Looking for a reliable
cardiac raw material supplier?

We I.V.DO that™

Technical note

Cardiovascular

Medix Biochemica

Contents

Introduction

Cardiovascular diseases (CVD) are a group of disorders affecting the heart and blood vessels. Accounting for an estimated one third of all deaths worldwide, CVDs are the number one global cause of mortality. Rapid diagnostics as well as reliable identification and monitoring of high-risk individuals is vital for lowering risk of CVD-related death and disability. Cardiac biomarkers are a varied group of molecules whose increased concentrations relate to the presence and the risk of future cardiovascular events. There is a growing need for accurate biomarkers for diagnostics and risk stratification, as efficient treatment and prevention of CVD rely on early detection of patients with, or at risk of, these diseases.

Several cardiac markers are currently used in clinical practice to support diagnosis, risk assessment, and treatment follow-up related to different CVD pathophysiological processes. For example, cardiac muscle damage causes cardiac troponin (cTn) to be released into the bloodstream by myocardial cells. Elevated serum levels of cTn thus indicate heart injury, and immunoassays for cTn form the cornerstone of diagnosing acute myocardial infarction (AMI). Current cTn assay methods allow AMI to be ruled out as early as one hour after onset of symptoms. As another example, the blood concentration of commonly used cardiac biomarker D-dimer correlates with the thrombolytic activity of the body. D-dimer immunoassays thus provide a useful tool for excluding pulmonary embolism and deep vein thrombosis.

Medix Biochemica provides a wide selection of premium-quality monoclonal antibodies, antigens and biological samples for cardiac marker detection. The monoclonal antibodies have optimized, industrial-scale in vitro production methods, certified batch-to-batch consistency, and expert customer service. This expertese has made Medix Biochemica one of the most important antibody suppliers for the in vitro diagnostic (IVD) community.

The results shown in this technical note are from prototype assays (unoptimized), indicating proof of concept with clinical samples. Further assay optimization may be required to obtain the best performance.

cTnI

Troponin is a regulatory protein complex involved in the calcium-mediated process of muscle contraction and relaxation in cardiac and skeletal muscle filaments. The troponin complex consists of three subunits: troponin I, T, and C. The names of the subunits reflect their biological functions; troponin I affects the myosin-actin interactions, troponin T mediates the binding of troponin to tropomyosin, and troponin C binds calcium ions.[1]

Troponin I and T have myocardial tissue-specific isoforms, cardiac troponin I (cTnI) and cardiac troponin T (cTnT). cTnI is expressed exclusively in the heart, but cTnT has occasionally also been detected in diseased skeletal muscles. The same isoform of troponin C is expressed in both myocardium and slow-twitch skeletal muscles and therefore it cannot be used as a cardiac marker, whereas cTnI and cTnT have become the most widely used biomarkers for detecting myocardial injury. After cardiac muscle damage, cardiac troponin is released into the bloodstream by myocardial cells due to loss of membrane integrity. Therefore, elevated serum levels of cTnI and cTnT indicate heart injury, but are independent of the mechanism causing it.[1,2]

Serum cTnI has superior specificity and sensitivity compared to other routinely used biomarkers, such as creatine kinase (CK-MB), lactate dehydrogenase, and myoglobin. Therefore, measurement of cardiac troponin is the cornerstone of diagnosis of acute myocardial infarction (AMI). Current guidelines recommend serial measurements of cardiac troponin levels and the use of the 99th percentile as an assay-specific cardiac troponin level cut-off value for AMI diagnosis. Similar to CK-MB, cardiac troponin is typically detectable within 4–6 hours after the onset of symptoms. However, current assay technologies allow fast and precise detection of cardiac troponin at very low concentrations, and enable ruling out AMI as early as an hour after symptom onset. After infarction, cardiac troponin concentrations remain elevated for several days.[3,4]

In addition to AMI, elevated level of cTnI may occur due to other conditions, such as renal failure, sepsis, and hypertension. Furthermore, high cTnI concentration serves as an adverse prognostic indicator in patients with acute coronary syndromes (ACS).[2]

The 210 residues long amino acid sequence of the 24-kDa human cTnI is highly conserved between various animals, which enables several human cTnI assays to be effectively adapted for animal use. The initial section of the protein sequence, however, is less conserved, and thus human-specific antibodies are also available.[1]

Medix Biochemica has more than three decades of experience in producing high-quality monoclonal antibodies against cTnI. Currently, the product portfolio includes seven anti-cTnI monoclonal antibodies (9701, 9703, 9705, 9707, RC9701, RC9707 and RC9750). Three of the antibodies are recombinant chimeric antibodies, consisting of constant region (Fc) from human and variable region (Fv) from mouse or chicken, depending on the antibody. In addition, Medix Biochemica offers a recombinant cTnI antigen, native cTnI and Troponin complex antigens, and biological samples.

Anti-human cTnI monoclonal antibodies and antigens

cTnI antibody	Product code	Concentration (mg/mL)	Shelf life (months at +2–8°C)	Subclass	Applications tested
9701	100129	5	36	IgG_1	ELISA, LF
RC9701	140000	5	N/D	Human IgG_1	ELISA
9703	100181	5	12	IgG_1	ELISA, LF
9705	100125	1	36	IgG_1	ELISA, LF
9707	100180	5	18	IgG_1	ELISA, LF
RC9707	140020	5	N/D	Human IgG_1	ELISA
RC9750	700050	5	15	IgG_1	ELISA

cTn antigen	Product code
Recombinant cTnI, 100 µg	610102
Native cTnI	550-11
Native cardiac Troponin Complex (cTn ITC)	550-08

Pair recommendations

Capture \ Detection	9701 / RC9701	9703	9705	9707 / RC9707*	RC9750
9701 / RC9701	–	+	+	+	+
9703	–	–	+	–	–
9705	+	+	–	+	+
9707 / RC9707*	–	–	–	–	–
RC9750	+	–	+	+	–

*9707 and RC9707 are not recommended as capture antibodies due to the cross-reactivity with skeletal Troponin I (14%)

RC9750 is recommended as a very sensitive capture antibody, and 9701 & 9705 can be used together for increased detection with RC9750. For increased sensitivity with other cTnI antibodies 2+1 or 2+2 antibody approach is recommended. For example capture 9701/RC9701 & 9705, detection 9703 & 9707/RC9707.

Troponin antigen recognition by antibodies

Capture \ Antigen	cTnI	cTn I-C	cTn I-T-C
9701 / RC9701	+	+	–
9703	+	+	–
9705	–	+	+
9707 / RC9707*	–	(+)	(+)
RC9750	–	+	+

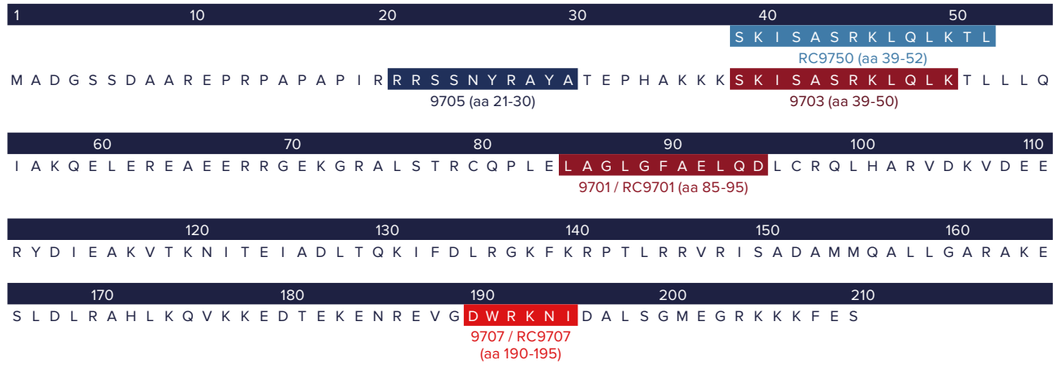
Product	Epitope (amino acids)
9701 / RC9701	85–95
9703	39–50
9705	21–30
9707 / RC9707	190–195
RC9750	39–52

Kinetic parameters

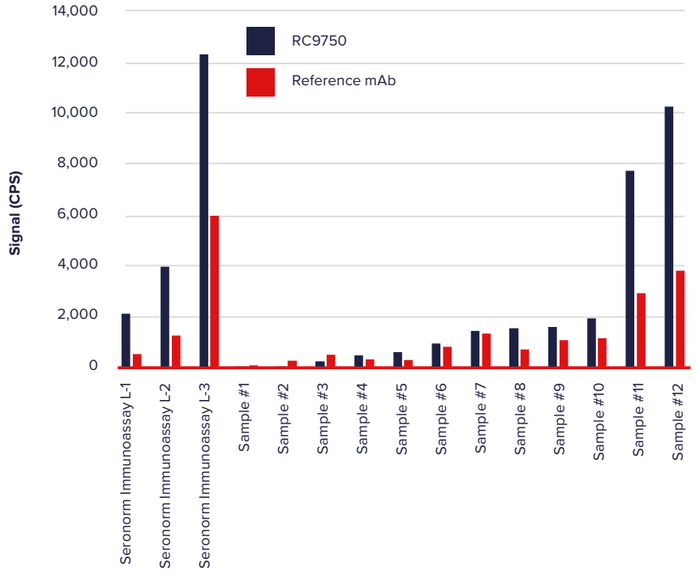
cTnI antibody	Association rate constant, k_{on}	Dissociation rate constant, k_{off}	Affinity constant, K_A
9701	4.1×10^5 1/Ms	5.6×10^{-4} 1/s	$K_A = 0.7 \times 10^9$ 1/M, $K_D = 1.4 \times 10^{-9}$ M = 1.4 nM
RC9701	2.5×10^5 1/Ms	3.3×10^{-4} 1/s	$K_A = 7.8 \times 10^8$ 1/M, $K_D = 1.3 \times 10^{-9}$ M = 1.3 nM
9703*	N/D	N/D	$K_A = 1.0 \times 10^9$ 1/M, $K_D = 1.0 \times 10^{-9}$ M = 1.0 nM
9705	7.0×10^5 1/Ms	4.5×10^{-5} 1/s	$K_A = 1.6 \times 10^{10}$ 1/M, $K_D = 6.4 \times 10^{-11}$ M = 0.064 nM
9707	1.9×10^6 1/Ms	5.8×10^{-6} 1/s	$K_A = 3.3 \times 10^{11}$ 1/M, $K_D = 3.0 \times 10^{-12}$ M = 0.003 nM
RC9707	1.7×10^6 1/Ms	2.7×10^{-4} 1/s	$K_A = 6.1 \times 10^9$ 1/M, $K_D = 7.1 \times 10^{-10}$ M = 0.71 nM
RC9750	3.3×10^4 1/Ms	1.1×10^{-4} 1/s	$K_A = 3.1 \times 10^8$ 1/M, $K_D = 6.5 \times 10^{-9}$ M = 6.5 nM

* Affinity constant for 9703 has been determined using cTnI antigen, and for other antibodies cTn I-T-C antigen.

