BOWEI-BIOTECH
for better bioassays

Therapeutic Drug Monitoring (TDM)

Shanghai Bowei Biotechnology

Therapeutic Drugs Monitoring (TDM)

Introduction

Therapeutic drug monitoring (TDM) is a clinical practice for therapy optimization by measuring the concentration of drug in biological samples, based on the fact that the concentration of drug in these samples correlates better to the pharmacological activity than dosage for evaluating efficacy or toxicity. TDM provides a strategy to maximize drug efficacy while preventing the emergence of concentration-dependent adverse drug reactions, and so helps clinician to optimize a patient's clinical outcome in various clinical situations by managing their medication regimen.

TDM has been performed for more than 50 years as a clinical routine. Today, in an era of *Personalized Medicine* with more understanding of the molecular mechanisms behind inter- and intra-individual variability in drug exposure and effects, TDM will play a more important role in clinical pharmacology. Immunoassay is one of the main choices for TDM due to its ability for analyzing a wide range of analytes and the advantages like high sensitivity, high-throughput, and inherent specificity.

Bowei-Bio has over 15 years of expertise in producing high-quality antibodies targeting various small-molecule drugs, as well as in developing immunoassays using these antibodies. Currently, our antibodies, conjugates and immunoassay kits cover more than 50 pharmaceuticals for which TDM is strongly recommended. We will continue to focus on this growing area, striving to expand our product offerings to better serve our customers and contribute to the advancement of personalized medicine.

Drugs

- Immunosuppressive Drugs
__Tacrolimus, Cyclosporin A, Sirolimus, Everolimus,Mycophenolic Acid, Mizoribine, Azathioprine
- Antibiotics Drugs
__Meropenem, Teicoplanin, Vancomycin, Linezolid, Rifampicin, Polymyxin B, Amikacin, Isoniazid, Chloramphenicol, Sulfonamide, Ceftiofur, Cephalexin
- Triazole Antifungal Drugs
__Voriconazole, Posaconazole, Itraconazole, Isavuconazole, Fluorocytosine
- Gabapentinoids Drugs
__Gabapentin, Pregabalin
- Antiepileptic Drugs
__Valproic Acid, Carbamazepine, Oxcarbazepine, 10-Hydroxycarbazepine (MHD), Topiramate, Phenytoin, Phenobarbital, Levetiracetam, Lamotrigine
- Anticancer Drugs
__Methotrexate, Busulfan, Venetoclax, 5-Fluorouracil, Paclitaxel, Docetaxel, Imatinib, Dasatinib, Afatinib, Crizotinib, Sunitinib
- Antipsychotic Drugs
__Olanzapine, Clozapine, Risperidone, Quetiapine, Amisulpride,
- Antihypertensive Drugs
__Empagliflozin, Amlodipine, Enalaprilat, Digoxin
- Inflammatory Bowel Disease Drugs
__Infliximab, Adalimumab, Methotrexate, 6-Methylmercaptopurine, 6-Thioguanine
- Others
__Acetaminophen, Diclofenac

Therapeutic drugs monitoring

TDM of immunosuppressive Drugs

Introduction

The discovery and application of immunosuppressive drugs (ISDs) in organ transplantation has dramatically reduced acute graft rejection and improved long-term graft survival. Given the narrow therapeutic index and large inter-patient pharmacokinetic variability of ISDs, TDM of ISDs has become an integral part of organ transplant programs for optimizing therapeutic effectiveness and minimizing unwanted adverse effects.

Cyclosporine (CSA), tacrolimus (FK506), sirolimus (RAPA), everolimus (EvE) and mycophenolate mofetil are five major ISDs used in modern transplantations. Although HPLC and LC-MS are considered as the reference method for monitoring of these ISDs, most laboratories adopt immunoassay for clinic TDM because of its automation, short analytical run times, and less requirement for specialized testing personnel.

Bowei-Bio has engaged in the field of ISD analysis for more than 15 years, and now provides a panel of high-quality antibodies and conjugates for immunoassay of several important ISDs. Extraction reagents are also available for pretreatment of whole blood sample for testing FK506, CSA, RAPA and EvE. Based on the use of these combinations, accurate immunoassays can be developed with close correlation to that obtained by HPLC-MS/MS and well-accepted commercial kits.

Products

ISDs	Conjugate	Antibody
Tacrolimus (FK506)	√	√
Cyclosporin A (CSA)	√	√
Sirolimus (RAPA)	√	√
Everolimus (EvE)	√	√
Mycophenolic Acid (MPA)	√	√
Mizoribine (MZR)	√	
Azathioprine （AZA）	√	

Therapeutic drugs monitoring

Tacrolimus (FK506)

Tacrolimus (FK506) is an immunosuppressive drug that acts as a calcineurin inhibitor by blocking T-cell signal transduction pathways and downregulating the transcription of interleukin-2 (IL-2). As a first-line immunosuppressant, FK506 has been clinically used for over 30 years and is still widely employed for preventing rejection reactions or graft-versus-host disease (GVHD) following solid organ and hematopoietic stem cell transplantation. Given that FK506 has a narrow therapeutic window, excessively high blood concentrations will increase the risk of nephrotoxicity, neurotoxicity, and infections, whereas insufficient concentrations may lead to transplant rejection or GVHD. Therefore, monitoring FK506 concentrations in whole blood is crucial for guiding clinical medication. Immunoassay is the most commonly used technique for TDM of FK506 in the past decades. Our anti-FK506 McAbs can be used for establishing sensitive and accurate FK506 immunoassays.

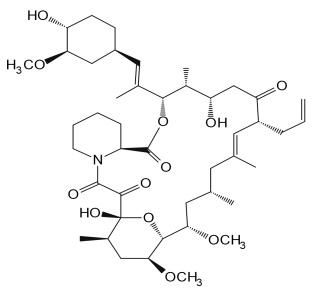

Fig. 1. The chemical structure of FK506

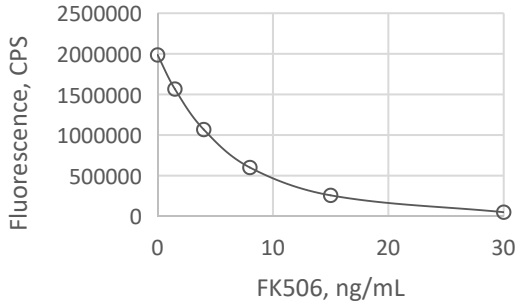

Fig. 2. Typical calibration curve of FK506-DELFIA using McAb-39

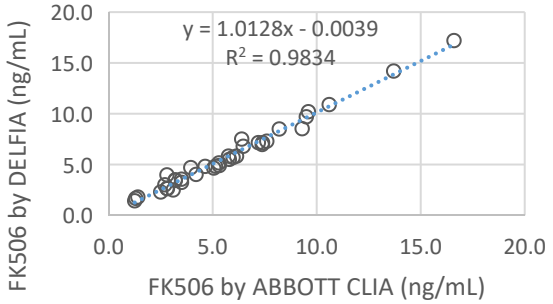

Fig. 3. The agreement between the FK506 concentration determined by DELFIA using McAb-39 and ABBOTT FK506-CLIA

Product Type	Catalog #	Description
Mouse monoclonal antibody	• Anti-FK506 McAb-39	Used for testing FK506 with LOD < 0.5ng/mL by DELFIA. The key performances of FK506-DELFIA using McAb-39 are shown in Fig. 2 and Fig. 3.
Mouse monoclonal antibody	• Anti-FK506 McAb-60	Used for developing FK506 immunoassay with similar performance compared to that by using McAb-39.
Conjugate	• FK506-BSA • FK506-PEG-Biotin	Paired with anti-FK506 McAbs for FK506 testing.

Therapeutic drugs monitoring

Cyclosporin-A (CSA)

Cyclosporine (Cyclosporine-A, Ciclosporin, CsA)) is a cyclic undecapeptide immunosuppressant consisting of seven N-methyl amino acids, four MeLeu residues, and a D-amino acid. It was introduced in the early 1980's to transplantation medicine as the first calcineurin inhibitor. It acts specifically and reversibly on lymphocytes, producing selective suppression of cell-mediated immunity. Up to now, CSA is still a key drug used in solid organ transplantation to prolong graft survival in human liver, heart, and kidney transplantation by preventing graft rejection. Like other immunosuppressants, CsA exhibits a narrow therapeutic window and considerable interindividual variability, TDM is required to optimize dosing and to balance the risk of rejection with drug-related toxicities. Our anti-CSA McAb can be used for establishing accurate CSA immunoassays, which has been well-evaluated and show excellent performance with regard to sensitivity, precision and accuracy.

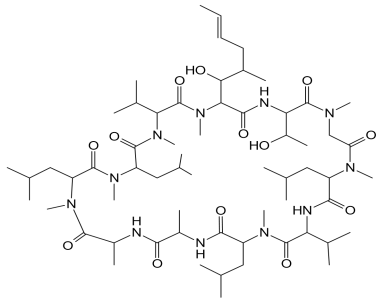

Fig .1. The chemical structure of CSA

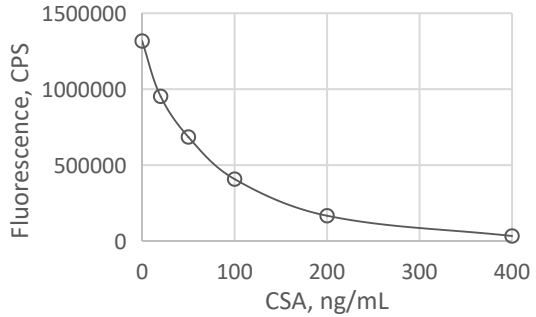

Fig.2. Typical calibration curve of CSA-DELFIA using McAb-6D6A8

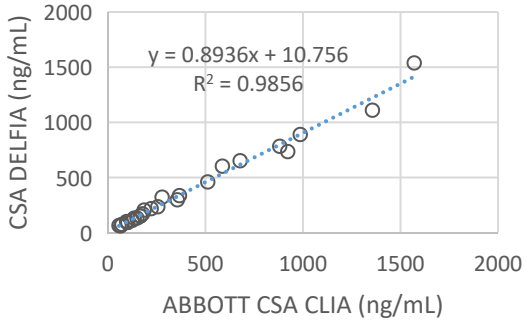

Fig. 3. Agreement between the CSA concentration determined by DELFIA using McAb-6D6A8 and ABBOTT CSA-CLIA

Product Type	Catalog #	Description
Mouse monoclonal antibody	• Anti-CSA McAb-6D6A8	Used for developing CSA immunoassay with LOD < 10ng/mL by DELFIA. The key performances of the CSA-DELFIA using McAb-6D6A8 are shown in Fig. 2 and Fig. 3.
Conjugate	• CSA-BSA	Paired with anti-CSA antibodies for CSA testing.

Therapeutic drugs monitoring

Sirolimus (RAPA)

Sirolimus (also known as rapamycin, RAPA) is a macrolide compound that inhibits antibody production, T-lymphocyte activation and proliferation. The trough concentration (C0) of RAPA is highly correlated with its efficacy and toxicity in transplantation medication. The therapeutic index of sirolimus differs depending on whether or not the drug is co-administered with calcineurin inhibitors. Generally, the target C0 of sirolimus in combination with cyclosporine are between 5 and 15 ng/mL. TDM is important in optimizing RAPA exposure since under- or overdosing of the drug can impact both the clinical efficacy and adverse effects profile. Among different techniques for RAPA monitoring, immunoassay is the most amenable for routine clinic use. Our anti-RAPA McAb-33 can be used for developing sensitive and accurate RAPA-immunoassays with LOD <0.5ng/mL. In addition, we also provide a stabilizer to effectively enhance the storage stability of RAPA calibrators, quality controls or reference materials. With the aid of the stabilizer, RAPA calibration materials can be stored in solution for a long time without the need for lyophilization to maintain its stability.

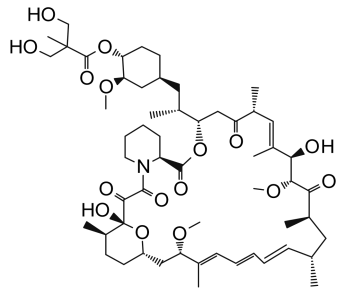

Fig. 1. The chemical structure of RAPA

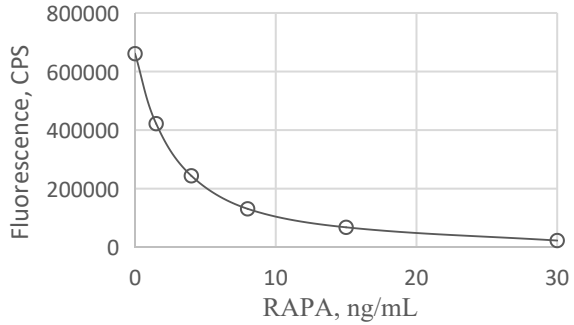

Fig.2. Typical calibration curve of RAPA-DELFIA using McAb-33

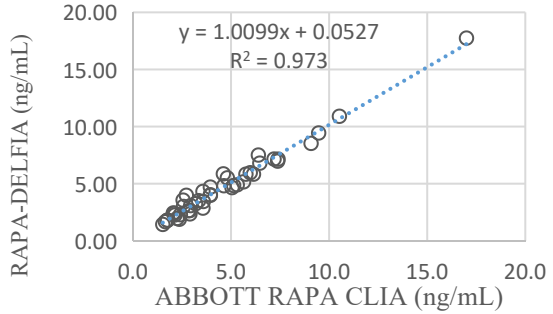

Fig. 3. Agreement between the RAPA concentration obtained by DELFIA using McAb-33 and ABBOTT RAPA-CLIA

Product Type	Catalog #	Description
Mouse monoclonal antibody	• Anti-RAPA McAb-33	Used for developing RAPA immunoassay with LOD < 0.5ng/mL by DELFIA. The key performances of the RAPA-DELFIA using McAb-33 are shown in Fig. 2 and Fig. 3.
Conjugate	• RAPA-BSA	Paired with anti-RAPA antibody for RAPA testing.
Stabilizing agent	• RAPA stabilizer-9	Used for enhancing the storage stability of RAPA in whole blood calibrators, quality controls and reference materials.

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Therapeutic drugs monitoring

Everolimus (EvE)

Everolimus is a synthetic derivative of sirolimus indicated for all solid transplant recipients for anti-rejections. EvE has a similar action mechanism as sirolimus, but appears to have a greater stability and solubility as well as more favorable pharmacokinetics. TDM of EvE is essential for dose optimization due to its narrow therapeutic index, large inter- and intra-individual variations in bioavailability and clearance, and potential interaction with concomitantly administered drugs. The proposed therapeutic range is trough blood concentration of 3.0–8.0ng/mL. Our anti-EvE McAbs can be used to develop sensitive and accurate EvE-immunoassay with good correlation with LC-MS/MS.

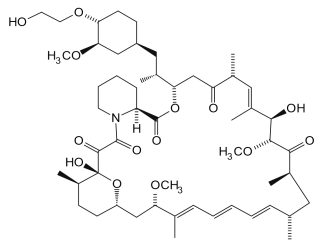

Fig. 1. The chemical structure of EvE

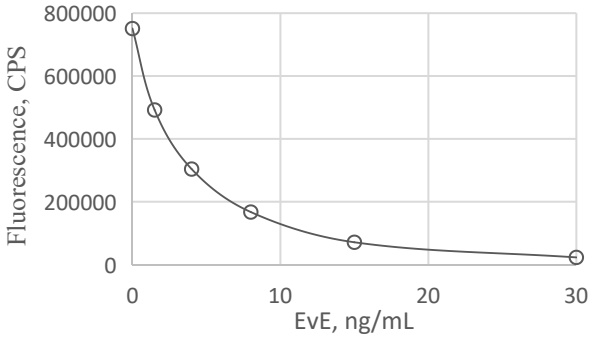

Fig.2. The typical calibration curve of EvE-DELFIA using McAb-H

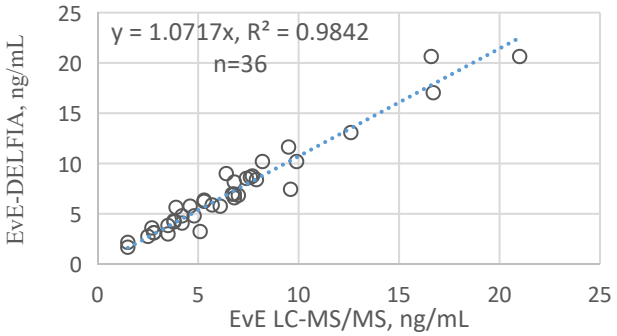

Fig. 3. Agreement between the EvE concentration obtained by DELFIA using McAb-H and LC-MS/MS

Product Type	Catalog #	Description
Mouse monoclonal antibody	• Anti-EvE McAb-H	Used for developing EvE immunoassay with LOD < 0.5ng/mL by DELFIA. The cross-reactivity with sirolimus is ~88%, similar to that currently used in commercial EvE immunoassays. The possible interference caused by co-therapy or transition of the two drugs should be considered for immunoassays using McAb-H.
Mouse monoclonal antibody	• Anti-EvE McAb-1615	Used for developing EvE immunoassay with similar performance compared to that by using McAb-H.
Mouse monoclonal antibody	• Anti-EvE McAb-54	The cross-reactivity is ~26% with sirolimus. LOD < 2.0ng/mL by DELFIA using this more specific McAb.
Conjugate	• EvE-BSA	Paired with anti-EvE antibodies for EvE testing.

Therapeutic drugs monitoring

Mycophenolic acid (MPA)

Mycophenolic acid (MPA) is an immunosuppressants widely used for maintenance therapy in solid organ transplantation. MPA exerts immunosuppressive effects by reversible and uncompetitive inhibition of inosine monophosphate dehydrogenase (IMPDH). Incorporation of MPA monitoring as a standard of practice in transplant medicine is important because of following reasons: 1) MPA predose concentration predicts the risk for development of acute rejection; 2) more than 10-fold interindividual variation of MPA AUC values exists in transplant patients receiving a fixed dose of MMF; 3) close monitoring of MPA is required when a major change in immunosuppression is planned such as steroid withdrawal. Our anti-MPA McAb can be used to establish MPA immunoassay with LOD < 3ng/mL, sensitive enough for determination of not only total MPA but also the free fraction of it. The free MPA is pharmacologically active and exists in blood at a level of about 2% of total MPA.

