BOWEI-BIOTECH
for better bioassays

Biomarkers of Health and Aging

Shanghai Bowei Biotechnology

Biomarkers of Health and Aging

Introduction

The biomarker of health and aging is defined as a wide range of biological indicators which reflect the underlying physiological processes, including the normative and pathogenic ones. Since these markers are closely associated with health and aging, detection of them may have utility in clinical diagnosis, epidemiological studies, health surveys and as outcomes in intervention studies that aim to promote the health of humans. Some of these markers can even be prudently applied as predictor for features of health, survival, or wellbeing. Bowei-Bio has concentrated on analysis of these biomarkers for several years, and released a series of antibodies and conjugates for detection of these targets. We will continue to deepen our effort in this area to launch more products to support *in-vitro* diagnosis and basic researches.

Products

Biomarkers of Health and Aging	Conjugate	Antibody
Creatinine (Cr)	√	√
S-Adenosylhomocysteine (SAH)	√	√
S-Adenosylmethionine (SAM)	√	√
Symmetric Dimethylarginine (SDMA)	√	√
Asymmetric Dimethylarginine (ADMA)	√	√
8-Hydroxy-2′-Deoxyguanosine (8OHdG)	√	√
Phosphorylated H2AX (γ-H2AX)	√	√
Nicotinamide Adenine Dinucleotide (NAD)	√	√
Uric Acid (UA)	√	√

Biomarkers of Health and Aging

Creatinine (Cr)

Creatinine (Cr) is primarily an endogenous compound generated by the non-enzymatic hepatic conversion of creatine. Dysregulation of Cr metabolism can contribute to a wide range of diseases. Reliable serum Cr (Scr) quantification is important for correct classification of kidney disease and early identification of kidney injury. Scr levels also have a close relationship with health status and medications. Jaffe-based creatinine method is a classic technique for creatinine estimation, but it sometimes exhibits considerable analytical bias due to the limited specificity. The more specific enzymatic methods are also subject to various interferences, such as ascorbate, increased monoclonal IgM and dopamine, etc., leading to falsely elevated or reduced SCr concentrations.

Measurement of SCr by immunoassays is potentially a more promising option, because of the intrinsically high binding specificity between the antibody and its target antigen. Our mouse anti-Cr McAb can be used for developing highly sensitive and specific Cr immunoassays.

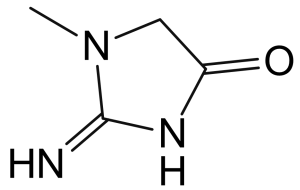

Fig. 1. The chemical structures of Cr

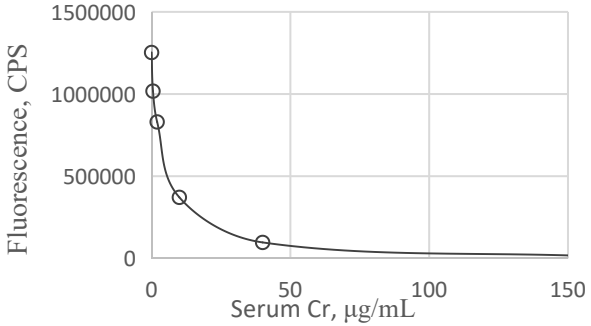

Fig. 2. Typical calibration curve of Cr-DELFIA using McAb-1653

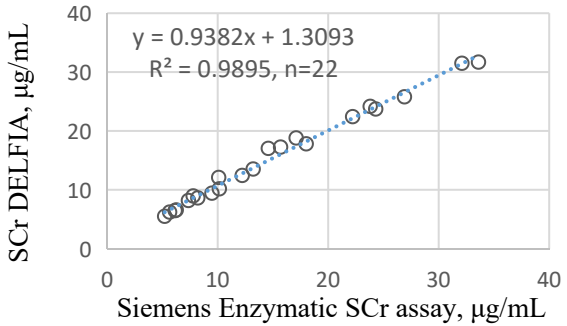

Fig. 3. The correlation of SCr values obtained by enzymatic assay and DELFIA using McAb-1653

Product Type	Catalog #	Description
Mouse monoclonal antibody	• Anti-Cr McAb-1653	Used for developing Cr immunoassay, with excellent correlation with the enzymatic methods (Fig. 3); LOD was <0.2μg/mL by Cr-DELFIA. No cross-reaction with creatine up to 1000μg/mL The key performances of the McAb-1653 based SCr-immunoassay are shown in Fig. 2 and Fig. 3.
Conjugate	• Cr-PEG-Biotin • Cr-PEG-Protein	Paired with the anti-Cr antibodies for Cr testing. Cr-PEG-Protein can be used in immunochromatographic assays, and Cr-PEG-Biotin can be used in pair with the streptavidin coated magnetic beads for Cr CLIA.