Binding epitopes

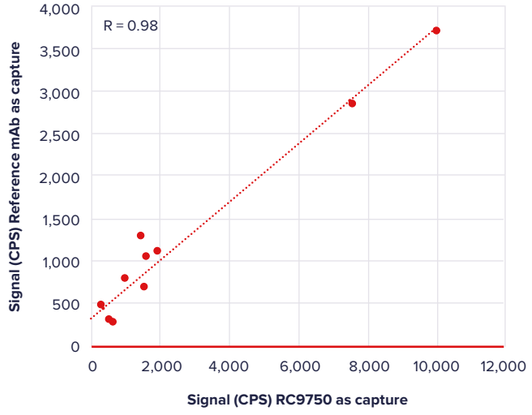


Comparison results of RC9750 and a reference antibody with clinical samples



Seronorm controls and clinical samples with elevated cTnI concentrations were measured with a fluoroimmunoassay (FIA) using antibodies RC9750 or reference mAb for capture and antibodies 9701 and 9705 as a mixture for detection. Both capture antibodies are binding to the epitope located in amino acid region 39-52 in cTnI.

Correlation of cTnI RC9750 FIA assay



Correlation of sandwich assays in clinical sample measurement using RC9750 and a reference antibody binding to the same amino acid region. Correlation is excellent and signal levels are high when using RC9750.

D-dimer

D-dimers are fragments of fibrin that form when blood clots are broken down in an enzymatic process. Plasmin cleaves cross-linked insoluble fibrin molecules into differently sized fibrin degradation products (FDPs). D-dimers are among these FDPs, and consist of two cross-linked D fragments of the fibrin protein. Under physiological conditions, D-dimers are usually non-covalently bonded to E-fragments, which are also fibrin fragments.[6–11]

In healthy individuals, the plasma concentration of D-dimers is low. However, many pathological conditions increase the thrombolytic activity of the body and thus correlate with an increased D-dimer blood concentration. Such conditions include thrombosis, malignancies, infections, and severe inflammation, for example. The physiological plasma levels of D-dimer are higher in women than in men, and the D-dimer concentration also increases with age.[8,9]

In clinical diagnostics, D-dimer testing can be utilized for ruling out pulmonary embolism and deep vein thrombosis (DVT). D-dimer is detectable in blood approximately two hours after signs of thrombus formation and has a half-life of eight hours. Although D-dimer is not specific for thromboembolic diseases, it is used to support the diagnosis of disseminated intravascular coagulation (DIC), as well as in monitoring patients during and after anticoagulant treatment for recurrent DVT.[7,8,11,12]

Medix Biochemica's product selection includes eight high-quality monoclonal IgG antibodies with versatile specificities for the detection of D-dimer. The D-dimer antibodies have varying specificities towards fibrinogen and fibrin degradation products (FDPs). This allows their utilization in the specific detection of the D-dimer monomer (~180 kDa) as well as in different sandwich ELISA assays. The pairing properties have proven suitable for sandwich ELISA applications.

Anti-human D-dimer monoclonal antibodies and native antigens

D-dimer antibody	Product code	Concentration (mg/mL)	Shelf life (months at +2–8°C)	Subclass	Applications tested
1401	100204	5	18	IgG_3	ELISA, IT
1402	100205	5	12	IgG_{2b}	ELISA, IT
1403	100228	5	36	IgG_{2a}	ELISA, IT
1404	100479	5	24	IgG_1	ELISA, IT
1405	100480	5	36	IgG_1	ELISA, IT
1407	100482	5	24	IgG_1	ELISA, IT
1408	100799	5	24	IgG_1	ELISA, IT
1409	100800	5	24	IgG_1	ELISA, IT

D-dimer antigen	Product code	Grade
Native D-dimer	200-09	> 50% (SDS-PAGE)
Native D-dimer	200-12	> 80% (SDS-PAGE)
Native D-dimer	200-13	> 95% (SDS-PAGE)

Cardiovascular

Pair recommendations

Capture \ Detection	1401	1402	1403	1404	1405	1407	1408	1409
1401	–	–	+	+	+	+	+ +	+ +
1402	–	–	–	+	–	–	–	–
1403	–	–	–	+	–	–	–	–
1404	–	+	+	–	+	–	–	–
1405	+	+	+	+	–	+	+	–
1407	+	+	–	–	–	–	–	–
1408	+ +	+	+	–	–	+	–	+ +
1409	+	–	–	–	–	–	+ +	–

Following pairs are especially recommended for the below mentioned assays:
FIA: 1408 (capture) - 1409 (detection), 1409 - 1408, 1401 - 1408, 1401 - 1409, and 1408 - 1401
IT: 1403 - 1404 and 1404 - 1407

Binding properties

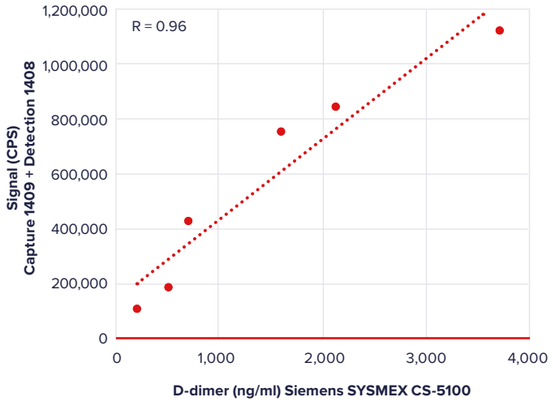
D-dimer antibody	FDP-E	FDP-D	FDP-X	FDP-Y	Fibrinogen
1401	–	–	–	+	–
1402	–	+	+	+	+
1403	–	+	+	+	+
1404	–	+	–	–	–
1405	–	+	–	–	–
1407	–	+	+	+	–
1408	–	+	–	+	–
1409	–	+	+	+	–

D-dimer antibodies bind to fibrin degradation products (FDP-D, FDP-X, and FDP-Y) and fibrinogen with differing specificities. The molecular configuration of the fragments has been described in Walker & Nesheim, 1999 .[11]

Kinetic parameters

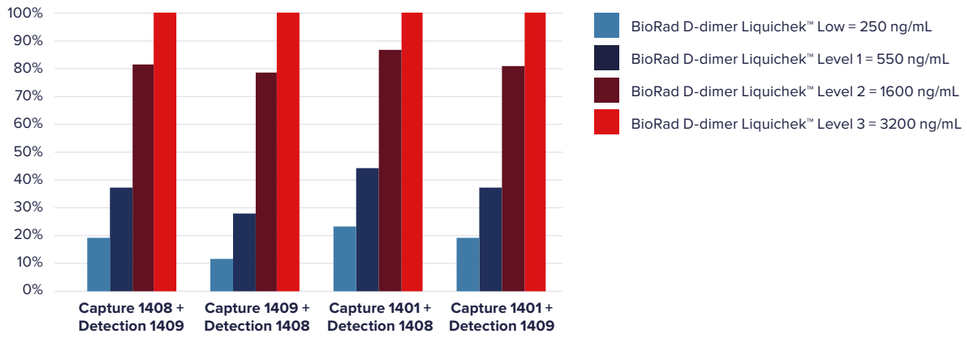
D-dimer antibody	Association rate constant, k_{on}	Dissociation rate constant, k_{off}	Affinity constant, K_A
1401	4.2×10^5 1/Ms	1.7×10^{-4} 1/s	$K_A = 2.5 \times 10^9$ 1/M, $K_D = 4.6 \times 10^{-10}$ M = 0.46 nM
1402	4.2×10^5 1/Ms	7.2×10^{-5} 1/s	$K_A = 5.8 \times 10^9$ 1/M, $K_D = 2.2 \times 10^{-10}$ M = 0.22 nM
1403	9.8×10^5 1/Ms	2.7×10^{-5} 1/s	$K_A = 3.7 \times 10^{10}$ 1/M, $K_D = 2.8 \times 10^{-11}$ M = 0.03 nM
1404	5.4×10^5 1/Ms	8.8×10^{-4} 1/s	$K_A = 6.2 \times 10^8$ 1/M, $K_D = 2.2 \times 10^{-9}$ M = 2.2 nM
1405	2.8×10^5 1/Ms	8.4×10^{-5} 1/s	$K_A = 3.4 \times 10^8$ 1/M, $K_D = 3.4 \times 10^{-9}$ M = 3.4 nM
1407	3.9×10^5 1/Ms	5.5×10^{-4} 1/s	$K_A = 7.0 \times 10^9$ 1/M, $K_D = 2.1 \times 10^{-10}$ M = 0.21 nM
1408	4.3×10^5 1/Ms	1.0×10^{-4} 1/s	$K_A = 4.2 \times 10^9$ 1/M, $K_D = 2.9 \times 10^{-10}$ M = 0.29 nM
1409	3.5×10^5 1/Ms	Does not dissociate	K_A = N/A, K_D = N/A

Correlation of D-dimer FIA assay



Correlation of D-dimer concentration in clinical samples between reference IVD method (Siemens SYSMEX) and a sandwich FIA using D-dimer antibodies 1409 for capture and 1408 for detection.

Results with serum controls



D-dimer antibodies were tested in sandwich FIA using Bio-Rad Liquichek™ D-Dimer Quality Control materials. The 100% level equals to 3200 D-dimer ng/ml (Fibrinogen Equivalent Units; FEU). The combination of clones 1409 (capture) and 1408 (detection) resulted in the least amount of non-specific binding combined with high detection sensitivity.

