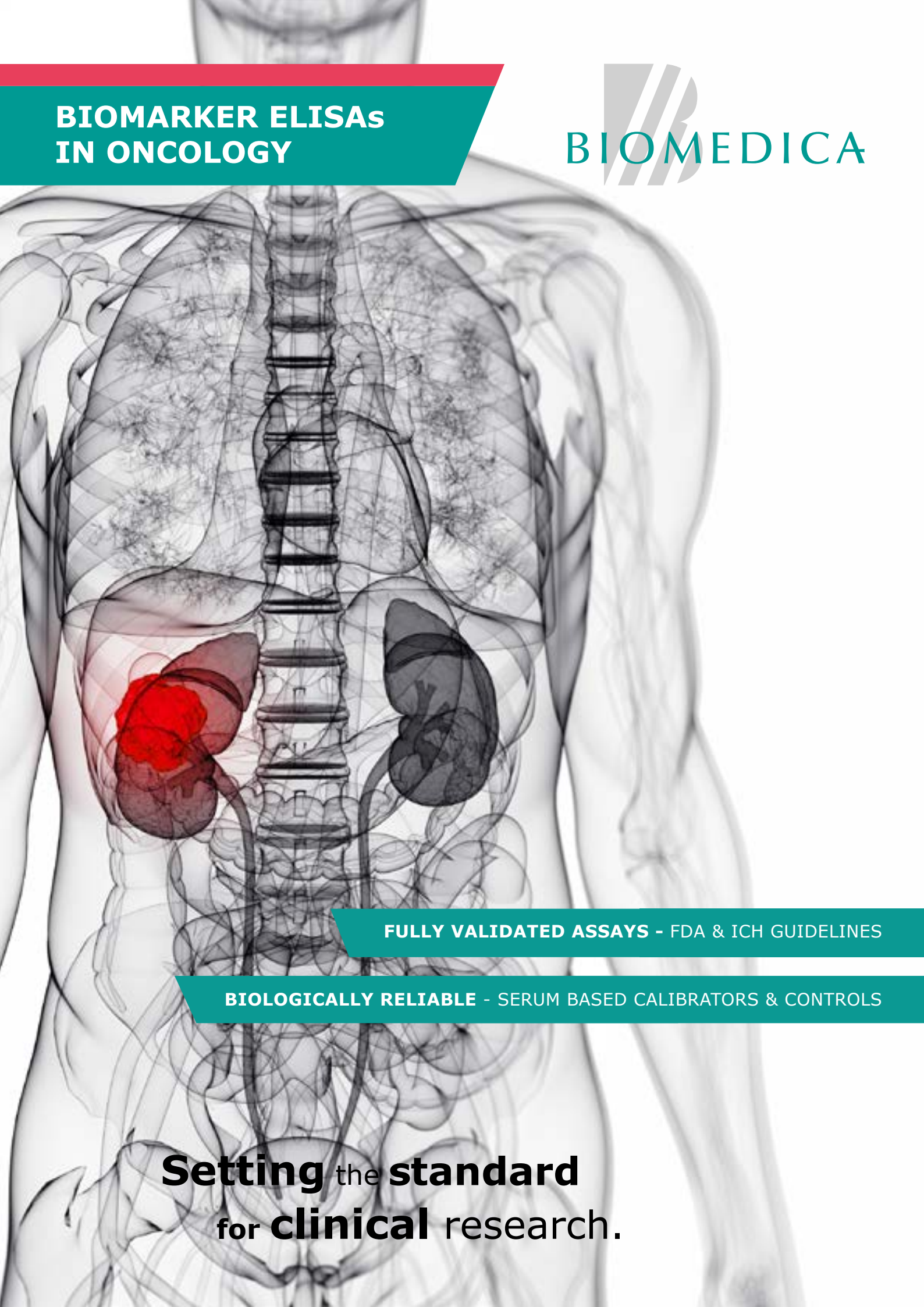
BIOMARKER ELISAs IN ONCOLOGY

BIOMEDICA



FULLY VALIDATED ASSAYS - FDA & ICH GUIDELINES

BIOLOGICALLY RELIABLE - SERUM BASED CALIBRATORS & CONTROLS

Setting the **standard**
for clinical research.

