



Technical Information

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Focus on Nephrology: The Role of Biomarkers in CKD-MBD

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Chronic renal insufficiency is very often accompanied by dysfunctions of the cardiovascular as well as the skeletal system. This matter of fact is reflected in the new disease nomenclature CKD-MBD (chronic kidney disease – mineral bone disorder, disorder of bone and mineral metabolism in patients with chronic kidney disease). The detection of concomitant diseases such as renal osteopathy and vascular calcification is very often only possible by using examination methods that are expensive, invasive and / or burdened by radiation exposure (e.g. bone biopsy, heart catheter examination, x-ray examination, etc.) Due to the numerous comorbidities and high chronic disease burden in patients with renal insufficiency, nephrology is a very interesting field for the establishment of biomarkers. Ideally, biomarkers can distinguish between health and disease conditions. The difference regarding risk factors lies in the fact that biomarkers are associated with the status or progress of a disease: A biomarker of CHD for example should correlate with the severity degree of the changes in coronary vessels. A risk factor, by contrast, has been involved in the development of a disease, but does not have to be associated with its severity degree at a certain point in time.

Biomarkers should be simple, inexpensive, minimally invasive, and serially measurable parameters that have good predictive value for the presence and severity of a particular disease. An optimal biomarker would at the same time be associated with a high diagnostic and prognostic sensitivity, would clearly reflect “the hard facts” of treatment outcome within the frame of therapy monitoring and could thus replace invasive, more expensive, and potentially hazardous examinations. For logical reasons, such parameters are used as biomarkers that are derivable from pathophysiology and, in addition, stand up to epidemiologically and therapeutically oriented clinical testing. Conveniently, typical biomarkers in medicine are components of serum or plasma. BNP is such an example. It is synthesized in the heart in parallel with the volume load and is released into the circulation. The BNP level is helpful in assessing the hydration status and the cardiac function in a patient. BNP is at the same time a prognostic marker and a tool for therapy monitoring.

CKD-MBD is a parade field for the application of biomarkers. For about a decade nephrology has recognized the prominent importance of bone and mineral disorder in chronic renal insufficiency for the treatment quality and outcome of patients with chronic renal failure. Here it is necessary to define biomarkers as tools for diagnosis and monitoring with regard to the triad of CKD-MBD consisting of bone metabolism and mineral metabolism disorder as well as cardiovascular disease. Attention should be paid to changes in concentrations that may reflect a genuine disease association or may only result from degradation or elimination kinetics in renal insufficiency or dialysis.

Biomarkers in the area of CKD-MBD can perform the following functions:

1. Biomarkers may aid in the non-invasive diagnosis of renal osteodystrophy. Although requested time and again, the gold standard, i.e. bone punch biopsy, is a method of investigation that is performed only rarely due to the discomfort it causes to the patient. Established serum parameters such as PTH and total AP may only inaccurately describe the presence and precise nature of a bone metabolism disorder. Biomarkers can, above all, be used to evaluate the extent of bone turnover and thus determine the subtype of renal osteopathy. The latter is important to control well-established therapeutic strategies (use of vitamin D, calcimimetics, phosphate binding agents etc.)

A. Examples: BAP, TRAP5b, Calcidiol, OPG

2. Biomarkers may help to assess the extent of vascular calcification (VC). VC is a prominent predictor of morbidity and mortality in patients suffering from an advanced stage of CKD or terminal renal insufficiency. Biomarkers may, for example, be used as an indirect measure of coronary calcification because the gold standard, i.e. multislice CT scan, is not unconditionally available. Moreover, biomarkers can indicate the presence of risk factors and thereby provide information for a therapeutic approach.

A. Examples: OPG, MGP, AP, BAP

3. Biomarkers may predict the risk of mortality in CKD or dialysis patients. Regardless of the association with a particular underlying disease, several biomarkers are established survival factors in patients with CKD. Some factors are both disease markers in the field of CKD-MBD and mortality markers. Besides, biomarkers may also reflect the success of therapy, but this has still to be clarified by larger studies.