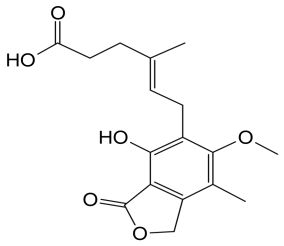

Fig. 1. The chemical structure of MPA

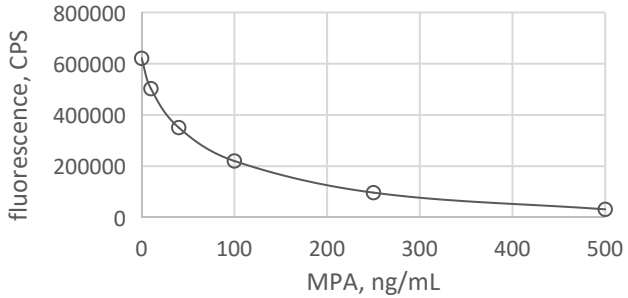

Fig.2. The typical calibration curve of MPA-DELFIA using McAb-6

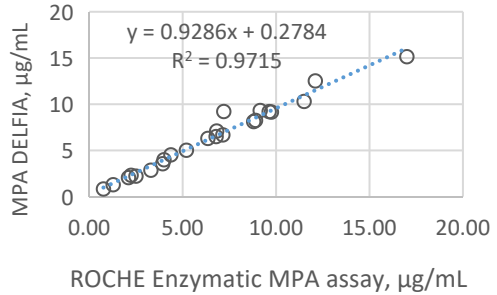

Fig. 3. Agreement between the MPA concentration obtained by DELFIA using McAb-6 and Roche enzymatic MPA-assay

Product Type	Catalog #	Description
Mouse monoclonal antibody	• Anti-MPA McAb-6	Used for developing MPA immunoassay with LOD < 3ng/mL by DELFIA. McAb-6 shows no cross-reactivity with 7-O-MPA-glucuronide (MPAG), the major inactive metabolite of MPA at 200µg/mL, which is usually present in plasma at 20- to 100-fold higher concentrations than MPA. McAb-6 displays similar reactivity with acyl-glucuronide, a metabolite of MPA with pharmacological potency comparable to MPA. This feature makes immunoassay using it well-suited for MPA monitoring because it detects both the parent drug and its active metabolite, but not the inactive metabolite.
Conjugate	• MPA-BSA	Paired with anti-MPA McAb for MPA testing.

Therapeutic drugs monitoring

Extraction Reagents

Calcineurin inhibitors like tacrolimus (FK506) and cyclosporine A (CSA), along with mTOR inhibitors sirolimus (RAPA) and everolimus (EvE), are widely used to improve graft survival after organ transplantation. Due to their narrow therapeutic windows and significant pharmacokinetic variability, TDM has been used for decades to minimize the side effects, enhance therapeutic outcomes, and ensure the patient adherence. In practice, TDM of these ISDs is usually conducted with whole blood as samples due to the drug's predominantly distribution in erythrocytes. This characteristic necessitates specific pretreatment of sample to release ISDs from blood cells before detection.

We have developed several target specific extraction reagents for treating whole blood sample which can effectively releases tacrolimus, sirolimus, cyclosporine-A, or EvE from their binding proteins, while simultaneously precipitating the blood protein. These extraction reagents have been well-evaluated by analysis of clinical samples.

Product Type	Catalog #	Description
Extraction reagent	• Extraction-FK506	Used for release FK506 in whole blood for FK506-immunoassay
Extraction reagent	• Extraction-CSA	Used for release CSA in whole blood for CSA-immunoassay
Extraction reagent	• Extraction-RAPA	Used for release RAPA in whole blood for RAPA-immunoassay
Extraction reagent	• Extraction-EvE	Used for release EvE in whole blood for EvE-immunoassay

Therapeutic drugs monitoring

TDM of Antibiotics Drugs

Introduction

The discovery of antibiotics started a new era for controlling bacterial infection of human beings, animals and agriculture. After several decades' application, the use of antibiotics today is challenged by the rapid increase of multidrug-resistant bacteria (MDR). This situation in together with the fact that very few new antibiotics are available in recent years, makes dose optimization strategy based on TDM for existing drug therapies become increasingly important.

Besides the role for hindering the continued rise of antimicrobial resistance, TDM guided antibiotic therapy is also useful for improving clinical outcome from infections, especially for the critically ill, obese and older patients with altered PK/PD; among these patients, multiple factors may influence the achievement of PK/PD targets, thus making the antibiotic dosing of these patients notoriously difficult.

Bowei-Bio provides a group of antibodies and conjugates for developing accurate antibiotics immunoassays, which covers most of the antibiotics highly recommended for performing TDM, including polymyxin B, teicoplanin, vancomycin, linezolid, meropenem, amikacin, rifampicin, and isoniazid, etc. More antibodies and conjugates for immunoassay of antibiotics will be launched by us in the future.

Products

Antibiotics Drugs	Conjugate	Antibody
Meropenem	√	√
Teicoplanin	√	√
Vancomycin	√	√
Linezolid	√	√
Rifampicin	√	√
Polymyxin-B	√	√
Amikacin	√	√
Isoniazid	√	√
Chloramphenicol	√	√
Sulfonamide	√	√
Ceftiofur	√	
Cephalexin	√	

Therapeutic drugs monitoring

Meropenem

Meropenem is a first-line β-lactam antibiotic widely used in the treatment of complicated and serious infections. Owing to its wide inter-individual variability in pharmacokinetic, standard dosing is not adequate for optimal therapy of critically ill patients or patients with renal insufficiency, TDM of meropenem is useful for achieving personalized drug administration. Our anti-Meropenem McAb can be used for developing sensitive and specific meropenem immunoassays for accurate monitoring of this drug.

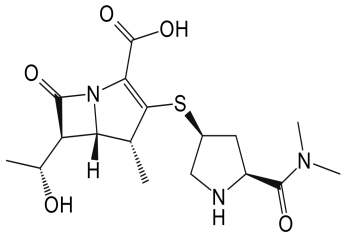

Fig. 1. The chemical structure of meropenem

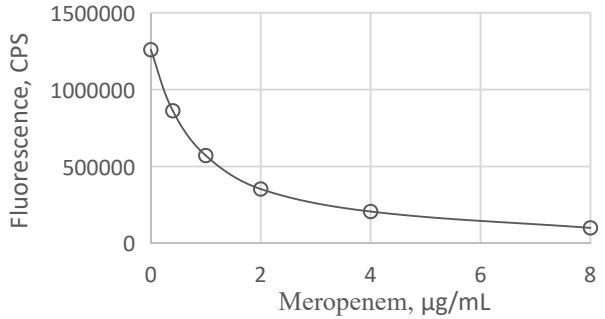

Fig.2. Typical calibration curve of meropenem-DELFIA using McAb-15

Product Type	Catalog #	Description
Mouse monoclonal antibody	• Anti-Meropenem McAb-15	Used for developing immunoassay with LOD < 0.1μg/mL by DELFIA. The cross-reactivities are less than 0.2% with imipenem, doripenem, biapenem and ertapenem.
Conjugate	• Meropenem-PEG-BSA • Meropenem-PEG-Biotin	Paired with anti-meropenem antibodies for meropenem testing.

Therapeutic drugs monitoring

Teicoplanin

Teicoplanin is a glycopeptide antibiotic used for treatment of infections caused by drug-resistant gram-positive bacteria. The lowest plasma trough teicoplanin concentration for effective treatment of the majority of severe infections was defined as 10μg/mL or greater. However, standard dosing does not reliably produce trough concentrations greater than 10μg/mL in seriously ill patients and those with renal impairment. Although teicoplanin is less toxic than vancomycin, teicoplanin trough concentrations ≥ 60μg/mL are regarded as toxic and may be associated with nephrotoxicity, hepatotoxicity, and thrombocytopenia. TDM of teicoplanin is recommended to be practiced at least within certain subpopulations with serious infections in order to achieve optimal drug concentrations by dose adjustments.

Teicoplanin is a mixture of five major components designated A2-1 to A2-5 and a more polar component A3-1 [Fig. 1]; A2-2 and A2-3 in patient plasma account for 93% of the total teicoplanin. The antibody used for developing reliable teicoplanin immunoassay need to recognize all the major components of the drug with similar affinity. Our anti-teicoplanin McAb well meets this requirement, and the immunoassay based on use of it show good regression with the HPLC by assaying clinical serum samples [Fig. 3].

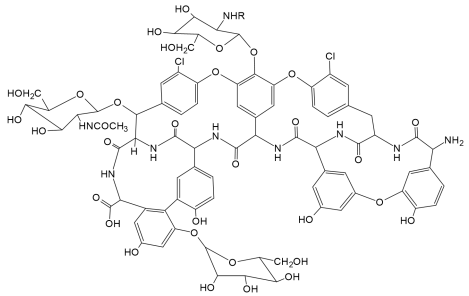

Fig. 1. The chemical structure of Teicoplanin.
A2-1 R = -(CH2)-CH=CH-C5H11; A2-2 R = -(CH2)6-CH(CH3)2; A2-3 R= C9H19; A2-4 R = -(CH2)6-CH(CH3) (C2H5); A2-5 R = -(CH2)7-CH(CH3)2

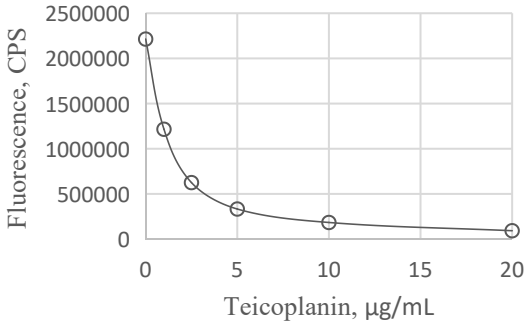

Fig.2. Typical calibration curve of Teicoplanin-DELFIA using McAb-mix

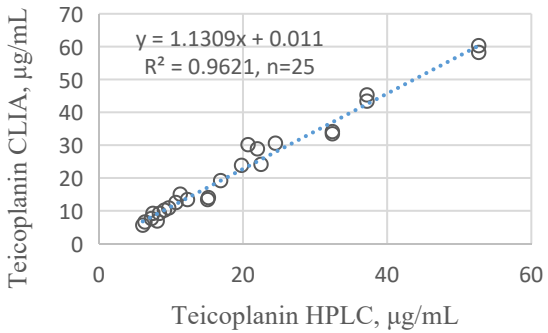

Fig. 3. Agreement between the Teicoplanin concentration obtained by HPLC and CLIA using McAb-mix

Product Type	Catalog #	Description
Mouse monoclonal antibody	• Anti-Teicoplanin McAb-mix	Used for detection of teicoplanin with LOD <0.2μg/mL by DELFIA based on use of the McAb-mix, a mixture of three clones of McAbs.
Conjugate	• Teicoplanin-OVA • Teicoplanin-PEG-Biotin	Paired with anti-Teicoplanin antibodies for Teicoplanin testing.

Therapeutic drugs monitoring

Vancomycin (VAN)

Vancomycin is a glycopeptide antibiotic indicated for treatment of methicillin-resistant staphylococcus aureus, coagulase-negative Staphylococci and other gram-positive organisms. Although it has been extensively used in clinical practice for over 60 years, today it's still one of the most important antibiotic, partly due to the continuous rise of MRSA in the past decades. Because of the its complexity in dosing, narrow therapeutic window, and the adverse drug reactions related to nephrotoxicity and ototoxicity, TDM of vancomycin becomes crucial for achieving a targeted vancomycin level. Among different techniques for vancomycin concentration monitoring, immunoassay is an important choice owing to its simplicity and practicality. Our mouse anti-VAN McAb-XL28 can be used for developing accurate VAN immunoassay. Excellent correlation was obtained between the DELFIA using McAb-XL28 and the commercial ABBOTT CLIA for quantifying vancomycin in clinical samples.

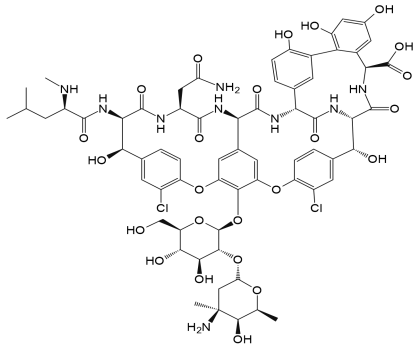

Fig. 1. The chemical structure of VAN

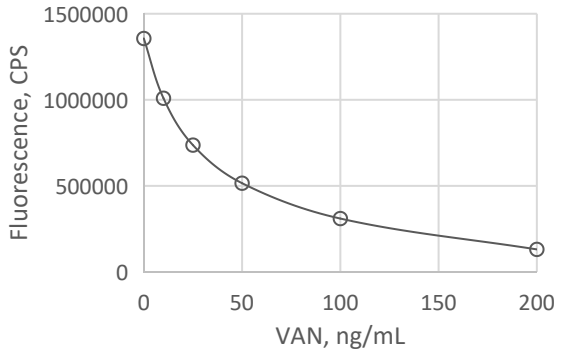

Fig.2. Typical calibration curve of VAN-DELFIA using McAb-XL28

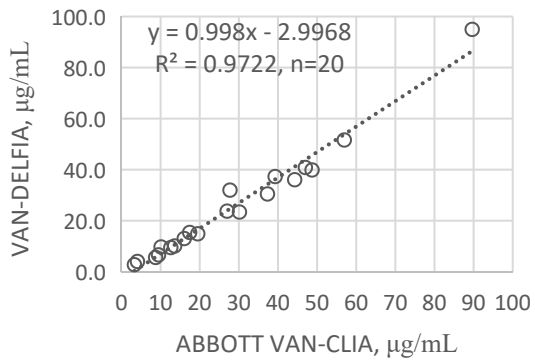

Fig. 3. Agreement between the VAN concentration obtained by ABBOTT CLIA and DELFIA using McAb-XL28

Product Type	Catalog #	Description
Mouse monoclonal antibody	• Anti-VAN McAb-XL28	Used for detection of vancomycin with LOD <5ng/mL by DELFIA. No cross-reactivities were detected with teicoplanin, cefotaxime, ceftriaxone, and gentamicin at 100µg/mL.
Conjugate	• Vancomycin-BSA	Paired with anti-VAN antibodies for VAN testing.

Therapeutic drugs monitoring

Linezolid (LZD)

Linezolid (LZD) is a synthetic oxazolidinone antibiotic approved for therapy of severe infections caused by methicillin- or vancomycin-resistant Gram-positive bacteria, as well as drug resistant tuberculosis with excellent early bactericidal activity. LZD is metabolized by arylamine N-acetyltransferase-2 (NAT2). Single-nucleotide polymorphisms (SNPs) in NAT2 gene result in two phenotypes, fast acetylators and slow acetylators. Patients with rapid acetylators had a higher risk of microbiological failure and relapse than those with slow acetylators. The minimum inhibitory concentrations are reported to be about 2 μg/mL for S. aureus, E. faecalis, E. faecium, S. pneumoniae, and coagulase-negative streptococcus isolates; in the meanwhile, LZD trough concentrations exceeding 8–10 μg/mL are associated with the increased risk of hematologic toxicity and other adverse effects like peripheral neuropathy and suppression of bone marrow. TDM is helpful for optimizing LZD dose to achieve target therapeutic range and improve the clinical outcomes of patients. Our mouse anti-linezolid McAb can be used to develop sensitive and specific LZD immunoassay.

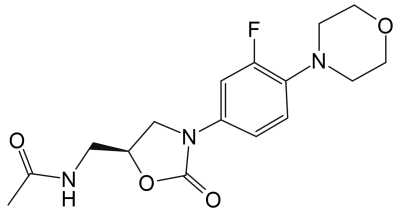

Fig. 1. The chemical structure of LZD

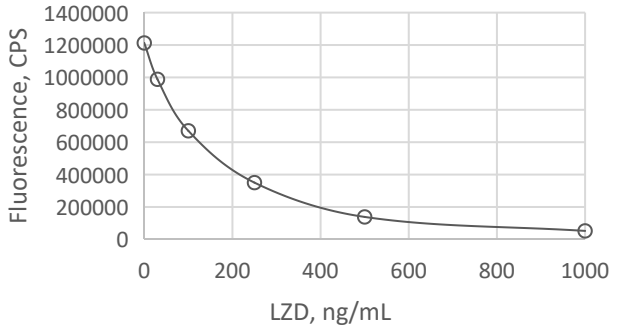

Fig.2. Typical calibration curve of LZD-DELFIA using McAb-27

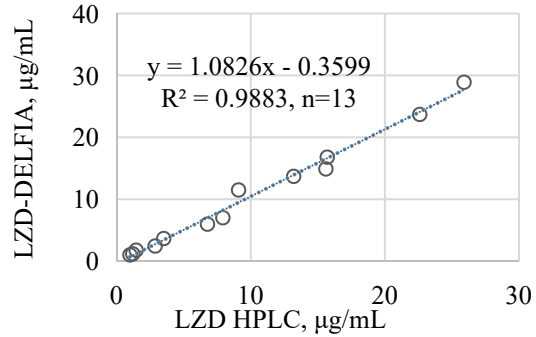

Fig. 3. Agreement between the LZD concentration obtained by HPLC and DELFIA using McAb-27

Product Type	Catalog #	Description
Mouse monoclonal antibody	• Anti-LZD McAb-27	Used for detection of LZD with LOD <10ng/mL by DELFIA. The cross-reactivities of the McAb-27 with the major inactive metabolites of LZD, PNU-142586 and PNU-142300 at 100 μg/mL each, was less than 0.1%.
Conjugate	• LZD-OVA	Paired with anti-LZD antibody for LZD testing.

