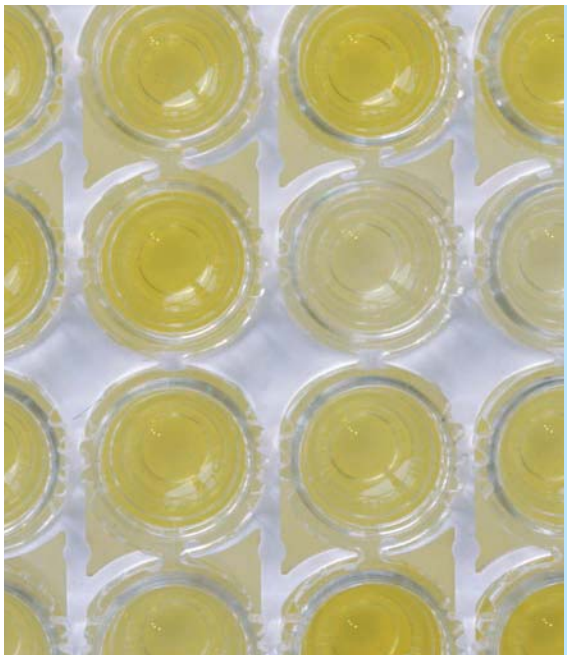
Osteoprotegerin / sRANKL

Valuable tools for research and routine



Bone Metabolism

Arterial Calcification

ELISAs for:

- OPG
- OPG (Mouse/Rat)
- total sRANKL
- sRANKL (Mouse/Rat)

Mouse/Rat Assays worldwide exclusive!

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OPG (ELISA)

Osteoprotegerin (OPG) or Osteoclast Inhibiting Factor (OCIF) is a glycoprotein with anti-resorptive characteristics which plays an important role in the regulation of bone degradation. The soluble receptor OPG prevents the differentiation and activation of osteoclasts and inhibits osteolytic processes. The biological importance of this system is demonstrated by the induction of severe osteoporosis in mice by targeted ablation of OPG/OCIF and by the induction of osteopetrosis by targeted ablation of OPG-L/ODF or overexpression of OPG/OCIF.

A first clinical study in postmenopausal women confirmed the **potent and sustained anti-resorptive activity of OPG**. Further clinical studies show that the expression of OPG is dependent of age and an adequate oestrogen supply. Other studies show that OPG expression was induced in bone marrow cells after proliferation of adherent stromal cells. There was an age-dependent decrease in the expression of OPG in cultured human bone marrow cells that indicates a mechanism explaining the age-related increase in the capacity of stromal/osteoblast cells to support osteoclastogenesis.

It could be demonstrated that OPG blocks behaviour indicative of pain in mice with bone cancer. The treatment with OPG blocks cancer-induced skeletal degradation, skeletal pain and pain-related neurochemical reorganisation of the spinal cord. The clinical studies show that OPG has a great potential for the treatment of osteoporosis and bone tumour-associated pain.

Tumour cells can produce cytokines and thereby can activate T-cells. Osteoblasts or activated T-cells induce the differentiation of osteoclast precursor cells to osteoclasts and activate osteoclasts through the binding of OPGL to RANK. OPG binds as „decoy"-receptor to OPGL and thus inhibits the differentiation and activation of osteoclast precursor cells and osteoclasts

Increased serum OPG is believed to be a **marker of bone metastatic spread in prostate cancer** patients (Jung et al. 2001). Even more OPG (and BSP) were found as independent prognostic factors for PCa-related death (Jung et al. 2004).