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SAM, SAH, and the methylation index

S-Adenosyl-L-methionine (SAM) is present in all living cells, and plays a critical role as a precursor in cellular biochemistry for transmethylation, transsulfuration and polyamine synthesis. For transmethylation, SAM acts as a universal methyl donor for transferring the methyl group to a variety of acceptors, and SAM is conversed to S-adenosylhomocysteine (SAH) in the same process. Any interferences of these reactions can affect wide spectrum of processes including gene expression, protein synthesis, membrane fluidity, and may result birth defects, cardiovascular disease, cancers, liver disease and many other diseases. Consequently, SAM, SAH, and their ratio (the methylation index) can be used as useful markers for study/diagnosis of different diseases or the potentially unfavorable health conditions. To meet the demands for reliable immunoassay of SAM and SAH, Bowei-Bio issued several clones of McAbs which allow accurate detection of SAH and SAM separately or simultaneously by various formats of immunoassays.

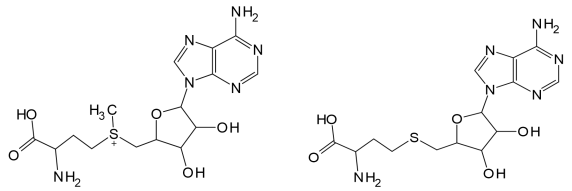

Fig. 1. The chemical structure of SAM (left) and SAH (right)

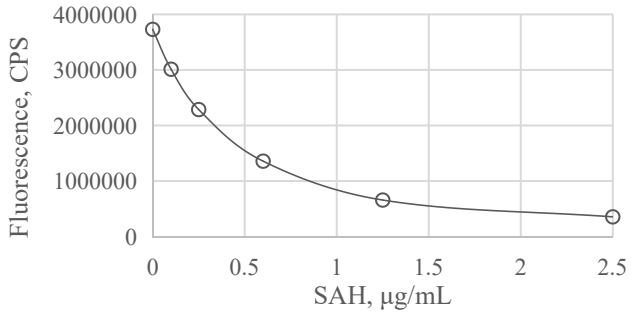

Fig. 2. Typical calibration curve of SAH-DELFIA using anti-SAH McAb-9

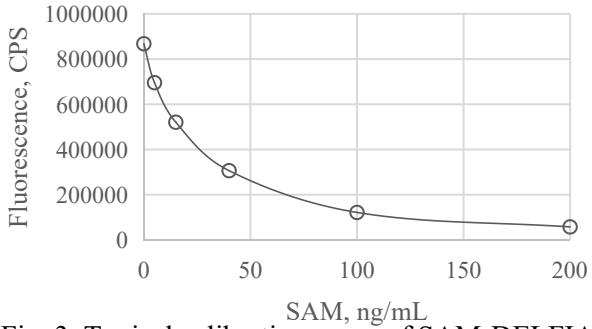

Fig. 3. Typical calibration curve of SAM-DELFIA using anti-SAM McAb-7

Product Type	Catalog #	Description
Mouse monoclonal antibody	• Anti-SAH McAbs-9	Used for SAH testing with LOD < 20ng/mL by DELFIA. The cross-reactivities with SAM, adenosine, L-methionine, methythioadenosine, ADP, and ATP are < 0.3%
Conjugate	• SAH-BSA	Paired with the anti-SAH antibody for SAH testing
Mouse monoclonal antibody	• Anti-SAM McAb-7	Used for SAM testing with LOD < 1.7ng/mL by DELFIA. No cross-reactivity was detected with SAH, adenosine, L-methionine, methythioadenosine, ADP, and ATP up to 5000ng/mL.
Conjugate	• SAM-BSA • SAM-PEG-Biotin	Paired with the anti-SAM antibody for SAM testing

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Symmetric Dimethylarginine (SDMA)

SDMA is uremic toxin with effect of suppression of NO production. Increased blood level of SDMA is an established risk factor for cardiovascular events and all-cause mortality in patients with serious diseases.