DKK-1 • free sRANKL • OPG • Periostin • Semaphorin 4D

Dickkopf-1 (DKK-1) ELISA (BI-20413)

Method	Sandwich ELISA, HRP/TMB
Sample type	Serum, cell culture supernatants
Sample size	20 µl / test, 12x8 tests
Standard range	0 – 160 pmol/l
Detection limit	1.7 pmol/l
Assay time	3.5 h
Use	CE marked – for IVD use in the EU
References	45

- Marker for bone metastasis and osteolytic bone lesions
- Potential prognostic marker and therapeutic target

Free soluble RANKL ELISA (BI-20462)

Method	Sandwich ELISA, HRP/TMB
Sample type	Serum, plasma (heparin)
Sample size	150 µl / test, 12x8 tests
Standard range	0 – 2 pmol/l
Detection limit	0.01 pmol/l
Assay time	Overnight assay
Use	CE marked – for IVD use in the EU
References	100+

Osteoprotegerin (OPG) ELISA (BI-20403)

Method	Sandwich ELISA, HRP/TMB
Sample type	Serum, plasma
Sample size	20 µl / test, 12x8 tests
Standard range	0 – 20 pmol/l
Detection limit	0.07 pmol/l
Assay time	5.5 h
Use	CE marked – for IVD use in the EU
References	96

- Dysregulated in primary bone cancers and cancers metastasizing to the bone
- Associated with tumor invasiveness
- Therapeutic target

Periostin ELISA (BI-20433) **NEW**

Method	Sandwich ELISA, HRP/TMB
Sample type	Serum, plasma, urine, cell culture supernatants
Sample size	10 µl / test, 12x8 tests
Standard range	0 – 4000 pmol/l
Detection limit	20 pmol/l
Assay time	5.5 h
Use	Research use only

- Increases cell survival and invasiveness
- Potential prognostic marker and therapeutic target

Soluble Semaphorin 4D ELISA (BI-20405) **NEW**

Method	Sandwich ELISA, HRP/TMB
Sample type	Plasma
Sample size	10 µl / test, 12x8 tests
Standard range	0 – 2000 pmol/l
Detection limit	12 pmol/l
Assay time	4.5 h
Use	Research use only

- Pro-angiogenic
- Inducer of tumor cell invasiveness
- Potential therapeutic target

Total soluble Neuropilin-1 ELISA (BI-20409) **NEW**

Method	Sandwich ELISA, HRP/TMB
Sample type	Serum, plasma
Sample size	10 µl / test, 12x8 tests
Standard range	0 – 12 nmol/l
Detection limit	0.09 nmol/l
Assay time	4 h
Use	Research use only

- Antagonist of VEGF-mediated angiogenesis
- Potential diagnostic marker in cervical cancer
- Potential therapeutic target

Neuropilin-1 • Sclerostin • Endostatin • Big Endothelin • FGF23

Sclerostin ELISA (BI-20492)

Method	Sandwich ELISA, HRP/TMB
Sample type	Serum, plasma (EDTA, heparin), urine, cell culture supernatants
Sample size	20 µl / test, 12x8 tests
Standard range	0 – 240 pmol/l
Detection limit	3.2 pmol/l
Assay time	Overnight assay
Use	Research use only
References	100+

- Dysregulated in cancers targeting the bone
- Marker for cancer-induced osteolytic bone loss
- Therapeutic target

Bioactive Sclerostin ELISA (BI-20472) **NEW**

Method	Sandwich ELISA, HRP/TMB
Sample type	Serum, plasma (EDTA, citrate), urine, cell culture supernatants
Sample size	20 µl / test, 12x8 tests
Standard range	0 – 320 pmol/l
Detection limit	1.9 pmol/l
Assay time	3.5 h
Use	Research use only

Endostatin ELISA (BI-20742) **NEW**

Method	Sandwich ELISA, HRP/TMB
Sample type	Serum, plasma, urine
Sample size	10-20 µl / test, 12x8 tests
Standard range	0 – 800 pmol/l
Detection limit	4 pmol/l
Assay time	4.5 h
Use	Research use only

- Anti-angiogenic
- Potential prognostic marker, especially in combination with VEGF
- Therapeutic target

Endostatin mouse/rat ELISA (BI-20742MR) **NEW**

Method	Sandwich ELISA, HRP/TMB
Sample type	Serum, plasma
Sample size	5 µl / test, 12x8 tests
Standard range	0 – 32 nmol/l
Detection limit	0.24 nmol/l
Assay time	2.5 h
Use	Research use only

Big Endothelin ELISA (BI-20082H)

Method	Sandwich ELISA, HRP/TMB
Sample type	Serum, plasma
Sample size	50 µl / test, 12x8 tests
Standard range	0 – 3 pmol/l
Detection limit	0.02 pmol/l
Assay time	5.5 h
Use	marked – for IVD use in the EU
References	42

- Promotes proliferation, survival, neovascularization, and invasiveness
- Indicates poor prognosis

FGF23 (C-terminal) ELISA (BI-20702)

Method	Sandwich ELISA, HRP/TMB
Sample type	Serum, plasma
Sample size	50 µl / test, 12x8 tests
Standard range	0 – 20 pmol/l
Detection limit	0.08 pmol/l
Assay time	Overnight assay
Use	CE marked – for IVD use in the EU
References	10

