BIOMARKER ELISAs IN ONCOLOGY

Setting the standard for clinical research.

FULLY VALIDATED ASSAYS - FDA & ICH GUIDELINES

BIOLOGICALLY RELIABLE - SERUM BASED CALIBRATORS & CONTROLS
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**
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**
Marked – for IVD use in the EU

**References**
100+

**Dysregulated in primary bone cancers and cancers metastasizing to the bone**

**Associated with tumor invasiveness**

**Therapeutic target**

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**
Marked – for IVD use in the EU

**References**
96

**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**
<table>
<thead>
<tr>
<th>Assay Type</th>
<th>Method</th>
<th>Sample Type</th>
<th>Sample Size</th>
<th>Standard Range</th>
<th>Detection Limit</th>
<th>Assay Time</th>
<th>Use</th>
<th>References</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sclerostin ELISA (BI-20492)</td>
<td>Sandwich ELISA, HRP/TMB</td>
<td>Serum, plasma (EDTA, heparin), urine, cell culture supernatants</td>
<td>20 µl / test, 12x8 tests</td>
<td>0 – 240 pmol/l</td>
<td>3.2 pmol/l</td>
<td>Overnight assay</td>
<td>Research use only</td>
<td>100+</td>
<td>Dysregulated in cancers targeting the bone</td>
</tr>
<tr>
<td>Bioactive Sclerostin ELISA (BI-20472) NEW</td>
<td>Sandwich ELISA, HRP/TMB</td>
<td>Serum, plasma (EDTA, citrate), urine, cell culture supernatants</td>
<td>20 µl / test, 12x8 tests</td>
<td>0 – 320 pmol/l</td>
<td>1.9 pmol/l</td>
<td>3.5 h</td>
<td>Research use only</td>
<td></td>
<td>Anti-angiogenic</td>
</tr>
<tr>
<td>Endostatin ELISA (BI-20742)</td>
<td>Sandwich ELISA, HRP/TMB</td>
<td>Serum, plasma, urine</td>
<td>10-20 µl / test, 12x8 tests</td>
<td>0 – 800 pmol/l</td>
<td>4 pmol/l</td>
<td>4.5 h</td>
<td>Research use only</td>
<td></td>
<td>Promotes proliferation, survival, neovascularization, and invasiveness</td>
</tr>
<tr>
<td>Endostatin mouse/rat ELISA (BI-20742MR) NEW</td>
<td>Sandwich ELISA, HRP/TMB</td>
<td>Serum, plasma</td>
<td>5 µl / test, 12x8 tests</td>
<td>0 – 32 nmol/l</td>
<td>0.24 nmol/l</td>
<td>2.5 h</td>
<td>Research use only</td>
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<tr>
<td>Big Endothelin ELISA (BI-20082H)</td>
<td>Sandwich ELISA, HRP/TMB</td>
<td>Serum, plasma</td>
<td>50 µl / test, 12x8 tests</td>
<td>0 – 3 pmol/l</td>
<td>0.02 pmol/l</td>
<td>5.5 h</td>
<td>marked – for IVD use in the EU</td>
<td>42</td>
<td></td>
</tr>
<tr>
<td>FGF23 (C-terminal) ELISA (BI-20702)</td>
<td>Sandwich ELISA, HRP/TMB</td>
<td>Serum, plasma</td>
<td>50 µl / test, 12x8 tests</td>
<td>0 – 20 pmol/l</td>
<td>0.08 pmol/l</td>
<td>Overnight assay</td>
<td>marked – for IVD use in the EU</td>
<td>10</td>
<td>Marker for tumor-induced osteomalacia</td>
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</table>
Features & Benefits

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

Assay Characteristics & Performance

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

Typical Standard Curve

![Typical Standard Curve](image)

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
Main Finding

“Low DKK-1 serum levels are associated with poor prognosis in PTC patients and DKK-1 could potentially serve as a biomarker for early diagnosis. 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. DKK-1 plays an important role in the dysfunction of osteoblasts observed in MM. Inhibition of DKK1 correlates with the extent of bone disease, and DKK-1 serum levels decrease in myeloma patients responding to treatment, irrespective of the regimen chosen. The combination with bortezomib, which enhances bone formation, seems to be preferred for the management of myeloma patients with osteolytic disease.

