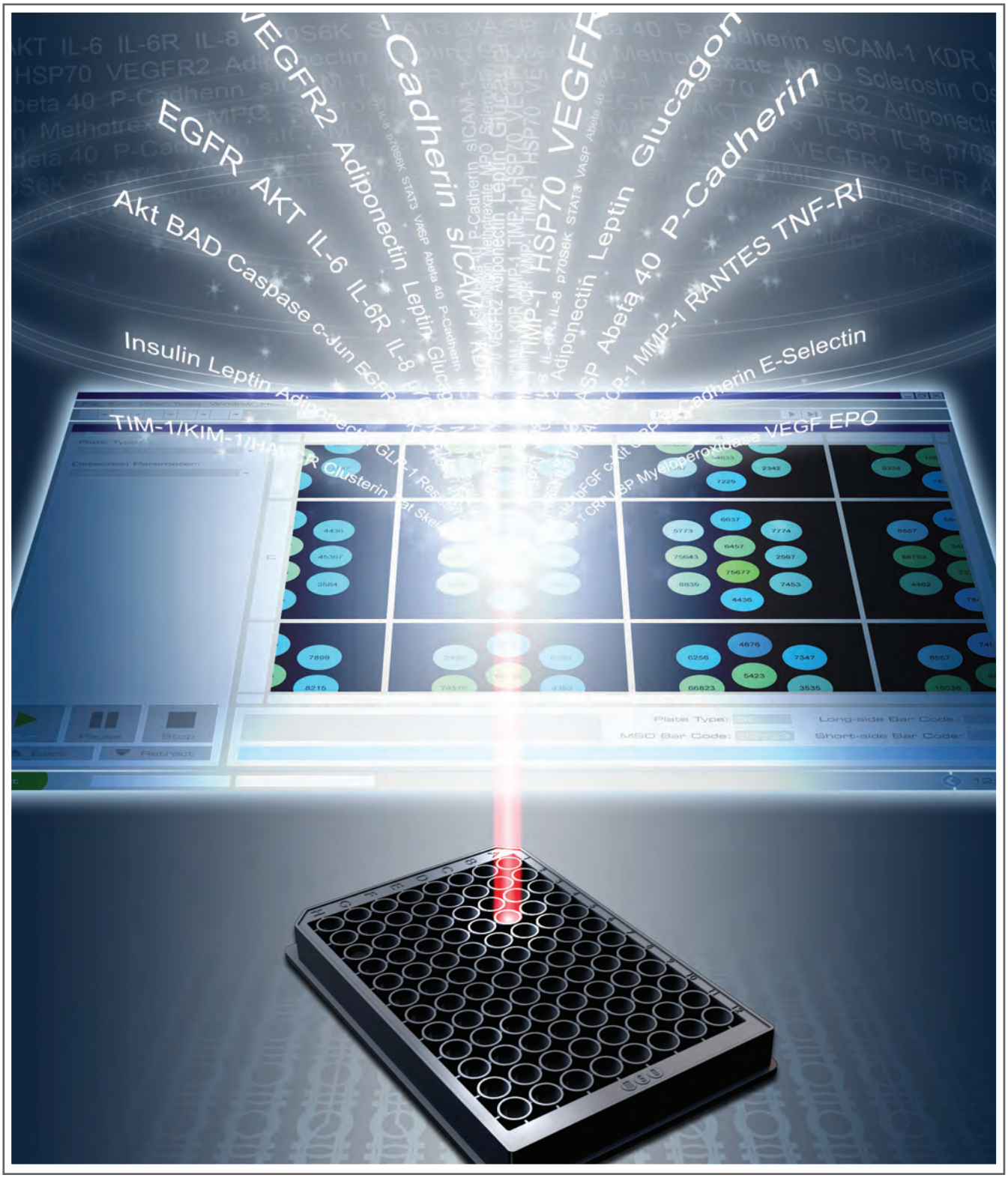
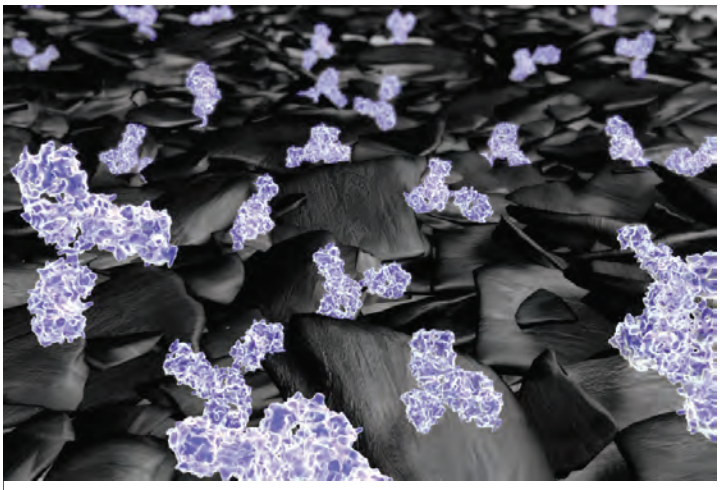
MSD® TECHNOLOGY PLATFORM