- Marker for tumor-induced osteomalacia

DKK-1 ELISA (Cat. No. BI-20413) CE

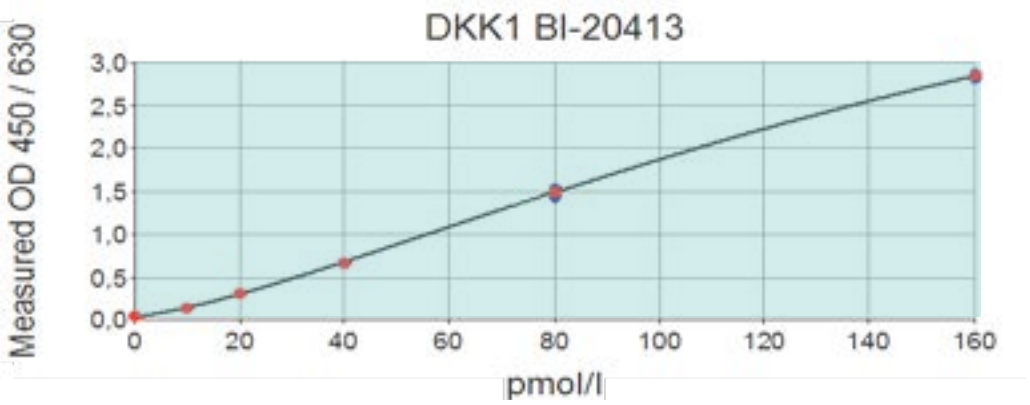
Features & Benefits

- CE marked
- Low sample volume – 20 µl / well
- No sample predilution

Assay Characteristics & Performance

Method	Sandwich ELISA, HRP/TMB, 12 x 8 detachable strips
Sample type	Serum
Standard range	0 – 160 pmol/l (equal to 0 – 4128 pg/ml)
Conversion factor	1 pg/ml = 0.05 pmol/l (MW: 25.8 kDa)
Sample volume	20 µl / well
Detection limit	1.7 pmol/l (0 pmol/l + 3 SD; equal to 43.9 pg/ml)
Incubation time	2 h / 1 h / 30 min
Precision	Intra-assay (n=5) ≤ 3%. Inter-assay (n=9) ≤ 3%.

Typical Standard Curve



Related Products

- Sclerostin ELISA, Cat. No. BI-20492
- Bioactive Sclerostin ELISA, Cat. No. BI-20472
- OPG ELISA, Cat. No. BI-20403
- Free soluble RANKL ELISA, Cat. No. BI-20462
- Periostin ELISA, Cat. No. BI-20433

DKK-1 IN ONCOLOGY

DKK-1 is a 25.8 kDa secreted protein functioning as antagonist of the canonical Wnt signaling pathway. DKK-1 is involved in embryonic development, tissue differentiation and homeostasis as well as carcinogenesis.

DKK-1 is centrally involved in the regulation of bone remodeling by inhibiting the differentiation of osteoblasts. Thus, its dysregulation is associated with various bone pathologies.
DKK-1 has emerged as a biomarker of cancer progression and prognosis as well as potential therapeutic target in various types of malignancies.

Areas of Interest

- Breast and prostate cancer
- Multiple myeloma
- Cutaneous malignant melanoma
- Hepatocellular carcinoma
- Gastrointestinal cancers
- Lung cancer
- Pancreatic cancer
- Papillary thyroid cancer
- Osteosarcoma
- MGUS

ASSOCIATION BETWEEN DICKKOPF-1 (DKK-1) AND CANCER

Reference	Type	Study Design
Sato L et al., *Cancer Res, 2010; 70(13):5326–5336*	Multiple	Patients with various cancers (n=906), healthy controls (n=207)
Mazon M et al., *Cancers, 2016; 8(7):62*		Review
Göbel A et al., *Breast Cancer Res Treat, 2017; 164(3):737–743.*	Breast	Women with primary estrogen positive breast cancer treated with adjuvant tamoxifen or aromatase inhibitors (n=45)
Göbel A et al., *Cancer Res Treat, 2015; 154:623–631.**		In vivo animal model of human breast cancer. Human breast cancer cell line with a high bone-metastatic potential.
Liang B et al., *Onco Targets Ther., 2015; 8:3115–3122.*	Gastro-intestinal	Systematic review and meta-analysis (n=5076 from 15 studies)
Fouad YM et al., *Scand J Gasteroenterol., 2016; 51(9):1133–1137*	Hepato-cellular	HCC patients (n=50), patients with chronic HCV infection (n=20), patients with liver cirrhosis (as control group, n=20)
Dong LL et al., *Diagn Pathol, 2014; 9:52.*	Lung	Patients with NSCLC (n=150), healthy controls (n=150)
Feldmann R et al., *Dermatology, 2011; 222(2):171–175.**	Melanoma	Patients with cutaneous melanoma (n=82)
Terpos E et al., *Am J Hematol, 2014; 89(1):34–40.**	Multiple Myeloma	Patients with relapsed or refractory myeloma (n=106) who received lenalidomide plus dexamethasone
Heider U et al., *Eur J Haematol, 2009; 82(1):31–38.*		Myeloma patients (n=101) receiving chemotherapy followed by autologous stem cell transplantation
Kaiser M et al., *Europ J Haemat, 2008; 80(6):490–494.*		Untreated MM patients (n=184), monoclonal gammopathy of undetermined significance patients (n=33)
Terpos E et al., *Metabolism, 2018; 80:80–90.*		Review
Han SX et al., *Oncotarget., 2015; 6(23):19907–19917.*	Pancreatic	Patients with pancreatic adenocarcinoma (n=140) and control patients (n=92)
Zhao JP et al., *Genetics and Molecular Research, 2015; 14, (4): 18886–18894.**	Papillary Thyroid	PTC patients (n=132) and healthy controls (n=40)
Rachner TD et al., *BMC Cancer, 2014; 14:649.**	Prostate	Patients with prostate cancer (n=80), serum
Browne AJ et al., *Cell Death and Disease, 2016; 7(2): e2119.**		Prostate cancer cells
Hall CL et al., *Prostate, 2008; 68(13): 1396–1404.*		Prostate cancer (PC) tissue microarrays (n=309) stained for DKK-1 protein by immunohistochemistry
D'Amelio P et al., *BMC Clinical Pathology, 2014; 14:11.**		Patients who underwent prostate biopsy (n=159)