Reference Table

<table>
<thead>
<tr>
<th>Reference</th>
<th>Type</th>
<th>Study Design</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sato L et al., <em>Cancer Res</em>, 2010; 70(13):5326–5336</td>
<td>Multiple</td>
<td>Patients with various cancers (n=906), healthy controls (n=207)</td>
</tr>
<tr>
<td>Mazon M et al., <em>Cancers</em>, 2016; 8(7):62</td>
<td>Breast</td>
<td>Review</td>
</tr>
<tr>
<td>Liang B et al., <em>Onco Targets Ther.</em>, 2015; 8:3115–3122.</td>
<td>Hepatocellular</td>
<td>Systematic review and meta-analysis (n=5076 from 15 studies)</td>
</tr>
<tr>
<td>Fouad YM et al., <em>Scand J Gastroenterol.</em>, 2016; 51(9):1133–1137</td>
<td>Lung</td>
<td>HCC patients (n=50), patients with chronic HCV infection (n=20), patients with liver cirrhosis (as control group, n=20)</td>
</tr>
<tr>
<td>Dong LL et al., <em>Diagn Pathol</em>, 2014; 9:52.</td>
<td>Multiple Myeloma</td>
<td>Patients with NSCLC (n=150), healthy controls (n=150)</td>
</tr>
<tr>
<td>Feldmann R et al., <em>Dermatology</em>, 2011; 222(2):171–175.*</td>
<td>Melanoma</td>
<td>Patients with cutaneous melanoma (n=82)</td>
</tr>
<tr>
<td>Terpos E et al., <em>Am J Hematol</em>, 2014; 89(1):34–40.*</td>
<td>Multiple</td>
<td>Patients with relapsed or refractory myeloma (n=106) who received lenalidomide plus dexamethasone</td>
</tr>
<tr>
<td>Heider U et al., <em>Eur J Haematol</em>, 2009; 82(1):31–38.</td>
<td>Multiple</td>
<td>Myeloma patients (n=101) receiving chemotherapy followed by autologous stem cell transplantation</td>
</tr>
<tr>
<td>Kaiser M et al., <em>Europ J Haemat</em>, 2008; 80(6):490–494.</td>
<td>Multiple Myeloma</td>
<td>Untreated MM patients (n=184), monoclonal gammopathy of undetermined significance patients (n=33)</td>
</tr>
<tr>
<td>Terpos E et al., <em>Metabolism</em>, 2018; 80:80–90.</td>
<td>Multiple</td>
<td>Review</td>
</tr>
<tr>
<td>Han SX et al., <em>OncoTarget.</em>, 2015; 6(23):19907–19917.</td>
<td>Pancreatic Thyroid</td>
<td>Patients with pancreatic adenocarcinoma (n=140) and control patients (n=92)</td>
</tr>
<tr>
<td>Zhao JP et al., <em>Genetics and Molecular Research</em>, 2015; 14, (4): 18886–18894.*</td>
<td>Papillary Thyroid</td>
<td>PTC patients (n=132) and healthy controls (n=40)</td>
</tr>
<tr>
<td>Rachner TD et al., <em>BMC Cancer</em>, 2014; 14:649.*</td>
<td>Prostate</td>
<td>Patients with prostate cancer (n=80), serum</td>
</tr>
<tr>
<td>Browne AJ et al., <em>Cell Death and Disease</em>, 2016; 7(2): e2119.*</td>
<td>Prostate</td>
<td>Prostate cancer cells</td>
</tr>
<tr>
<td>Hall CL et al., <em>Prostate</em>, 2008; 68(13): 1396–1404.</td>
<td>Prostate</td>
<td>Prostate cancer (PC) tissue microarrays (n=309) stained for DKK-1 protein by immunohistochemistry</td>
</tr>
<tr>
<td>D’Amelio P et al., <em>BMC Clinical Pathology</em>, 2014; 14:11.*</td>
<td>Prostate</td>
<td>Patients who underwent prostate biopsy (n=159)</td>
</tr>
</tbody>
</table>

* 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."
Features & Benefits

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

Assay Characteristics & Performance

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

Typical Standard Curve

![Typical Standard Curve](image)

