may be necessary to set new reference values for PINP for cases using bone resorption inhibitors. In patients using denosumab, PINP fell below the reference lower limit in 50%. In patients with bone resorption inhibitors including denosumab, it may be necessary to examine new reference values for PINP.