Therapeutic drugs monitoring

Rifampicin

Rifampicin is a potent antibiotic for first line therapy of tuberculosis (TB). Rifampicin exhibits concentration dependent killing of mycobacteria. Different factors like age, gender, weight, doses/formulations, gastro-intestinal disorders, may alter the absorption and bioavailability of rifampicin, thus altering the drug levels. Low plasma levels of rifampicin tends to cause slow response to therapy, treatment failure or acquired drug resistance. TB patients with further complicated conditions like diabetes or HIV are at increased risks for drug-drug interactions and poor drug absorption. In these cases, TDM can be used to optimize patient management and improve clinical outcomes. Our anti-rifampicin McAb can be used to develop ultrasensitive rifampicin immunoassay with LOD <5ng/mL. Based on the outstanding sensitivity and the relatively steady ratio of saliva/serum concentration, saliva can potentially be employed as sample for rifampicin monitoring, even though the salivary rifampicin level is only about 10 percent of that in serum.

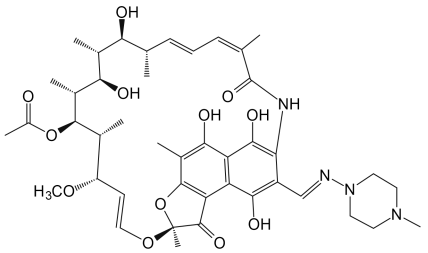

Fig. 1. The chemical structure of rifampicin

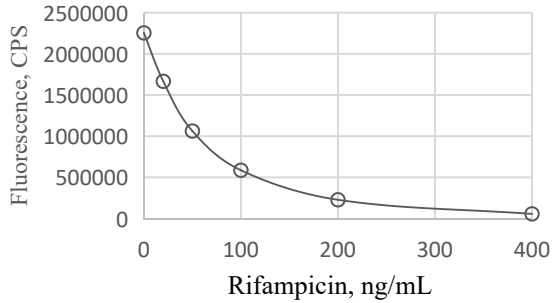

Fig. 2. Typical calibration curve of rifampicin-DELFIA using McAb-3

Product Type	Catalog #	Description
Mouse monoclonal antibody	• Anti-Rifampicin McAb-3	Used for developing rifampicin immunoassay with LOD < 5ng/mL by DELFIA. The McAb-3 shows 0.46% of cross-reactivity with 25-desacetyl-rifampicin, the main metabolite of rifampicin. The cross-reactivities with rifabutin and rifamycin were 0.2% and 1.7%, respectively.
Conjugate	• Rifampicin-BSA • Rifampicin-PEG-Biotin	Paired with anti-rifampicin antibodies for rifampicin testing.

Therapeutic drugs monitoring

Polymyxin-B

Polymyxin-B is a cationic lipopeptide antibiotic introduced into medical practice in the 1950s. For a long time, it obtained only limited use due to its severe nephro- and neurotoxicity and a narrow therapeutic range. With the expansion of multidrug-resistant (MDR) gram-negative bacteria in recent decades, Polymyxin-B has become extremely in demand in emergency medicine as 'last line' drug due to its activity against many of these MDR strains. The clearance and distribution of polymyxin-B change significantly in critically ill patients. Impairment of kidney function leads to decreased clearance of the drug and an increased risk of toxicity. The use of extracorporeal techniques, e.g., renal replacement therapy, plasmapheresis, and hemodialysis, also complicates the pharmacokinetics of polymyxin-B. Therefore, the blood level of polymyxin-B is difficult to predict in these patients, and TDM is of great value for optimizing the clinical use of this drug. Polymyxin-B is a multi-component antibiotic with polymyxin B1 and B2 as major components. Currently, LC-MS/MS is the main technique for polymyxin-B analysis, which mainly focuses on determining the total concentration of polymyxin B1 and B2. To realize more convenient determination of polymyxin B, Bowei-Bio has generated a clone of McAb which can be used for establish accurate immunoassay for Polymyxin-B monitoring.

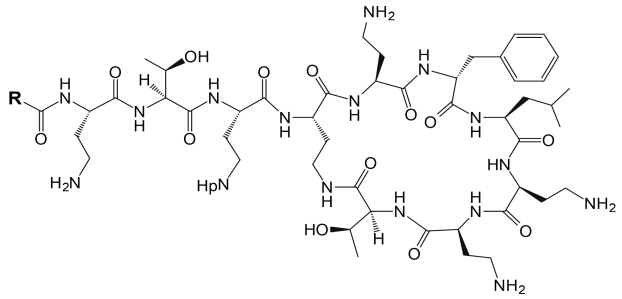

Fig. 1. The chemical structure of polymyxin-B.
R = 6-methyloctanoic acid for polymyxin B1, 6-methylheptanoic acid for B2, octanoic acid for B3, and heptanoic acid for B4.

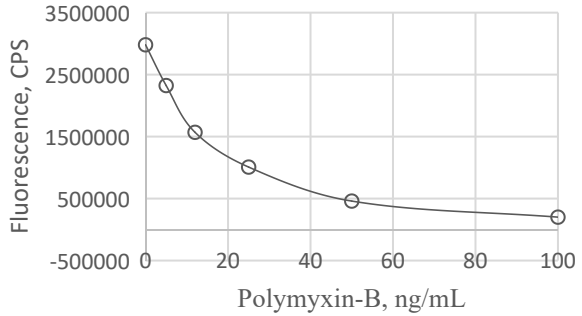

Fig. 2. Typical calibration curve of Polymyxin-B-DELFIA using McAb-16

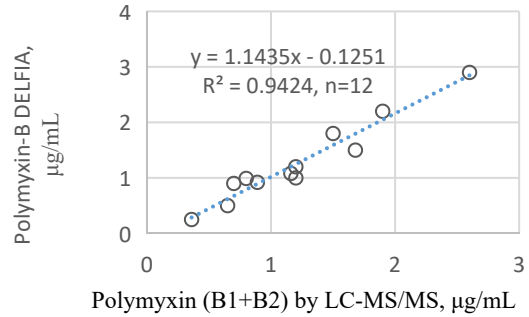

Fig. 3. Agreement between the Polymyxin-B concentration obtained by DELFIA using McAb-16 and LC-MS/MS

Product Type	Catalog #	Description
Mouse monoclonal antibody	• Anti-Polymyxin-B McAb-16	Used for detection of total concentration of polymyxin B1 and B2. LOD <10ng/mL by DELFIA. The cross-reactivity with polymyxin-E is less than 0.3%.
Conjugate	• Polymyxin-B-BSA	Paired with anti-Polymyxin-B McAb for Polymyxin-B testing.

Therapeutic drugs monitoring

Amikacin (AMK)

Amikacin (AMK) is a semi-synthetic aminoglycoside antibiotic that actions by disrupting bacterial protein synthesis after binding to the 30S ribosome of susceptible organisms. It is effective for a broad spectrum of bacterial infections, especially severe multidrug-resistant Gram-negative bacteria, such as Pseudomonas aeruginosa, while also showing activity against Nocardia spp. and Mycobacterium spp. Like other aminoglycosides, AMK has narrow therapeutic index with significant intra- and inter-individual pharmacokinetic variability. AMK is associated with ototoxicity and nephrotoxicity when being overdosed, in the meanwhile, a high proportion of patients fail to achieve the therapeutic target for AMK efficacy when with insufficient medication, potentially placing them at higher risk of treatment failure. TDM of AMK is helpful for optimizing dosage regimens to achieve improved safety and efficacy. Our anti-AMK McAb can be used to develop AMK immunoassay with LOD less than 65pg/mL, which show no cross-reactivity with other aminoglycoside antibiotics with similar structure.

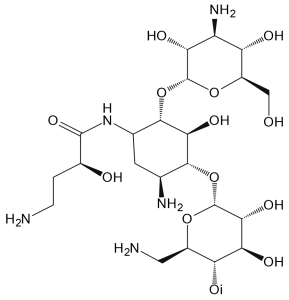

Fig. 1. The chemical structure of AMK

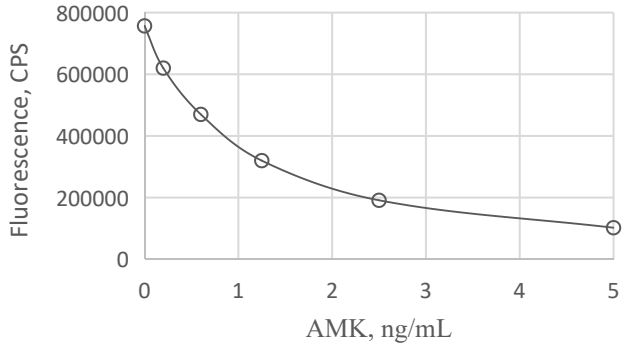

Fig. 2. Typical calibration curve of AMK-DELFIA using McAb-36

Product Type	Catalog #	Description
Mouse monoclonal antibody	• Anti-AMK McAb-36	Used for developing AMK immunoassay with LOD < 65pg/mL by DELFIA. No cross-reaction was detected with kanamycin and topomycin up to 100μg/mL.
Conjugate	• AMK-OVA	Paired with anti-AMK antibodies for AMK testing.

Therapeutic drugs monitoring

Isoniazid (INH)

Isoniazid (INH)), has been widely used as the first-line anti-TB drug for more than 70 years. Up to now, there is still more than 8 million new patients per year receiving INH treatment. Isoniazid has considerable inter- and intra-pharmacokinetic variation related to the expression level of N-acetyltransferase, the major pathway of isoniazid metabolism. Accordingly, the population is divided into slow (SAs) and rapid acetylators (RAs), which will lead to greatly different blood INH levels. INH treatment is associated with abnormal elevation of alanine aminotransferase (ALT) levels in approximately 20% of patients and hepatotoxicity in 1% to 2% of patients. Overdose of INH increases the risk of hepatotoxicity, whereas low plasma levels of the drug may lead to poor response to therapy. Due to the widespread use and large inter-patient variability of the plasma levels of INH, a regular TDM of INH is useful to predict the acetylation profile and to prescribe doses associated with optimal efficacy and safety.

Immunoassays play a crucial role for TDM of various kinds of drugs, however, immunoassay of INH has seldom been reported, partly because of the challenge for generating specific anti-INH antibodies, since INH and its major metabolite, isonicotinic acid, share the same isonicotinyl group. To realize accurate INH immunoassay, Bowei-Bio has generated a clone of McAb which show high specificity for binding INH. INH immunoassay based on this McAb shows good correlation with HPLC-MS/MS.

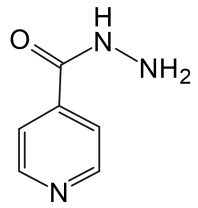

Fig. 1. The chemical structure of INH

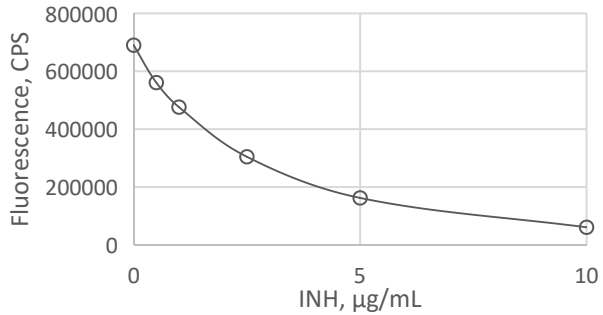

Fig. 2. Typical calibration curve of INH-DELFIA using McAb-6

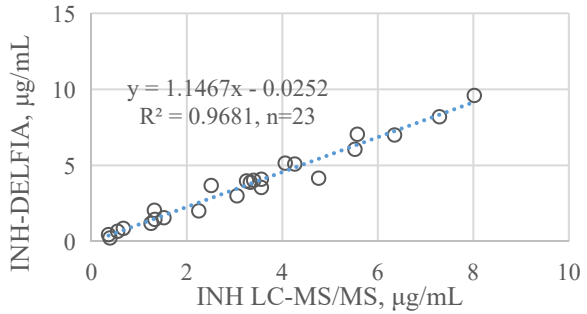

Fig. 3. Agreement between the INH concentration obtained by DELFIA using McAb-6 and LC-MS/MS

Product Type	Catalog #	Description
Mouse monoclonal antibody	• Anti-INH McAb-6	Used for developing INH immunoassay with LOD < 0.12µg/mL by DELFIA. The cross-reactivity of McAb-6 is less than 1.6% with acetylisoniazid, isonicotinic acid, hydrazine, and acetylhydrazine, the four main metabolites of INH.
Conjugate	• INH-Protein	Paired with anti-INH McAb for INH testing.

Therapeutic drugs monitoring

TDM of Antifungal Drugs

Introduction

Invasive fungal infection (IFI) is associated with significant morbidity and mortality, triazole antifungal drugs have played a key role for management of this serious infection. Numerous factors determine the outcome of IFI, but very few of them are under the control of the clinicians. The successful management of IFI continues to be a difficult challenge to clinicians. The choice of drug and dosing regimen based on the TDM is among the factors which the clinician can dictate.

Antifungal TDM is now generally indicated for the triazoles, among which, TDM of fluconazole is recommended only in some rare circumstances, while the TDM of itraconazole, voriconazole and posaconazole are highly recommended because of the marked variability of blood drug levels caused by inconsistent absorption, metabolism, elimination and interaction with concomitant medications. Presently, the most commonly utilized techniques for TDM of triazoles include HPLC and LC-MS, however, there are very limited number of laboratories performing these assays due to the limited sample throughput, long time-consuming, requirement for experienced staff and specialized facilities.

Bowei-Bio has developed a panel of monoclonal antibodies and conjugates for accurate immunoassay of triazole antifungal drugs. We expected that immunoassay for TDM of antifungal drugs will become a more convenient, rapid, and cost-effective alternative to HPLC and LC-MS, and assist individualized anti-fungal treatment.

Products

Antifungal Drugs	Conjugate	Antibody
Voriconazole (VRC)	√	√
Posaconazole (PSC)	√	√
Itraconazole (ITC)	√	√
Isavuconazole (ISA)	√	*
Fluorocytosine (FLC)	√	

* Be available soon

Therapeutic drugs monitoring

Voriconazole (VRC)

Voriconazole (VRC) is a second-generation triazole licensed for treatment of invasive aspergillosis, candidiasis, and serious infections caused by Scedosporium/Fusarium species. Trough concentration of VRC in plasma correlates well with its efficacy and toxicity. VRC shows a large inter- and intra-individual pharmacokinetic variability, mainly caused by different bioavailability, polymorphisms of the gene encoding the CYP2C19 enzyme, drug-drug interactions, and liver diseases. The large variability in VRC plasma concentrations together with the narrow therapeutic window makes individualized dosing adjustments based on TDM necessary to optimize efficacy and to minimize toxicity. According to the British Society for Medical Microbiology (BSMM), VRC plasma concentrations should be determined in the first 5 days of therapy and regularly thereafter. Our anti-VRC McAb can be used for developing accurate VRC immunoassay with excellent correlation with HPLC for analyzing clinical samples.

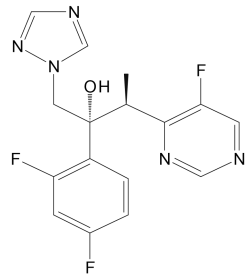

Fig. 1. The chemical structure of VRC

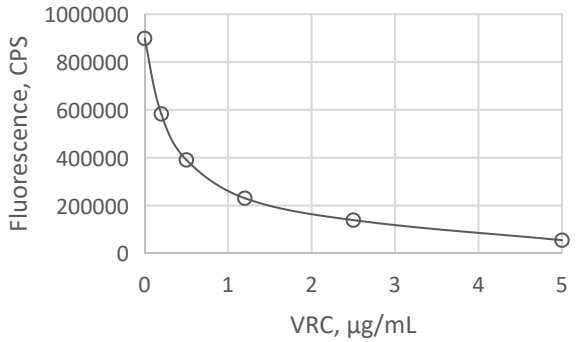

Fig. 2. Typical calibration curve of VRC-DELFIA using McAb-1618

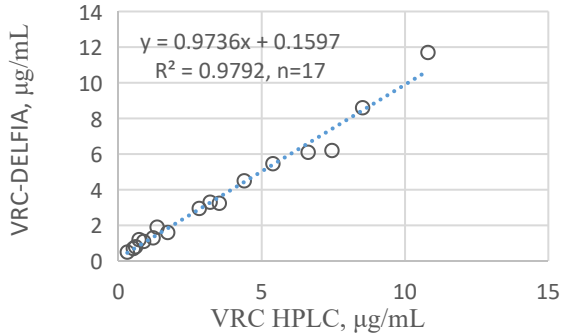

Fig. 3. The correlation of VRC concentration obtained by HPLC and DELFIA using McAb-1618

Product Type	Catalog #	Description
Mouse monoclonal antibody	• Anti-VRC McAb-1618	Used for developing VRC immunoassay with LOD < 0.1µg/mL and excellent correlation with HPLC. No significant cross-reactivities were observed with 30 µg/mL of fluconazole, itraconazole, posaconazole, and 10 µg/mL of the inactive N-oxide metabolite of voriconazole.
Conjugate	• VRC-BSA	Paired with anti-VRC antibody for VRC testing.

Therapeutic drugs monitoring

Posaconazole (PSC)

Posaconazole (PSC) is a second-generation triazole agent with potent and broad antifungal activity. Due to the large inter- and intra-individual variation in bioavailability and drug-drug interactions, the concentration of blood PSC varies considerably in different patients. A significant relationship exists between a higher incidence of clinical failure and lower PSC concentrations. In meanwhile, too high posaconazole levels may cause gastrointestinal reactions, hepatic injury, secondary hypertension, hypokalemia, and occasionally metabolic alkalosis. It is believed that the upper limit of the posaconazole concentration should be around 3745 ng/mL [*2023, Med Mycol 61:myad079.*]. TDM based on different techniques has been performed to ensure adequate drug exposure and limited adverse reactions. Our anti-PSC McAb can be used for developing accurate immunoassays for convenient and reliable PSC monitoring.