In veterinary diagnostics, SDMA correlates well with glomerular filtration rate (GFR) in small animals, such as dogs and cats. SDMA increases earlier than creatinine (CREA), and so it is more sensitive for diagnosis of both active and chronic kidney disease. Unlike CREA, SDMA is not impacted by lean body mass. The SDMA Test now become an essential parameter for early detection of kidney diseases of small animals. Our anti-SDMA McAb and the paired SDMA conjugates can be used for developing accurate immunoassay for SDMA determination in different clinical samples.

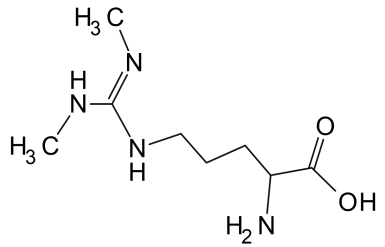

Fig. 1. The chemical structures of SDMA

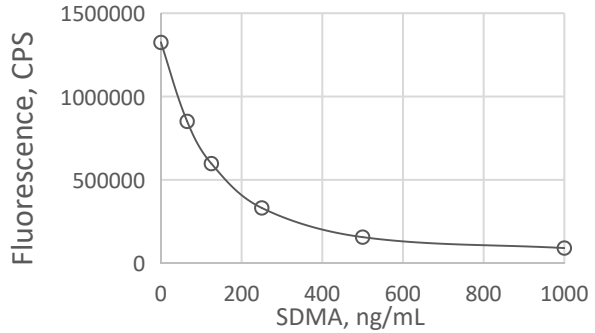

Fig. 2. Typical calibration curve of SDMA-DELFIA using McAb-54

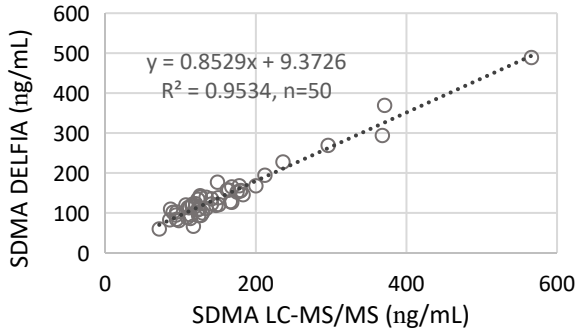

Fig. 3. The correlation of SDMA values obtained by LC-MS/MS and DELFIA using McAb-54

Product Type	Catalog #	Description
Mouse monoclonal antibody	• Anti-SDMA McAb-54	Used for SDMA determination with LOD < 10ng/mL by DELFIA. The cross-reactivities with ADMA and MMA were < 0.18% and < 1.5%, respectively.
Rabbit polyclonal antibody	• Anti-SDMA-BSA PcAb-0221-6	Used for SDMA determination with LOD < 27ng/mL by DELFIA. The cross-reactivities with ADMA and MMA were < 1.26% and < 2.72%, respectively.
Conjugate	• SDMA-PEG-OVA • SDMA-PEG-Biotin	Paired with the anti-SDMA antibodies for SDMA testing.

Biomarkers of Health and Aging

Asymmetric Dimethylarginine (ADMA)

Asymmetric dimethylarginine (ADMA) is an endogenous competitive inhibitor of endothelial nitric oxide synthase (NOS). ADMA inhibits eNOS by displacement of the physiological substrate, L-arginine, from the enzyme. The inhibition leads to decreased NO production in the endothelium of vessel walls. The abnormal higher ADMA levels are associated with diseases associated with an impaired endothelial L-arginine-NO pathway and endothelial dysfunction, such as atherosclerosis, hypercholesterolemia, chronic heart failure, diabetes mellitus, and hypertension. Growing evidence indicates that elevated ADMA plasma levels can be used as a strong predictor for cardiovascular disease.

To establish rapid and feasible method for ADMA determination, we generated anti-ADMA monoclonal antibody which shows good affinity and specificity for SDMA determination.