A. Examples: FGF, OPG, MGP, AP, BAP

Outlook: The field of biomarker research in nephrology is a fast developing one. Taking the example of the development of our knowledge about PTH assays where we have only recently discovered the significance of a species-specific detection method, this fact becomes vividly clear.

Moreover, new parameters with good potential to become established as valuable biomarkers come into the market at a rapid pace. Less than 10 years ago FGF23 found its way into nephrology and promises to become an important marker and a frequently used monitoring tool for phosphate metabolism. Other promising markers are now at the stage of experimental and clinical testing (e.g. MGP, Gla-rich protein GRP).

In summary, the use of biomarkers may be a simple and inexpensive method for the early monitoring of our patients as regards disease incidence and course of treatment. Thus, biomarkers can, properly used and optimized, help improve the treatment outcome of our patients.

FGF-23 Fibroblast Growth Factor 23

FGF-23 is produced in osteoblast precursor cells and is a potent regulator of phosphate and vitamin D metabolism.

Phosphate plays an essential role in the stability of skeletal bones and energy metabolism as well as in DNA synthesis and intracellular signal cascades.

FGF-23 inhibits in combination with cofactor Klotho phosphate reabsorption in renal proximal tubular cells via FGF-23 receptors (increased phosphate loss, reduced serum phosphate) and decreases calcitriol synthesis by suppressing alpha-1-hydroxylase.

FGF-23 in Osteology

FGF-23 is involved in a variety of diseases accompanied by hypophosphatemia caused by renal phosphate loss. Moreover, the clinical pictures show distinctly reduced calcitriol synthesis and osteomalacia or vitamin D resistant rickets.

1. Tumor-induced osteomalacia / hypophosphatemia (TIO; paraneoplastic overexpression of FGF-23)
2. Autosomal dominant hypophosphatemic rickets (ADHR; due to mutation in FGF-23 protein, FGF-23 cannot be inactivated by endopeptidases)
3. X-linked hypophosphatemia (XHL, mutation in degrading enzyme (PHEX))
4. Craniofacial dysplasia with hypophosphatemia (increased FGF-23 levels caused by mutation of FGF receptor 1)
5. Fibrous dysplasia of bone (overproduction of FGF-23 due to mutation in G-protein subunit G5a/GNAS1)

FGF-23 in Nephrology

1. Elevated FGF-23 values are seen in chronic renal insufficiency and correlate negatively with GFR.
2. Increased serum FGF-23 levels may help maintain normophosphatemia in early chronic renal insufficiency until creatinine clearance is reduced to approximately 30 mL/min and hyperphosphatemia develops due to exhausted regulatory mechanisms and concurrently decreased calcitriol and sHPT.
3. Monitoring of FGF-23 and serum phosphate in early chronic renal insufficiency allows, if necessary, to institute phosphate reduction therapy at an earlier stage.
4. Creatinine levels within the normal range do not exclude disorders of phosphate metabolism.
5. In the ArMoRR study published by Guitierrez et al. in August 2008, it was demonstrated that the FGF-23 level at the beginning of hemodialysis therapy may be seen as an independent risk marker. Patients showing FGF-23 levels within the highest range developed a 5.7fold higher risk of death within one year.

References

- Guitierrez et al.: Fibroblast Growth Factor 23 and Mortality among Patients Undergoing Hemodialysis. N Eng J Med 2008; 359: 584-92
- Chi-yuan Hsu: FGF-23 and Outcomes Research – When Physiology meets Epidemiology. N Engl J Med 2008; 359 6
- Andreas L. Serra et al.: Phosphatemic Effect of Cinacalcet in Kidney Transplant Recipients With Persistent Hyperparathyroidism. American Journal of Kidney Diseases 2008