* DKK-1 measured with Biomedica DKK-1 ELISA

Main Finding

"The majority of cancer patients presented elevated DKK1 levels compared to healthy controls and thus confirmed previous data supporting the usefulness of DKK1 as a serological biomarker of cancer."

"Dysregulation of DKK1 has been associated with bone pathologies and has now emerged as a potential biomarker of cancer progression and prognosis for several types of malignancies."

"DKK-1 serum levels were reduced in breast cancer patients receiving an adjuvant therapy with tamoxifen, possibly contributing to its bone-protective properties."

"...combined use of low concentration of statins and amino-bisphosphonates [...] significantly suppresses breast cancer-derived DKK-1 to levels where it can no longer inhibit Wnt-mediated osteoblast differentiation."

"Serum DKK1 is a potential biomarker with high sensitivity and specificity for screening GI cancers."

"Serum DKK1 could potentially be used for early diagnosis of HCC and complement measurement of AFP in the diagnosis of HCC."

"DKK-1 was overexpressed in NSCLC, and DKK-1 in serum was a good predictor of poor prognosis in patients with NSCLC."

"Low DKK-1 serum levels are associated with poor prognosis in PTC patients and DKK-1 could potentially be used as a biomarker leading to earlier diagnosis of PTC."

"The combination with bortezomib, which enhances bone formation, seems to be preferred for the management of myeloma patients with osteolytic disease."

"DKK-1 levels decrease in myeloma patients responding to treatment, irrespective of the regimen chosen. These data suggest that myeloma cells are the main source of circulating DKK-1 protein and provide a framework for clinical trials on anti-DKK-1 treatment in MM."

"... correlation between DKK-1 serum concentration and the amount of lytic bone disease, indicating that DKK-1 is an important factor for the extent of bone disease and supporting the hypothesis of DKK-1 as a therapeutic target in myeloma bone disease."

"DKK-1 plays an important role in the dysfunction of osteoblasts observed in MM. Inhibition of DKK1 reduced tumor growth as an indirect effect via modification of the tumor microenvironment."

"Serum levels of DKK1 and CA19-9 were elevated in PC patients in the early-stage cases. These levels increased with the advancement of clinical stage."

"Our in vivo data indicate that a decrease in Dkk-1 could be a sign of loss of tumor control."

"High DKK-1 serum levels are associated with a poor survival in patients with prostate cancer."

"p38 MAPK regulates DKK-1 in prostate cancer and may present a potential target in osteolytic prostate cancers."

"These data support a model in which DKK-1 is a molecular switch that transitions the phenotype of PCa osseous lesions from osteolytic to osteoblastic."

"DKK-1 might be predictive for patients negative at first biopsy who will develop PCa and in the prognosis of bone metastases."

SOLUBLE SEMAPHORIN 4D (Cat. No. BI-20405)

