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News on current events in osteoporosis and rheumatology

Serum biomarker profile associated with high bone turnover and BMD in postmenopausal women

N°57 – December 2008

Early diagnosis of onset osteoporosis is essential for the delivery of effective therapy. Biochemical markers of bone turnover provide a means of evaluating skeletal dynamics that complements static measurements of bone mineral density (BMD) by dual energy X-ray absorptiometry. Conventional clinical measurements of bone turnover, primarily the estimation of collagen and its breakdown products in the blood or urine, lack both sensitivity and specificity as a reliable diagnostic tool. In this study [1], the serum proteome of 58 postmenopausal women with high or low/normal bone turnover (training set) was analyzed by surface-enhanced laser-desorption/ionization time-of-flight (SELDI-TOF) mass spectrometry, and a diagnostic fingerprint was identified using a variety of statistical and machine-learning tools. The diagnostic fingerprint was validated in a separate test set, consisting of serum samples from an additional 59 postmenopausal women obtained from the same Mayo cohort, with a gap of 2 y.

Specific protein peaks that discriminate between postmenopausal patients with high or low/normal bone turnover were identified and validated. Multiple supervised learning approaches were able to classify the level of bone turnover in the training set with 80% sensitivity and 100% specificity. In addition, the individual protein peaks were also significantly correlated with BMD measurements in these patients. Four of the major discriminatory peaks in the diagnostic profile were identified as fragments of interalpha-trypsin-inhibitor heavy chain H4 precursor (ITIH4), a plasma kallikrein-sensitive glycoprotein that is a component of the host response system.

These data suggest that these serum protein fragments are the serum-borne reflection of the increased osteoclast activity, leading to the increased bone turnover that is associated with decreasing BMD and presumably an increased risk of fracture. In conjunction with the identification of the individual proteins, this protein fingerprint may provide a novel approach to evaluate high bone turnover states.

1. Bhattacharyya S et al. *J Bone Miner Res.* 2008; 23: 1106-1117

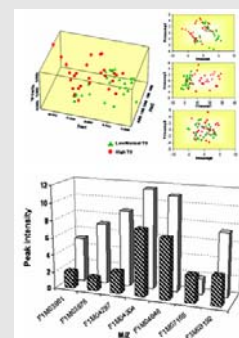
Serum biomarker profile associated with high bone turnover and BMD in postmenopausal women

Biochemical markers of bone turnover provide a means of evaluating skeletal dynamics that complements static measurements of bone mineral density (BMD) by DXA. The serum proteomics approach is a new tool to identify new markers of bone turnover.

The principal components analysis show that the plot of the samples against the first three principal components clearly indicates the efficient differentiation between the samples with or without high bone turnover. Clear differences between the sample groups are indicated along the planes of the first vs the second principal components and also the first vs the third principal components as shown in the 2-D plots.

The diagnostic fingerprint of postmenopausal women with high (striped bars) and low/normal (white bars) bone turnover show clear differences.

In conjunction with the identification of the individual proteins, this protein fingerprint may provide a novel approach to evaluate high bone turnover states.



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