FGF-23 (C-Term) 2nd Generation

Fibroblast Growth Factor 23

C-terminal

Cat. No.:	60 - 6100
Tests:	96
Method:	ELISA
Range:	1.5 - 1500 RU/ml
Sensitivity:	1.5 RU/ml
Incubation time:	3.5 hours
Sample volume:	100 µl
Sample type:	Serum, plasma, cell culture
Sample preparation:	It is recommended to collect the sample in the morning after a 12-hour fasting period. Plasma samples are stable up to 6 days when stored at +4°C.
Reference values:	20.9 – 125.9 RU/ml (N = 84)

Species: Human

FGF-23 Intact, Human

Fibroblast Growth Factor 23

Intact

Cat. No.:	60 - 6500
Tests:	96
Method:	ELISA
Range:	6- 200 pg/ml (can be extended to 650 pg/ml)
Sensitivity:	1.0 pg/ml
Incubation time:	3.5 hours
Sample volume:	150 µl
Sample type:	EDTA plasma, cell culture
Sample preparation:	It is recommended to collect the sample in the morning after a 12-hour fasting period. Intact FGF-23 is very instable. Therefore, collection and testing or storage should take place promptly. Store samples at -20 °C or below. Avoid repeated freezing and thawing of specimens.

Reference values: 7 - 29.3 pg/ml

Species: Human

Specificity: Antibodies recognize FGF-23 amino acids 186-206 and 51-69.

FGF-23 Intact, Human (Kainos)

Fibroblast Growth Factor 23

Intact

Cat. No.: CY-4000

Tests: 96

Method: **ELISA**

Range: 8 – 800 pg/ml

Sensitivity: 3.0 pg/ml

Incubation time: 3.5 hours

Sample volume: 50 µl

Sample type: Serum

Sample preparation: Intact FGF-23 is very instable. Therefore, collection and testing or storage should take place promptly. Store samples at -20 °C or below. Avoid repeated freezing and thawing of specimens.

Reference values: 10 – 50 pg/ml

Species: Human

Klotho, Human

Cat. No.:	27998
Tests:	96
Method:	ELISA
Range:	93.75 - 6000 pg/ml
Sensitivity:	6.15 pg/ml
Incubation time:	2 hours
Sample volume:	100 µl
Sample type:	Serum, EDTA plasma
Sample preparation:	Collection, testing and samples storage should take place promptly. Store samples at -20 °C or below. Avoid repeated freezing and thawing of specimens.
Reference values:	239 – 1266 pg/ml
Species:	Human
Specificity:	No cross-reactions observed with: osteopontin, human VEGF or PDGF.

Intended use:

Klotho is a single-pass trans-membrane anti-aging protein (1014 amino-acids, 130 kDa, chromosomal location in 13q12 in humans) that has been recently shown to have wide and important biological effects. Its expression occurs mainly in the kidney and in the parathyroid. Its extra-cellular domain is wide whereas its intra-cellular part is very short; it also exists as a soluble protein.

In humans, Klotho polymorphisms have been associated both in a positive and negative way to bone mineral density, life expectancy, cardiovascular events (e.g., ischemic stroke, carotid atherosclerosis), biomarkers of metabolic syndrome (e.g., uric acid levels, lipid and glucose metabolisms), and even to cognitive ability.

BAP (Quidel®) **Bone-specific Alkaline Phosphatase**

CE / FDA

Enzyme activity of bound BAP is measured

Cat. No.: 8012
Tests: 96
Method: **ELISA**
Range: 2-140 U/l (1-70 µg/ml)
Sensitivity: 0.7 U/l
Incubation time: 3.5 hours
Sample volume: 20 µl
Sample type: Heparinized plasma, serum, cell culture
Sample preparation: Plasma samples should not be treated with EDTA or citrate because of the inhibition of the BAP enzyme. Keep samples refrigerated at 2-8 °C for storage of less than 5 days.
For long-term storage freeze specimens at -20 °C or below.

Reference values:	Female	25 - 44 years Premenopausal	11.6 - 29.6 U/l
	Female	≥ 45 years Postmenopausal	14.2 - 42.7 U/l
	Male	> 25 years	15.0 - 41.3 U/l

Reference values from children are available.