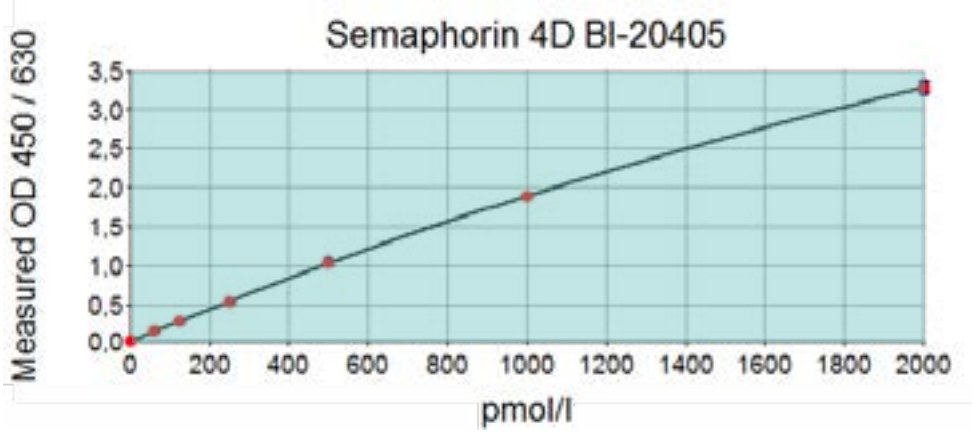
Features & Benefits

- Highly specific – epitope mapped antibodies
- Low sample volume – 10 µl / well

Assay Characteristics & Performance

Method	Sandwich ELISA, HRP/TMB, 12 x 8 detachable strips
Sample type	Plasma (EDTA, heparin, citrate)
Standard range	0 – 2,000 pmol/l (equal to 0 – 157,800 pg/ml)
Conversion factor	1 ng/ml = 0.014 pmol/l (MW: 78.9 kDa)
Sample volume	10 µl / well
Detection limit	12 pmol/l (0 pmol/l + 3 SD; equal to 947 pg/ml)
Incubation time	3 h / 1 h / 30 min
Precision	Intra-assay (n=5) ≤ 8%. Inter-assay (n=11) ≤ 11%.

Typical Standard Curve



Related Products

- Endostatin ELISA, Cat. No. BI-20742
- Big Endothelin ELISA, Cat. No. BI-20082H
- C-terminal FGF23 ELISA, Cat. No. BI-20702
- Intact FGF23 ELISA, Cat. No. BI-20700

SEMAPHORIN 4D IN ONCOLOGY

Semaphorin 4D (Sema4D, CD100) is a type I integral membrane glycoprotein expressed as a disulphide-linked homodimer. It is over-expressed in a wide variety of cancers including malignancies of prostate, colon, breast, lung, and pancreas, as well as cervical and ovarian malignancies, head and neck squamous cell carcinoma, and osteosarcoma.

The extracellular region of Sema4D can be proteolytically cleaved to generate soluble molecule retaining its biological activity. The type 1 matrix metalloproteinases mediating this cleavage are upregulated in many malignant cells. Among the three receptors binding soluble and transmembrane Semaphorin 4D, Plexin B1 has the highest affinity and is expressed on antigen presenting cells, endothelial and epithelial cells, as well as on some cancer cells.

Sema4D activates endothelial cells and promotes tumor angiogenesis and tumor progression. Furthermore, it influences vascular permeability and might thereby regulate extravasation. Apart from its pro-angiogenic properties, Sema4D acts on receptor-positive malignant cells where it promotes survival, proliferation, and migration. Within the tumor microenvironment Sema4D influences the infiltration and differentiation of immune cells creating an anti-inflammatory milieu. Moreover, Sema4D suppresses osteoblast differentiation and hence, promotes the formation of bone metastasis.

Elevated expression of Sema4D is generally associated with a poor prognosis in several malignancies. However, as a therapeutic target, interferences with Sema4D signaling provides the possibility to enhance anti-tumor immune responses and inhibit tumor progression. Recently, high expression of soluble Sema4D in the plasma of patients with head and neck squamous cell carcinoma has been reported. This finding indicates that determination of Sema4D plasma levels might be useful biomarker in the context of cancer progression, prognosis, and therapy.

Areas of Interest

- Breast cancer
- Cervical cancer
- Colorectal cancer
- Ovarian cancer
- Gastric cancer
- Head and neck cancer
- Lung cancer
- Multiple myeloma
- Pancreatic cancer
- Prostate cancer
- Sarcomas