NT-proBNP & proBNP

Natriuretic peptides function as protective hormones that counteract the physiological abnormalities of heart injury and myocardial dysfunction through their diuretic, natriuretic, and vasodilatory effects. The most relevant biomarkers of this family include B-type natriuretic peptide (BNP) and N-terminal prohormone of natriuretic peptide (NT-proBNP), which have been established as effective novel biomarkers for heart failure.[13,14]

The cardiac hormone BNP is predominantly released from cardiac myocytes in ventricles in response to myocardial wall stress secondary to volume and pressure overload. Initially, BNP is secreted as a biologically inactive 108-amino acid pro-BNP that is proteolytically cleaved to form the 32-amino acid bioactive BNP and its biologically inactive N-terminal fragment, the 76-amino acid NT-proBNP molecule.[13] NT-proBNP and BNP are secreted in a 1:1 ratio, but due to the longer half-life of NT-proBNP in the circulation (90–120 minutes compared with 20 minutes for BNP) the plasma concentrations of NT-proBNP are usually 6–10 times higher than BNP.[14–16]

The levels of both BNP and NT-proBNP are significantly increased in the plasma of patients with asymptomatic and symptomatic cardiac dysfunction and provide a hemodynamic measure of myocardial injuries.[16] Therefore, serum BNP and NT-proBNP tests have become valuable tools to confirm or exclude the presence of cardiovascular diseases, heart failure in particular. In addition, BNP and NT-proBNP assays have shown good clinical and statistical performance in providing independent prognostic information for risk stratification.[17–19]

Due to its longer half-life, NT-proBNP has the advantage of being more stable than BNP in clinical testing. However, NT-proBNP is affected more by age and renal function than BNP, and therefore requires careful assessment in the elderly and in patients with compromised renal function.[15]

Medix Biochemica offers nine high-quality monoclonal antibodies for the detection of NT-proBNP (1306, RC1306, 1307, RC1307, 1308, 1309, 1310, 1311, and 1312). Two of the antibodies are recombinant chimeric antibodies, consisting of constant region (Fc) from human and variable region (Fv) from mouse. In addition, the product portfolio includes one recombinant NT-proBNP antigen and one recombinant proBNP antigen in three product sizes, as well as biological samples. New BNP antibodies will be soon available.

Anti-human NT-proBNP monoclonal antibodies with recombinant antigens and biological samples

NT-proBNP antibody	Product code	Concentration (mg/mL)	Shelf life (months at +2–8°C)	Subclass	Applications tested
1306	100521	5	18	IgG_1	ELISA, CLIA, LF
RC1306	140010	5	N/D	Human IgG_1	ELISA
1307	100719	5	12	IgG_1	ELISA, CLIA, LF
RC1307	140011	5	N/D	Human IgG_1	ELISA
1308	100712	5	24	IgG_{2b}	ELISA, CLIA, LF
1309	100710	5	12	IgG_1	ELISA, CLIA, LF
1310	100718	5	N/D	IgG_1	ELISA, CLIA, LF
1311	100716	5	N/D	IgG_1	ELISA, CLIA, LF
1312	100717	5	N/D	IgG_1	ELISA, CLIA, LF

NT-proBNP & proBNP antigen	Product code
Recombinant NT-proBNP, 100 µg	610090
Recombinant proBNP, 50 µg	710017
Recombinant proBNP, 500 µg	710043
Recombinant proBNP, 1000 µg	710042

Biological sample	Product code
NT-proBNP Serum Samples	991-24-S-NTPBNP

Pair recommendations

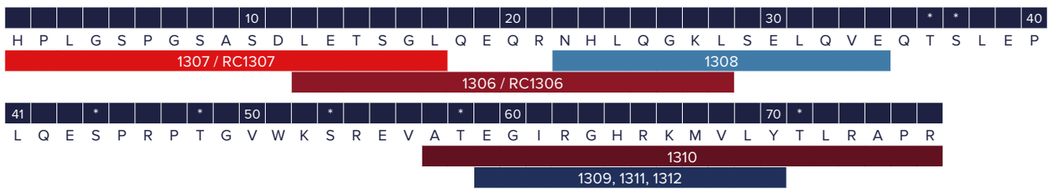
Capture \ Detection	1306 / RC1306	1307 / RC1307	1308	1309	1310	1311	1312
1306 / RC1306	–	+	–	+	+	+	+
1307 / RC1307	+	–	+	+	+	+	+
1308	–	+	–	+	+	+	+
1309	+	+	+	–	–	–	–
1310	+	+	+	–	–	–	–
1311	+	+	+	–	–	–	–
1312	+	+	+	–	–	–	–

Following pairs are especially recommended for the below mentioned assays:
CLIA: 1306 (capture) – 1309 (detection), 1306 – 1311, 1306 – 1312, 1308 – 1309, 1308 – 1310, 1308 – 1311 and 1308 – 1312

Kinetic parameters

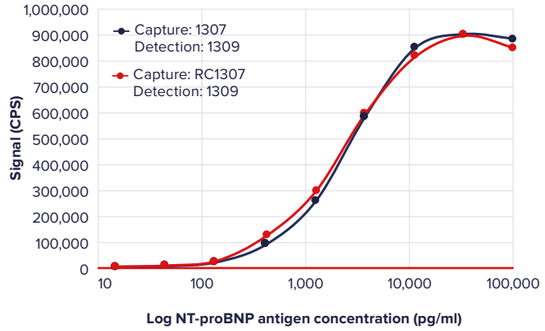
NT-proBNP antibody	Association rate constant, k_{on}	Dissociation rate constant, k_{off}	Affinity constant, K_A
1306	5.1×10^5	5.5×10^{-4}	$K_A = 9.2 \times 10^8$, $K_D = 1.7 \times 10^{-9}$ M = 1.7 nM
RC1306	2.3×10^5	4.7×10^{-4}	$K_A = 4.9 \times 10^8$, $K_D = 3.9 \times 10^{-9}$ M = 3.9 nM
1307	4.4×10^5	4.0×10^{-5}	$K_A = 1.1 \times 10^{10}$, $K_D = 9.0 \times 10^{-11}$ M = 0.09 nM
RC1307	1.2×10^6	2.3×10^{-4}	$K_A = 5.2 \times 10^9$, $K_D = 2.3 \times 10^{-10}$ M = 0.23 nM
1308	1.0×10^6	8.7×10^{-4}	$K_A = 1.2 \times 10^9$, $K_D = 1.0 \times 10^{-9}$ M = 1.0 nM
1309	9.5×10^5	1.4×10^{-4}	$K_A = 6.6 \times 10^9$, $K_D = 2.1 \times 10^{-10}$ M = 0.21 nM
1310	2.0×10^6	3.4×10^{-4}	$K_A = 5.8 \times 10^9$, $K_D = 1.9 \times 10^{-10}$ M = 0.19 nM
1311	7.5×10^5	1.1×10^{-4}	$K_A = 7.1 \times 10^9$, $K_D = 1.6 \times 10^{-10}$ M = 0.16 nM
1312	2.1×10^6	5.0×10^{-4}	$K_A = 4.1 \times 10^9$, $K_D = 2,5 \times 10^{-10}$ M = 0.25 nM

Binding epitopes



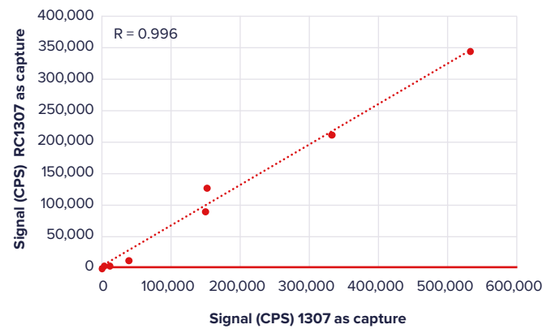
* Potential glycosylation sites

NT-proBNP standard curves of mouse 1307 and recombinant RC1307



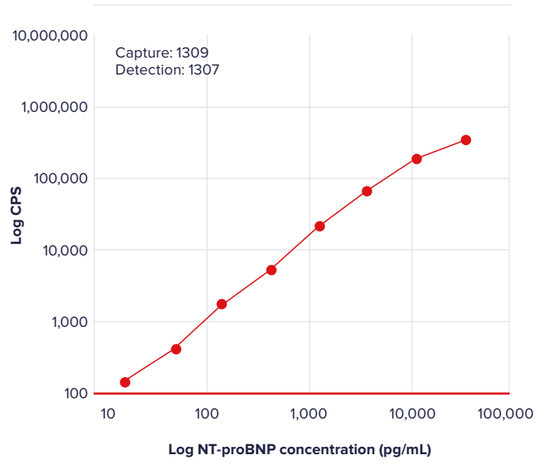
Sandwich FIA standard curves for recombinant NT-proBNP antigen using antibodies 1307 or RC1307 (capture) and 1309 (detection). Sensitivity of these antibodies 1307 (mouse antibody) and RC1307 (recombinant chimeric antibody) is the same.

Correlation of NT-proBNP FIA assay



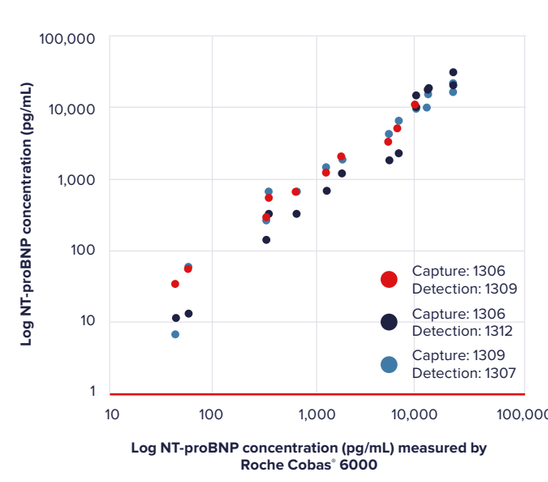
Correlation of NT-proBNP detection in serum samples using sandwich FIA. Antibodies 1307 (mouse antibody) or RC1307 (recombinant chimeric antibody) were used for capture and 1309 for detection. Mouse 1307 and recombinant RC1307 antibodies correlate well in the assay.