Species: Human, rabbit, porcine, dog, cat, sheep, goat, bovine, horse, baboon, rhesus macaque, cynomolgus macaque
Cross reaction: Minimal cross-reactivity to liver (3-8 %), intestinal (0.4 %) and placental (0 %) alkaline phosphatases.

Intended use:

BAP (bone specific alkaline phosphatase) is a highly specific marker of osteoblast activity during bone remodeling. Measurement of BAP is intended for use as an aid in:

- management of postmenopausal osteoporosis and Paget's disease.
- monitoring postmenopausal women on hormonal or bisphosphonate therapy.
- predicting skeletal response to hormonal therapy in postmenopausal women.
- diagnostic analysis metastasis.

See also reference:

Clinical & Technical Monograph: Bone specific alkaline phosphatase (BAP).

BAP Control (Serum)

Cat. No.: 4820
Set of 4 times 0.5 ml (4 levels)
Average: 9, 19, 46, 85 U/l

TRAP5b, Human (Quidel®) Tartrate-resistant acid phosphatase

CE

Enzyme activity is measured

Cat. No.: 8036
Tests: 96
Method: **ELISA**
Range: 2.5 - 15.5 U/l
Sensitivity: 0.2 U/l
Incubation time: 2 hours
Sample volume: 50 µl
Sample type: Serum, Heparin-plasma, cell culture
Sample preparation: Whole blood and Serum can be stored 8 hours at room temperature, Serum and Heparin-plasma for 2 days at 2-8 °C, 1 month at -20 °C or for longer storage at -80 °C.
Maximum 3 freeze- and thaw cycles.

Reference values:	Postmenopausal women	Mean 2.89 U/l – SD 0.94
	Premenopausal women	Mean 1.33 U/l – SD 0.73
	Men	Mean 1.91 U/l – SD 0.57

Reference values from children are available.

Species: Human, (rhesus macaque)

Intended use:

TRAP5b is highly specific for osteoclasts in-vivo, although it has been shown to be secreted by alveolar macrophages under certain conditions. As a bone marker, TRAP5b is unique in that it reflects the number of osteoclasts and, as changes in bone resorption are usually associated with changes in osteoclast number, TRAP5b is a useful indicator of bone resorption.

TRAP5b is not linked specifically to osteoclast mediated collagen degradation, rather it is secreted by active osteoclasts whether or not they are metabolizing bone substrate. In certain disease states where bone resorption and the number of active osteoclasts is uncoupled, this may be very significant. TRAP5b data may also be seen as supportive of other resorption data indicating an increase in the number of active osteoclasts.

In general, in-vivo TRAP5b data correlate highly with other markers of bone resorption including DPD, NTX and CTX. As a serological bone resorption marker there is substantial synergy with bone formation markers, particularly BAP. It may therefore be beneficial to look at both BAP and TRAP5b using the same sample type, Serum.

TRAP 5b is considered as the most important marker of bone resorption rate in renal failure patients. Bone metabolism markers like CTX, NTX, BAP and osteocalcin accumulate in blood because the markers are not cleared by the dysfunctional kidney. This can lead to elevated marker levels in renal osteodystrophy, a bone disease affecting the majority of renal failure patients, causing misinterpretation of bone marker results.

TRAP5b is inactivated rapidly during circulation and degraded into fragments, before clearance from blood circulation through the liver. Therefore renal dysfunction does not affect enzymatically active intact TRAP5b levels. Even in liver failure, inactive fragments accumulate in blood, while enzymatically active intact TRAP5b molecules do not accumulate.

Serum TRAP5b demonstrates little variation over the day. This represents a great advantage over serum and urinary markers which demonstrate variations of up to 137 % over the day. TRAP5b also demonstrates minimal response to fasting, whereas other markers decrease up to 18 % during fasting. Due to its low biological noise, the signal-to-noise ratio of TRAP5b in disease and therapy situations may in fact be larger than for other serum and urinary telopeptides markers.

Changes of the TRAP activity during a therapy monitoring allow the judgment of the efficiency of anti-resorptive therapies.