ASSOCIATION BETWEEN SEMPAHORIN 4D AND CANCER

Reference	Type	Study Design
Yang YH et al., *PLOS ONE 2016; 11: e0150151.*	Breast	MC3T3-E1, 293T (ATCC) and breast cancer cells
Malik MF et al., *Oncol Rep. 2015; 34(2):1049–1057.*		Breast cancer tumor (n=147) and normal mammary tissue (n=22)
Liu H et al., *Microvasc. Res. 2014; 93:1–8.*	Cervical	Cervical cancer patients (n=232)
Wang JS et al., *World J. Gastroenterol. 2015; 21(7):2191–2198.*	Colorectal	Colorectal carcinoma patients (n=86)
Ikeya T et al., B*MC Cancer. 2016 Jul 25; 16:525.*		Patients, who underwent surgery for colorectal cancer (n=226)
Ding X et al., *Onco Targets Ther. 2016; 9:1189–1204.*		HUVEC and colorectal cancer (CRC) cell lines
Chen Y et al., *Cell. Mol. Biol. Lett. 2018; 23:2.*	Ovarian	HUVEC and ovarian cancer cell line A2780
Chen Y et al., *Int. J. Mol. Sci. 2012; 13:13264–13274.*		Epithelial ovarian cancer (EOC) patients (n=124), healthy controls (n=40)
Chen Y et al., *Asian Pac. J. Cancer Prev. 2013; 14:5883–5890.*		Epithelial ovarian cancer (EOC) patients (n=67), ovarian cancer cell lines
Li H et al., *World J Gastroenterol. 2018; 24(5):593–601*	Gastric	Gastric carcinoma and adjacent normal tissues (n=290)
Derakhshandeh R et al., *Oncotarget 2018; 9(13):11126–11144*	Head and Neck	HNSCC patients (n=33), healthy donors (n=10)
Chen WG et al., *Clin Exp Metastasis. 2019; 36(1):39–56*	Lung	Human lung cancer cells (PC9 and A549) and MC3T3-E1 mouse osteoblast precursor cells
Terpos E et al., *Blood Cancer J. 2018; 8(5):42.*	Multiple Myeloma	MM patients (n=72), healthy controls (n=25)
Kato S et al., *Cancer Sci. 2011; 102(11):2029–2037.*	Pancreatic	Human pancreatic cancer cell lines, paraffin-embedded pancreatic cancer tissue sections (n=99)
Damola A et al., *The Prostate 2013; 73(12):1326–1335.*	Prostate	Primary cancer cell lines
Campos M et al., *Oncol. Lett. 2013; 5(5):1527–1535.*	Sarcomas	Tumor tissue samples and tumor free tissue from patients diagnosed with STS (n=65)

Main Findings

"We observe a decrease in the number of bone metastases in mice injected with breast cancer cells when Sema4D is silenced by RNA interference."

"A decreased expression of Sema4D, plexin-B1 and -B2 was associated with local recurrence and poor prognosis."

"Sema4D autocrine within tumor cells contributes to enhanced invasion and tumor progression through increased motility of cervical cancer and VEGF-C/-D-mediated lymphangiogenesis. Sema4D might be useful as a molecular marker of poor prognosis in cervical cancer."

"HIF-1α and Sema4D protein expression was significantly correlated with prognosis of colorectal carcinoma… only Sema4D expression played a significant role in predicting patient prognosis."

"The expression of Sema4D and PlexinB1 were both found to be significantly related to stage, depth of tumor invasion, lymph node metastasis, lymphatic invasion, and venous invasion, and was found to be an independent risk factor for a worse survival."

"Targeting Sema4D might serve as a parallel option for antiangiogenic therapy for CRC, particularly when traditional anti-VEGF therapies fail or tumors develop resistance to strategies targeting a single angiogenic signaling pathway."

"VEGF and SEMA4D had a positive correlation with the malignant degree of ovarian cancer, and SEMA4D can serve as an independent prognostic factor."

"SEMA4D expression and histologic grade were independent indicators of overall survival (OS) and progress-free survival (PFS) for EOC patients."

"SEMA4D expression was an independent indicator of overall survival (OS) and progression-free survival (PFS) for EOC patients. Furthermore, higher expression of SEMA4D in ovarian cancer cell lines and their supernatants were found than that in a human primary cultured ovarian cell line and its supernatant."

"Combined detection of wTAM markers, CD68 and Sema4D, in gastric carcinoma tissue shows potential to predict the trend of gastric carcinoma progression."

"Sema4D was detected in plasma of HNC patients at significantly higher levels (115.44 ± 39.37) compared to healthy donors (38.60 ± 12.73) ($p < 0.0001$)."

"These results provide the first evidence that HIF-1α-induced Sema4D expression and secretion play important roles in lung cancer osteolytic bone metastasis by inhibiting osteoblast differentiation, thereby providing potential strategies for the treatment of bone metastasis via targeting osteoblasts."

"Our data suggest that Sema4D is elevated in MM patients and correlate with adverse myeloma features and increased bone resorption, providing a possible target for novel therapeutic approaches in MM."

"The overexpression of Sema4D and of its receptor, plexinB1, was found to be significantly correlated with clinical factors, such as lymph node metastasis, distant metastasis, and poor prognosis in patients with PDAC."

"Sema4D stimulation increases the motility and anchorage independent growth."

"CD100 [SEMA4D] expression was identified to significantly correlate with global and local survival free of disease in patients. CD100 expression levels are suitable for evaluation of tumors from STS patients to determine prognosis."