NT-proBNP standard curve



Sandwich FIA standard curve for recombinant NT-proBNP antigen using antibodies 1309 (capture) and 1307 (detection).

Correlation of NT-proBNP FIA assay



Correlation NT-proBNP concentrations in clinical samples between reference IVD method (Roche Cobas® 6000) and a fluoroimmunoassay (FIA) using NT-proBNP antibodies 1306 or 1309 for capture, and 1307, 1309 or 1312 for detection. NT-proBNP antibodies demonstrate excellent assay sensitivity correlating well with the reference IVD assay.

ST2

ST2 belongs to the interleukin (IL)-1 receptor-like family of proteins expressed in cardiomyocytes in response to mechanical stress. The protein is expressed both in a transmembrane receptor form (ST2L) and a soluble decoy receptor form (sST2). IL-33, which is involved in reducing fibrosis and hypertrophy, is the ligand for both forms. Binding of IL-33 to ST2L promotes signaling that exerts protective effects on cardiomyocytes. On the contrary, sST2 acts as a decoy receptor; when it is bound to IL-33 it prevents the beneficial signaling thus inducing fibrosis and hypertrophy.[20,21]

Current clinical assays measure sST2 whose elevated concentrations are strongly associated with adverse outcomes in heart failure.[39] The recommended cut-off for sST2 concentration in heart failure is 35 ng/mL, when assessed by Presage ST2 assay which has been approved for prognostication of heart failure in Europe and USA.[40]

Unlike natriuretic peptides, sST2 is not affected by age, sex, body mass index, and renal function when used as biomarkers in a clinical setting.[39] Furthermore, sST2 is the strongest predictor of mortality from both acute and chronic heart failure.[26,41,42] Besides being a prognostic biomarker for mortality, sST2 could be used to guide treatment decisions in the future. It has been demonstrated that patients with elevated sST2 levels may particularly benefit from high-dose beta blockers and mineralocorticoid inhibitors.[22–28]

Medix Biochemica offers seven monoclonal antibodies for the detection of ST2. Three of the ST2 antibodies recognize both free sST2 and sST2 bound to interleukin 33 (IL-33) (10201, 10202 and 10203), while the other four are specific to free sST2 alone (10204, 10205, 10206 and 10207). In addition, the product portfolio includes one recombinant ST2 antigen.

Anti-human ST2 monoclonal antibodies and recombinant antigen

ST2 antibody	Product code	Concentration (mg/mL)	Specificity	Shelf life (months at +2–8°C)	Subclass	Applications tested
10201	100680	5	Free sST2 and sST2 bound to IL-33	24	IgG_1	ELISA, CLIA
10202	100681	5	Free sST2 and sST2 bound to IL-33	N/D	IgG_1	ELISA, CLIA
10203	100682	5	Free sST2 and sST2 bound to IL-33	12	IgG_1	ELISA, CLIA
10204	100683	5	Free sST2	36	IgG_1	ELISA, CLIA
10205	100684	5	Free sST2	36	IgG_1	ELISA, CLIA
10206	100685	5	Free sST2	24	IgG_1	ELISA, CLIA
10207	100686	5	Free sST2	N/D	IgG_1	ELISA, CLIA

ST2 antigen	Product code
Recombinant ST2, 50 µg	710020
Recombinant ST2, 500 µg	710047
Recombinant ST2, 1000 µg	710046

Pair recommendations

Capture \ Detection	10201	10202	10203	10204	10205	10206	10207
10201	–	–	–	+	+	+	+
10202	–	–	–	+	+	+	+
10203	–	–	–	+	+	+	+
10204	+	+	+	–	+	+	–
10205	+	+	+	+	–	–	–
10206	+	+	+	+	–	–	–
10207	+	+	+	–	–	–	–

Kinetic parameters

ST2 antibody	Association rate constant, k_{on}	Dissociation rate constant, k_{off}	Affinity constant, K_A
10201	4.4×10^5	1.6×10^{-4}	$K_A = 2.9 \times 10^9$, $K_D = 5.4 \times 10^{-10}$ M = 0.54 nM
10202	5.2×10^4	8.6×10^{-5}	$K_A = 6.0 \times 10^8$, $K_D = 2.6 \times 10^{-9}$ M = 2.6 nM
10203	5.0×10^5	1.6×10^{-4}	$K_A = 3.2 \times 10^9$, $K_D = 4.7 \times 10^{-10}$ M = 0.47 nM
10204	2.5×10^5	5.1×10^{-4}	$K_A = 4.9 \times 10^8$, $K_D = 2.3 \times 10^{-9}$ M = 2.3 nM
10205	2.8×10^5	4.8×10^{-4}	$K_A = 5.8 \times 10^8$, $K_D = 2.0 \times 10^{-9}$ M = 2.0 nM
10206	4.9×10^5	1.1×10^{-4}	$K_A = 4.5 \times 10^9$, $K_D = 2.3 \times 10^{-10}$ M = 0.23 nM
10207	5.2×10^5	2.6×10^{-4}	$K_A = 2.0 \times 10^9$, $K_D = 6.9 \times 10^{-10}$ M = 0.69 nM

ST2 detection

ST2 standard curve

Correlation of ST2 CLIA assay

Correlation of ST2 detection in clinical samples between reference IVD method (Presage® ST2, Critical Diagnostics) and a chemiluminescence immunoassay (CLIA) using ST2 antibodies 10201 for capture and 10206 for detection.

Correlation of ST2 FIA assay

Correlation ST2 concentrations in clinical samples between reference IVD method (Presage® ST2, Critical Diagnostics) and a fluoroimmunoassay (FIA) using ST2 antibodies 10203 for capture and 10207 for detection.

Galectin-3

Galectin-3 (Mac-2 antigen, IgE-binding protein, L-29, or CBP30) is a soluble 35-kDa lectin that binds to the β-galactoside sugars that are found on several proteins.[29] It consists of two characteristic domains: a C-terminal carbohydrate recognition domain (CRD), and an N-terminal domain with a unique proline-glycine-alanine-thyrosine-rich (PGAY) repeat motif that enables oligomerization.[30,31] Galectin-3 is abundantly expressed across various different cell and tissue types. It is found both intracellularly and extracellularly,[31] and its biological functions are dependent on the subcellular localization. Galectin-3 binds to several different proteins and mediates diverse physiological responses, including cell cycle, cell adhesion and apoptosis, tissue development, immune responses, neoplastic transformation, angiogenesis and metastasis.[30–32]

Galectin-3 is a pro-inflammatory and pro-fibriotic marker involved in fibrosis of various organs, including heart, vessels, lungs, liver, and kidneys.[29,33] Its expression is upregulated in chronic inflammatory diseases, heart failure, hypertension and atherosclerotic lesions, and it is involved in several pathophysiological processes including cancer, liver cirrhosis, and diabetes mellitus.[29,34,35] In addition, Galectin-3 induces pathologic atrial remodeling in atrial fibrillation patients.[36–38] It is an accurate diagnostic and prognostic marker of poor outcomes and high mortality in patients with myocardial ischemia, acute ischemic stroke and chronic heart failure, whose prognosis is dependent on accurate and timely diagnosis.[38–40]

Medix Biochemica offers five monoclonal antibodies for the detection of Galectin-3, and a recombinant antigen.

Anti-human Galectin-3 monoclonal antibodies and recombinant antigen

Galectin-3 antibody	Product code	Concentration (mg/mL)	Subclass	Applications tested
10301	100730	5	IgG_1	ELISA, CLIA
10302	100731	5	IgG_1	ELISA, CLIA
10303	100732	5	IgG_1	ELISA, CLIA
10304	100733	5	IgG_1	ELISA, CLIA
10305	100734	5	IgG_1	ELISA, CLIA

Galectin-3 antigen	Product code
Recombinant Galectin-3, 100 µg	610144

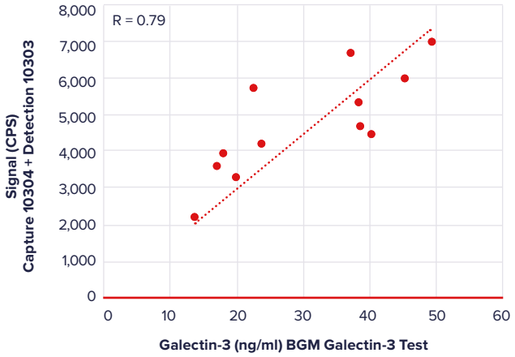
Pair recommendations

Capture \ Detection	10301	10302	10303	10304	10305
10301	–	+	+	+	+
10302	+	–	–	+	+
10303	+	–	–	+	+
10304	+	+	+	–	–
10305	+	+	+	–	–

Kinetic parameters

Galectin-3 antibody	Association rate constant, k_{on}	Dissociation rate constant, k_{off}	Affinity constant, K_A
10301	$5{,}2 \times 10^4$	$1{,}9 \times 10^{-4}$	$K_A = 2.8 \times 10^8$, $K_D = 4.3 \times 10^{-9}$ M = 4.3 nM
10302	$3{,}2 \times 10^5$	$1{,}2 \times 10^{-4}$	$K_A = 2.7 \times 10^9$, $K_D = 3.7 \times 10^{-10}$ M = 0.37 nM
10303	$2{,}9 \times 10^5$	$3{,}0 \times 10^{-4}$	$K_A = 9.7 \times 10^8$, $K_D = 2.2 \times 10^{-9}$ M = 2.2 nM
10304	$5{,}9 \times 10^5$	$9{,}0 \times 10^{-5}$	$K_A = 6.5 \times 10^9$, $K_D = 1.5 \times 10^{-10}$ M = 0.15 nM
10305	$6{,}1 \times 10^5$	$1{,}3 \times 10^{-4}$	$K_A = 4.8 \times 10^9$, $K_D = 2.4 \times 10^{-10}$ M = 0.24 nM

Correlation of Galectin-3 FIA assay



Correlation of Galectin-3 detection in serum samples between reference IVD method (Galectin-3, BG Medicine) and a fluoroimmunoassay (FIA) using Galectin-3 antibodies 10304 for capture and 10303 for detection. The results show proof of concept with clinical samples. Further assay optimization may be required to obtain the best performance.