Furthermore, increased TRAP5b values in serum and plasma were found in diseases with enhanced bone resorption:

- Paget's disease
- Hemodialysis
- Follow up after kidney transplantation
- Hyperthyreosis

Method Description:

The Quidel® TRAP5b Assay is a 2-step direct capture Enzym-Immunoassay.

Naturally occurring, inactive TRAP5b fragments in the serum may interfere with the detection of TRAP5b in physiological samples. The Quidel® TRAP5b Assay avoids the influence of the inactive fragments by using two different monoclonal antibodies. The assay employs two unique monoclonal antibodies, Trk49 and Trk62, generated with immunization of purified TRAP5b from human bone cells. The first antibody, Trk49, is highly specific to inactive TRAP5b fragments; the second antibody, Trk62, is highly specific for intact, active TRAP5b. Trk49 binds inactive TRAP5b fragments, thereby making Trk62 more available to bind active TRAP5b in the microwell. The resulting TRAP5b assay is very specific with high precision and a wide range of linearity.

PTH 1-84 Intact, Human

CE / FDA

Cat. No.:	7022
Tests:	96
Method:	ELISA
Range:	7 - 210 pg /ml
Sensitivity:	1.57 pg/ml
Incubation time:	3.5 hours
Sample volume:	25 µl
Sample type:	Serum, EDTA plasma
Sample preparation:	Samples should be tested immediately or stored frozen at -20 °C or below.
Reference values:	10.4 – 66.5 pg/ml
Species:	Human
Cross reaction:	Human PTH 1-34: 2 %; human PTH 39-84: 0.02 %
Standards:	Synthetic human intact PTH 1-84
Specificity:	Antibodies directed against human PTH 39-84 and PTH 1-34, detect intact PTH.

Intended use:

PTH (Parathyroid hormone, Parathormone, Parathyrin) is biosynthesized in the parathyroid gland as a pre-proparathyroid hormone, a larger molecular precursor consisting of 115 amino acids. Following sequential intracellular cleavage of a 25-amino acid sequence, pre-proparathyroid hormone is converted to an intermediate, a 90-amino acid polypeptide, parathyroid hormone. By additional proteolytic modification, parathyroid hormone is then converted to parathyroid hormone, an 84 amino acid polypeptide. In healthy individuals, regulation of parathyroid hormone secretion normally occurs via a negative feedback action of serum calcium on the parathyroid glands. Intact PTH is biologically active and clears very rapidly from the circulation with a half-life of less than four minutes. PTH undergoes proteolysis in the parathyroid glands, but mostly peripherally, particularly in the liver but also in the kidneys and bone, to give N-terminal fragments and longer lived C-terminal and Mid-region fragments.

Intact PTH assays are important for the differentiation of primary hyperparathyroidism from other (non-parathyroid-mediated) forms of hypercalcemia, such as cancer, sarcoidosis and thyrotoxicosis. The measurement of parathyroid hormone is the most specific way of making the diagnosis of primary hyperparathyroidism. In the presence of hypercalcemia, an elevated level of parathyroid hormone virtually establishes the diagnosis. In over 90 % of patients with primary hyperparathyroidism, the parathyroid hormone will be elevated.

The most common other cause of hypercalcemia, namely hypercalcemia of malignancy, is associated with suppressed levels of parathyroid hormone or PTH levels within the normal range. When intact PTH level is plotted against serum calcium, the intact PTH concentration for patients with hypercalcemia of malignancy is almost always found to be inappropriately low when interpreted in view of the elevated serum calcium.

Unlike C-terminal and Mid-region PTH, which typically are grossly elevated in subjects with renal insufficiency, intact PTH assays are less influenced by the declining renal function.

PTH values are typically undetectable in hypocalcemia due to total hypoparathyroidism, but are found within the normal range in hypocalcemia due to partial loss or inhibition of parathyroid function.

Recent studies supported the existence of a large „non PTH 1-84 fragment“ missing a part of the amino-terminal site of the molecule. All „Intact PTH“ assays cross-react with this fragment. It has been shown that this fragment may cause wrongly increased detections levels in dialysis patients. For this reason it is recommended to use the „Bioactive Intact PTH“ assay for dialysis patients.