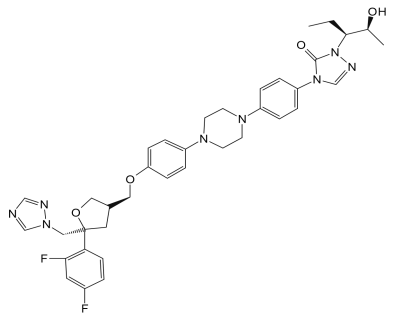

Fig. 1. The chemical structure of PSC

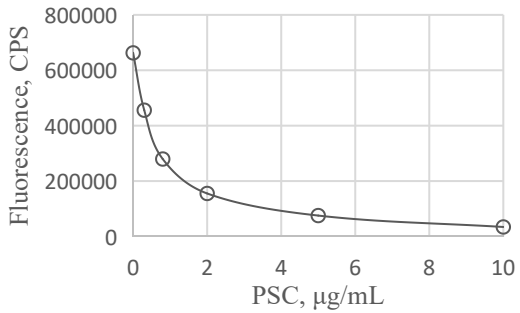

Fig. 2. Typical calibration curve of PSC-DELFIA using McAb-5

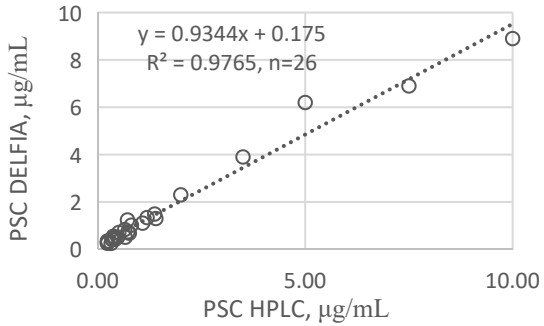

Fig. 3. The correlation of PSC concentration obtained by HPLC and DELFIA using McAb-5

Product Type	Catalog #	Description
Mouse monoclonal antibody	• Anti-PSC McAb-5	Used for developing PSC immunoassay with LOD <0.2μg/mL and good correlation with HPLC. The cross-reactivities with itraconazole and OH-itraconazole are 1.3% and 2%, respectively.
Conjugate	• PSC-BSA	Paired with anti-PSC antibody for PSC testing.

Therapeutic drugs monitoring

Itraconazole (ITC)

Itraconazole (ITC) is a broad-spectrum triazole anti-fungal drug used to treat and prevent infections caused by dermatophytes, yeasts, dimorphic and dematiaceous fungi and molds. It is also used in prophylaxis of fungal infections in some immunosuppressive pathologies. ITC has irregular absorption, especially in patients with pathologic conditions that may affect the gastrointestinal system, including neutropenic patients, those with AIDS, and organ transplant recipients. ITC has a variable dose–concentration relationship and alterations in kinetics during long-term treatment. Like all of the triazoles, ITC exhibits multiple drug interactions, most notably with cytochrome P450-inducing drugs. Accordingly, TDM of ITC is helpful for optimizing clinical efficacy when it is used in prophylaxis and therapy of invasive fungal infections. Our anti-ITC McAbs can be used for developing accurate immunoassays for convenient and reliable ITC monitoring.

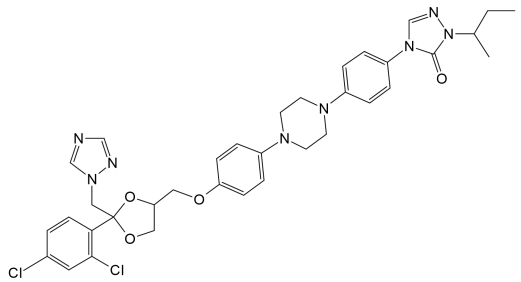

Fig. 1. The chemical structure of ITC

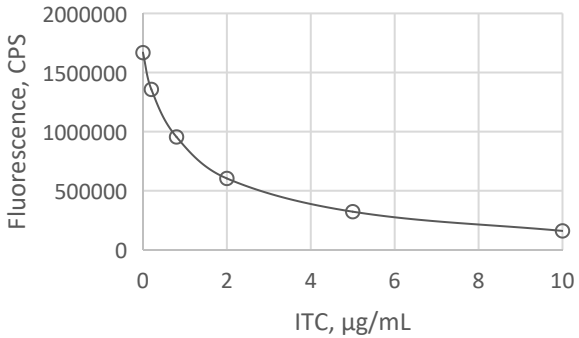

Fig. 2. Typical calibration curve of ITC-DELFIA using McAb-49

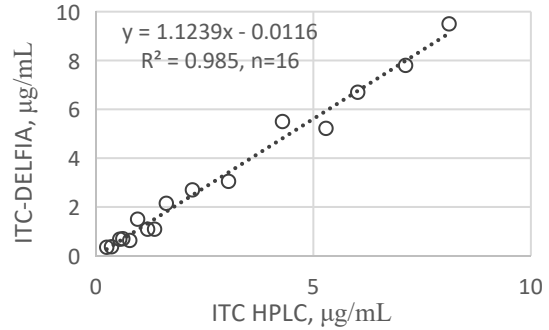

Fig. 2. The correlation of ITC concentration obtained by HPLC and DELFIA using McAb clone-49

Product Type	Catalog #	Description
Mouse monoclonal antibody	• Anti-ITC McAb-49	Used for testing ITC with LOD <0.1μg/mL by DELFIA. The cross-reactivities is < 2.2% with hydroxy-itraconazole, keto-itraconazole, N-desaklylitraconazole and posaconazole.
Mouse monoclonal antibody	• Anti-ITC McAb-25	Used for testing ITC with LOD <0.03μg/mL by DELFIA. The cross-reactivities is about 50% with hydroxy-itraconazole and 4.5% with posaconazole. Immunoassay using McAb-25 also reflects plasma hydroxy-itraconazole concentrations (the active metabolite of itraconazole).
Conjugate	• ITC-BSA	Paired with anti-ITC antibodies for ITC testing.

Therapeutic drugs monitoring

TDM of Gabapentinoids Drugs

Introduction

The gabapentinoid group consists of gabapentin and pregabalin, two of the most widely prescribed drugs with their structure similar to the inhibitory neurotransmitter gamma-aminobutyric acid. Gabapentinoids were initially used as anticonvulsant to treat seizure disorders, and up to now also has been used to treat anxiety, pain, postoperative nausea, substance abuse issues, and vomiting. In recent years, there are growing evidences indicating that gabapentinoids are associated with dependence and misuse, especially for patients suffering from opiate addiction, in which case gabapentinoids are used either to reinforce the effects of opiates or to reduce withdrawal sensations. The association of gabapentinoids with opiates or other sedatives is particularly dangerous due to their synergistical enhancement on central depressant. Monitoring of gabapentinoids is helpful to monitor patient adherence, to help physicians decide the best treatment for the patient and to avoid unnecessary prescription of opioids which are used for treatment of neuropathic pain but show high risk of addiction. Our monoclonal antibodies and conjugates can be used for establishing accurate immunoassay for monitoring of gabapentinoids.

Products

Gabapentinoids Drugs	Conjugate	Antibody
Gabapentin (Gaba)	√	√
Pregabalin (Preg)	√	√

Therapeutic drugs monitoring

Gabapentin (Gaba)

Gabapentin (Gaba) is an anticonvulsant drug, initially used for adjunctive treatment of partial seizures, and later for treatment of cancer- and childbirth-related pain. It also has utility in diabetic neuropathy, migraine disorders, restless leg syndrome, and in the treatment of mood disorders, panic attacks, and social phobias. For seizure control, most patients exhibit predose plasma concentrations between 2 to 20 µg/mL. The major side effects of it include somnolence, dizziness, ataxia, fatigue, nystagmus, and an increased risk of respiratory depression. TDM of gabapentin is helpful for establishing compliance and detecting individual patient thresholds for saturation of gabapentin absorption. Due to renal elimination, gabapentin monitoring may be useful for optimizing the dose in the renal-compromised patient. Moreover, although Gaba was once believed to be safe and have a low potential for abuse, there has been an increasing number of case reports that gabapentin is being misused for its subjective pleasurable effects. Monitoring of Gaba will facilitate government authorities in regulating its abuse. Our anti-Gaba McAb can be used to develop sensitive immunoassays for convenient and reliable Gaba monitoring.

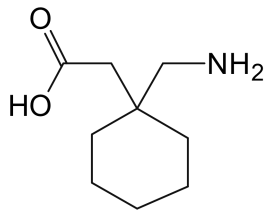

Fig. 1. The chemical structure of Gaba

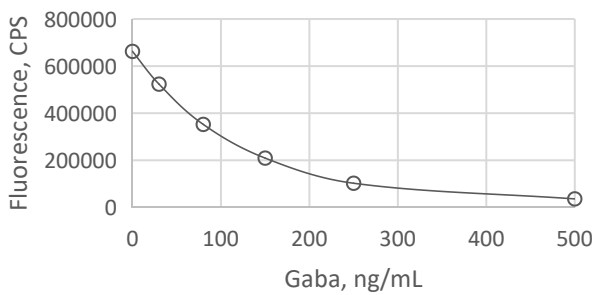

Fig. 2. Typical calibration curve of Gaba-DELFIA using McAb-3

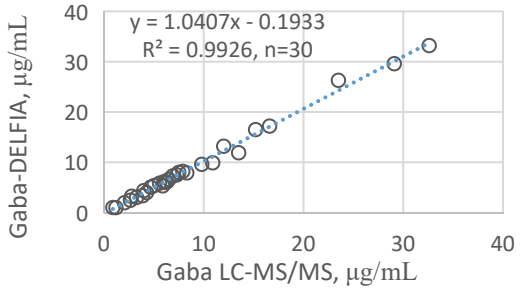

Fig. 3. The correlation of Gaba concentration obtained by LC-MS/MS and DELFIA using McAb-3

Product Type	Catalog #	Description
Mouse monoclonal antibody	• Anti-Gaba McAb-3	Used for developing Gaba immunoassay with LOD <2.5ng/mL by DELFIA. No cross-reactivity was detected with pregabalin, γ-Hydroxybutyric Acid and γ-aminobutyric acid at 50µg/mL. No metabolite cross-reactivity issues are involved in Gaba immunoassay since this drug is not metabolized in humans.
Conjugate	• Gaba-PEG-BSA	Paired with anti-Gaba antibody for Gaba testing.

Therapeutic drugs monitoring

Pregabalin (Preg)

Pregabalin (Preg) is a well-recognized central nervous system depressant. It binds to the α-2-δ subunit of voltage-gated calcium channels, decreasing the release of several excitatory neurotransmitters and blocking the development of hyperalgesia and central sensitization. It was used for the treatment of seizures, neuropathic pain, anxiety disorder (GAD) or social anxiety disorder (SAD), spinal cord injury, and fibromyalgia. The side effects of Preg are less severe compared to other anti-epileptic drugs, being the most frequently reported somnolence, angioedema, dizziness, blurred vision, dry mouth, and weight gain. The TDM of pregabalin is a useful to achieve the therapeutic effect while minimizing the risk of side effects in critically ill patients, especially in those with severe renal impairment. Moreover, the abuse of Preg has increased substantially over the last decade, monitoring of this drug will facilitate government authorities in regulating its abuse. Our anti-Preg McAb can be used to develop sensitive immunoassays for convenient and reliable Preg monitoring.

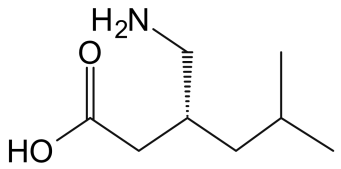

Fig. 1. The chemical structure of Preg

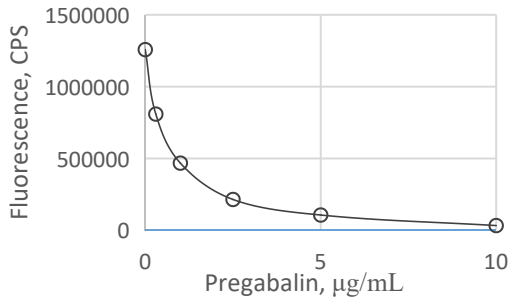

Fig. 2. The typical calibration curve of Preg-DELFIA using McAb-16

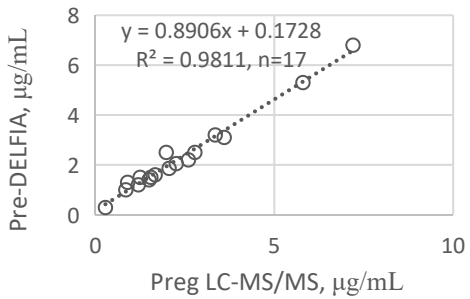

Fig. 3. The correlation of Preg concentration obtained by LC-MS/MS and DELFIA using McAb-16

Product Type	Catalog #	Description
Mouse monoclonal antibody	• Anti-Preg McAb-16	Used for developing Preg immunoassay with LOD <20 ng/mL and good correlation with HPLC. No cross-reactivity was detected with gabapentin, γ-Hydroxybutyric Acid and γ-aminobutyric acid at 50μg/mL.
Conjugate	• Preg-BSA	Paired with anti-Preg antibody for Preg testing.

Therapeutic drugs monitoring

Antiepileptic Drugs

Introduction

Therapeutic Drug Monitoring (TDM) is a crucial clinical tool in the management of epilepsy, a group of neurological disorders characterized by recurrent epileptic seizures. As antiepileptic drugs (AEDs) exhibit significant interindividual variability in pharmacokinetics—affected by factors such as age, gender, liver/kidney function, genetic polymorphisms, and concurrent medications—TDM plays an indispensable role in optimizing treatment outcomes.

TDM is particularly valuable in specific clinical scenarios: initiating AED therapy to rapidly achieve effective concentrations, monitoring adherence (low drug levels often indicate poor compliance), adjusting dosages during pregnancy or renal/hepatic impairment, and managing polytherapy (where drug-drug interactions may alter AED concentrations). By individualizing dosage regimens based on TDM results, clinicians can significantly reduce the risk of treatment failure and adverse drug reactions, thereby improving the quality of life for epilepsy patients.

Bowei-Bio has engaged in the area of AED analysis for many years, and launched a group of antibodies and conjugates for accurate immunoassay of AEDs which are of high level of recommendation for TDM.

Products

Antiepileptic Drugs	Conjugate	Antibody
Valproic acid (VPA)	√	√
Carbamazepine (CBZ)	√	√
Oxcarbazepine (OXC)	√	√
10-hydroxycarbazepine (MHD)	√	√
Topiramate (TPA)	√	√
Phenytoin	√	√
Phenobarbital	√	√
Levetiracetam	√	*
Lamotrigine	√	*

*: Available soon

Therapeutic drugs monitoring

Valproic acid (VPA)

Valproic acid (VPA) has been applied for treatment of different types of epilepsy for over 50 years. More recently, it has also been proposed for the management of neurological disorder, cancer, addictions and used as an antiviral complement. Clinical use of VPA is associated with severe, and sometimes fatal hepatotoxicity. The therapeutic plasma levels of VPA are between 50-120 μg/mL. Periodic monitoring of plasma VPA level is important for successful therapy and effective control of its adverse effects. Among different techniques for VPA monitoring, immunoassay is the most practical choice for clinic VPA determination because of its speed, simplicity, availability of automated instruments, and the reliable results that correlate well with chromatographic methods. Our anti-VPA McAb can be used to develop accurate immunoassay for reliable VPA monitoring.

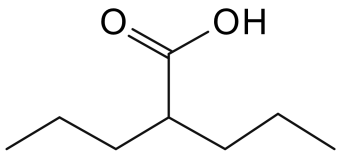

Fig. 1. The chemical structure of VPA

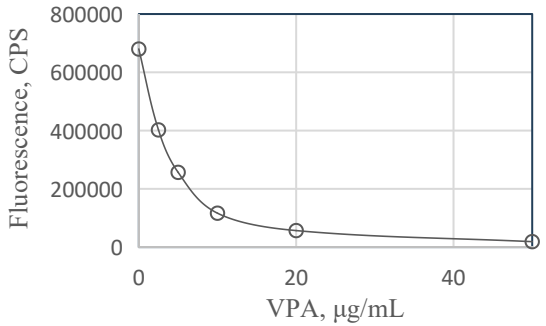

Fig. 2. Typical calibration curve of the VPA-DELFIA using McAb-22

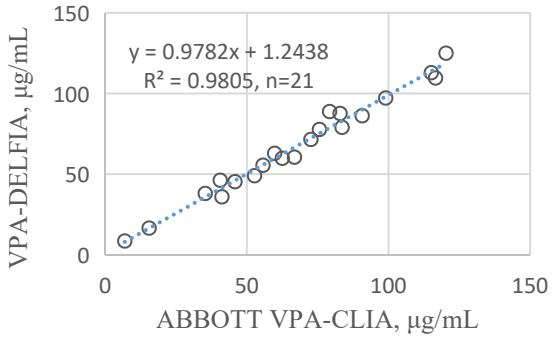

Fig. 3. Comparison of the VPA con. obtained by DELFIA and ABBOTT CLIA

Product Type	Catalog #	Description
Mouse monoclonal antibody	• Anti-VPA McAb-22	Used for testing VPA with LOD < 0.2μg/mL by DELFIA. The cross-reactivity with 4-ene-VPA was 2.7%. No cross-reactivity was detected with 4-hydroxy valproic acid, and 3-hydroxy valproic acid at 150μg/mL.
Conjugate	• VPA-BSA	Paired with anti-VPA antibodies for VPA testing.

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Therapeutic drugs monitoring

Carbamazepine (CBZ)

Carbamazepine (CBZ) is an antiepileptic drug for controlling various types of epileptic seizures. CBZ was approved in US in 1974, and today it is still one of the most important antiepileptic drug (AED). Besides the usage as AED, CBZ is also indicated for treatment of trigeminal or glossopharyngeal neuralgia, and is the drug of choice in the management of schizophrenia, bipolar disorder, aggression, and posttraumatic stress disorder. Both the therapeutic and toxic effects of CBZ are closely correlated with its plasma concentration more than with dose. When the blood level of CBZ is maintained within the therapeutic window, it demonstrates definite efficacy, and works well as a monotherapy for epilepsy. However, there are often significant variations in drug concentrations among different patients because numerous factors affect the in vivo pharmacokinetics. This frequently leads to subtherapeutic or excessive drug concentrations, leading to treatment failure or toxicity. TDM of CBZ enables timely adjustment of medication regimens, facilitating effective and safe anti-epileptic treatment. Bowei-Bio has generated two clones of McAbs for CBZ immunoassay; one is for selective detection of CBZ, and another for detection of the total concentration of CBZ and its active metabolite (carbamazepine-10,11-epoxide, CBZE).