GDF-15

Growth differentiation factor 15 (GDF-15), also known as MIC1, Placental TGF-β, NSAID-activated gene or PDF, is a stress responsive cytokine member of the transforming growth factor-β (TGF-β) superfamily. Upon proteolytic cleavage, the N-terminal pro-peptide is released from the precursor protein and GDF-15 is secreted as a dimer.[59] Under normal physiological states, GDF-15 is expressed weakly in several tissues and becomes upregulated during injury and inflammation.[60,61] Increased GDF-15 levels are associated with different malignancies including heart failure (HF), atherosclerosis, acute coronary syndrome (ACS)[62], chronic kidney disease,[63] and cancer.[64]

GDF-15 mediates anti-inflammatory effects in atherosclerosis and acute myocardial infarction by directly inhibiting myeloid cell recruitment, and may prevent hypertrophy and apoptosis by participating in protective signaling pathways.[61,65,66] Conversely, GDF-15 contributes to inflammation, pathologic hypertrophy, left ventricular remodeling, and apoptosis in atherosclerosis and myocardial infarction.[62]

GDF-15 is a consistent biomarker of mortality in HF and ACS, and an early predictor of cardiovascular events. As a result, detection of high levels of GDF-15 may provide additional diagnostic value by offering the possibility of early intervention in serious morbidities, including cardiovascular diseases.[59,67,68] Likewise, GDF-15 may have prognostic value in risk stratification, staging, and etiology of HF.[62,68–70]

Medix Biochemica offers five monoclonal antibodies for the detection of GDF-15, which bind to two different epitope groups. Two of the GDF-15 antibodies bind to epitope group 1 (4901, 4902), while the other three antibodies bind to epitope group 2 (4903, 4904, 4905).

Anti-human GDF-15 monoclonal antibodies

GDF-15 antibody	Product code	Concentration (mg/mL)	Subclass	Applications tested
4901	100688	5	IgG_1	ELISA, CLIA
4902	100658	5	IgG_1	ELISA, CLIA
4903	100836	5	IgG_1	ELISA, CLIA
4904	100837	5	IgG_1	ELISA, CLIA
4905	100838	5	IgG_1	ELISA, CLIA

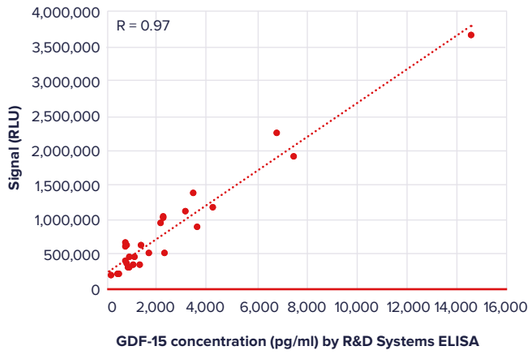
Pair recommendations

		Detection				
		4901	**4902**	**4903**	**4904**	**4905**
Capture	**4901**	–	–	+	+	+
	4902	–	–	+	+	+
	4903	+	+	–	–	–
	4904	+	+	–	–	–
	4905	+	+	–	–	–

Kinetic parameters

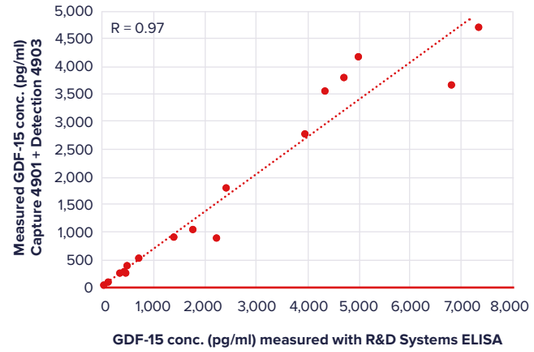
GDF-15 antibody	Association rate constant, k_{on}	Dissociation rate constant, k_{off}	Affinity constant, K_A
4901	6.6×10^5	N/A	N/A
4902	5.6×10^5	N/A	N/A
4903	7.9×10^5	N/A	N/A
4904	5.0×10^5	1.3×10^{-4}	$K_A = 3.7 \times 10^9$, $K_D = 1.4 \times 10^{-9}$ M = 1.4 nM
4905	7.3×10^5	N/A	N/A

Correlation of GDF-15 CLIA assay



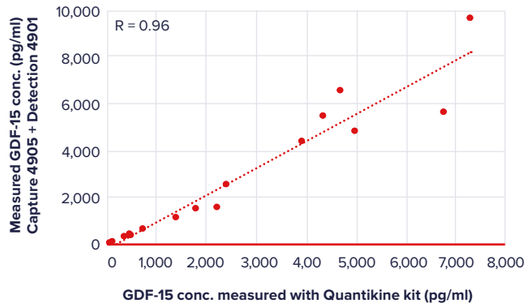
Correlation of GDF-15 detection in clinical samples between a reference method (ELISA, R&D Systems) and a chemiluminescence immunoassay (CLIA) using GDF-15 antibodies 4904 for capture and 4901 for detection.

Correlation of GDF-15 FIA assay



Correlation of GDF-15 detection in clinical samples between a reference method (ELISA, R&D Systems) and a fluoroimmunoassay (FIA) using GDF-15 antibodies 4901 for capture and 4903 for detection.

Correlation of GDF-15 FIA assay



Correlation of GDF-15 detection in clinical samples between a reference method (ELISA, R&D Systems) and a fluoroimmunoassay (FIA) using GDF-15 antibodies 4905 for capture and 4901 for detection.

FABP3

Fatty acid-binding proteins (FABP) are a family of lipid chaperones involved in the transport and metabolism of fatty acids. So far, at least nine members of the family have been identified. FABPs are 14–15 kDa proteins that reversibly bind hydrophobic ligands, such as fatty acids, with high affinity.[19] Heart-type FABP (H-FABP, also known as FABP3) is a cytosolic, low-molecular-weight protein present in abundance in the myocardium, but also in small quantities in the brain, kidney and skeletal muscle.[13,19]

In the case of acute myocardial infarction (AMI), FABP3 is released from the porous cell membranes of ischemic myocardial cells into circulation due to its small size.[12,20] Therefore, FABP3 is used as a biochemical marker in the early diagnosis of AMI and acute coronary syndrome[12,20], and can provide even better sensitivity than other commonly used markers including cTnI, CK-MB, and myoglobin 0–6 hours after the onset of chest pain.[21] However, the concentration of FABP3 is affected by age and renal condition.[12,19] Also, special attention needs to be addressed to additional analytical issues, such as optimum cut-off value.[13,41–43]

Medix Biochemica offers three different monoclonal antibodies for the detection of human FABP3 (2302, 2303, and 2304). All of the antibodies are specific for FABP3 and show no cross-reactivity with FABP1 and FABP4. Additionally, Medix Biochemica has one recombinant FABP3 antigen and two native antigens in the product selection.

Anti-human FABP3 monoclonal antibodies and antigens

FABP3 antibody	Product code	Concentration (mg/mL)	Shelf life (months at +2–8°C)	Subclass	Applications tested
2302	100292	5	18	IgG_1	ELISA, LF, IT
2303	100293	5	24	IgG_1	ELISA, LF, IT
2304	100294	5	24	IgG_1	ELISA, LF, IT

FABP3 antigen	Product code	Form
Recombinant FABP3, 100 µg	610043	Lyophilized
Native FABP3	276-10	Liquid
Native FABP3	276-12	Lyophilized

Pair recommendations

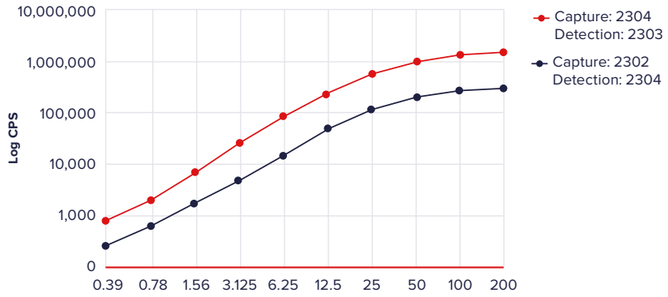
		Detection		
		2302	**2303**	**2304**
Capture	**2302**	–	–	+
	2303	–	–	+
	2304	+	+	–

Following pair is especially recommended for the IT assay: 2302 – 2304

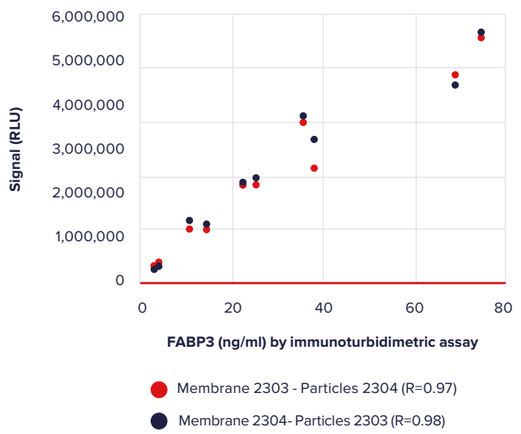
Kinetic parameters

FABP3 antibody	Association rate constant, k_{on}	Dissociation rate constant, k_{off}	Affinity constant, K_A
2302	2.9×10^5 1/Ms	4.5×10^{-3} 1/Ms	$K_A = 6.5 \times 10^7$ 1/M, $K_D = 1.6 \times 10^{-8}$ M = 16 nM
2303	4.0×10^5 1/Ms	1.6×10^{-3} 1/Ms	$K_A = 2.5 \times 10^8$ 1/M, $K_D = 4.1 \times 10^{-9}$ M = 4.1 nM
2304	3.5×10^5 1/Ms	1.2×10^{-4} 1/Ms	$K_A = 2.8 \times 10^9$ 1/M, $K_D = 3.5 \times 10^{-10}$ M = 0.35 nM

FABP3 standard curves

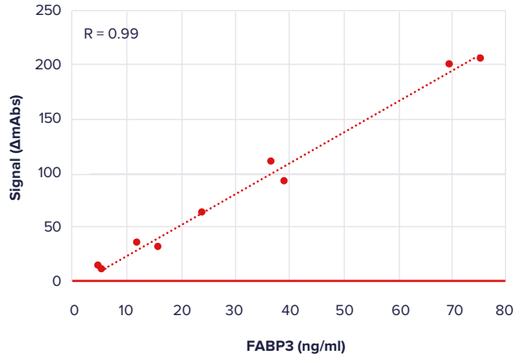


Correlation of FABP3 FLF assay



FABP3 detection in clinical samples correlates well between reference method (immunoturbidimetric assay) and fluorometric lateral flow assay (FLF) with antibody pairs 2304 - 2303 and 2303 - 2304.