25-OH-Vitamin D direct



Cat. No.: K2109
Tests: 96
Method: **ELISA**
Range: ~ 3 - 320 nmol/l
Sensitivity: 2.0 nmol/l
Incubation time: 24 hours
Sample volume: 30 µL
Sample type: Serum, cell culture
Sample preparation: Samples are stable for 24 hours at 2-8 °C.
Long-term storage at -20 °C or below.
Avoid repeated freeze/thaw cycles.

Reference values: 1 ng/ml = 2.5 nmol/l
1 nmol/l = 0.4 ng/ml

Deficiency (seriously deficient) < 12 ng/ml resp. < 30 nmol/l
Insufficiency (deficient) 12 - 30 ng/ml resp. 30 - 75 nmol/l
Sufficiency (adequately supplied) > 30 ng/ml resp. > 75 nmol/l

Species: Human
Specificity: 25-OH-Vitamin D₂ 23.4 %
25-OH-Vitamin D₃ 100.0 %
Vitamin D₂ & D₃ 2.0 %

Intended use:

Vitamin D is a steroid hormone involved in the intestinal absorption of calcium and the regulation of calcium homeostasis. There are two different forms of Vitamin D, named D₃ and D₂, which are very similar in structure. The Vitamin D₂ is a synthetic product, which is predominantly absorbed by fortified food.

Physiological Vitamin D₃ levels result not only from dietary uptake but can also be produced from a cholesterol precursor, 7-dehydrocholesterol, in the skin during sun exposure. In the liver, the vitamin is hydroxylated to 25-hydroxyvitamin D (25-OH-Vitamin D), the major circulating metabolite of Vitamin D. Although 1,25-(OH)₂ Vitamin D portrays the biological active form of Vitamin D, which is synthesized in the kidney, it is widely accepted that the measurement of circulating 25-OH-Vitamin D provides better information with respect to patients Vitamin D status and allows its use in diagnose hypovitaminosis.

The concentration of 25-OH-Vitamin D decreases with age and a deficiency is common among elderly persons. Clinical applications of 25-OH-Vitamin D measurements are the diagnosis and therapy control of postmenopausal osteoporosis, rickets, osteomalacia, renal osteodystrophy, pregnancy, neonatal hypocalcemia and hyperparathyroidism. In addition, a prevalence of subclinical Vitamin D deficiency has been discussed in different European countries.

Vitamin D intoxication mostly occurs during a large intake of pharmaceutical preparations of Vitamin D and may lead to hypercalcemia, hypercalcuria and nephrocalcinosis in susceptible infants.

Sclerostin TECO[®]

Regulation of Bone Turnover

Cat. No.: TE1023
Tests: 96
Method: **ELISA**
Range: 0.25 – 4 ng/ml
Sensitivity: 0.15 ng/ml
Incubation time: 20 hours
Sample volume: 25 µl
Sample type: Serum, Cell culture
Sample preparation: Non-lipemic human serum is recommended. Centrifuge collected blood samples within 4 hours. Serum is stable for 3 days at room temperature, 5 days at 2 – 8 °C, 2 years at -20 °C. For longer storage at -80°C. Maximum 3 freeze- and thaw cycles.

Reference values: Sclerostin Values are dependent on age and gender.

Subjects	Mean ng/ml	Mean pmol/l	SD ng/ml	SD pmol/l	N
Pre-menopausal female	0.56	24.64	0.13	5.72	60
Post-menopausal female	0.69	30.36	0.20	8.80	60
Men	0.74	32.56	0.27	11.44	18
All subjects	0.61	26.65	0.19	8.38	138

Clinically Healthy Subjects 16 and 91 years.