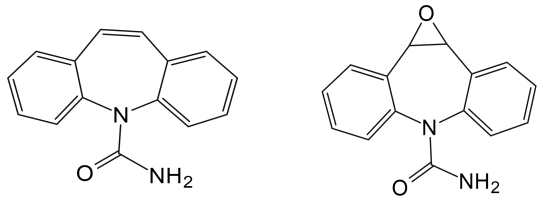

Fig. 1. The chemical structure of CBZ (left) and CBZE (right)

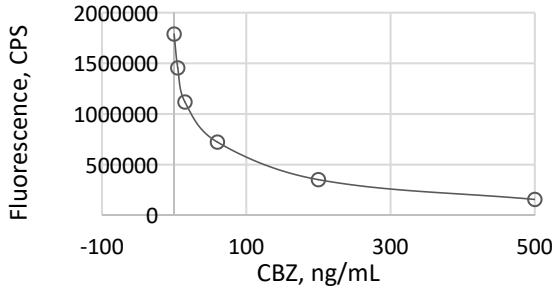

Fig. 2. Typical calibration curve of the CBZ-DELFIA using McAb-33

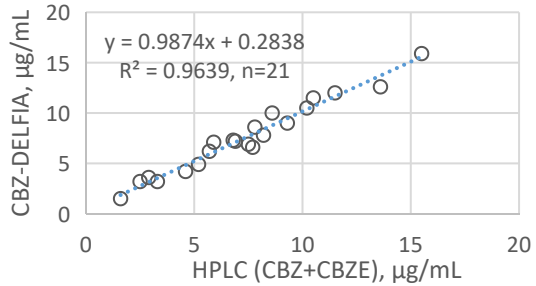

Fig. 3. Comparison of the CBZ con. obtained by HPLC and DELFIA using McAb-33

Product Type	Catalog #	Description
Mouse monoclonal antibody	• Anti-CBZ McAb-33	The LOD is < 0.05 µg/mL for CBZ-DELFIA; Its cross-reactivities with CBZE and oxcarbazepine, are 97% and 0.6%, respectively. McAb-33 is highly suitable for detecting total concentration of CBZ and CBZE.
Mouse monoclonal antibody	• Anti-CBZ McAb-2	The LOD is < 0.5 µg/mL for CBZ-DELFIA. Its cross-reactivity with CBZE is about 7.2%. Since the concentration of CBZE in plasma is 1/5 to 1/20 of that of CBZ, the positive bias introduced by this cross-reactivity is insignificant. McAb-2 can be used for detection of the parent drug CBZ.
Conjugate	• CBZ-PEG-BSA	Paired with anti-CBZ antibodies for CBZ testing.

Therapeutic drugs monitoring

Oxcarbazepine (OXC) and Oxcarbazepine Metabolite (MHD)

Oxcarbazepine (OXC) is a dibenzazepine carboxamide derivative widely used in treatment of epilepsy. As a prodrug, OXC is converted in the body into its active metabolite 10-monohydroxycarbamazepine (MHD). MHD exists in blood with two enantiomers (S)-MHD and (R)-MHD at a ratio of approximately 4:1 for patients treated with oxcarbazepine. Both the S- and R-enantiomers have similar pharmacological activity. Although OXC has the advantages of good tolerability and mild adverse reactions, TDM of OXC and MHD is helpful to guide OXC medication, especially for patients during pregnancy, in renal insufficiency, and at the extremes of age. TDM of OXC or MHD is also used to determine the significance of potential drug interactions or rule out noncompliance. Our anti-OXC McAb-11 can be used to develop OXC-immunoassay with excellent specificity and sensitivity without significant interference from its metabolite MHD and other structurally similar compounds. The anti-MHD McAb-22 can be used to establish accurate immunoassays for MHD monitoring.

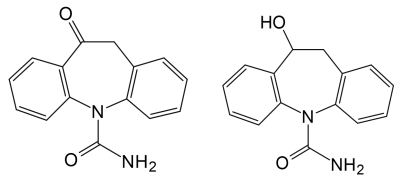

Fig. 1. The chemical structures of OXC (left) and MHD (right)

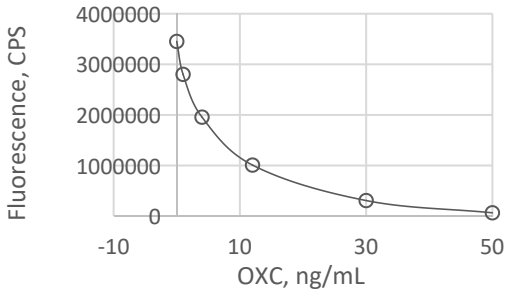

Fig. 2. Typical calibration curve of the OXC-DELFIA using McAb-11

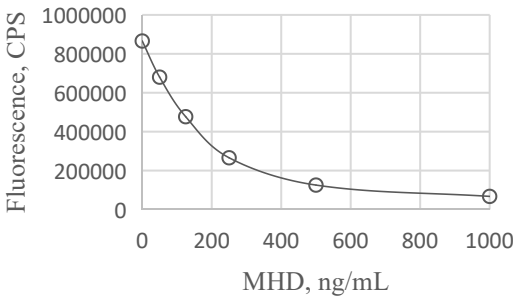

Fig. 3. Typical calibration curve of the MHD-DELFIA using McAb-22

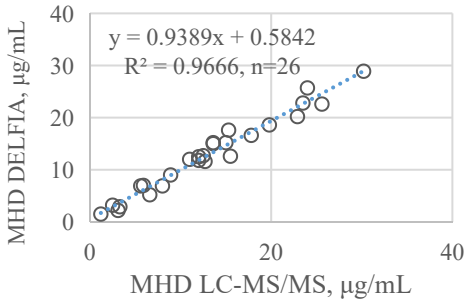

Fig. 4. Comparison of the MHD values obtained by LC-MS/MS and DELFIA using McAb-26

Product Type	Catalog #	Description
Mouse monoclonal antibody	• Anti-MHD McAb-22	Used for testing MHD with LOD < 2ng/mL by DELFIA. The cross-reactivities are < 4.6% with OXC, < 4.9% with carbamazepine, and < 0.15% with 10,11-Dihydro-10,11-dihydroxycarbamazepine.
Conjugate	• MHD-PEG-BSA	Paired with anti-MHD antibodies for MHD testing.
Mouse monoclonal antibody	• Anti-OXC McAb-11	Used for testing OXC with LOD < 0.35ng/mL by DELFIA. The cross-reactivities are < 0.00125% with MHD, < 0.0032 with carbamazepine 10,11-epoxide, and < 0.0065 with carbamazepine. No cross-reaction was detected with MHD-O-glucuronide at 40µg/mL
Conjugate	• OXC-PEG-BSA	Paired with anti-OXC antibodies for OXC testing.

Therapeutic drugs monitoring

Topiramate (TPA)

Topiramate (TPA) is a broad-spectrum anticonvulsant commonly used for treatment of epilepsy. Because of its multiple mechanisms of action, TPA is also used for variety of indications such as bipolar disorder, obesity, eating disorders, migraine headaches, posttraumatic stress and cancers. Despite the relatively wide therapeutic range (about 2-15μg/mL) and relative absence of severe adverse effects, topiramate monitoring is still helpful for addressing therapeutic failure, optimizing individual therapy, assessing compliance, and managing co-medications especially when co-administered with drugs that may alter liver enzyme metabolism. Among these methods used for TPA monitoring, immunoassay is regarded as the most practical choice for clinic TPA-TDM because of its speed, simplicity, the availability of automated instruments, and the reliable results that correlate well with chromatographic methods. Our anti-TPA McAb can be used to develop accurate immunoassay for reliable TPA monitoring.

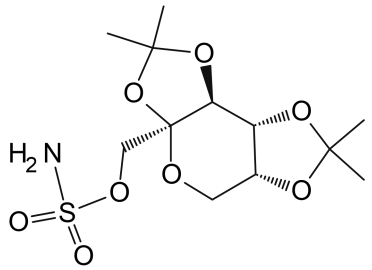

Fig. 1. The chemical structure of TPA

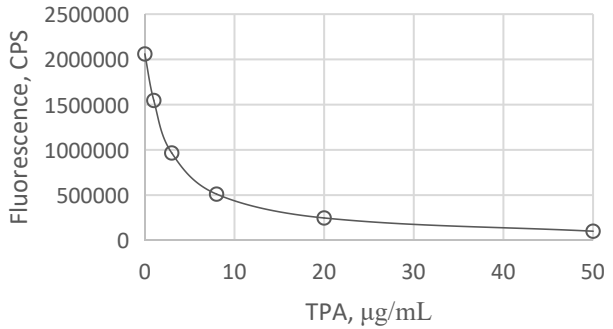

Fig. 2. Typical calibration curve of the TPA-DELFIA using PcAb-7-3

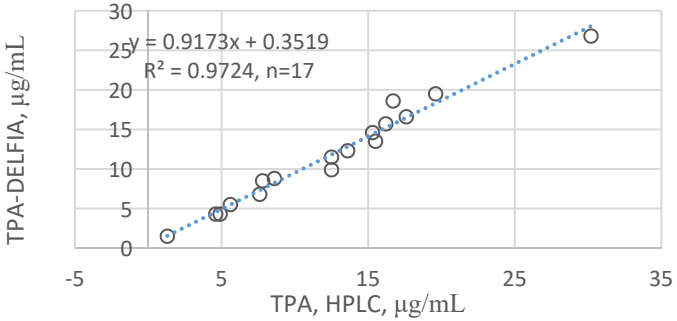

Fig. 3. Comparison of the TPA con. obtained by HPLC and DELFIA using PcAb-7-3

Product Type	Catalog #	Description
Rabbit polyclonal antibody	• Anti-TPA-BSA PcAb-7-3	Used for testing TPA with LOD < 0.5μg/mL by DELFIA. The cross-reactivities of the PcAb 7-3 with the main metabolites of TPA were 1.2% for 10-OH TPM, 0.56% for 9-OH TPM, less than 0.05% for 2,3-desisopropylidene TPM and 4,5-desisopropylidene TPM. No cross-reactivity was detected with phenytoin, phenobarbitol, primidone, valproic acid and tolbutamide. The key performances of the TPA-DELFIA based on the use of PcAb -7-3 are presented in Fig. 2 and 3.
Conjugate	• TPA-PEG-OVA	Paired with anti-TPA antibody for TPA testing.

Therapeutic drugs monitoring

Phenytoin/Phenobarbital

Phenytoin and phenobarbital are two classic anticonvulsants widely used for management of patients with epilepsy. Because of the narrow therapeutic window (10-20μg/mL for phenytoin and 15-40μg/mL for phenobarbital) and the good relationship between serum concentration and clinical efficacy and toxicity, TDM is an important adjunct to therapy in order to optimize the dosage regimen for effective therapy and prevention of drug toxicity. Numerous methods are available for monitoring the concentrations of phenytoin and phenobarbital in serum, including gas chromatography, HPLC, and immunoassays. Among these techniques, immunoassay is regarded as the most applicable one for routine clinical application. Our anti-phenytoin and anti-phenobarbital PcAbs can be used to develop sensitive immunoassays for drug monitoring.

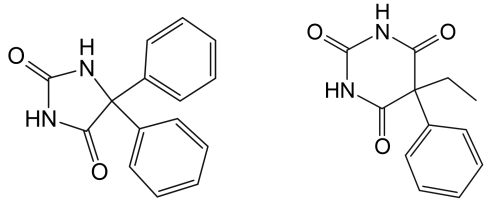

Fig. 1. The chemical structures of phenytoin (left) and phenobarbital (right)

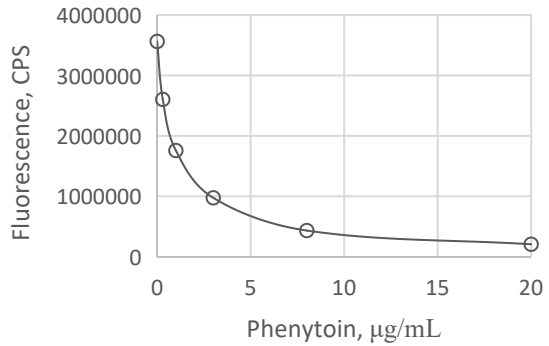

Fig. 2. Typical calibration curve of phenytoin-DELFIA using PcAb-0221

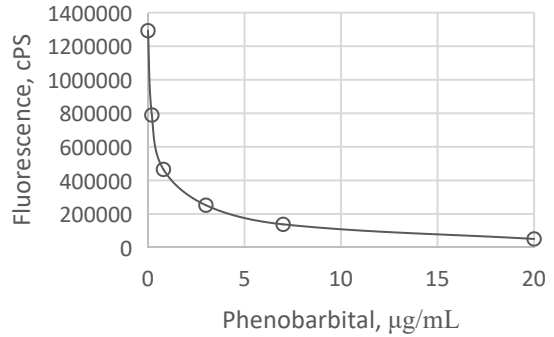

Fig. 3. Typical calibration curve of phenobarbital-DELFIA using PcAb-0216

Product Type	Catalog #	Description
Rabbit polyclonal antibody	• Anti-Phenytoin-BCP PcAb 0221	Used for testing phenytoin with LOD <0.1μg/mL by DELFIA. The cross-reactivity with 4-HPPH (5-(4-hydroxyphenyl)-5-phenylhydantoin), the major metabolite of phenytoin, is < 4.6%. No cross-reactivity to oxaprozine was detected.
Conjugate	• Phenytoin-PEG-BSA	Paired with anti-phenytoin antibodies for phenytoin testing
Rabbit polyclonal antibody	• Anti-phenobarbital-BSA PcAb 0216	Used for testing phenobarbital with LOD <0.1μg/mL by DELFIA. The cross-reactivity with p-hydroxyphenobarbital, the major metabolite of phenobarbital, is < 2.7%.
Conjugate	• Phenobarbital-PEG-BCP	Paired with anti-phenobarbital antibodies for phenobarbital testing

Therapeutic drugs monitoring

TDM of Anticancer Drugs

Introduction

Most anticancer drugs are usually characterized by steep dose-response curve, narrow therapeutic window, and highly variable pharmacokinetics. These factors often cause patients' plasma drug concentrations to deviate from the therapeutic range, which may either compromise tumor treatment efficacy or induce severe adverse reactions, such as life-threatening myelosuppression. Conducting therapeutic drug monitoring (TDM) for such drugs holds significant clinical value in ensuring therapeutic efficacy while controlling adverse effects. Although there are still challenges for fully implementing TDM in daily oncology practice because of the difficulties in establishing appropriate therapeutic windows for some tumor types, the common use of combination chemotherapies, and the analytical challenges with prodrugs, dosage optimization by TDM is surely helpful for improving the use of the antineoplastic agents because of the benefits including enhancement of compliance, improvement of response rates, minimization of pharmacokinetic variability among patients, optimized dose adjustment in patients with hepatic and (or) renal dysfunction, and detection of drug interactions.

Recent advances in anticancer drug TDM derive from technological innovations and deeper pharmacogenomic insights. While LC-MS is widely used for sensitive, specific and multiplexed detection of drugs, immunoassays remain indispensable in antitumor drug TDM with the advantages of rapid analysis, simple operation, high automation and cost-effectiveness. Bowei-Bio has launched a group of antibodies and conjugates for accurate immunoassay of several key anticancer drugs that is of high level of recommendation to use TDM.

Products

Anticancer drugs	Conjugate	Antibody
Methotrexate	√	√
Busulfan	√	√
Venetoclax	√	√
5-Fluorouracil	√	√
Paclitaxel	√	√
Docetaxel	√	√
Imatinib	√	√
Dasatinib	√	
Afatinib	√	
Crizotinib	√	
Sunitinib	√	

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Therapeutic drugs monitoring

Methotrexate (MTX)

Methotrexate (MTX) is widely used to treat various kinds of oncologic and non-oncologic diseases. Although it can be administered over a wide range of dose, serious adverse effects may occur when high-dose MTX therapy is applied for management of acute lymphoblastic leukemia, lymphoma, breast cancer, and osteosarcoma. In such cases, drug monitoring is essential for its toxicity assessment and the subsequent leucovorin rescue. Immunoassay provides a useful tool for accurate and convenient MTX determination. Our anti-MTX McAb can be used to develop sensitive and specific immunoassays for accurate MTX monitoring.

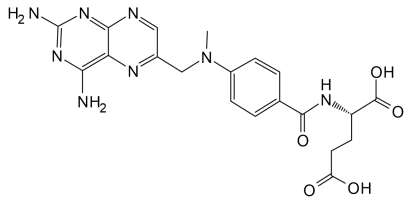

Fig. 1. The chemical structure of MTX

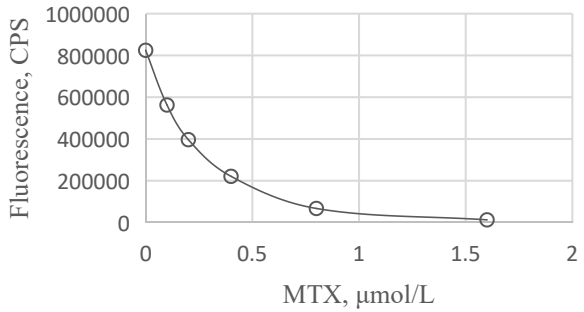

Fig. 2. Typical calibration curve of the MTX-DELFIA using McAb-6SQ

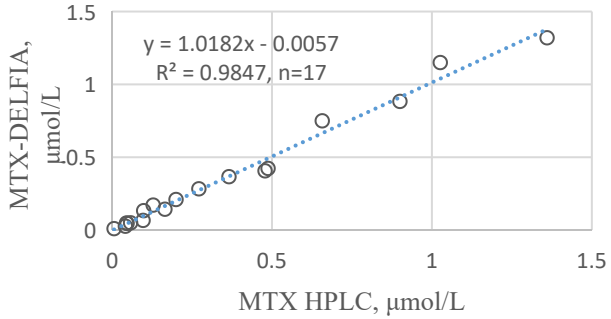

Fig. 3. Comparison of HPLC and MTX-DELFIA using McAb-6SQ on measurement of clinical samples

Product Type	Catalog #	Description
Mouse monoclonal antibody	• Anti-MTX McAb-6SQ	Used for developing MTX immunoassay with excellent correlation with HPLC measurement. LOD was 0.02µmoL/L by DELFIA. The cross-reactivities was < 1.6% for 7-Hydroxymethotrexate, <0.1% for folate, 5MTHFA and folinic acid.
Conjugate	• MTX-BSA	Paired with anti-MTX antibody for MTX testing.