Correlation of FABP3 IT assay



FABP antibody pair 2302 - 2304 demonstrate excellent assay sensitivity with clinical samples in immunoturbidimetric assay (IT).

Copeptin

Copeptin, which is a 39-aminoacid glycopeptide, forms the C-terminal part of pre-provasopressin (pre-proAVP). Pre-proAVP is a precursor protein synthesized in hypothalamus and consists of a signal peptide, arginine vasopressin (AVP, also known as antidiuretic hormone [ADH]), neurophysin II and copeptin. The components of pre-proAVP are cleaved during axonal transportation from hypothalamus to pituitary gland.[44]

AVP is released into the bloodstream in response to changes in plasma osmolarity and reduced cardiac output. However, it is unstable in isolated plasma and thus cannot be used as a biomarker. As copeptin is co-synthesized with AVP and is found in equimolar amounts with AVP in the bloodstream, and because it is stable in plasma for days it can be used as a surrogate biomarker of AVP release.[34]

Several trials have assessed the diagnostic and prognostic value of copeptin in various cardiovascular diseases, especially in acute coronary syndromes (ACS) and heart failure.[45]

Copeptin is a promising biomarker for improving the diagnostics of ACS when used in combination with troponins.[35] Using copeptin in combination with cardiac troponin I (cTnI), for example, allowed safely ruling out acute myocardial infarction with a negative predictive value of over 99% in patients presenting with suspected ACS.[36] In addition, copeptin can potentially be used to predict outcomes of acute and chronic heart failure.[46–47]

Medix Biochemica has four monoclonal antibodies (4801, 4802, 4804, and 4806) for the detection of copeptin.

Anti-human copeptin monoclonal antibodies

Copeptin antibody	Product code	Concentration (mg/mL)	Subclass	Applications tested
4801	100638	5	IgG_1	ELISA
4802	100639	5	IgG_1	ELISA
4804	100649	5	IgG_1	ELISA
4806	100648	5	IgG_1	ELISA

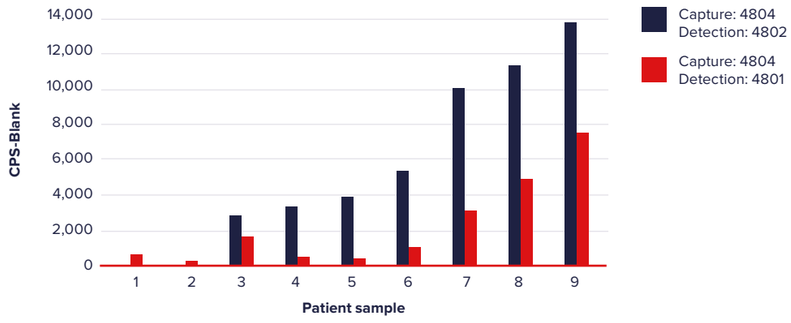
Pair recommendations

Capture \ Detection	4801	4802	4804	4806
4801	–	–	+	+
4802	–	–	+	+
4804	+	+	–	–
4806	+	+	–	–

Binding epitopes

Copeptin standard curves

Copeptin results with clinical samples



Detection of Copeptin in clinical samples using Copeptin antibodies 4804 for capture and 4801 or 4802 for detection in FIA assay.

Myoglobin

Myoglobin is an oxygen-binding cytosolic heme protein and belongs to the globin family together with hemoglobin and neuroglobin. Globin-family proteins have a characteristic globin fold consisting of eight alpha-helices and a heme group. Myoglobin is found in oxidative striated muscles and cardiac myocytes as well as in smooth muscle cells acting as an oxygen storage depot.[48]

Myoglobin is a sensitive marker for muscle damage, and is rapidly released after acute myocardial injury (AMI).[23] Myoglobin is the earliest marker to rise after AMI, and appears in blood 1–3 hours post AMI, reaches its maximum in 4–7 hours and goes back to baseline after 24–36 hours.[26] However, because of its rapid kinetics, the use of myoglobin as a biomarker may miss patients who do not show early signs of infarction.[23] In addition, myoglobin is less heart-specific than for example CK-MB and FABP3[27], and has limited specificity for patients with renal insufficiency and skeletal muscle injury.[49,50,52]

Currently, Medix Biochemica offers three monoclonal antibodies (7001, 7004, and 7005) for the specific detection of myoglobin. In addition, Medix Biochemica offers recombinant and native myoglobin antigens.

Anti-human myoglobin monoclonal antibodies and antigens

Myoglobin antibody	Product code	Concentration (mg/mL)	Shelf life (months at +2–8°C)	Subclass	Applications tested
7001	100378	5	24	IgG_{2b}	ELISA, LF, IT
7004	100354	5	24	IgG_1	ELISA, LF, IT
7005	100078	5	36	IgG_1	ELISA, LF, IT

Myoglobin antigen	Product code
Recombinant Myoglobin, 100 µg	610030
Native Myoglobin	431-11

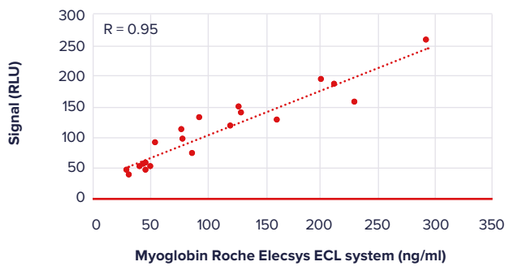
Kinetic parameters

Myoglobin antibody	Affinity constant, K_A
7001	1×10^8 1/M
7004	7×10^9 1/M
7005	1×10^9 1/M

Pair recommendations

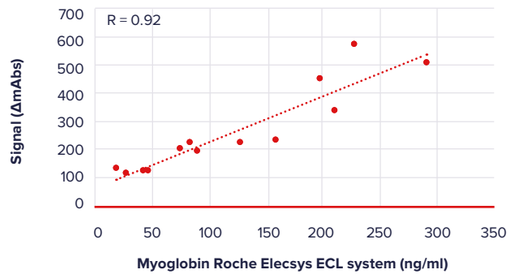
		Detection		
		7001	**7004**	**7005**
Capture	**7001**	–	+	+
	7004	+	–	+
	7005	+	+	–

Correlation of Myoglobin LF assay



Correlation of Myoglobin detection in clinical samples between reference IVD method (Roche Elecsys ECL system) and lateral flow assay (LF) using Myoglobin antibodies 7001 for capture and 7005 for detection.

Correlation of Myoglobin IT assay



Correlation of Myoglobin detection in clinical samples between reference IVD method (Roche Elecsys ECL system) and immunoturbidimetric assay (IT) using Myoglobin antibodies 7004 and 7005.

CK-MB

Creatine kinase (CK, also known as creatine phosphokinase or phospho-creatine kinase) is a member of a highly conserved family of phosphoryl transfer enzymes called phosphagen (guanidino) kinases and is expressed in various cells and tissue types. CK catalyzes the reversible transfer of phosphate from phosphocreatine to ADP to yield ATP and creatine.[22] CK consists of two subunits, which can be either the M (muscle) or B (brain) type. In humans, there are three different isoenzymes, BB, MM, and MB.[12,23] The CK-MB isoenzyme, also known as CK-2, is predominantly found in the heart muscle, and serves as a biomarker for cardiac muscle injury.[13,51,52]

CK-MB is present in high concentration uniquely in the myocardium, but it can be found in smaller concentrations in skeletal muscle and the brain. The levels of CK-MB are normally very low or undetectable in the blood, but increase rapidly in both heart and skeletal diseases with highest concentrations in the cardiac muscle (22% in the cardiac muscle compared to 1–3 % in the skeletal muscle). Measurement of CK-MB concentration in plasma or serum is used as a tool for the diagnosis of acute myocardial infarction (AMI), and is routinely determined in emergency patients. CK-MB measurement is especially valuable in the 20% of AMI patients that are clinically asymptomatic.[13,49,50]

Medix Biochemica has two monoclonal antibodies (7501 and 7502) against human creatine kinase MB isozyme. The antibody 7502 is specific for CK-MB isoform, with less than 10% cross-reactivity to isoforms CK-BB or CK-MM. In addition, Medix Biochemica offers native CK-MB antigens.

Anti-human CK-MB monoclonal antibodies and native antigens

CK-MB antibody	Product code	Concentration (mg/mL)	Shelf life (months at +2–8°C)	Subclass	Applications tested
7501	100630	5	24	IgG_1	ELISA
7502	100086	5	18	IgG_1	ELISA

CK-MB antigen	Product code	Grade
Native CK-MB	190-24	Purified (Control Grade)
Native CK-MB	190-24A	> 98% (SDS-PAGE)
Native CK-MB	190-24-R2	Highly purified

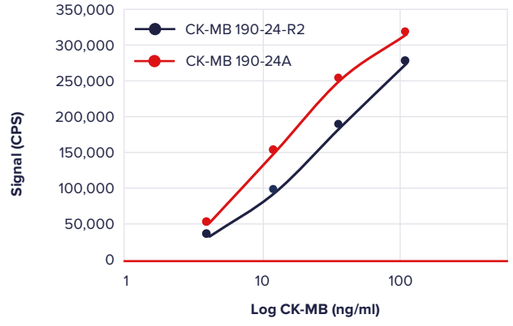
Pair recommendations

		Detection
		7502
Capture	**7501**	+

Kinetic parameters

CK-MB antibody	Affinity constant, K_A
7501	2×10^9 1/M
7502	1×10^8 1/M

CK-MB standard curves



Sandwich FIA standard curves for two CK-MB antigens using antibodies 7501 (capture) and 7502 (detection).