Species: Human

Intended use

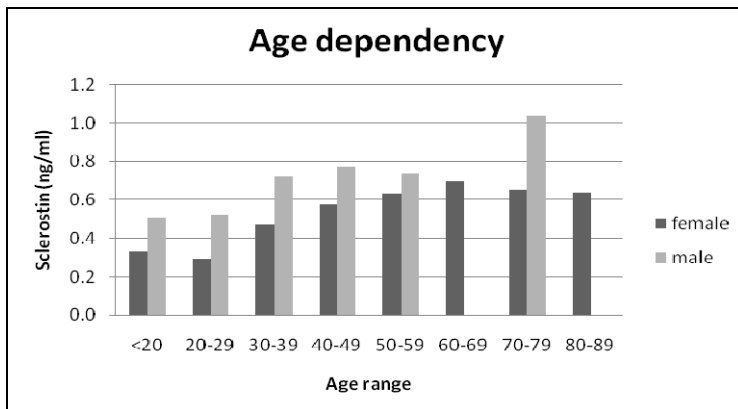
Sclerostin is the protein product of the SOST gene, which is located at 17q12-21 and highly conserved across vertebrate species. The highest expression of sclerostin throughout the adult skeleton has been observed in hypertrophic chondrocytes and osteocytes.

Sclerostin blocks canonical Wnt signaling by binding to the Wnt coreceptors LRP5/6, inhibiting bone formation by regulating osteoblast function and promoting osteoblast apoptosis. Sclerostin also antagonizes bone morphogenetic protein (BMP) action (e.g. osteoblast differentiation), but does not inhibit direct BMP-induced responses. Sclerostin expression is down-regulated by Parathyroid hormone (PTH), as well as, by the mechanical stimulation of bone.

Reduced expression of sclerostin can result in van Buchem disease, while a complete absence results in Sclerosteosis. Patients affected by Sclerosteosis show progressive hyperostosis and sclerosis of the skull, mandible and all long bones. Bone mineral density (BMD), bone volume, bone formation rate, and bone strength are significantly increased, while overall skeletal morphology appears to be normal. A predominance of sclerostin causes reduced bone quality (Osteoporosis pseudoglioma (OPPG) syndrome). Down-regulation of sclerostin might be used as a treatment for diseases such as osteoporosis, promote osseointegration of implants, prevent periprosthetic bone loss, or treat non-union in fractures. Local enhancement of sclerostin expression might be used to prevent cancer metastasis and minimize further expansion of ectopic bone formation.

- Sclerosteosis
- Van Buchem disease
- Osteoporosis pseudoglioma (OPPG) syndrome
- Follow up efficacy of osteoporosis therapy

Values Normal Subjects by Age and Gender (Mean \pm SD)



OPG, Human (Quidel®)

Osteoprotegerin

Cat. No.: 8034
Tests: 96
Method: **ELISA**
Range: 1.5 - 60 pmol/l
Sensitivity: 0.13 pmol/l
Incubation time: 3 hours
Sample volume: 100 µl (diluted 1:3, cell culture direct)
Sample type: Serum, plasma (EDTA, Citrate, Heparin), cell culture, synovial fluid
Sample preparation: No activity loss for 8 hours at room temperature or after 2 weeks at 4 °C. Store samples at -20 °C for longer storage. Serum is stable up to 3 freeze and thaw cycles, Heparin only stable for 1 freeze and thaw cycle. Before use, thaw samples at low temperature and mix them thoroughly. Hemolyzed or lipemic sera may cause erroneous results.

Reference values: Average 4.1 ± 0.33 pmol/l

Species: Human, baboon, rhesus macaque

Intended use:

Osteoprotegerin (OPG) is a secretory glycoprotein belonging to the TNF receptor super family. OPG inhibits the binding of RANK to RANKL and thus inhibits the recruitment, proliferation and activation of osteoclasts. Since OPG exhibits an inhibitory effect on osteoclasts activation, it acts as a soluble factor in the regulation of bone mass.

Changes in the homeostasis of the RANKL/RANK/OPG systems causes disturbances in bone remodeling shown by bone damages in patients with postmenopausal osteoporosis, Paget's disease, bone loss due to cancer metastases and rheumatoid arthritis.