Therapeutic drugs monitoring

Busulfan (Bu)

Allogeneic hematopoietic cell transplantation (allo-HCT) is used to treat several types of cancers such as lymphoma, leukemia, and multiple myeloma. Busulfan (Bu) is an important component of many conditioning regimens for allo-HCT. The high Bu plasma levels have been shown to increase the chance of veno-occlusive disease, while low levels are associated with recurrence of disease or graft rejection. Due to its complex action and metabolism, and a large inter- and intra-individual variability (especially in children), TDM of Bu is critical for controlling the risk of adverse consequences and in the meanwhile maintaining enough therapeutic effects. Compared to the commonly used LC-MS/MS, HPLC and GC-MS/MS for Bu monitoring, immunoassay is regarded as a more convenient choice for routine clinic use. However, high quality anti-Bu antibody is seldom available in current market because of the instability of Bu which poses challenges for antibody preparation.

Our monoclonal anti-Bu antibody can be used for developing accurate Bu immunoassays with excellent correlation with HPLC-MS/MS. The high sensitivity of immunoassay based on the use of McAb-9 makes it feasible to use not only plasma but also dried blood spot as sample for Bu monitoring.

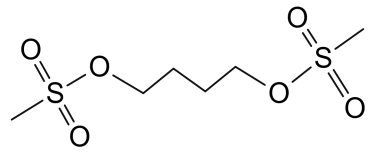

Fig. 1. The chemical structure of Busulfan

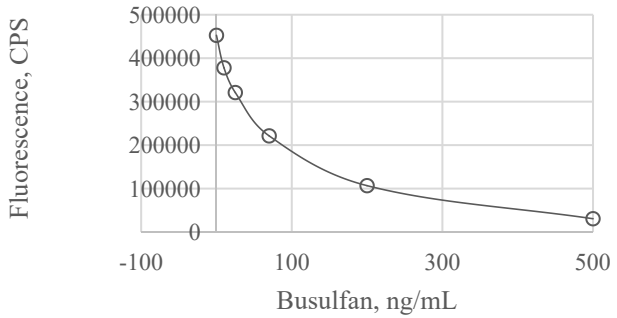

Fig. 2. The typical calibration curve of the Bu-DELFIA using McAb-9

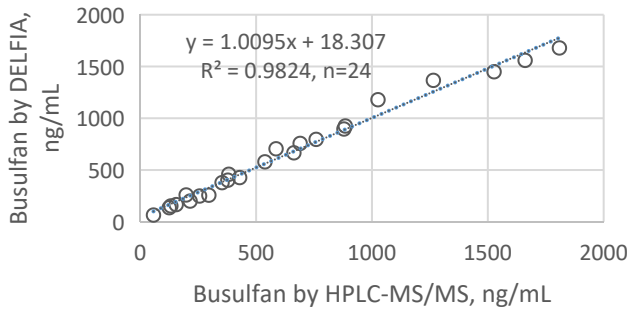

Fig. 3. Agreement between the Bu concentration determined by LC-MS/MS and DELFIA using McAb-9

Product Type	Catalog #	Description
Mouse monoclonal antibody	• Anti-Bu McAb-9	Used for developing Bu immunoassay with LOD <10ng/mL by DELFIA. No cross-reactivities were observed with 20 µg/mL of Bu metabolites including tetramethyl sulfone, tetrahydrothiophene, and tetrahydrothiophene-3-ol-1,1-dioxide.
Conjugate	• Bu-Protein	Paired with anti-Bu antibody for Bu testing.
Bu derivative	• Bu derivative	Used for preparing calibrators or quality controls with improved stability than Bu.

Therapeutic drugs monitoring

Venetoclax

Venetoclax has emerged as a breakthrough for treatment of chronic lymphocytic leukemia and acute myeloid leukemia. Due to its high selectivity for BCL-2 protein, venetoclax shows superior efficacy and better safety compared to nonvenetoclax group of drugs. However, when venetoclax is administered at a fixed dose, the plasma concentration of venetoclax will vary widely between individuals. Especially when venetoclax is co-administered with a strong CYP3A4 inhibitor, the blood Cmax of venetoclax may be increased more than two times. On these grounds, close monitoring of the blood venetoclax concentration is highly recommended with an aim to reduce the risk of tumor-lysis syndrome and other complications. Venetoclax monitoring has so far relied mainly on HPLC and LC-MS/MS, two techniques that potentially showing superior selectivity and accuracy if being well-optimized. However, immunoassay would be a more convenient, faster, more automatic and cost-effective choice for venetoclax determination. Our polyclonal anti-venetoclax antibody can be used for developing accurate venetoclax immunoassays that show excellent correlation with HPLC-MS/MS.

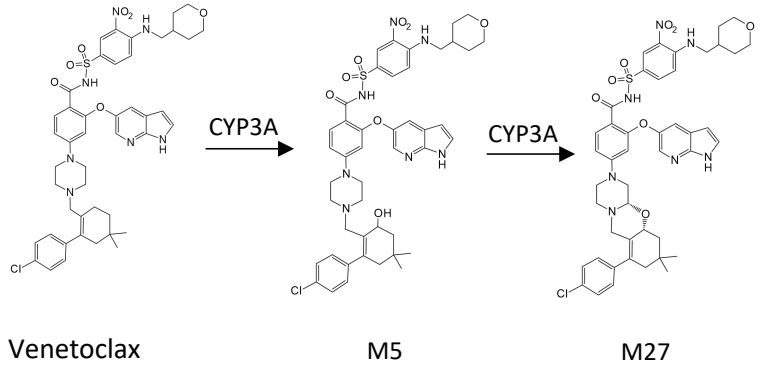

Fig. 1. The chemical structure of venetoclax and its major metabolism route

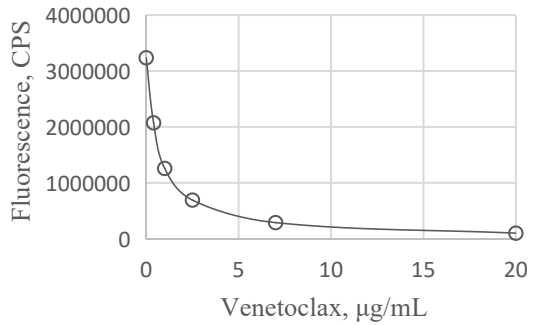

Fig.2. Typical calibration curve of the Venetoclax-DELFIA using PcAb-1119

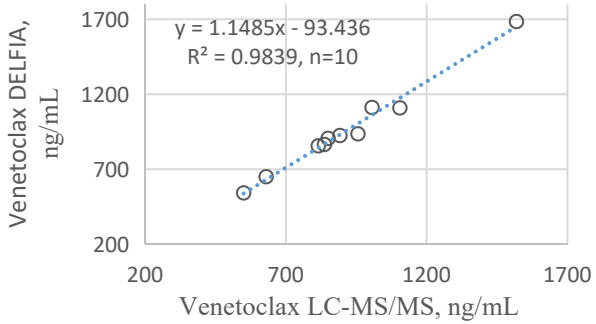

Fig.3. Agreement between the Venetoclax concentration determined by LC-MS/MS and DELFIA using PcAb-1119

Product Type	Catalog #	Description
Rabbit polyclonal antibody	• Anti-venetoclax-BSA PcAb-1119	Used for developing venetoclax immunoassays with LOD <0.05µg/mL by DELFIA. No cross-reactivity was detected with M27 up to 5000ng/mL.
Conjugate	• Venetoclax-Protein	Paired with anti-venetoclax antibody for venetoclax testing.

Therapeutic drugs monitoring

5-Fluorouracil (5FU)

5-Fluorouracil (5FU) is an analogue of uracil with its hydrogen at the C-5 position of the pyrimidine ring substituted by fluorine. In the past several decades, 5FU continues to be the cornerstone as a cytotoxic agent for treatment of head and neck, breast, lung, liver, stomach, pancreas, and colon cancers. Due to its relatively narrow therapeutic index and the substantial inter-individual variability in drug exposure and therapy response, a high proportion of the patients exhibit drug levels outside the therapeutic range at standard doses, and more than 50% of patients do not benefit from standard 5FU therapies [*N Engl J Med 2005;352: 476–87].* Therefore, TDM of 5FU can be used as an effective tool to reduce the occurrence of adverse effects as well as to improve the efficacy of treatment.

To establish a rapid, sensitive, accurate and easy to use method for 5FU monitoring, we generated a clone of anti-5FU McAb which can be used to establish accurate 5FU immunoassay which show close correlation to LC-MS/MS.

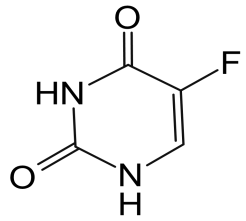

Fig. 1. The chemical structure of 5FU

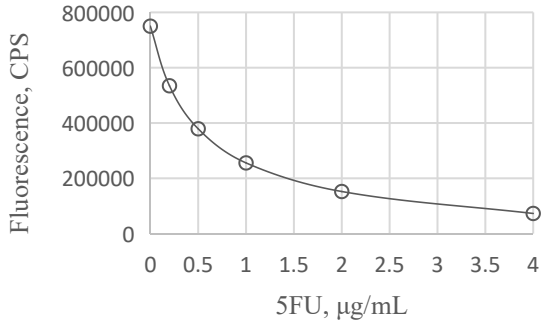

Fig. 2. Typical calibration curve of the 5FU-DELFIA using McAb-17

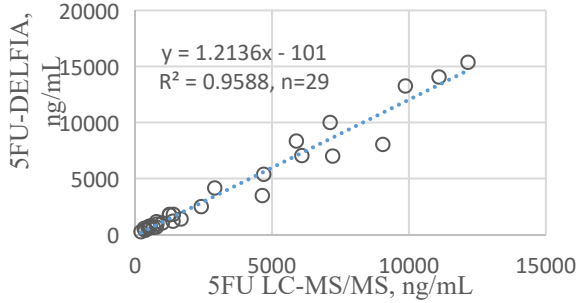

Fig. 3. The correlation of 5FU values obtained by LC-MS/MS and 5FU-DELFIA using McAb-17

Product Type	Catalog #	Description
Mouse monoclonal antibody	• Anti-5FU McAb-17	Used for testing 5FU with LOD < 46ng/mL by DELFIA. The cross-reactivities are < 2.5% for dihydro-5-FU, the main metabolite of 5FU, and <0.6% for tegafur, fluorouridine, uracil, thymine, thymidine, uridine, capecitabine, 5'-deoxy-5-fluorouridine and 5'-deoxy-5-fluorocytidine.
Conjugate	• 5FU-BSA	Paired with anti-5FU antibodies for developing 5FU immunoassay.

Therapeutic drugs monitoring

Paclitaxel (PTX)

Paclitaxel (PTX) is a diterpene alkaloid isolated from Taxus species which shows anti-tumor efficacy by stabilizing microtubules to stop division and proliferation of the tumorous cells. PTX is used to treat multiple types of tumor including stomach, lung, breast, ovary, head and neck, and endometrial cancer. As an active and broad-spectrum natural anti-cancer drug, PTX also shows relatively low toxicity. However, due to the high inter- and intra-patient variability in PTX pharmacokinetics and the close relationship between haematological toxicity and plasma exposure, TDM of PTX can used to achieve the pharmacokinetically guided dose individualization, and based on this, to improve the outcome of patient undergoing chemotherapy of this drug.

Among various techniques for PTX monitoring, immunoassay is well-suited for routine use due to the easy availability of automatic instrumentation, low requirements for sample pretreatment, and cost-effectiveness. Our anti-PTX McAb and its paired conjugate can be used for developing sensitive and accurate PTX immunoassay.

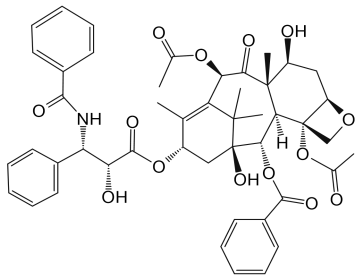

Fig. 1. The chemical structure of PTX

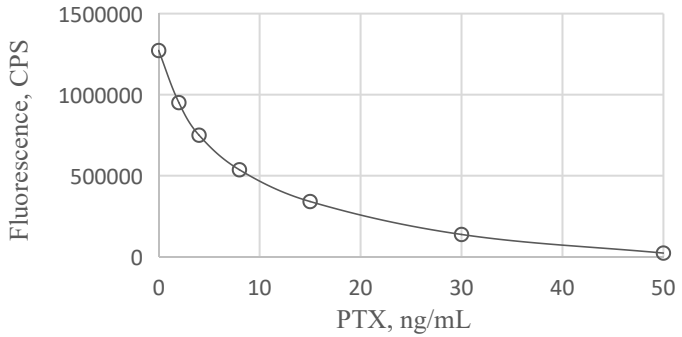

Fig. 2. Typical calibration curve of the PTX-DELFIA using McAb-15

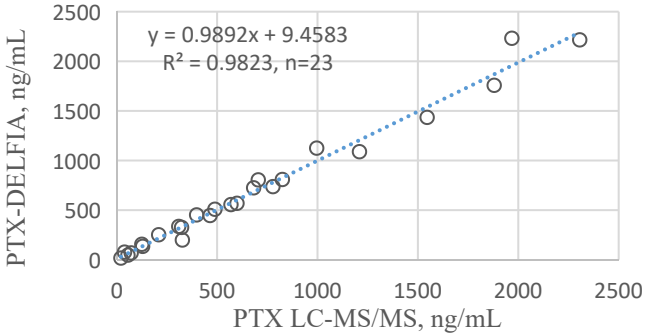

Fig. 3. The correlation between the LC-MS/MS and DELFIA using McAb-15 for analyzing clinical samples.

Product Type	Catalog #	Description
Mouse monoclonal antibody	• Anti-PTX McAb-15	Used for testing PTX with LOD < 0.8ng/mL by DELFIA. The cross-reactivity of McAb-15 is about 16% for 6α-hydroxy-paclitaxel, the main metabolite of PTX, which will introduce 0.16-1.6% of overestimation of PTX. The cross-reactivity is <2.5% for docetaxel and < 0.3% for cephalomannine and baccatin III.
Conjugate	• PTX-PEG-BSA	Paired with anti-PTX antibodies for developing PTX immunoassay.

Therapeutic drugs monitoring

Docetaxel

Docetaxel is a a widely used chemotherapeutic agent for the treatment of several solid cancers, including non-small cell lung cancer, metastatic castration resistant prostate cancer, breast cancer, and head and neck cancer. Because of the large inter-individual variability in the pharmacokinetics of docetaxel, the drug exposure may vary among patients as much as 10-folds if the dosing is based only on the body surface area [*Eur J Cancer. 2004; 40:1170-1178.*]. The unpredictable drug exposure will lead to poor efficacy or severe toxicities such as neutropenia, anemia, diarrhea, asthenia, alopecia, and nausea [*Ann Oncol. 2007; 18:168-172.*]. Up to now, it is still a challenge to apply PK-guided dose management for docetaxel therapy, mainly because of the lack of accurate, easy-to-use and cost-effective analytical tools for monitoring the plasma drug concentrations. Our anti-docetaxel McAb and its paired conjugate can be used for developing sensitive and accurate docetaxel immunoassay.

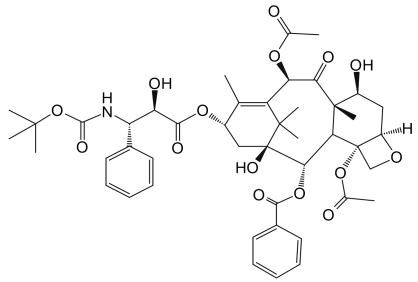

Fig. 1. The chemical structure of docetaxel

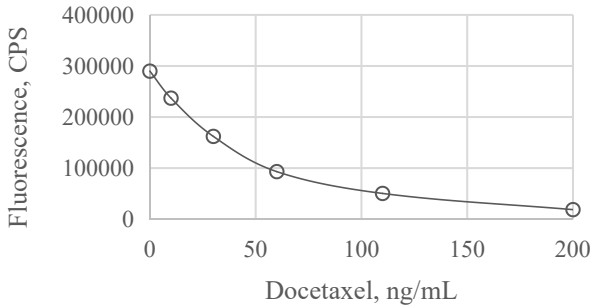

Fig.2. Typical calibration curve of the docetaxel-DELFIA using McAb-7

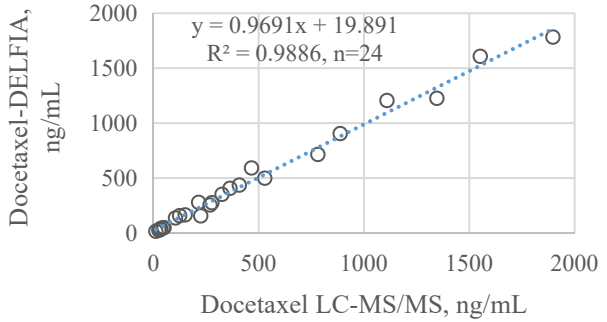

Fig. 3. The correlation between the LC-MS/MS and DELFIA using McAb-7 for analyzing clinical samples.