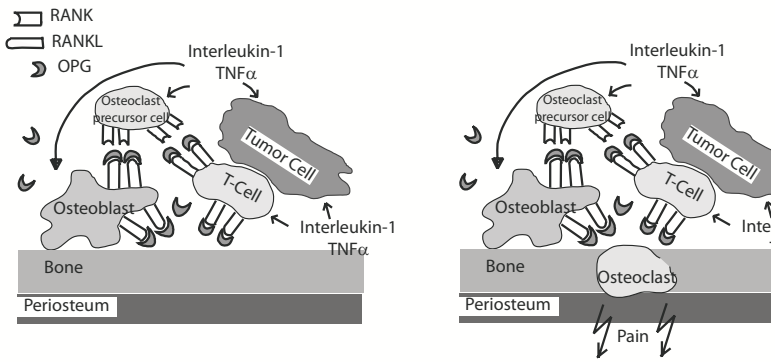

Figure 1: *Tumour cells can produce cytokines and thereby can activate T-cells. Osteoblasts or activated T-cells induce the differentiation of osteoclast precursor cells to osteoclasts and activate osteoclasts through the binding of OPGL to RANK. OPG binds as a „decoy" receptor to OPGL and thus inhibits the differentiation and activation of osteoclast precursor cells and osteoclasts. RANKL = Receptor Activator of Nuclear factor-κB ligand; RANK = Receptor Activator of Nuclear factor-κB; OPG = Osteoprotegerin = OCIF (osteoinductive factor)*

Intake of oral contraceptives is associated with increased OPG serum levels. This may contribute to the positive effects of oral contraceptives on the skeleton (Hofbauer et al. 2004).

Recent findings suggest that OPG and RANKL may play an important role in the development of vascular disease. Jono et al. (2002) and Schoppet et al. (2003) showed that **serum OPG levels are associated with the presence and severity of coronary artery disease**. They conclude that alterations of the OPG system may contribute to the pathogenesis of human vascular disease. The mechanism by which serum OPG levels were increased in advanced coronary artery disease is still unknown. Another study showed that OPG is upregulated in symptomatic human carotid atherosclerosis with possible implications for plaque stability (Golledge et al. 2004).

Indications

- Study of the bone metabolism
- Osteoporosis
- Prediction of relative risk for non-traumatic fracture
- Atherosclerosis

OPG	
Matrix	Serum, EDTA plasma, Heparin plasma, Citrate plasma
Sample volume	20 µL
Test principle	ELISA
Cat. No.	K 1011

OPG (Mouse/Rat)	*(for research use only)*
Matrix	Plasma, serum, cell culture supernatants, urine
Sample volume	100 µL
Test principle	ELISA
Cat. No.	KR1020

total sRANKL (ELISA)

Receptor activator of NF-κB ligand (RANKL), a member of the tumor necrosis factor ligand superfamily, is expressed on cells of the osteoblastic lineage and activated T lymphocytes. RANKL has been shown to exist in **three forms**, a cell-bound form of 316 amino acids, a truncated form with a shorter cytoplasmicdomain generated by enzymatic cleavage, and a soluble form (sRANKL). All forms of RANKL activateNF-κB (RANK), a receptor located on osteoclasts and dendritic cells. **RANKL** is the essential factor for osteoclast formation, fusion, activation, and survival, resulting in bone resorption and bone loss. Diel and Jakob et al. (2014) emphasised the importance of osteoclast-activation by tumor cells during metastasising into the bone. Bone and bone marrow should be included into the oncologic therapy as inhibition of bone regeneration is an important principle of metastasising. Moreover, RANKL is known to have several immunological effects, including T cell activation and regulation of various functions of antigen-presenting dendritic cells, as well as inhibition of apoptosis, induction of cluster formation, and stimulation of cytokine production. The biological effects of RANKL are counterbalanced by the endogenous antagonist osteo-protegerin (OPG) which binds to and neutralizes RANKL.

The **biological importance of RANKL** is demonstrated by induction of severe osteopetrosis and complete absence of osteoclasts in RANKL knock-out mice. In addition, these mice exhibit defects in the differentiation of T and B cells, lack lymph nodes, and have defects in thymus differentiation. Activated T cells which are important in the pathogenesis of inflammatory and immune-mediated diseases produce increased levels of RANKL expression. In these disorders, RANKL represents the link between bone metabolism and the immune system. Thus, an excessive production of RANKL has been implicated in the pathogenesis of rheumatoid arthritis, periodontal disease, and malignant tumors such as multiple myeloma and T cell leukaemia. Moreover, RANKL may also be involved in certain aspects of vascular diseases (arterial calcification, atherosclerosis) and the development of the lactating breast. RANKL is regulated by various hormones, cytokines, and drugs that have been shown to regulate bone metabolism, including glucocorticoids. A low level of RANKL is an independent predictor of nontraumatic fracture. This finding may gain relevance for assessment of fracture risk (Schett et al. 2004).