TOTAL SOLUBLE NEUROPILIN-1 ELISA (Cat. No. BI-20409)

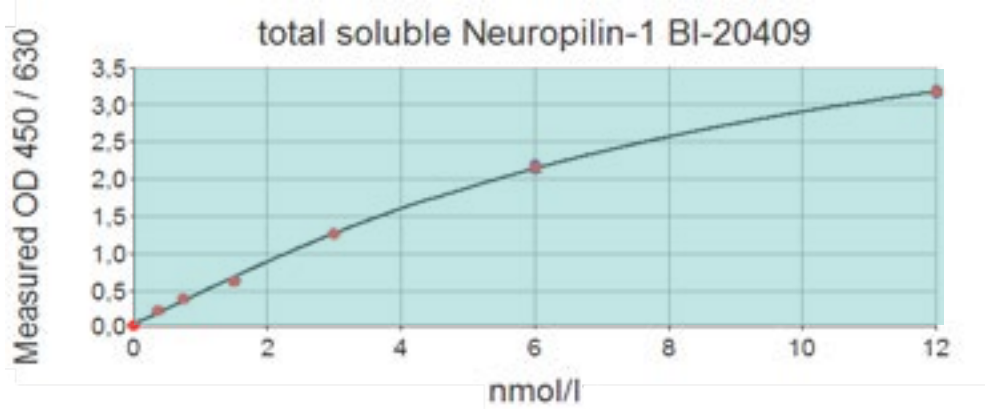
Features & Benefits

- Measures ligand bound and uncomplexed soluble NRP1
- Highly specific – epitope mapped antibodies
- Low sample volume – 10 µl / well

Assay Characteristics & Performance

Method	Sandwich ELISA, HRP/TMB, 12 x 8 detachable strips
Sample type	Serum, plasma (EDTA, heparin, citrate), cell-culture supernatant
Standard range	0 – 12 nmol/l (equal to 0 – 836 ng/ml)
Conversion factor	1 ng/ml = 0.014 nmol/l (MW: 69.7 kDa)
Sample volume	10 µl / well
Detection limit	0.09 nmol/l (0 nmol/l + 3 SD; equal to 6.27 ng/ml)
Incubation time	30 min / 2 h / 1 h / 30 min
Precision	Intra-assay (n=6) ≤ 11%. Inter-assay (n=12) ≤ 10%.

Typical Standard Curve



Related Products

- Endostatin ELISA, Cat. No. BI-20742
- Big Endothelin ELISA, Cat. No. BI-20082H
- C-terminal FGF23 ELISA, Cat. No. BI-20702
- Intact FGF23 ELISA, Cat. No. BI-20700

NEUROPILIN-1 IN ONCOLOGY

Neuropilin-1 (NRP1) is a single-pass transmembrane glycoprotein of 923 amino acids, composed of a large extracellular region, a short transmembrane domain and a short cytoplasmic tail.

Due to alternative splicing or shedding, the extracellular region can be released into circulation as soluble Neuropilin. Multiple ligands bind to the extracellular region of NRP1, like class III semaphorins which have a key role in axonal guidance, or members of the VEGF family of angiogenic cytokines. Ligand-binding to transmembrane NRP1, which has co-receptor function, leads to signaling via receptor proteins containing a PDZ domain. By contrast, ligand-binding to soluble Neuropilin-1 (sNRP1) has antagonistic properties by acting as decoy.

NRP1 is expressed by a variety of cells and tissues. For instance, the transmembrane protein is expressed by neuronal cells, endothelial cells, vascular smooth muscle cells, cardiomyocytes, osteoblasts, naïve T cells or platelets. NRP1 is also expressed in a variety of cancers suggesting a critical role in tumor progression. As a co-receptor for VEGF, NRP1 is implicated in vascularization and tumor growth and is seen as a potential target for cancer therapies.

Areas of Interest

- Breast cancer
- Hepatocellular carcinoma
- Glioblastoma
- Cholangiocarcinoma
- Adenocarcinoma
- Gastric cancer
- Non-small lung cancer
- Melanoma
- Ovarian carcinoma
- Oral squamous cell carcinoma
- Osteosarcoma
- Acute myeloid leukemia
- Bladder cancer
- Squamous cell carcinoma
- Colorectal cancer
- Nasopharyngeal carcinoma