Lp-PLA2

Lipoprotein-associated phospholipase A2 (Lp-PLA2), also known as platelet-activating factor acetylhydrolase, is a calcium-independent serine lipase belonging to the phospholipase A2 superfamily. It is an enzyme secreted by macrophages and lymphocytes in atherosclerotic plaques, and is strongly correlated with atherogenic risk. About 80% of the Lp-PLA2 circulates bind to low-density lipoproteins (LDL), while nearly 20% are bound to high-density lipoproteins (HDL). Lp-PLA2 promotes modifications in LDL in the arterial wall, thus generating oxidized phospholipids. Such oxidized phospholipids can advance atherosclerosis by promoting inflammation and endothelial dysfunction.[71–76] Higher levels of Lp-PLA2 within the atherosclerotic plaque may represent increased risk of plaque instability, rupture, and production of blood clots.[76–78]

Lp-PLA2 is a vascular-specific marker of inflammation not influenced by obesity, and a strong and independent predictor of atherosclerotic cardiovascular events.[78] High levels of both Lp-PLA2 and C-reactive protein (CRP) constitute a very high risk of cardiovascular events in individuals with low or moderately elevated LDL cholesterol. In addition to major risk factors such as high LDL and low HDL levels, diabetes, and hypertension, Lp-PLA2 can be used to determine which patients are at risk of developing atherosclerotic cardiovascular disease.[78]

Medix Biochemica offers four monoclonal antibodies for the detection of Lp-PLA2 and one recombinant antigen.

Anti-human Lp-PLA2 monoclonal antibodies and recombinant antigen

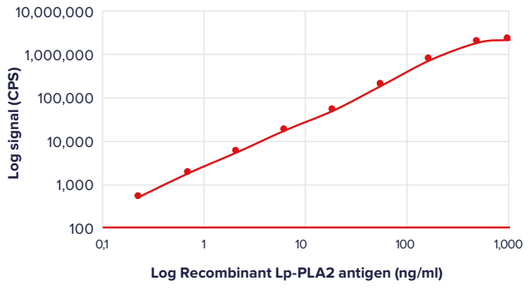
Lp-PLA2 antibody	Product code	Concentration (mg/mL)	Shelf life (months at +2–8°C)	Subclass	Applications tested
11202	100751	5	24	IgG_1	ELISA
11205	100818	5	N/D	IgG_1	ELISA
11207	100753	5	18	IgG_1	ELISA
11209	100755	5	N/D	IgG_1	ELISA

Lp-PLA2 antigen	Product code
Recombinant Lp-PLA2	400-60

Pair recommendations

Capture \ Detection	11202	11205	11207	11209
11202	–	+	+	+
11205	+	–	+	+
11207	+	+	–	–
11209	+	+	–	–

Lp-PLA2 standard curve



Sandwich FIA standard curve for recombinant Lp-PLA2 antigen using antibodies 11205 (capture) and 11202 (detection).

MPO

Myeloperoxidase (MPO) is an enzyme that belongs to the heme-peroxidase superfamily. It is highly expressed in neutrophils and monocytes and released during their activation. Accordingly, MPO is involved in the antimicrobial innate immune response.[28]

MPO has a 150-kDa homodimeric structure that consists of two 15-kDa light chains and two variable-weight heavy chains bound to a heme group.[29] It catalyzes the conversion of hydrogen peroxide to hypochlorous acid, which has strong anti-microbial and detoxification properties but can also cause oxidative damage to the host tissue. In addition to playing a role in the host immune response, MPO has been identified in atheromatous plaques[30] and can exert several proatherogenic effects. These include oxidation of low-density lipoprotein (LDL) and high-density lipoprotein (HDL)[31] as well as induction of vascular dysfunction through reducing nitric oxide bioavailability.[32]

Several studies have indicated that MPO could be used as a cardiovascular disease risk marker along with traditional markers, especially in patients with unstable coronary artery disease.[31]

Medix Biochemica provides three high-quality monoclonal antibodies (1701, 1702 and 1703) against MPO, and a native MPO antigen.

Anti-human MPO monoclonal antibodies and native antigen

MPO antibody	Product code	Concentration (mg/mL)	Shelf life (months at +2–8°C)	Subclass	Applications tested
1701	100266	5	36	IgG_1	ELISA
1702	100267	5	36	IgG_1	ELISA
1703	100268	5	36	IgG_1	ELISA

MPO antigen	Product code
Native MPO	426-10

Pair recommendations

Capture \ Detection	1701	1702	1703
1701	–	+	+
1702	–	–	+
1703	+	+	–

Kinetic parameters

MPO antibody	Association rate constant, k_{on}	Dissociation rate constant, k_{off}	Affinity constant, K_A
1701	1×10^6 1/Ms	1×10^{-3} 1/s	$K_A = 1 \times 10^9$ 1/M, $K_D = 1 \times 10^{-9}$ M
1702	8×10^5 1/Ms	2×10^{-3} 1/s	$K_A = 5 \times 10^8$ 1/M, $K_D = 2 \times 10^{-9}$ M
1703	9×10^5 1/Ms	2×10^{-4} 1/s	$K_A = 5 \times 10^9$ 1/M, $K_D = 2 \times 10^{-10}$ M

Cardiovascular

References:

