A REGULATORY MARKER OF BONE TURNOVER

Features and benefits

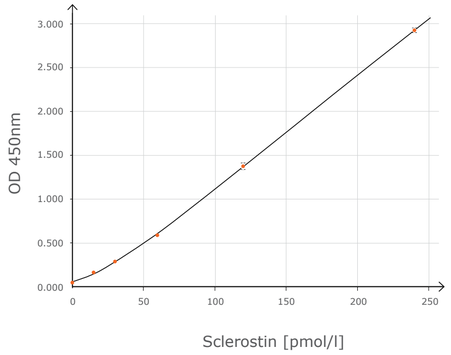
- Fully validated for use with human serum and plasma samples
- For the measurement of human samples
- 20 µl sample volume only!
- High sensitivity
- 6 standards + 1 control (all in human serum matrix!)
- Convenient ready to use protocol

Assay characteristics

- Method: Sandwich ELISA, HRP/TMB
- Sample type: Serum, plasma (Citrate, EDTA, Heparin)
- Sample size: 20 µl / test
- Standard range: 0 - 240 pmol/l
- Detection limit: 2.6 pmol/l
- Incubation: overnight / 1 h / 30 min (room temperature)
- Unit conversion: 1 pg/ml = 0.044 pmol/l

URINE PROTOCOL AVAILABLE

Sclerostin standard curve



Related Biomedica Bone Products

- DKK-1 ELISA, Cat.No. BI-20413
- OPG ELISA, Cat.No. BI-20403
- Ampli-sRANKL ELISA, Cat.No. BI-20452
- Cathepsin K ELISA, Cat.No. BI-20432

Setting the **standard** **for** **clinical** research.

SCLEROSTIN ELISA

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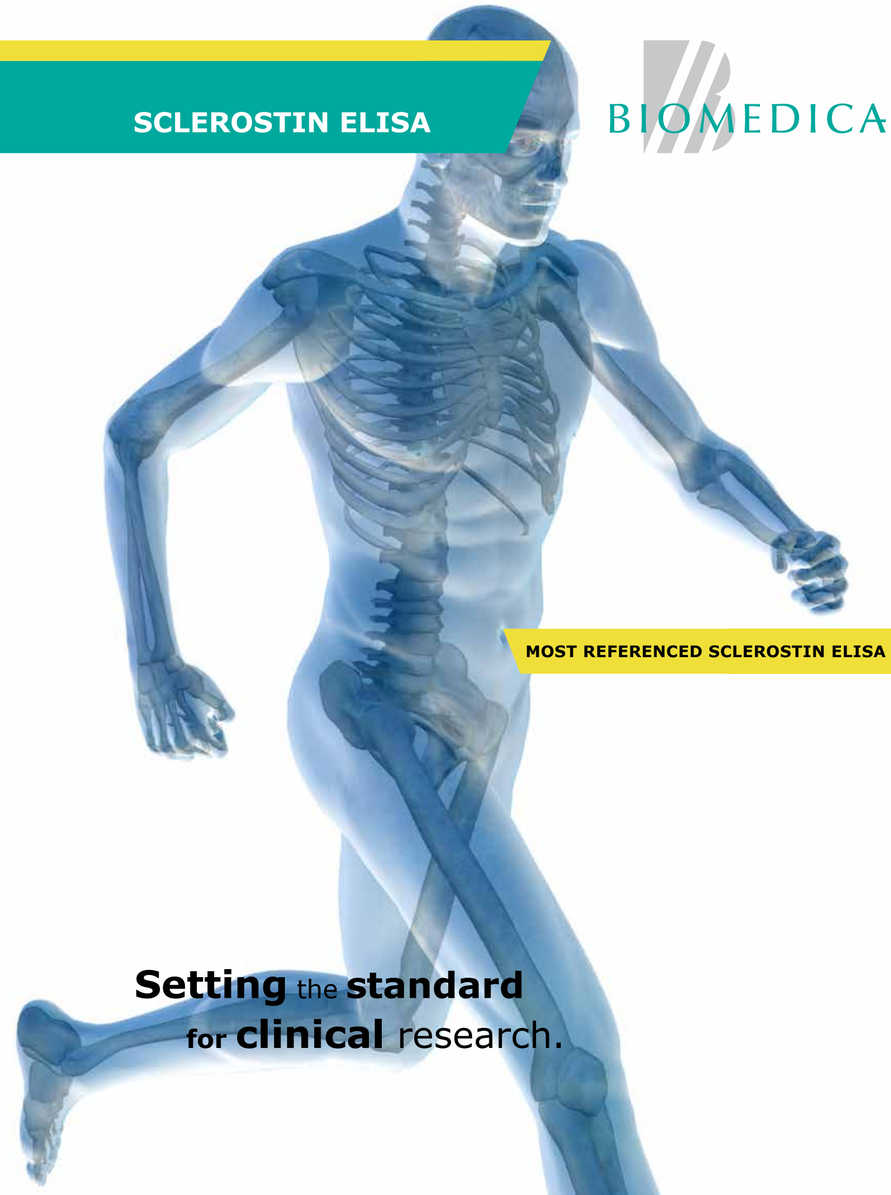