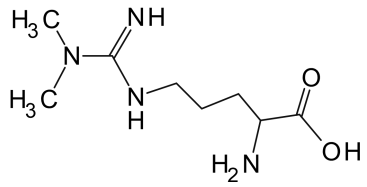

Fig. 1. The chemical structures of ADMA

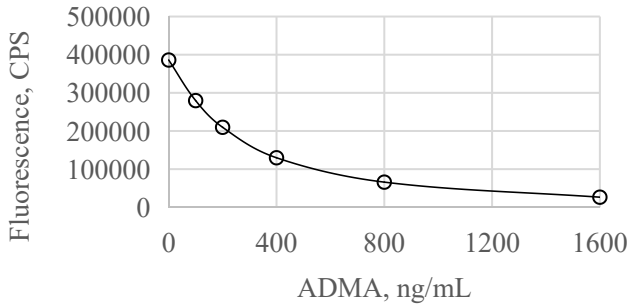

Fig. 2. Typical calibration curve of ADMA-DELFIA using McAb-D8

Product Type	Catalog #	Description
Mouse monoclonal antibody	• Anti-ADMA McAb-D8	Used for ADMA testing with LOD < 15ng/mL by ADMA-DELFIA. Its cross-reactivity with SDMA and MMA, the two major cross-reactants in blood, is approximately 0.1% and 1.2%, respectively.
Conjugate	• ADMA-PEG-OVA • ADMA-PEG-Biotin	Paired with the anti-ADMA antibodies for ADMA testing.

Biomarkers of Health and Aging

8-Hydroxy-2′-Deoxyguanosine (8-OHdG)

Reactive oxygen species play an important role in different kinds of DNA damages which is known to contribute to age-related degenerative processes and diseases. Among the identified oxidative DNA damage products, 8-hydroxy-2′-deoxyguanosine (8-OHdG) is one of the predominant forms of oxidative DNA lesion. 8-OHdG is produced by hydroxyl radical attack at the C-8 position of DNA guanine followed by a one-electron oxidation [*Free Radic. Biol. Med. 1999, 26 (1/2), 129–135*]. The production and release of 8-OHdG in body fluids and tissues has a close relationship with aging and pathogenesis of different disorders. Determination of 8-oxodG level has been cited as a preferential non-invasive biomarker of DNA damage induced by oxidative stress. Our anti-8-OHdG McAb-34 enables the development of specific and sensitive 8-OHdG immunoassay. The 8-OHdG immunoassay using McAb-34 exhibits 0.001% of cross-reactivity with 8-hydroxyguanine (8-OHG), 10-times improved than that using McAb-clone-N45.1, which is currently the most extensively utilized McAb worldwide. Furthermore, the sensitivity of 8-OHdG immunoassay achieved by using McAb-34 is markedly improved than that of N45.1-based immunoassays.

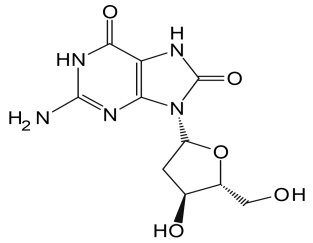

Fig. 1. The chemical structure of 8-OHdG

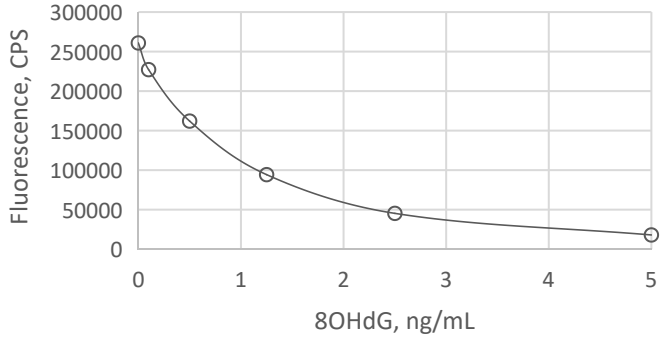

Fig. 2. Typical calibration curve of 8-OHdG-DELFIA using McAb-34

Product Type	Catalog #	Description
Mouse monoclonal antibody	• Anti-8-OHdG McAb-34	Used for testing 8-OHdG with LOD < 0.05ng/mL by DELFIA. The cross-reactivity with 8-OHG is < 0.001%. No cross-reactivities were detected with guanosine, uracil, thymine, guanine, urea and creatinine up to 50μg/mL.
Conjugate	• 8-OHdG-PEG-Biotin • 8-OHdG-PEG-OVA	Paired with the anti-8-OHdG antibodies for 8-OHdG testing.