1. Adamcova M, Popelova-Lencova O, Jirkovsky E et al. (2016). Cardiac troponins-Translational biomarkers in cardiology: Theory and practice of cardiac troponin high-sensitivity assays. Biofactors 42:133–148.
2. Babuin L & Jaffe AS (2005). Troponin: the biomarker of choice for the detection of cardiac injury. CMAJ 173:1191–1202.
3. Westermann D, Neumann JT, Sorensen NA & Blankenberg S (2017). High-sensitivity assays for troponin in patients with cardiac disease. Nat Rev Cardiol 14: 472–483.
4. Neumann JT, Sorensen NA, Schwemer T et al. (2016). Diagnosis of Myocardial Infarction Using a High-Sensitivity Troponin I 1-Hour Algorithm. JAMA Cardiol 1:397–404.
5. Jin et al. Troponin T Isoform Regulation and Structure-Function Relationships. Basic Appl. Myol. 2000;20:17–26.
6. Jacobs B, Obi A & Wakefield T (2016). Diagnostic biomarkers in venous thromboembolic disease. J Vasc Surg Venous Lymphat Disord 4:508–517.
7. Adam SS, Key NS & Greenberg CS (2009). D-dimer antigen: current concepts and future prospects. Blood 113:2878–2887.
8. Giannitsis E, Mair J, Christersson C et al. (2017). How to use D-dimer in acute cardiovascular care. Eur Heart J Acute Cardiovasc Care 6:69–80.
9. Linkins LA & Takach Lapner S (2017). Review of D-dimer testing: Good, Bad, and Ugly. Int J Lab Hematol 39 Suppl 1:98–103.
10. Soomro AY, Guerchicoff A, Nichols DJ et al. (2016). The current role and future prospects of D-dimer biomarker. Eur Heart J Cardiovasc Pharmacother 2:175–184.
11. Walker JB & Nesheim ME (1999). The molecular weights, mass distribution, chain composition, and structure of soluble fibrin degradation products released from a fibrin clot perfused with plasmin. J Biol Chem 274:5201–5212.
12. Pulivarthi S & Gurram MK (2014). Effectiveness of d-dimer as a screening test for venous thromboembolism: an update. N Am J Med Sci 6:491–499.
13. Kehl DW, Iqbal N, Fard A et al. (2012). Biomarkers in acute myocardial injury. Transl Res 159:252–264.
14. Ghashghaei R, Arbit B & Maisel AS (2016). Current and novel biomarkers in heart failure: bench to bedside. Curr Opin Cardiol 31:191–195.
15. Downie PF, Talwar S, Squire IB et al. (1999). Assessment of the stability of N-terminal pro-brain natriuretic peptide in vitro: implications for assessment of left ventricular dysfunction. Clin Sci (Lond) 97:255–258.
16. Suzuki T, Lyon A, Saggar R et al. (2016). Editor's Choice-Biomarkers of acute cardiovascular and pulmonary diseases. Eur Heart J Acute Cardiovasc Care 5:416–433.
17. Buchan A, Bennett R, Coad A et al. (2015). The role of cardiac biomarkers for predicting left ventricular dysfunction and cardiovascular mortality in acute exacerbations of COPD. Open Heart 2:e000052–2014–000052. eCollection 2015.
18. Martindale JL, Wakai A, Collins SP et al. (2016). Diagnosing Acute Heart Failure in the Emergency Department: A Systematic Review and Metaanalysis. Acad Emerg Med 23:223–242.
19. Pu DR, Chiong JR & Zhou QC (2010). Clinical applications of N-terminal pro B-type natriuretic peptide in heart failure and other cardiovascular diseases. Heart Fail Rev 15:293–304.
20. Januzzi JL,Jr (2013). ST2 as a cardiovascular risk biomarker: from the bench to the bedside. J Cardiovasc Transl Res 6:493–500.
21. Wettersten N & Maisel AS (2016). Biomarkers for Heart Failure: An Update for Practitioners of Internal Medicine. Am J Med 129:560–567.
22. Daniels LB & Bayes-Genis A (2014). Using ST2 in cardiovascular patients: a review. Future Cardiol 10:525–539.
23. Dieplinger B, Januzzi JL, Jr, Steinmair M et al. (2009). Analytical and clinical evaluation of a novel high-sensitivity assay for measurement of soluble ST2 in human plasma–the Presage ST2 assay. Clin Chim Acta 409:33–40.
24. Gaggin HK, Szymonifka J, Bhardwaj A et al. (2014). Head-to-head comparison of serial soluble ST2, growth differentiation factor-15, and highly-sensitive troponin T measurements in patients with chronic heart failure. JACC Heart Fail 2:65–72.
25. Bayes-Genis A, de Antonio M, Vila J et al. (2014). Head-to-head comparison of 2 myocardial fibrosis biomarkers for long-term heart failure risk stratification: ST2 versus galectin-3. J Am Coll Cardiol 63:158–166.
26. Binas et al. The prognostic value of sST2 and galectin-3 considering different aetiologies in non-ischaemic heart failure. Open Heart 2018;5(1):e000750.
27. Gaggin HK, Motiwala S, Bhardwaj A et al. (2013). Soluble concentrations of the interleukin receptor family member ST2 and beta-blocker therapy in chronic heart failure. Circ Heart Fail 6:1206–1213.
28. Maisel A, Xue Y, van Veldhuisen DJ et al. (2014). Effect of spironolactone on 30-day death and heart failure rehospitalization (from the COACH Study). Am J Cardiol 114:737–742.43.
29. Suthahar et al. (2018) Galectin-3 activation and inhibition in heart failure and cardiovascular disease: an update. Theranostics 8(3):593–609.
30. Barondes et al. (1994) Galectins. Structure and function of a large family of animal lectins. J Biol Chem 269:20807–10.
31. Dumic et al. (2006) Galectin-3: an open-ended story. Biochim Biophys Acta 1760:616–35.
32. Funasaka et al. Galectin-3 in angiogenesis and metastasis. Glycobiology 2014;24(10):886–91.
33. Henderson et al. (2006) Galectin-3 regulates myofibroblast activation and hepatic fibrosis. Proc Natl Acad Sci USA 28;103(13):5060–5.
34. Binh et al. (2013) Galectin-3 in preneoplastic lesions of glioma. J Neurooncol 111(2):123–32.
35. Pugliese et al. (2014) Galectin-3 in diabetic patients. Clin Chem Lab Med 52(10):1413–23.
36. Clementy et al. (2018) Galectin-3 in atrial fibrillation: mechanism and therapeutic implications. Int J Mol Sci 19(4):pii:E976.
37. de Boer et al. (2013) Galectin-3 in heart failure with preserved ejection fraction. Eur J Heart Fail 15(10):1095–101.
38. Wang et al. (2018) Serum galectin-3 and poor outcomes among patients with acute ischemic stroke. Stroke 49(1):211–214.
39. Gehlken et al. (2018) Galectin-3 in heart failure: an update of the last 3 years. Heart Fail Clin 14(1):75–92.
40. Kang et al. (2018) Galectin-3 in patients with coronary heart disease and atrial fibrillation. Clin Chim Acta 478:166–170.
41. Furuhashi M, Ura N, Hasegawa K et al. (2003). Serum ratio of hearttype fatty acid-binding protein to myoglobin. A novel marker of cardiac damage and volume overload in hemodialysis patients. Nephron Clin Pract 93:C69–74.
42. Furuhashi M & Hotamisligil GS (2008). Fatty acid-binding proteins: role in metabolic diseases and potential as drug targets. Nat Rev Drug Discov 7:489–503.
43. McMahon CG, Lamont JV, Curtin E et al. (2012). Diagnostic accuracy of heart-type fatty acid-binding protein for the early diagnosis of acute myocardial infarction. Am J Emerg Med 30:267–274.
44. Dobsa L & Edozien KC (2013). Copeptin and its potential role in diagnosis and prognosis of various diseases. Biochem Med (Zagreb) 23:172–190.
45. Struck J, Morgenthaler NG & Bergmann A (2005). Copeptin, a stable peptide derived from the vasopressin precursor, is elevated in serum of sepsis patients. Peptides 26:2500–2504.
46. Schurtz G, Lamblin N, Bauters C et al. (2015). Copeptin in acute coronary syndromes and heart failure management: State of the art and future directions. Arch Cardiovasc Dis 108:398–407.
47. Maisel A, Mueller C, Neath SX et al. (2013). Copeptin helps in the early detection of patients with acute myocardial infarction: primary results of the CHOPIN trial (Copeptin Helps in the early detection Of Patients with acute myocardial INfarction). J Am Coll Cardiol 62:150–160.
48. Ellington WR & Suzuki T (2007). Early evolution of the creatine kinase gene family and the capacity for creatine biosynthesis and membrane transport. Subcell Biochem 46:17–26.
49. Danese E & Montagnana M (2016). An historical approach to the diagnostic biomarkers of acute coronary syndrome. Ann Transl Med 4:194.
50. Sanchez M, Gella FJ, Profilis C et al. (2001). Certification of the mass concentration of creatine kinase isoenzyme 2 (CK-MB) in the reference material BCR 608. Clin Chem Lab Med 39:858–865.
51. Hendgen-Cotta UB, Kelm M & Rassaf T (2014). Myoglobin functions in the heart. Free Radic Biol Med 73:252–259.
52. Penttilä I, Penttilä K & Rantanen T (2000). Laboratory diagnosis of patients with acute chest pain. Clin Chem Lab Med 38:187–197.
53. French JK & White HD (2004). Clinical implications of the new definition of myocardial infarction. Heart 90:99–106.
54. O'Brien PJ (2000). Peroxidases. Chem Biol Interact 129:113–139.
55. Andrews PC & Krinsky NI (1981). The reductive cleavage of myeloperoxidase in half, producing enzymically active hemimyeloperoxidase. J Biol Chem 256:4211–4218.
56. Daugherty A, Dunn JL, Rateri DL & Heinecke JW (1994). Myeloperoxidase, a catalyst for lipoprotein oxidation, is expressed in human atherosclerotic lesions. J Clin Invest 94:437–444.
57. Schindhelm RK, van der Zwan LP, Teerlink T & Scheffer PG (2009). Myeloperoxidase: a useful biomarker for cardiovascular disease risk stratification? Clin Chem 55:1462–1470.
58. Eiserich JP, Baldus S, Brennan ML et al. (2002). Myeloperoxidase, a leukocyte-derived vascular NO oxidase. Science 296:2391–2394.
59. Wollert, K. C., Kempf, T. & Wallentin, L. Growth Differentiation Factor 15 as a Biomarker in Cardiovascular Disease. Clin. Chem. 63, 140–151 (2017).
60. Xu, X., Li, Z. & Gao, W. Growth differentiation factor 15 in cardiovascular diseases: from bench to bedside. Biomarkers 16, 466–475 (2011).
61. Kempf, T. et al. GDF-15 is an inhibitor of leukocyte integrin activation required for survival after myocardial infarction in mice. Nat. Med. 17, 581–588 (2011).
62. George, M., Jena, A., Srivatsan, V., Muthukumar, R. & Dhandapani, V. GDF 15 - A Novel Biomarker in the Offing for Heart Failure. Curr. Cardiol. Rev. 12, 37–46 (2016).
63. Bao, X. et al. Growth differentiation factor-15 and incident chronic kidney disease: a population-based cohort study. BMC Nephrol. 22, 351 (2021).
64. Welsh, J. B. et al. Large-scale delineation of secreted protein biomarkers overexpressed in cancer tissue and serum. Proc. Natl. Acad. Sci. U. S. A. 100, 3410–3415 (2003).
65. Xu, J. et al. GDF15/MIC-1 functions as a protective and antihypertrophic factor released from the myocardium in association with SMAD protein activation. Circ. Res. 98, 342–350 (2006).
66. Kempf, T. et al. The transforming growth factor-beta superfamily member growth-differentiation factor-15 protects the heart from ischemia/reperfusion injury. Circ. Res. 98, 351–360 (2006).
67. Eggers, K. M., Kempf, T., Wallentin, L., Wollert, K. C. & Lind, L. Change in growth differentiation factor 15 concentrations over time independently predicts mortality in community-dwelling elderly individuals. Clin. Chem. 59, 1091–1098 (2013).
68. Anand, I. S. et al. Serial measurement of growth-differentiation factor-15 in heart failure: relation to disease severity and prognosis in the Valsartan Heart Failure Trial. Circulation 122, 1387–1395 (2010).
69. Wang, F. et al. Growth differentiation factor 15 in different stages of heart failure: potential screening implications. Biomark. Biochem. Indic. Expo. Response Susceptibility Chem. 15, 671–676 (2010).
70. Chow, S. L. et al. Role of Biomarkers for the Prevention, Assessment, and Management of Heart Failure: A Scientific Statement From the American Heart Association. Circulation 135, e1054–e1091 (2017).
71. Macphee, C. H. et al. Lipoprotein-associated phospholipase A2, platelet-activating factor acetylhydrolase, generates two bioactive products during the oxidation of low-density lipoprotein: use of a novel inhibitor. Biochem J 338 (Pt 2), 479–487 (1999).
72. Zalewski, A. & Macphee, C. Role of lipoprotein-associated phospholipase A2 in atherosclerosis: biology, epidemiology, and possible therapeutic target. Arterioscler Thromb Vasc Biol 25, 923–931 (2005).
73. Kolodgie, F. D. et al. Lipoprotein-associated phospholipase A2 protein expression in the natural progression of human coronary atherosclerosis. Arterioscler Thromb Vasc Biol 26, 2523–2529 (2006).
74. Stafforini, D. M. et al. Molecular basis of the interaction between plasma platelet-activating factor acetylhydrolase and low density lipoprotein. J Biol Chem 274, 7018–7024 (1999).
75. Corson, M. A. Phospholipase A2 inhibitors in atherosclerosis: the race is on. The Lancet 373, 608–610 (2009).
76. De Stefano, A. et al. Lp-PLA2, a new biomarker of vascular disorders in metabolic diseases. Int J Immunopathol Pharmacol 33, 2058738419827154 (2019).
77. Thompson, A. et al. Lipoprotein-associated phospholipase A2 and risk of coronary disease, stroke, and mortality: collaborative analysis of 32 prospective studies. The Lancet 375, 1536–1544 (2010).
78. Jellinger, P. S. et al. American Association of Clinical Endocrinologists and American College of Endocrinology Guidelines for Management of Dyslipidemia and Prevention of Cardiovascular Disease. Endocrine Practice 23, 1–87 (2017).

Medix Biochemica

More information on our products
medixbiochemica.com

Klovinpellontie 3, FI-02180 Espoo, Finland
medix@medixbiochemica.com

CPS = Counts per second
CLIA = Chemiluminescence immunoassay
ELISA = Enzyme-linked immunosorbent assay
FIA = Fluoroimmunoassay
IT = Immunoturbidimetry
LF = Lateral flow
N/A = Not Applicable
N/D = Not Determined

The results shown in this technical note are from prototype assays (unoptimized), indicating proof of concept with clinical samples. Further assay optimization may be required to obtain the best performance.