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 (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
<table>
<thead>
<tr>
<th>Reference</th>
<th>Type</th>
<th>Study Design</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yang YH et al., <em>PLOS ONE</em> 2016; 11: e0150151.</td>
<td>Breast</td>
<td>MC3T3-E1, 293T (ATCC) and breast cancer cells</td>
</tr>
<tr>
<td>Malik MF et al., <em>Oncol Rep.</em> 2015; 34(2):1049–1057.</td>
<td>Breast</td>
<td>Breast cancer tumor (n=147) and normal mammary tissue (n=22)</td>
</tr>
<tr>
<td>Wang JS et al., <em>World J. Gastroenterol.</em> 2015; 21(7):2191–2198.</td>
<td>Colorectal</td>
<td>Colorectal carcinoma patients (n=86)</td>
</tr>
<tr>
<td>Ding X et al., <em>Onco Targets Ther.</em> 2016; 9:1189–1204.</td>
<td>Colorectal</td>
<td>HUVEC and colorectal cancer (CRC) cell lines</td>
</tr>
<tr>
<td>Chen Y et al., <em>Cell. Mol. Biol. Lett.</em> 2018; 23:2.</td>
<td>Ovarian</td>
<td>HUVEC and ovarian cancer cell line A2780</td>
</tr>
<tr>
<td>Chen Y et al., <em>Asian Pac. J. Cancer Prev.</em> 2013; 14:5883–5890.</td>
<td>Ovarian</td>
<td>Epithelial ovarian cancer (EOC) patients (n=67), ovarian cancer cell lines</td>
</tr>
<tr>
<td>Li H et al., <em>World J Gastroenterol.</em> 2018; 24(5):593–601</td>
<td>Gastric</td>
<td>Gastric carcinoma and adjacent normal tissues (n=290)</td>
</tr>
<tr>
<td>Derakhshandeh R et al., <em>Oncotarget</em> 2018; 9(13):11126–11144</td>
<td>Head and Neck</td>
<td>HNSCC patients (n=33), healthy donors (n=10)</td>
</tr>
<tr>
<td>Chen WG et al., <em>Clin Exp Metastasis.</em> 2019; 36(1):39–56</td>
<td>Lung</td>
<td>Human lung cancer cells (PC9 and A549) and MC3T3-E1 mouse osteoblast precursor cells</td>
</tr>
<tr>
<td>Terpos E et al., <em>Blood Cancer J.</em> 2018; 8(5):42.</td>
<td>Multiple Myeloma</td>
<td>MM patients (n=72), healthy controls (n=25)</td>
</tr>
<tr>
<td>Damola A et al., <em>The Prostate</em> 2013; 73(12):1326–1335.</td>
<td>Prostate</td>
<td>Primary cancer cell lines</td>
</tr>
<tr>
<td>Campos M et al., <em>Oncol. Lett.</em> 2013; 5(5):1527–1535.</td>
<td>Sarcomas</td>
<td>Tumor tissue samples and tumor free tissue from patients diagnosed with STS (n=65)</td>
</tr>
</tbody>
</table>
## 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 progression-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

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

![Typical Standard Curve](image)

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 (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

<table>
<thead>
<tr>
<th>Reference</th>
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<tr>
<td>Naik A et al., <em>Scientific Reports</em> 2017; 7(1):3301.</td>
<td>Breast</td>
<td>Breast cancer patients (n=70), age-matched healthy controls (n=50)</td>
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<td>Yang S et al., <em>Disease markers</em> 2015; 2015:506428.</td>
<td>Cervical</td>
<td>Preoperative cervical cancer patients (n=64), controls (n=20)</td>
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<td>Shi F et al., <em>Oncogene.</em> 2018; 37(7):935-943.</td>
<td>Esophageal Squamous</td>
<td>Surgically resected ESCC and adjacent histologically normal tissues (n=383)</td>
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<td>Zhang Y et al., <em>Pathol. Oncol. Res.</em> 2016; 22(2):367–375.</td>
<td>Hepatocellular</td>
<td>HCC tissue specimen (n=16), matched normal liver specimen (n=16)</td>
</tr>
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<td>Chu W et al., <em>PloS One</em> 2014; 9(7):e101931.</td>
<td>Oral Squamous</td>
<td>OSCC cell lines transfected with a vector encoding NRP1</td>
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<td>Ben Q et al., <em>Pancreas</em> 2014; 43(5):744–749.</td>
<td>Pancreatic</td>
<td>Patients with resected pancreatic ductal adenocarcinomas (PDACs, n=172)</td>
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<td>Ding Y et al., <em>Exp Ther Med</em> 2018; 16(2):537–546.</td>
<td>Therapeutic Target</td>
<td>Female BALB/c nude mice (n=15), human gastric cancer cell lines</td>
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<td>Arpel A et al., <em>Oncotarget</em> 2016; 7(34):54723–54732.</td>
<td></td>
<td>Nude mice injected with breast cancer cells, murine 4T1 cells and human epithelial breast adenocarcinoma cell lines</td>
</tr>
<tr>
<td>Kumar A et al., <em>ACS Nano</em> 2014; 8(5):4205–4220.</td>
<td></td>
<td>Prostate cancer cells treated with NRP-1 targeted peptide linked to a lethal dose of a platinum (IV) drug</td>
</tr>
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**Main Findings**

"Circulating and tumor tissue expression of NRP-1 and circulating placental growth factor (PIGF) 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 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."
Setting the standard for clinical research.

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