

JUSTIN SILVER, MD

JERUSALEM, ISRAEL

TRAP 5b AS A MARKER OF BONE RESORPTION

Justin Silver
Jerusalem, Israel

Tartrate resistant acid phosphatase (TRAP; EC 3.1.3.2) has often been used to assess bone resorption. Although osteoclasts contain abundant TRAP and they are responsible for bone resorption, the total TRAP activities in the serum measured by colorimetric methods is not a sensitive index of bone turnover. TRAP 5 is further separated into 5a and 5b by electrophoresis. The two isoforms are almost identical, but they have a different carbohydrate content, 5a containing sialic acid that is not found in 5b. Only type 5b is derived from the osteoclast, and therefore assays have been developed (1-3). Takahashi et al (4) studied the TRAP isoforms, type-5a or type-5b, responsible for increased tartrate-resistant acid phosphatase (TRAP) activity in endstage renal disease (ESRD) and TRAP protein in rheumatoid arthritis (RA). They studied 24 sera each from healthy, ESRD and RA subjects. Type-5 TRAP activity and protein were quantitated by immunoassays. Isoform expression was determined by computerized imaging of non-denaturing polyacrylamide gels (PAGE) stained for TRAP activity. Other biochemical markers included: intact parathyroid hormone (iPTH), total and bone-specific alkaline phosphatase (TAP, BAP), N-telopeptides of type-I collagen (NTx), and free pyridinoline (Pyd). Isoform 5a was normal in both ESRD and RA. Isoform 5b was elevated in ESRD only. Both TRAP activity and protein correlated with iPTH, TAP and Pyd in ESRD sera. Increased TRAP activity in ESRD was due to increased osteoclastic isoform 5b and related to bone turnover. They concluded that heterogeneity of serum TRAP and preferential expression of isoforms has clinical significance in different diseases including ESRD and RA. Reichel et al (5) studied 141 hemodialysis patients and showed that TRAP 5b, bAP and osteocalcin had high correlations with intact PTH assays and the whole PTH assay. Importantly, none of the PTH assays was superior to any other PTH assay in predicting serum concentrations of the bone markers. In summary, TRAP 5b has the potential to be useful marker of osteoclastic bone resorption.

References

1. Halleen J.M., Alatalo S.L., Suominen H., Cheng S., Janckila A.J., and Vaananen H.K. 2000. Tartrate-resistant acid phosphatase 5b: a novel serum marker of bone resorption. *J.Bone Miner.Res.* 15:1337-1345.
2. Igarashi Y., Lee M.Y., and Matsuzaki S. 2001. Heparin column analysis of serum type 5 tartrate-resistant acid phosphatase isoforms. *J.Chromatogr.B Biomed.Sci.Appl.* 757:269-276.
3. Alatalo S.L., Halleen J.M., Hentunen T.A., Monkkonen J., and Vaananen H.K. 2000. Rapid screening method for osteoclast differentiation in vitro that measures tartrate-resistant acid phosphatase 5b activity secreted into the culture medium. *Clin Chem.* 46:1751-1754.
4. Takahashi K., Janckila A.J., Sun S.Z., Lederer E.D., Ray P.C., and Yam L.T. 2000. Electrophoretic study of tartrate-resistant acid phosphatase isoforms in endstage renal disease and rheumatoid arthritis. *Clin Chim.Acta* 301:147-158.
5. Reichel H., Esser A., Roth H.J., and Schmidt-Gayk H. 2003. Influence of PTH assay methodology on differential diagnosis of renal bone disease. *Nephrol Dial.Transplant.* 18:759-768.