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Phosphorylated H2AX (γ-H2AX)

DNA double-strand break (DSB) can be induced by a variety of factors, such as ionizing radiation, toxic chemicals, reactive oxygen species, and programmed biological processes. DSBs can cause genotoxicity and cell death, and thereafter lead to genomic instability and increased cancer risk. As a response of the cell to DSBs, phosphorylation of histone protein H2AX on serine-139 occurs rapidly, and numerous γ-H2AX focus are formed at the sites flanking DSBs. Based on this, γ-H2AX can be used as a sensitive marker for DNA DSB, and utilized for biodosimetry, drug development, radio- or chemotherapy monitoring, and study of the process of aging. Commonly used techniques for measuring the γ-H2AX level mainly include the microscopic examination of immuno-stained foci, flow cytometry analysis and whole cell-ELISA, etc. All these methods require the use of high quality of anti- γ-H2AX antibodies. Our anti-γ-H2AX McAbs allow accurate quantification of γ-H2AX level by different immunologic methods based on its high affinity and specific binding to γ-H2AX focus.

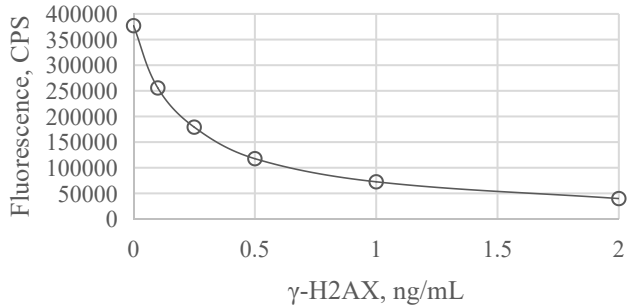

Fig. 2. Typical calibration curve of γ-H2AX-DELFIA using McAb-19

Product Type	Catalog #	Description
Mouse monoclonal antibody	• Anti-γ-H2AX McAb-19	Suitable for selectively detecting γ-H2AX by WB, ICC/IF, IHC-P, whole cell ELISA and other related techniques. LOD <0.02ng/mL by γ-H2AX-DELFIA with cross-reactivity < 0.06% for unmodified H2AX.
Mouse monoclonal antibody	• Anti-γ-H2AX McAb-46	Its cross-reactivity with H2AX is about 56%. Suitable for tracing total H2AX in histone protein, including γ-H2AX and unmodified H2AX. LOD <0.15ng/mL by γ-H2AX-DELFIA.
Conjugate	• γ-H2AX -PEG-Biotin	Paired with the anti-γ-H2AX antibodies for determination of γ-H2AX.

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Nicotinamide Adenine Dinucleotide (NAD)

Nicotinamide adenine dinucleotide (NAD) is an essential pyridine nucleotide, and has been investigated as an important target to extend lifespan and health-span. Age related NAD depletion due to the imbalance between NAD biosynthesis and degradation is associated with reduced energy production, impaired DNA repair and genomic instability. These findings provide insights into the development of nutraceutical intervention against age-associated metabolic complications. In view of the fact that the NAD levels are affected by aging related factors and a wide range of pathologies, accurate measurement of NAD is getting higher demands in various clinic and scientific fields. Different techniques have been proposed to analyze NAD in biological samples, e.g., enzymatic assays, chromatography, and LC-MS/MS. Our anti-NAD monoclonal antibody allows more convenient NAD determination by immunoassay.

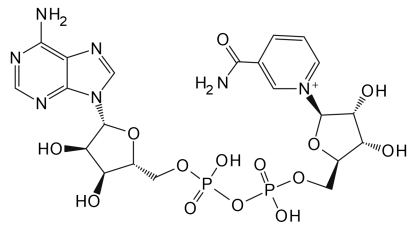

Fig. 1. The chemical structure of NAD

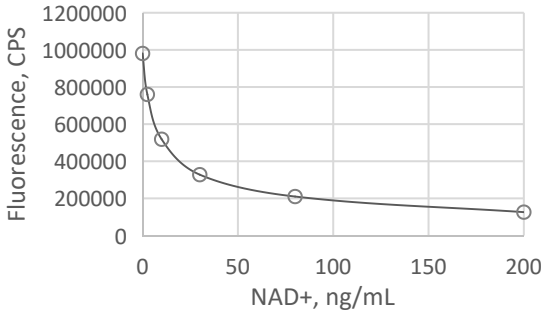

Fig. 2. Typical calibration curve of NAD-DELFIA using McAb-2

Product Type	Catalog #	Description
Mouse monoclonal antibody	• Anti-NAD McAb-2	Used for developing NAD immunoassay with LOD < 1ng/mL by DELFIA. The cross-reactivities were 1.26% with NAAD and 0.66% with β-NADPH
Conjugate	• NAD-PEG-Biotin • NAD-PEG-BSA	Paired with the anti-NAD antibody for NAD testing