The tests decribed allow to determine accurately the OPG/sRANKL ratio and to integrate the result into the therapy decision.

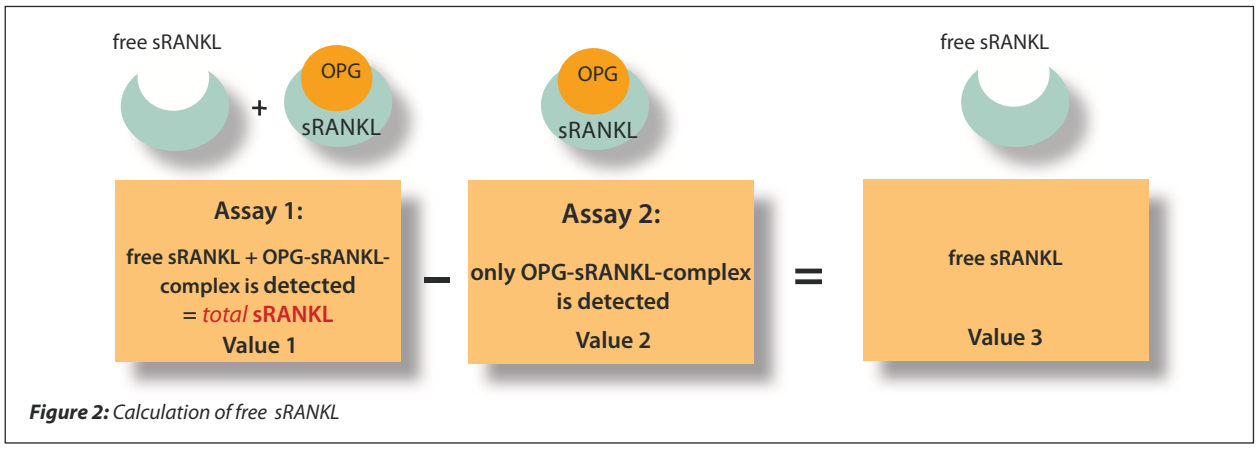

Figure 2: *Calculation of free sRANKL*

Why to measure „*total* sRANKL"?

The concentration of free sRANKL is rather low in human serum or plasma. That is why the determination of the very same is difficult in those matrices. This fact which lies in the nature of the parameter if measured in serum or plasma, inspired Immundiagnostik to develop a new kit for measuring total sRANKL. The antibody combination in our total sRANKL ELISA detects the OPG-sRANKL-complex. Running the assay with an excessive addition of OPG to the sample, the primarily present OPG-sRANKL-complex plus the newly evoked OPG-sRANKL-complex are detected (Value 1 in our chart). Running the assay without an ecxessive addition of OPG to the sample, only the primarily present OPG-sRANKL-complex in the sample is detected (Value 2 in our chart). Subtracting Value 2 from Value 1 will give you the value of free sRANKL in the sample (Value 3 in our chart).

Indications

- Study of the bone metabolism
- Osteoporosis
- Prediction of relative risk for non-traumatic fracture
- Atherosclerosis

***total* sRANKL**	
Matrix	Serum, plasma
Sample volume	50 µL
Test principle	ELISA
Cat. No.	K 1016

The advantages of our *total* sRANKL-ELISA:

- **Detects free and OPG bound sRANKL: higher sensitivity than sRANKL-ELISA (differentiates clearly within the normal range)**
- **Free sRANKL can be determined mathematically by carrying out the assay two times: once with a prior addition of OPG (free sRANKL and OPG-sRANKL-complex are detected), once without an addition of OPG (only OPG-sRANKL-complexes are detected)**
- **Only 50 µl sample volume is needed**
- **High stability of the analyte (can be kept frozen for years until analysed)**

sRANKL Mouse/Rat	*(for research use only)*
Matrix	Serum, cell culture supernatants
Sample volume	100 µL
Test principle	ELISA
Cat. No.	K 1019

← *For your research:*
sRANKL Mouse/Rat ELISA

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