Intended applications:

- Postmenopausal and senile osteoporosis
- Glucocorticoid dependent osteoporosis
- Diseases with locally increased resorption activity
- Therapy control of OPG treatments
- Arthritis
- Bone metastases
- Vascular calcification
- Renal cell carcinoma

Fetuin-A, Human



Cat. No.: KT-800
Tests: 96
Method: **ELISA**
Range: 12.5 - 370 ng/ml
Sensitivity: 5.0 ng/ml
Incubation time: 3 hours
Sample volume: 25 µl (prediluted 1:10,000)
Sample type: Serum
Sample preparation: Serum should be separated within 3 hours after blood collection, measure or store at -20 °C. Max. 3 freeze and thaw cycles.

Reference values: 0.35 - 0.95 g/l
Mean 0.57 g/l - SD 0.13 g/l

Species: Human

Intended use:

Fetuin-A synthesized in the liver is secreted into the blood stream and it is deposited, accumulated as a non-collagenous protein in mineralized bones and teeth.

Fetuin-A acts as an important circulating inhibitor of ectopic calcification, a frequently seen complication in degenerative diseases. Low Fetuin-A level may be associated with higher cardiovascular mortality in chronic renal failure, liver cancer and liver cirrhosis patients on long-term dialysis.

Human Fetuin-A represents a natural inhibitor of tyrosine kinase activity of the insulin receptor. Fetuin-A may play a significant role in regulating post-prandial glucose disposition, insulin sensitivity, weight gain, and fat accumulation and may be a novel therapeutic target in the treatment of type 2 diabetes, obesity, and other insulin-resistant conditions.

- Fetuin-A level (< 0.35 g/l) indicates a higher risk of cardiovascular calcification and increase mortality in ESRD-patients.
- Fetuin-A level (> 1.00 g/l) in elderly population, an independent risk factor of type II diabetes.
- Fetuin-A is an important predictor of death in acute myocardial infarction.
- Involved with the regulation of calcium metabolism and osteogenesis.

EPO **Erythropoietin**

CE / FDA

Cat. No.:	7025
Tests:	96
Method:	ELISA
Range:	10 - 336 mU/ml
Sensitivity:	1.2 mU/ml
Incubation time:	2.5 hours
Sample volume:	200 µl
Sample type:	Serum, Heparin- and EDTA Plasma
Sample preparation:	Due to diurnal variation it is recommended to collect the sample between 7:30 a.m. and 12:00 noon. Collect whole blood and allow the blood to clot at 2-8 °C. The serum should be promptly separated, preferably in a refrigerated centrifuge, and stored at -15 °C or below. Serum samples may be stored at 2-8 °C for a maximum of 24 hours. Serum samples, frozen at -15 °C, are stable for a maximum of 12 months. Avoid repeated freezing and thawing of specimens. For long-term storage, it is recommended to aliquot the samples prior to freezing. Before usage, all samples should be brought to room temperature and mixed by gentle inversion or swirling. Do not use grossly hemolyzed or lipemic samples.
Reference values:	4.3 - 32.9 mU/ml (2.5 - 97.5 percentile)
Species:	Human
Cross reaction:	No cross-reaction with ACTH and TSH.

Intended use:

Erythropoietin (EPO) is a highly glycosylated protein. Quantification of serum erythropoietin concentration serves as a diagnostic tool to determine the cause of anemia or erythrocytosis. Aplastic anemia, hemolytic anemia and anemia due to iron deficiency all result in serum EPO elevation. Whereas, EPO levels in patients with secondary anemia due to renal failure and other disorders such as acquired immune deficiency syndrome (AIDS) are generally inappropriately low for the degree of anemia. Some tumors produce EPO and in these cases, EPO may be used as a tumor marker to monitor the effectiveness of treatment. With the start of recombinant erythropoietin administration as biological therapy to the increase erythrocyte number, erythropoietin assays are also be used to support the prognosis and control of the response to a recombinant EPO treatment in anemic persons.

For further information please contact / Für weitere Informationen wenden Sie sich bitte an / Pour plus d'informations, veuillez contacter:

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always your partner

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