MESO SCALE DISCOVERY® (MSD) Technology

MESO SCALE DISCOVERY's MULTI-ARRAY® technology enables the detection of biomarkers in single and multiplex formats utilizing the next generation of electrochemiluminescence detection. The combination of electrochemiluminescence and patterned arrays bring speed and high density of information to research through miniaturization, organization, and parallel processing of biological assays. The MSD product line includes a diverse menu of single and multiplex assay kits for profiling biomarkers, cell signaling pathways, and other applications, as well as a suite of plates and reagents for assay development.



Antibodies on a carbon surface

MESO SCALE DISCOVERY
A division of Meso Scale Diagnostics, LLC.

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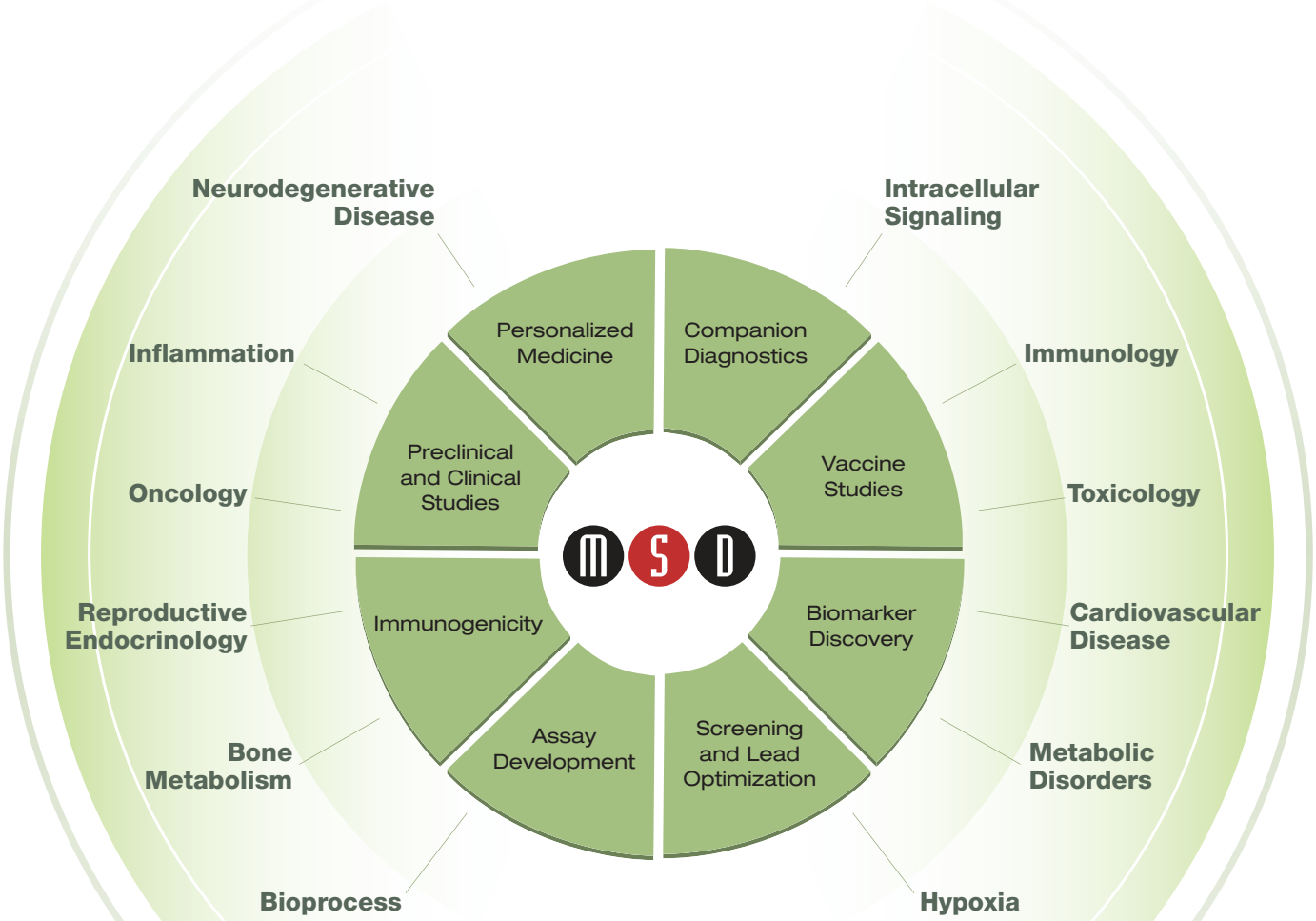
Rockville, MD 20850 USA
Phone: 1.240.314.2795
Fax: 1.301.990.2776
Email: customerservice@mesoscale.com
www.mesoscale.com