Product Type	Catalog #	Description
Mouse monoclonal antibody	• Anti-docetaxel McAb-7	Used for testing docetaxel with LOD < 0.16ng/mL by DELFIA. The percentage cross-reactivity is < 3.2% for paclitaxel, and < 0.26% for cephalomannine and baccatin III.
Conjugate	• Docetaxel-PEG-BSA	Paired with anti-docetaxel antibodies for docetaxel testing.

Therapeutic drugs monitoring

Imatinib

Imatinib, a selective tyrosine kinase (TKI) inhibitor, is the first commercial targeted anticancer agent which have transformed the prognosis of chronic myeloid leukemia (CML) with an overall survival rate of 88% at 8 years. Imatinib is regarded as the gold standard of first-line drug for management of CML patients. Prescription of imatinib requires close biological monitoring due to the potential adverse effects, particularly the hepatotoxicity, although it happens only occasionally, but serious. Our anti-Imatinib McAb can be used to develop sensitive and specific immunoassays for accurate imatinib monitoring.

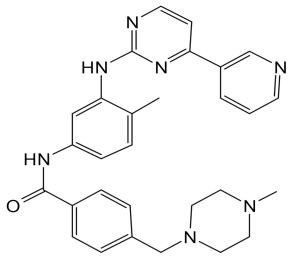

Fig. 1. The chemical structure of imatinib

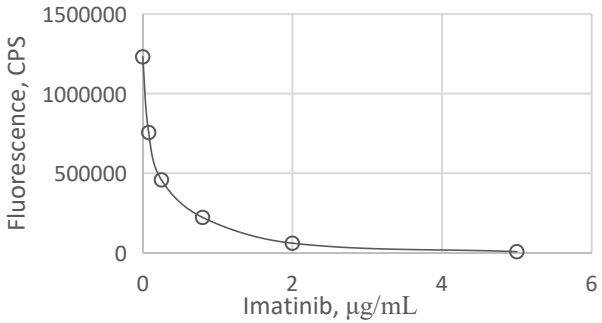

Fig. 2. Typical calibration curve of the imatinib-DELFIA using McAb-28

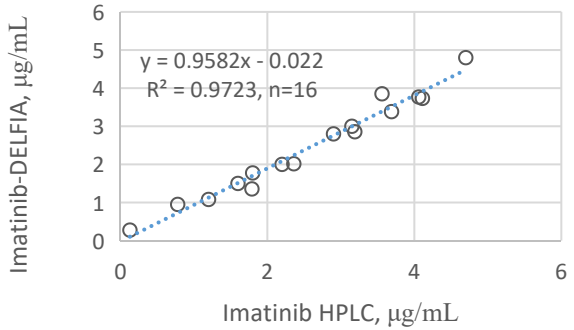

Fig. 3. Comparison of the imatinib concentration obtained by HPLC and DELFIA using McAb-28

Product Type	Catalog #	Description
Mouse monoclonal antibody	• Anti-imatinib McAb-28	Used for testing imatinib with LOD < 0.02µg/mL by DELFIA. Its cross-reactivity is 3.6% with N-desmethyl imatinib, the major metabolite of imatinib.
Conjugate	• Imatinib-BCP	Paired with anti-imatinib antibody for imatinib testing.

Therapeutic drugs monitoring

TDM of Atypical Antipsychotics Drugs

Introduction

Atypical antipsychotics are one class of drugs for treatment of severe mental illness (SMI), specifically schizophrenia and bipolar disorder. This class of drugs mainly includes aripiprazole, clozapine, olanzapine, quetiapine, paliperidone, and risperidone. Atypical antipsychotics are neurologically safer and have a broader spectrum of efficacy than "classical" neuroleptics. Although these second-generation of antipsychotics have common therapeutical features including effectiveness against the negative symptoms of schizophrenia and the advantage of not causing severe extrapyramidal symptoms and hyperprolactinemia, the TDM of patients treated with these drugs is however, very important for avoiding the onset of side and toxic effects due to high plasma levels of the drug caused by overdose or interactions with other drugs, and for improving the patient's compliance, thus leading to higher treatment efficacy.

Bowei-Bio has launched a panel of antibodies and conjugates which can be used for developing immunoassays for accurate monitoring of several main atypical antipsychotics.

Products

Atypical Antipsychotics Drugs	Conjugate	Antibody
Olanzapine	√	√
Clozapine	√	√
Risperidone	√	√
Quetiapine	√	√
Amisulpride	√	

Therapeutic drugs monitoring

Olanzapine (OLZ)

Olanzapine is one of the most commonly used atypical antipsychotic in the world for the treatment of schizophrenia and mania, and for maintenance of bipolar disorders. OLZ levels are linearly correlated with its dose, with ~ 60% bioavailability and ~ 93% protein binding in blood. OLZ exhibits high pharmacokinetic variability mainly because of the clinical and genetic factors. Several non-genetic factors, such as age, gender, smoking, co-medication or disease states, also influence OLZ levels. Under the recommended doses, the plasma OLZ concentration exhibits inter-individual variations of up to 25-folds. Toxicity can be induced when the OLZ level is higher than 100 ng/mL and there is a risk of death when the drug levels reach 160 ng/mL. To ensure therapeutic effectiveness and minimize the side effects, TDM of OLZ is highly recommended for individualizing the dosage for patients with schizophrenia. OLZ monitoring is also helpful in assessing the noncompliance which is a major issue in psychiatric treatment. Currently, LC-MS/MS and HPLC-UV are two major techniques for OLZ monitoring. In order to develop more convenient method for routine OLZ monitoring, we generated a clone of highly specific anti-OLZ McAb which can be used for accurate detection of OLZ by immunoassay.

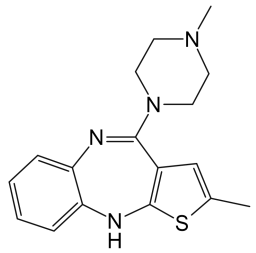

Fig. 1. The chemical structure of OLZ

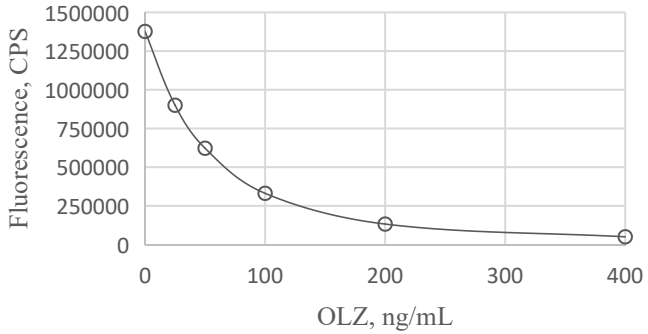

Fig. 2. Typical calibration curve of the OLZ-DELFIA using McAb-22

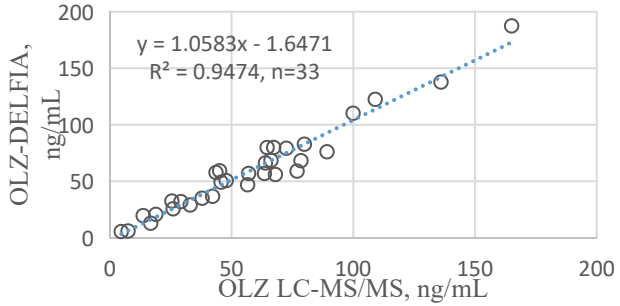

Fig. 3. Correlation between LC-MS/MS and OLZ-DELFIA using McAb-22 for measurement of clinical samples

Product Type	Catalog #	Description
Mouse monoclonal antibody	• Anti-OLZ McAb-22	Used for testing OLZ with LOD < 2ng/mL by DELFIA. The cross-reactivities of DELFIA using McAb-22 is < 3% for N-desmethyl olanzapine, and < 0.5% for olanzapine-10-N-glucuronide, N-desmethyl-2-carboxy olanzapine, olanzapine-10-N-glucuronide and 2-hydroxymethyl olanzapine. The cross-reactivity of McAb-22 with clozapine is about 9%. When OLZ is co-administered with clozapine or used in a replacement treatment, the interference of clozapine on OLZ immunoassay should be considered.
Conjugate	• OLZ-PEG-BSA	Paired with antibody for OLZ testing.

Therapeutic drugs monitoring

Clozapine

Clozapine is the most efficacious antipsychotic drug for treatment of resistant schizophrenia (TRS). It is estimated that as many as 30% of individuals with schizophrenia meet the criteria for TRS, and clozapine is considered valuable in 30–75% of this subgroup. Although the relationship between the therapeutic effect and its blood concentration is well-established, its blood level achieved on a given dose is highly variable because of the large inter-individual variation in pharmacokinetics which is related with genetics, medical conditions, drug-drug interactions, age, and changes in tobacco smoking habit. Monitoring the blood levels of clozapine is important in order to maximize treatment efficacy by alleviating symptoms associated with schizophrenia and minimize adverse effects. Our anti-clozapine McAb and its paired conjugate can be used for developing sensitive clozapine immunoassay for convenient clozapine monitoring.

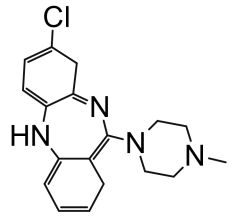

Fig. 1. The chemical structure of Clozapine

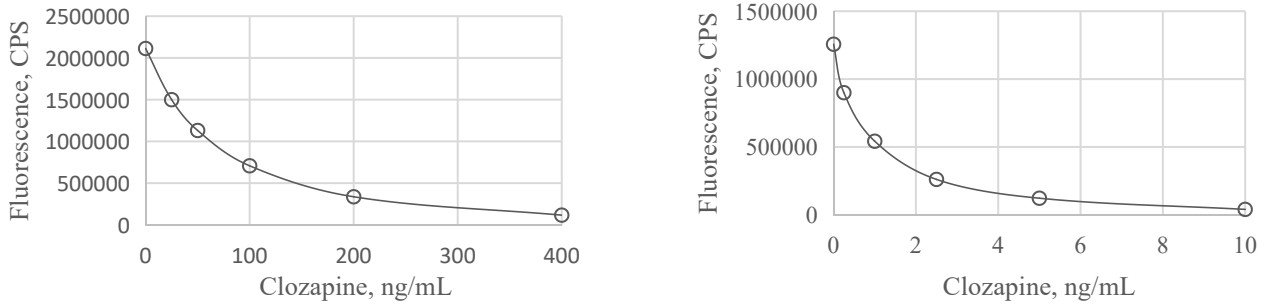

Fig. 2. Typical calibration curve of the clozapine-DELFIA based on the use of McAb-0119 (left) and McAb-12 (right)

Product Type	Catalog #	Description
Mouse monoclonal antibody	• Anti-clozapine McAb-0119	Used for testing clozapine with LOD < 5ng/mL by DELFIA. The cross-reactivity is about 8% with desmethylclozapine, the main metabolites of clozapine, which shows about 7% activity of its parent drug.
Mouse monoclonal antibody	• Anti-clozapine McAb-12	Used for testing clozapine with LOD < 0.1ng/mL by DELFIA. The cross-reactivity is about 2.9% with desmethylclozapine, the main metabolites of clozapine.
Conjugate	• Clozapine-BSA	Paired with antibody for clozapine testing.

Therapeutic drugs monitoring

Risperidone (Risp)

Risperidone (Risp) is a benzisoxazole derivative possessing dopamine D2-receptor and serotonin 5-HT2-receptor antagonist properties. As a second-generation atypical antipsychotic, it is approved for both acute and maintenance treatment of schizophrenia. Risp is metabolized in the liver with the participation of CYP2D6 to an active metabolite – 9-hydroxyrisperidone (9-OH-Risp) and other inactive metabolites. The most common adverse effects of Risp include irreversible extrapyramidal symptoms, neuroleptic malignant syndrome, headache, insomnia, agitation, and weight gain. The therapeutic plasma concentration of total Risp (parent drug plus 9-hydroxyrisperidone) shall be within the range of 20–60 ng/ml. TDM of Risp is useful for managing adverse effects, supporting compliance, ruling out therapeutic failure as a result of low drug exposure. Our anti-Risp-BSA PcAb can be used for developing sensitive immunoassay for convenient quantification of total concentration of Risp and 9-hydroxyrisperidone.

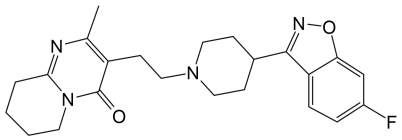

Fig. 1. The chemical structure of Risp

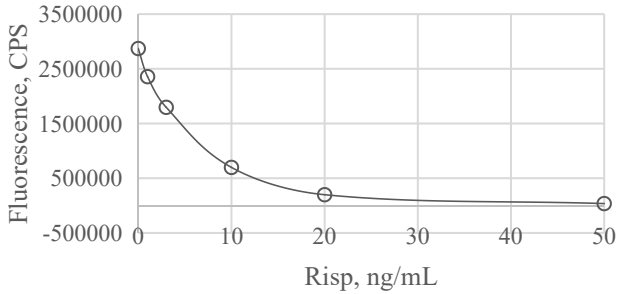

Fig. 2. Typical calibration curve of the Risp-DELFIA using PcAb-4

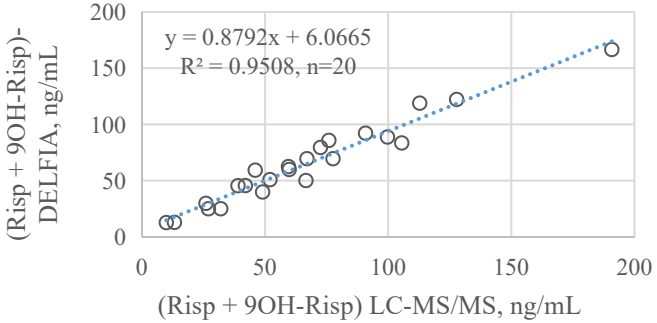

Fig. 3. Correlation between the LC-MS/MS and DELFIA using PcAb-4 for analysis of clinical samples.

Product Type	Catalog #	Description
Rabbit polyclonal antibody	• Anti-Risp-BSA PcAb-4	LOD < 0.1ng/mL by DELFIA using PcAb-4. The cross-reactivities of DELFIA using PcAb-4 is about 97.6% for 9-hydroxyrisperidone (9OH-Risp).
Conjugate	• Risp-PEG-OVA	Paired with antibody for Risp testing.

Therapeutic drugs monitoring

Quetiapine (QTP)

Quetiapine is a dibenzothiazepine derivative used in clinic as a second-generation antipsychotic. It is one of the most frequently prescribed antipsychotics not only for schizophrenia and bipolar disorders, but also in off-label-use for other psychiatric disorders. The antidepressant and mood-stabilizing properties of QTP are correlated with the concentration of the parent drug and its principal circulating metabolite, norquetiapine. Overdose of quetiapine can lead to coma, respiratory insufficiency and severe hypotension. Due to its sharp increase of use over the past 20 years, acute intoxications is very often, some of which have fatal outcomes. TDM is particularly useful in avoiding toxicity caused by high doses of QTP, improving pharmacotherapy, and allowing to better explain individual variability in drug response. Our anti-QTP PcAb can be used for developing sensitive immunoassay for detection of QTP and its metabolite norquetiapine. Monoclonal antibody designed for the specific detection of quetiapine is now in development.

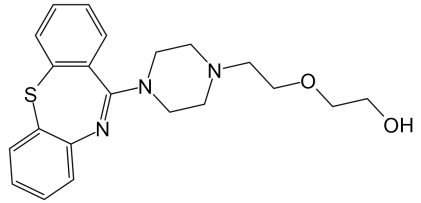

Fig. 1. The chemical structure of QTP

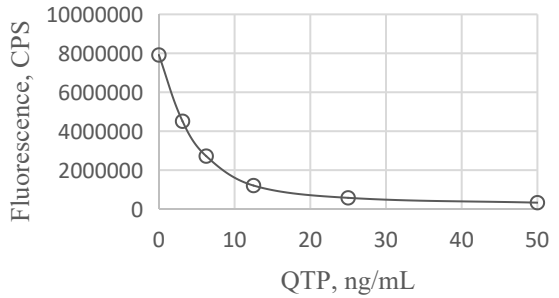

Fig. 2. Typical calibration curve of the QTP-DELFIA using PcAb-3

Product Type	Catalog #	Description
Rabbit polyclonal antibody	• Anti-QTP-BSA PcAb-1	LOD is < 0.1ng/mL by DELFIA. The cross-reactivities of DELFIA using PcAb-1 is about 53.6% for norquetiapine, and < 2.5% for Quetiapine sulfoxide and 7-hydroxyquetiapine.
Conjugate	• QTP-PEG-Biotin	Paired with anti-QTP antibody for QTP testing.

Therapeutic drugs monitoring

Antihypertensive and Anti-cardiovascular Drugs

Introduction

Hypertension affects more than 1.65 billion people worldwide, and is associated with increased risk of cardiovascular disease events (e.g. coronary heart disease, heart failure and stroke) and death**.** Antihypertensive treatment has proved effective in reduction of these risks. Nevertheless, pharmacological therapy are usually not effective in reaching target blood pressure values, and poor adherence has proven to be a main cause of the treatment failure, which is often associated to severe outcomes including myocardial infarction, chronic heart failure, stroke, end-stage renal disease, and overall mortality. Assessment of nonadherence is important to improve the clinical outcomes, and reduce disease burden and costs. TDM is a reliable and cost-effective choice among different methods for assessment of therapeutic adherence.

Bowei-Bio has developed a group of antibodies and conjugates designed for immunoassay-based detection of multiple cardiac disease related drugs, which we hope will offer a more rapid and cost-effective alternative to HPLC and LC-MS, for support of clinical cardiac disease management.