Uric Acid (UA)

Uric acid (2,6,8-trihydroxypurine, UA) is the end product of purine metabolism, which is found in urine as the major nitrogenous compound and present in other biological fluids such as serum and saliva; UA level in these samples is an indicator of metabolic alterations and disease development, e.g., hyperuricemia can occur in association with a number of conditions, and can possibly lead to gout and renal disease. Enzymatic analysis of UA using uricase is now widely accepted for clinical diagnosis. Uricase is very specific for oxidization of UA, it does not oxidize other purines and various UA derivatives such as 1-, 3-, 7-, and 9-methyl uric acid; however, these derivatives and xanthine are potential interferences in different uricase methods, as they are putative competitive inhibitor of uricase [*Proc. R. Soc. Lond. B. 1936 119, 114-140*] and present in biological matrices at variable levels. Further, uricase based methods show different sensitivity to some common interferences, e.g., endogenous bilirubin, hemoglobin, reduced glutathione, ascorbate and lipids. Immunoassay can be expected to be a alternative for UA enzymatic analysis due to the inherent specificity of immunoreaction. However, UA immunoassay has not yet been reported up to now, partly because of the difficulty for developing qualified antibody, due to the existence of various UA derivatives in blood and the interchange of UA structure under different pH environments. To explore new methodological possibilities for UA immuno-analysis, we generated an anti-UA monoclonal antibody which can be used for developing sensitive UA immunoassay.

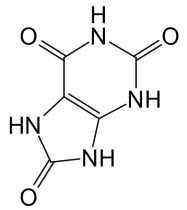

Fig. 1. The chemical structure of UA

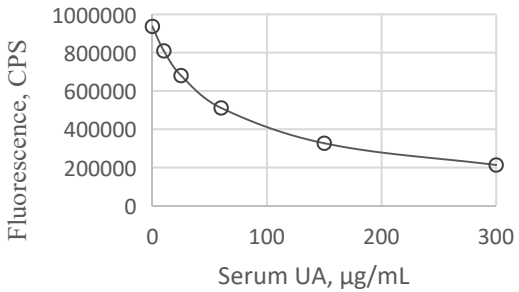

Fig. 2. Typical calibration curve of UA-DELFIA using McAb-44

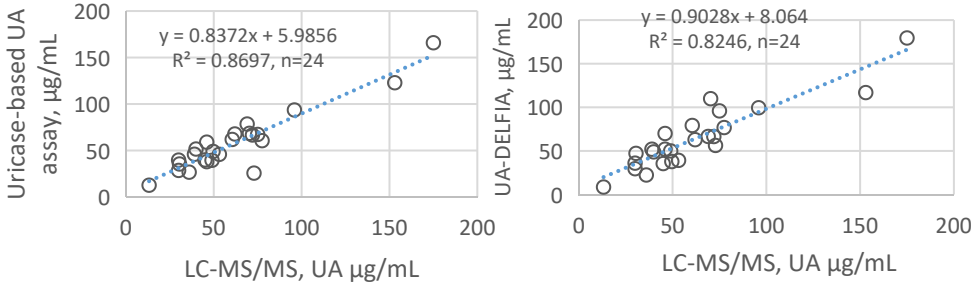

Fig. 3. The correlation of the UA LC-MS/MS with the uricase assay (left) or UA-DELFIA using McAb clone-44 (right)

Product Type	Catalog #	Description
Mouse monoclonal antibody	• Anti-UA McAb-44	LOD <3.9μg/mL by UA-DELFIA. The cross-reactivities of McAb-44 is < 1.2% for xanthine and <0.3% for hypoxanthine.
Conjugate	• UA-PEG-Biotin • UA-PEG-BSA	Paired with anti-UA antibodies for UA testing.