Spot the Difference

Company Overview

MESO SCALE DISCOVERY offers a unique, multiplexed immunoassay platform for the quantification of proteins in biological samples. With over 400 convenient assay kits and assay customization capabilities, MSD has enabled scientists to make accurate and precise determinations of levels of cytokines, phosphoproteins, and other biomarkers in different matrices. High quality data can be obtained in less time on the MSD platform with minimal effort and low cost. MSD's MULTI-ARRAY technology has been adopted by major pharmaceutical companies, clinical research organizations, biotech companies, personalized medicine companies, and academic and government institutions.

The graphic below illustrates the broad spectrum of applications of the MSD technology.



The benefits of MULTI-ARRAY technology are well recognized. Here are just a few peer-reviewed publications highlighting some of the advantages of the platform.

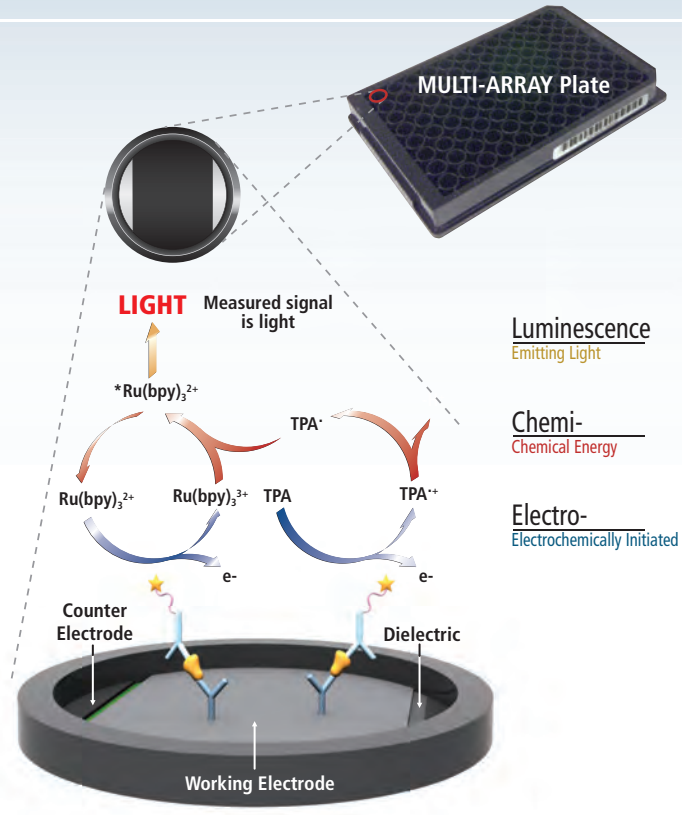
- ***high inter-laboratory reproducibility, low matrix effects and high reliability*** (Fichorova, R.N., et al. Anal Chem. 2008 80(12): 4741-51.)[1]
- ***reproducibility and cost-effectiveness over Western blot*** (Gowan, S.M., et al. Assay and Drug Dev Technol. 2007 5(3): 391-401.)[2]
- ***novel sandwich assay that provides sensitivity, accuracy, reproducibility and absolute quantification*** (Cao, L., et al. Cancer Research. 2008 68: 8039-8048.)[3]
- ***most suitable to detect low affinity anti-drug antibodies*** (Liang, M., et al. Assay and Drug Dev Technol. 2007 5(5): 1-8.)[4]