MOST REFERENCED SCLEROSTIN ELISA

Setting the **standard**
for **clinical** research.

SCLEROSTIN ELISA BI-20492

ELISA for the measurement of human Sclerostin in biological samples.

Sclerostin - a regulatory marker of bone turnover.

Areas of interest

- Osteoporosis
- Cancer-induced bone disease
- Rheumatoid arthritis
- Kidney disease

Bone remodeling

Bone remodeling is a lifelong coordinated process of bone resorption and formation which renews the skeleton whilst maintaining its structure. Osteoblasts and osteoclasts are specialized cells responsible for this process. In recent years considerable progress has been made identifying and characterizing molecules involved in the regulatory pathways of bone metabolism. These discoveries have in turn facilitated the development of new biochemical markers that reflect bone formation or bone resorption. These markers have been useful for the investigation of the pathophysiological process of metabolic bone disease and drug development in osteoporosis, rheumatoid arthritis, and metastatic bone disease.

Regulators of osteoclastic and osteoblastic activation

The discovery of the OPG/RANKL/RANK system has greatly changed our conception on the regulatory mechanisms of differentiation of osteoclasts and osteoblasts (1). The identification of RANKL as the essential cytokine for the formation and activation of osteoclasts has lead to the development of therapeutics that block RANKL activity and thus inhibits bone resorption (2). Most widely used osteoporosis therapies reduce bone loss by inhibiting bone resorption but have modest effects on increasing bone mass. The recent discovery of the Wnt signaling pathway and its regulators of osteoblastic activation have lead to the identification of novel therapeutic targets that increase bone formation (3). The activation of the Wnt signaling pathway leads to an increased proliferation and differentiation of osteoblastic precursor cells which favors the deposition of new bone and an increase of bone density. Wnt signaling is triggered when the appropriate Wnt peptide binds to a co-receptor complex at the osteoclast cell membrane involving low-density lipoprotein receptor-related protein (LRP) 5 or LRP6 and the Frizzled (Fz) receptor (3).

Sclerostin an antagonist of Wnt Signaling

Wnt signaling can be antagonized by secreted or intracellular inhibitors which prevent the formation of the Wnt-Frizzled-LRP5 complex. These antagonists may serve as potential therapeutic targets for bone formation. One of the most promising targets is sclerostin which has been identified as one of the major inhibitors of Wnt signaling (4). Studies in animals as well as in humans show that inhibition of the osteocyte-secreted sclerostin by an anti-sclerostin antibody induces bone formation. Sclerostin interacts with LRP5 and LRP6 and inhibits the binding of Wnt to its receptor, thus blocking bone formation (Fig. 1). Sclerostin is almost exclusively expressed in osteocytes. These cells are the most abundant cells in bone and possess mechanosensing appendices, stretching through a system of bone canaliculi. In response to mechanical loading, osteocytes secrete cytokines and modulate the Wnt signaling pathway. These cytokines control the differentiation of osteoblasts and thus regulate bone formation (3). Mutations of SOST, the gene encoding sclerostin, are linked to high-bone mass disorders seen in sclerosteosis and Van Buchems disease, indicating that osteocytes may act as master regulators of bone formation and localized bone remodeling (5).