Products

Antihypertensive and Anti-cardiovascular Drugs	Conjugate	Antibody
Empagliflozin	√	√
Amlodipine	√	√
Enalaprilat	√	√
Digoxin	√	√

Therapeutic drugs monitoring

Empagliflozin (EMPA)

Empagliflozin (EMPA) is a potent and selective inhibitor of sodium glucose cotransporter 2 (SGLT-2) used for the treatment of type-2 diabetes. Inhibition of SGLT2 leads to reduced renal glucose reabsorption, increased urinary glucose excretion and decreased serum glucose. EMPA plays an important role in the management of cardiovascular and kidney complications in patients with type-2 diabetes. For patients with HFpEF (heart failure with preserved ejection fraction), EMPA is effective to reduce cardiovascular death and heart failure hospitalization as well as to protect kidneys and improve quality of life. It is important to keep plasma levels of EMPA within the therapeutic range to ensure drug efficacy and safety, since insufficient EMPA levels can lead to hyperglycemia, increasing the risk of diabetic complications, while excessive levels can cause hypoglycemia, potentially leading to a coma [*Heart Fail Rev. 2021; 26(3):603-622; Diabetes Ther. 2020; 11(11):2521-2538*]. Our monoclonal anti-EMPA McAbs can be used to establish highly sensitive and specific EMPA immunoassay. The high sensitivity of EMPA immunoassay makes it possible to use saliva as sample with the merits of non-invasive collection, prompt availability, and potential accessibility in out-of-clinic settings, which will effectively improve therapeutic adherence.

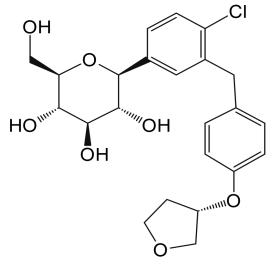

Fig. 1. The chemical structure of EMPA

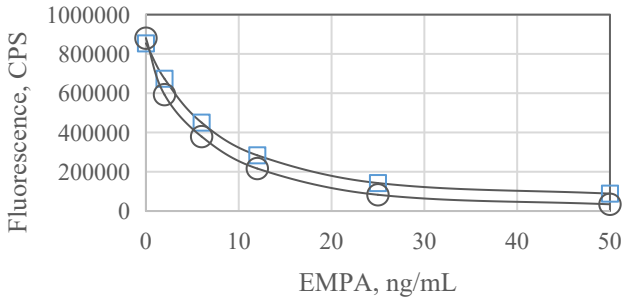

Fig.2. Typical calibration curve of EMPA-DELFIA using McAb-3 (Square) and McAb-40 (Circle)

Product Type	Catalog #	Description
Mouse monoclonal antibody	• Anti-EMPA McAb-3	Used for testing EMPA with LOD < 1.1ng/mL by DELFIA. No cross-reaction was detected with dapagliflozin, canagliflozin, and ertugliflozin at 10μg/mL in McAb-3 based DELFIA.
Mouse monoclonal antibody	• Anti-EMPA McAb-40	Used for testing EMPA with LOD < 0.35ng/mL by DELFIA. No cross-reaction was detected with dapagliflozin, canagliflozin, and ertugliflozin at 10μg/mL in McAb-40 based DELFIA.
Conjugate	• EMPA-BSA	Paired with anti-EMPA antibodies for EMPA testing.

Therapeutic drugs monitoring

Amlodipine

Amlodipine is a calcium channel antagonist of the dihydropyridine group. It is effective for treating hypertension, chronic stable angina, and vasospastic angina. It acts by exhibiting potent peripheral and coronary artery vasodilation, and shows high vascular selectivity, and little or no effect on cardiac conduction or contractility. The recommended dosages for amlodipine are based on clinical trials in which doses are increased until the desired effect is achieved or until unacceptable side effects (such as peripheral edema) appear. TDM of amlodipine is helpful for dose adjustment to minimize adverse effects and achieve satisfactory blood pressure control in hypertensive patients. Also, timely monitoring of amlodipine can assist to identify nonadherence to antihypertensive medications which may lead to several adverse outcomes. Our monoclonal anti-amlodipine McAb can be used to establish ultrasensitive immunoassay for amlodipine determination; the outstanding analytical sensitivity also makes it possible to use saliva or dried blood spot as samples for amlodipine monitoring.

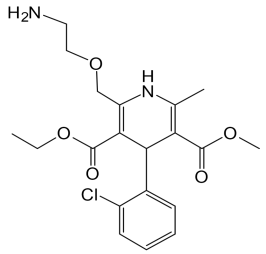

Fig. 1. The chemical structure of amlodipine

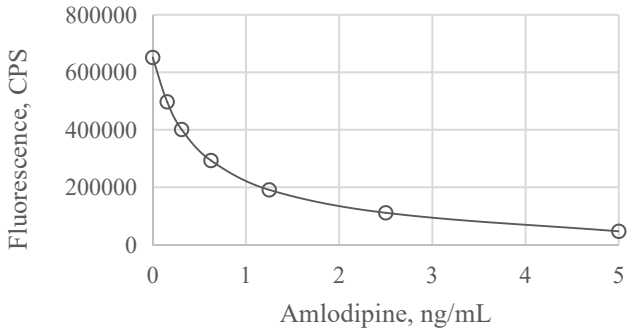

Fig.2. Typical calibration curve of the amlodipine-DELFIA based on the use of McAb-8

Product Type	Catalog #	Description
Mouse monoclonal antibody	• Anti-amlodipine McAb-8	Used for testing amlodipine with LOD < 0.05ng/mL by DELFIA.
Conjugate	• Amlodipine-BSA	Paired with antibodies for amlodipine testing.

Therapeutic drugs monitoring

Enalaprilat

Enalapril is an angiotensin-converting enzyme inhibitor (ACEI) widely used as an antihypertensive drug for treatment of arterial hypertension and chronic heart failure. Although some new antihypertensive drugs have been developed and are entering clinical practice, enalapril remains the critical drug for the therapy of chronic heart failure. Enalaprilat has a strong anti-hypotensive effect, due to its ability to inhibit the angiotensin-converting enzyme (ACE). The severity and duration of the anti-hypotensive effect of enalapril is largely determined by the rate of its hydrolysis to enalaprilat which varies significantly in patients, largely associated with activity of the CES1 enzyme. Under standard dose, the blood levels of enalaprilat may not reach the therapeutic range or, to the contrary, is higher, because of the gene polymorphism of CES1 and other genes, drug interactions and other factors. TDM of enalaprilat is helpful for improving clinical outcome by rational choice of therapy as well as for assessment of medication adherence. Our monoclonal anti-enalaprilat McAb can be used to establish highly sensitive and specific immunoassay for enalaprilat determination.

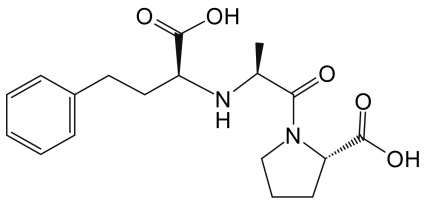

Fig. 1. The chemical structure of enalaprilat

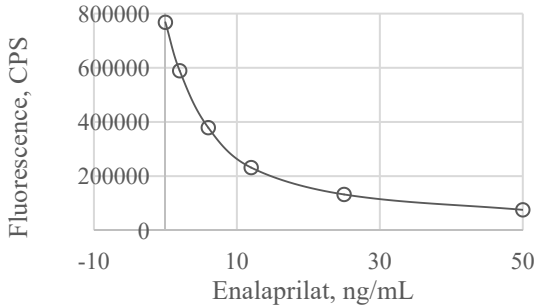

Fig.2. Typical calibration curve of enalaprilat-DELFIA using McAb-26

Product Type	Catalog #	Description
Mouse monoclonal antibody	• Anti-Enalaprilat McAb-26	Used for testing enalaprilat with LOD < 0.6ng/mL by DELFIA. The percentage cross-reactivity is < 0.46% with enalapril; no cross-reaction was detected with proline, phenylalanine, alanine-proline, and captopril up to 10ug/mL.
Conjugate	• Enalaprilat-BSA	Paired with antibodies for enalaprilat testing.

Therapeutic drugs monitoring

Digoxin

Digoxin is used to slow atrioventricular conduction, and is indicated for the treatment of supraventricular arrhythmias, such as atrioventricular reciprocating tachycardia and atrioventricular nodal reentrant tachycardia. The recommended therapeutic plasma concentrations of digoxin has traditionally been established between 0.8 to 2.0 ng/mL, more recently some studies have proposed to prudentially set this range to 0.5–0.9 ng/mL [*Eur. J. Heart Fail. 2016, 18, 1072–1081*]. Owing to the high potency, narrow therapeutic range, and the multiple pharmacokinetic interaction of digoxin with co-administered drugs, TDM is of utmost importance for accurate use of this valuable but potentially dangerous drug. Although a series of LC-MS/MS methods have been developed to quantify digoxin, but over the past several decades, immunoassay is always the major method of choice for digoxin monitoring in clinical laboratories. Our monoclonal anti-digoxin McAb can be used to establish highly sensitive digoxin immunoassay with results closely correlated with that obtained by ABBOTT-CLIA.

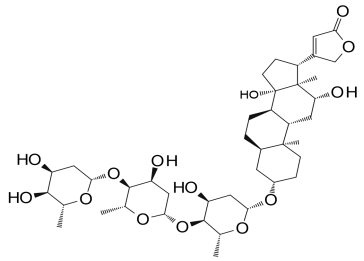

Fig. 1. The chemical structure of digoxin

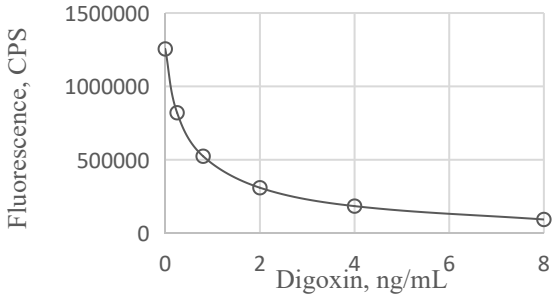

Fig. 2. Typical calibration curve of digoxin-DELFIA using McAb-2A4

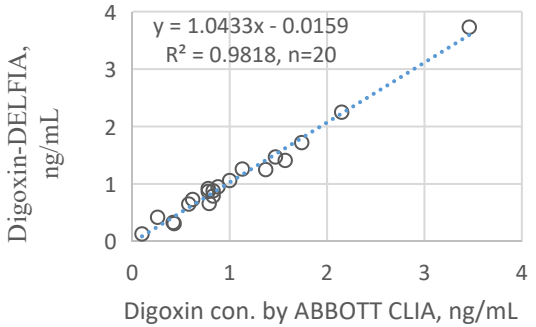

Fig. 3. The agreement between digoxin concentration determined by ABBOTT-CLIA and the DELFIA using McAb-2A4

Product Type	Catalog #	Description
Mouse monoclonal antibody	• Anti-Digoxin McAb-2A4	Used for testing digoxin with LOD < 0.1ng/mL by DELFIA. The key performances of the digoxin-DELFIA based on the use of McAb-2A4 are given in Fig. 2 and 3.
Conjugate	• Digoxin-BSA	Paired with anti-digoxin antibodies for digoxin testing.

Therapeutic drugs monitoring

TDM of Anti-IBD Drugs

Introduction

Inflammatory bowel disease (IBD), including Crohn's disease and ulcerative colitis, is characterized by chronic relapsing intestinal inflammation. The etiology of IBD involves a complex interaction between the genetic, environmental or microbial factors and the immune responses. IBD has become a worldwide health-care problem with a continually increasing incidence. Tumor necrosis factor (TNF)-α inhibitors and thiopurines are among the most important classes of medications utilized in the clinical management of IBDs. However, a significant proportion of patients loses response to these agents, or develops adverse effects during the course of the treatment. Monitoring of the drug, anti-drug antibodies (for TNF-α inhibitors) and metabolite levels (for thiopurines) can provide valuable insight into the possible etiology of unfavorable outcomes and formulate individualized treatment plans for patients accordingly.

Bowei-Bio has generated several conjugates and McAbs for monitoring of IBD medications, and will continuously expand the product portfolio to support the clinical management of IBD.

Products

Anti-IBD Drugs	Conjugate	Antibody
Infliximab (IFX)	√	√
Adalimumab (ADA)	√	√
Methotrexate (MTX)	√	√
6-methylmercaptopurine (6-MMP)	√	√
6-Thioguanine (6-TGN)	√	

Therapeutic drugs monitoring

Infliximab (IFX)

Infliximab (IFX) is a chimeric human-murine monoclonal antibody specific for human tumor necrosis factor (TNF-α) that is approved for reducing symptoms and for induction and maintenance of remission in patients with Crohn's disease (CD), ulcerative colitis (UC), and pediatric CD or UC refractory to conventional therapy. Other approved indications for IFX include rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis, and plaque psoriasis. Measurement of IFX concentrations in human blood has been utilized for optimizing IFX dosing and in managing inflammatory bowel disease (IBD) activity and aid in the management of both UC and CD. In addition, long-term IFX treatment can induce the formation of anti-drug antibody (ADA) that is associated with lower drug levels and clinical nonresponse. The detection of ADA is useful to determine the cause of nonresponse, helping to determine the kind of therapy switch. Our monoclonal anti-IFX McAb can be used to establish sensitive and specific immunoassay for determination of both the IFX and anti-IFX antibodies.

Product Type	Catalog #	Description
Mouse monoclonal antibody	• Anti-IFX McAb-22	When used for testing IFX, LOD <100ng/mL was obtained by competitive DELFIA with infliximab coated microwells. No cross-reaction with human IgG up to 10mg/mL.
Biopharmaceutical	• Infliximab	Paired with Anti-IFX McAb-22 for testing IFX or anti-IFX antibody by different formats of immunoassay.

Therapeutic drugs monitoring

Adalimumab (ADL)

Adalimumab (ADL) is a recombinant fully-human IgG1 monoclonal antibody specific for human TNF-α. ADL was created using phage display technology resulting in an antibody with human derived heavy and light chain variable regions and human IgG1:k constant regions. ADL is approved for reducing signs and symptoms, and induction and maintenance of remission in patients with CD and UC. Other approved indications for ADL include rheumatoid arthritis, juvenile rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis, plaque psoriasis, hidradenitis suppurativa, and intermediate, posterior, and panuveitis. ADL is effective in reducing disease activity, and offer significant benefits in quality of life and may have the potential to change the progression of the disease when given early. However, a large percentage of patients fail to respond to ADL therapy, or gradually lose the response over time, and require either drug dose-escalation or switch to an alternative agent in order to maintain response. There are complex reasons for loss of response to ADL treatment, one of the main causes of it is decreased drug levels due to the development of anti-ADL antibodies. Therefore, accurate monitoring of serum ADL and anti-ADL antibody levels is an important part of therapy for patients being treated with ADL. Our monoclonal anti-ADL McAb can be used to establish sensitive and specific immunoassay for determination of both the ADL and anti-ADL antibodies.

Product Type	Catalog #	Description
Mouse monoclonal antibody	• Anti- ADL McAb-33	McAb-33 can be used to establish competitive ADL-immunoassay, and also can be paired with itself to develop sandwich immunoassay for ADL quantification. LOD <50ng/mL can be obtained by both competitive and sandwich DELFIA. No cross-reaction with human IgG up to 10mg/mL. Competitive format is recommended as the first choice for its lack of “hook” phenomenon.
Biopharmaceutical	• Adalimumab	Paired with anti-ADL McAb for testing ADL or anti-ADL antibodies by different formats of immunoassay.

Bowei-biotech
for better bioassays

Therapeutic drugs monitoring

Methotrexate (MTX)

Methotrexate (MTX) is widely used to treat various kinds of oncologic and non-oncologic diseases. Although it can be administered over a wide range of dose, serious adverse effects may occur when high-dose MTX therapy is applied for management of acute lymphoblastic leukemia, lymphoma, breast cancer, and osteosarcoma. In such cases, drug monitoring is essential for its toxicity assessment and the subsequent leucovorin rescue. Immunoassay provides a useful tool for accurate and convenient MTX determination. Our anti-MTX McAb can be used to develop sensitive and specific immunoassays for accurate MTX monitoring.

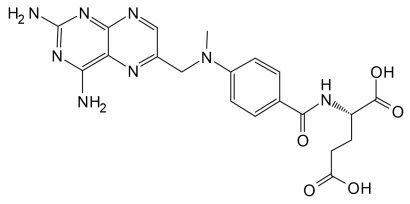

Fig. 1. The chemical structure of MTX

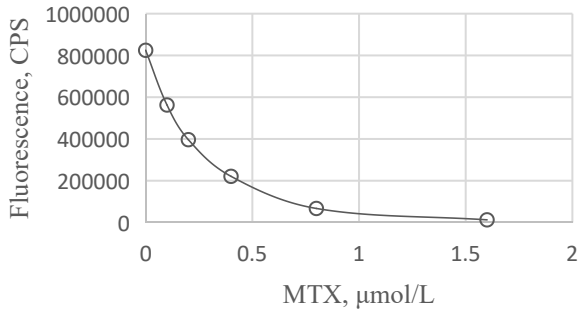

Fig. 2. Typical calibration curve of the MTX-DELFIA using McAb-6SQ

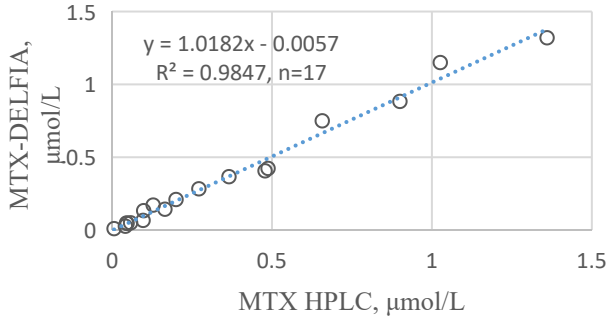

Fig. 3. Comparison of HPLC and MTX-DELFIA using McAb-6SQ on measurement of clinical samples

Product Type	Catalog #	Description
Mouse monoclonal antibody	• Anti-MTX McAb-6SQ	Used for developing MTX immunoassay with excellent correlation with HPLC measurement. LOD was 0.02µmoL/L by DELFIA. The cross-reactivities with was < 1.6% for 7-Hydroxymethotrexate, <0.1% for folate, 5MTHFA and folinic acid.
Conjugate	• MTX-BSA	Paired with anti-MTX antibody for MTX testing.