ASSOCIATION BETWEEN NEUROPILIN-1 AND CANCER

Reference	Type	Study Design
Naik A et al., *Scientific Reports 2017; 7(1):3301.*	Breast	Breast cancer patients (n=70), age-matched healthy controls (n=50)
Yang S et al., *Disease markers 2015; 2015:506428.*	Cervical	Preoperative cervical cancer patients (n=64), controls (n=20)
Shi F et al., *Oncogene. 2018; 37(7):935-943.*	Esophageal Squamous	Surgically resected ESCC and adjacent histologically normal tissues (n=383)
Li L et al., *J. Exp. Clin. Cancer Res. 2016; 35:16.*	Gastric	Gastric cancer patients (n=141), human gastric cancer cells MGC-803, SGC7901, BGC823, AGS, NCI-N87 and HGC-27
Zhang Y et al., *Pathol. Oncol. Res. 2016; 22(2):367–375.*	Hepato-cellular	HCC tissue specimen (n=16), matched normal liver specimen (n=16)
Lu J et al., *Mol. Med. Rep. 2015; 12(2): 2668–2676.*	Melanoma	Melanoma patients (n=381)
Dong JC et al., *J. Cell. Mol. Med. 2015; 19(9):2286–2295.*	Lung	SCID mice; HepG2, MCF-7, U87, PC-3, A549, H460, H358, H1299 and SK-MES-1 cells
Chu W et al., *PloS One 2014; 9(7):e101931.*	Oral Squamous	OSCC cell lines transfected with a vector encoding NRP1
Ben Q et al., *Pancreas 2014; 43(5):744–749.*	Pancreatic	Patients with resected pancreatic ductal adenocarcinomas (PDACs, n=172)
Matkar PN et al., *Oncotarget 2016; 7(43):69489–69506.*		Rowett Nude rats injected with BxPC-3 human pancreatic cancer cell
Chaudhary B et al., *Cancer Immunol. Immunother. 2014; 63(2):81–99.*	Therapeutic Target	Review
Ding Y et al., *Exp Ther Med 2018; 16(2):537–546.*		Female BALB/c nude mice (n=15), human gastric cancer cell lines
Arpel A et al., *Oncotarget 2016; 7(34):54723–54732.*		Nude mice injected with breast cancer cells, murine 4T1 cells and human epithelial breast adenocarcinoma cell lines
Kumar A et al., *ACS Nano 2014; 8(5):4205–4220.*		Prostate cancer cells treated with NRP-1 targeted peptide linked to a lethal dose of a platinum (IV) drug

Main Findings

"Circulating and tumor tissue expression of NRP-1 and circulating placental growth factor (PlGF) increase in advanced nodal and metastatic breast cancer compared with locally advanced disease."

"Both sNRP-1 and NRP-1 proteins were correlated with stage. sNRP-1 presented a high diagnostic ability of cervical cancer and CIN, with a sensitivity of 70.97% and a specificity of 73.68%."

"Here we revealed that over-expression of NRP1 correlates with poor prognosis in esophageal squamous cell carcinoma (ESCC). NRP1-knockdown suppressed ESCC cell proliferation and xenograft tumor growth."

"Gastric cancer tissues expressed higher levels of NRP-1 compared to normal gastric mucosa. Its expression correlated with clinical staging, tumor differentiation and pathological types. NRP-1 depletion inhibited cell proliferation by inducing cell cycle arrest in the G1/S phase."

"High expression of NRP-1 was significantly associated with intrahepatic metastasis (P = 0.036), Edmondson grade (P = 0.007), TNM classification (P = 0.0031), and portal vein invasion (P = 0.004). Furthermore, the HCC patients with high NRP-1 expression had shorter overall survival (OS), and recurrence-free survival (RFS)."

"Notably, increased NRP1 expression was correlated with a poorer overall, and disease-specific, 10-year survival (P=0.03 and P=0.002, respectively). Multivariate Cox regression analyses indicated that NRP1 is an independent prognostic marker for melanoma."

"shRNA-mediated NRP1 inhibition also significantly enhanced the radio-sensitivity of NSCLC cells both in vitro and in vivo. The over-expression of NRP1 was correlated with growth, survival and radio-resistance of NSCLC cells via the VEGF-PI3K-NF-κB pathway, and NRP1 may be a molecular therapeutic target for gene therapy or radio-sensitization of NSCLC."

"Our results indicate that NRP1 may regulate the epithelial-to-mesenchymal transition process in OSCC cell lines through NF-κB activation, and that higher NRP1 expression levels are associated with lymph node metastasis and poor prognosis in OSCC patients."

"Neuropilin 1 is highly expressed in PDACs, and high expression of NRP-1 is significantly correlated with angiogenesis, advanced tumor-node-metastasis stage, p T stage, node invasion, and poor postoperative overall survival."

"In vivo, loss of NRP-1 attenuated tumor perfusion and size, accompanied by reduction in endothelial-to-mesenchymal transition and fibrosis."

"NRP1 may enhance Treg tumour infiltration and a decrease in NRP1+ Tregs correlates with successful chemotherapy, suggesting a specific role for NRP1 in cancer pathology. As a therapeutic target, NRP1 allows simultaneous targeting of NRP1-expressing tumour vasculature, NRP1+ Tregs and pDCs."

"Anti-NRP-1 mAb suppressed the growth of gastric cancer xenograft tumors and downregulated the expression of vascular endothelial growth factor proteins within tumors in nude mice."

"In models with long term in vivo administration of the peptide, MTP-NRP1 not only reduced tumor volume but also decreased number and size of breast cancer metastases."

"The uptake of drug-loaded nanocarriers is dependent on the interaction with Nrp-1 in cell lines expressing high (PC-3) and low (DU-145) levels of Nrp-1, as confirmed through inductively coupled plasma mass spectrometry and confocal microscopy. Our preliminary investigations with platinum (IV)-functionalized gold nanoparticles along with a targeting peptide hold significant promise for future cancer treatment."

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