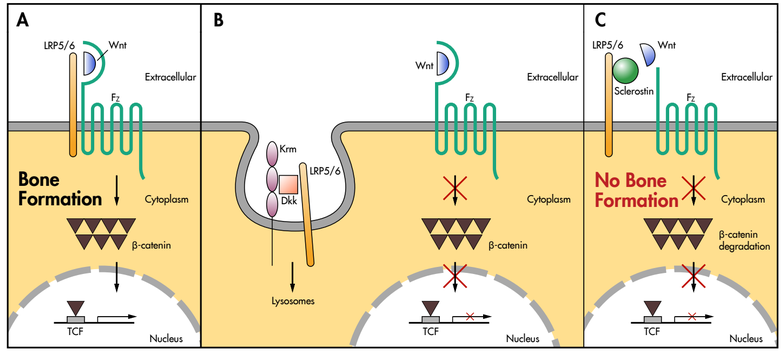

Fig. 1: Modified from Piters E. et al., Archives of Biochemistry and Biophysics 2008; 473: 112-116

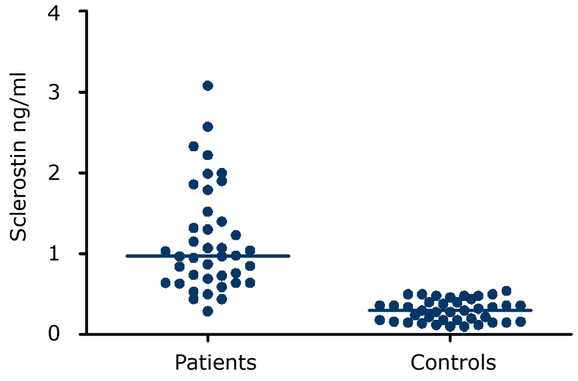

Fig. 2: Sclerostin serum levels (nanograms per milliliter) are higher in immobilized patients vs. healthy free-living subjects (P<0.0001). Data are presented as median. From: Gaudio A et al. J Clin Endocrinol Metab. 2010; 95 (5): 2248-2253. Copyright 2010, The Endocrine Society

Scientific findings

The precise physiological role of sclerostin in osteocytes is not yet fully understood, but numerous studies indicate that sclerostin expression decreases in the presence of mechanical loading, ultimately leading to enhanced osteogenesis (6). Downregulation of sclerostin expression is also caused by PTH. Bellido and co-workers have demonstrated that chronic elevation of PTH in mice reduces the expression of sclerostin in osteocytes (7). In a recent study serum sclerostin was negatively correlated with PTH levels and free estrogen index in postmenopausal women (8). These findings suggest that serum sclerostin levels are regulated by both estrogens and PTH in postmenopausal women. These observations are consistent with the recent findings of Mödder and co-workers demonstrating that in humans, circulating sclerostin levels are reduced by estrogen (9). Gaudio and co-workers have shown that sclerostin serum levels are significantly elevated in patients with immobilization-induced bone loss (Fig. 2) (10). These data are consistent with the hypothesis that sclerostin is a link between mechanical unloading and disuse osteoporosis in humans. A further study demonstrated the overexpression of sclerostin in the synovial tissues of patients with rheumatoid arthritis. These findings suggest that inflammatory cytokines may promote the imbalance between bone resorption and formation by affecting regulatory molecules of the Wnt pathway such as sclerostin (11). The role of sclerostin in multiple myeloma patients has been shown by Terpos and co-workers (12). Sclerostin is increased in the serum of patients with multiple myeloma and it correlates with advanced ISS stage, increased bone resorption, reduced osteoblast function and poor survival.

Future perspectives

Alterations of the Wnt signaling pathway and its regulatory molecule sclerostin have been shown to play an important role in bone turnover abnormalities associated with osteoporosis, multiple myeloma, bone metastasis and arthritis. The recent discovery of the Wnt signaling pathway has lead to the identification of new biological markers, such as sclerostin, that may be useful in understanding the regulatory mechanisms underlying bone formation. The development of neutralizing antibodies to sclerostin are found to be very promising therapeutic agents in diseases with elevated bone resorption. Treatments based on inhibition of sclerostin activity could provide a powerful way to restore bone strength of the osteoporotic skeleton.

Conclusion

The measurement of serum sclerostin levels is a novel approach in studying the regulation of bone mass, and may serve as a tool in detecting bone disorders and monitoring the efficiency of various therapies.

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