MSD Technology

MSD's electrochemiluminescence detection technology uses SULFO-TAG™ labels, which emit light upon electrochemical stimulation initiated at the electrode surfaces of MULTI-ARRAY and MULTI-SPOT® microplates.

Electrochemiluminescence Features:

- Minimal background signals and high signal to background ratios - the stimulation mechanism (electricity) is decoupled from the signal (light)
- Proximity - only labels bound near the electrode surface are detected, enabling non-washed assays
- Flexibility - labels are stable, non-radioactive, and conveniently conjugated to biological molecules
- Emission at ~620 nm - eliminates problems with color quenching
- Signal amplification - multiple excitation cycles of each label enhance light levels and improve sensitivity
- Flexible surface coatings to suit most any biology
- Carbon electrode plate surface has 10X greater binding capacity than polystyrene
- Custom surface coatings and patterns



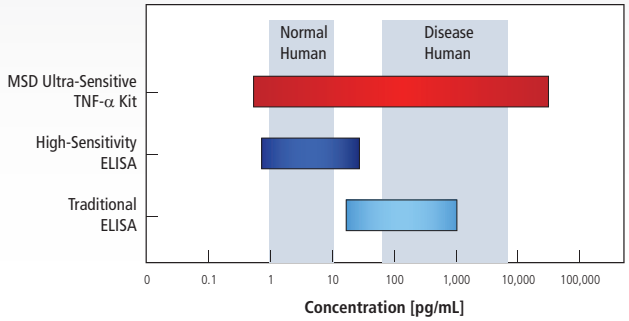
MULTI-ARRAY and MULTI-SPOT Features:

- Capability to simultaneously measure multiple analytes in the same well
- High density arrays for high throughput multiplexing of biomarkers
- The unique bar code label on each plate enables complete traceability back to MSD manufacturing records
- The MSD DISCOVERY WORKBENCH® software provides customers with a powerful tool for data analysis

MSD - SPOT THE DIFFERENCE®

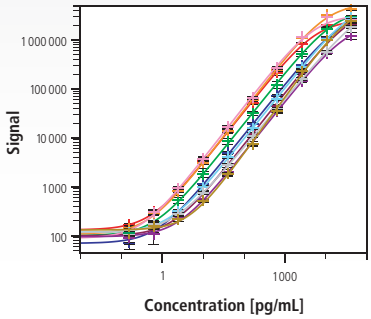
MESO SCALE DISCOVERY's unique spot patterns are the hallmark of its MULTI-ARRAY technology for the detection of biomarkers in single and multiplex formats. MSD offers an innovative platform for immunoassays that have ultra-low detection limits, provide up to five logs of linear dynamic range, use minimal sample, and handle difficult matrices easily. Combined, these advantages enable the measurement of native levels of biomarkers in normal and diseased samples without multiple dilutions. MSD's simple protocols and streamlined assay formats from MSD reduce workflow without compromising quality. The result is an increase in productivity while eliminating unnecessary costs.

Rapid, Robust, Reproducible



- Large dynamic range
- High sensitivity
- High precision
- Low background
- Conserves sample volume
- Simple protocols
- Reduces matrix effects
- Eliminates multiple dilutions

Multiplexing



- Multiple analytes in one well
- No compromise in performance or speed
- Catalog assay panels for rapid delivery
- Custom panels available

Assay Solutions and Services

- Over 300 single analyte kits
- Over 200 multiple analyte kits
- Customized multiplexed kits
- ELISA conversion packs
- QUICKPLEX® packs
- Prototype Printing Services
- Complimentary on-site scientific support
- Contract assay development

SECTOR® Instruments

- Ultra-fast read time
- No fluidics
- No user calibration required
- Reliable measurements
- Integrated data analysis tool
- Comprehensive validation packages
- Software support for 21 CFR Part 11 compliance
- Comprehensive service plans

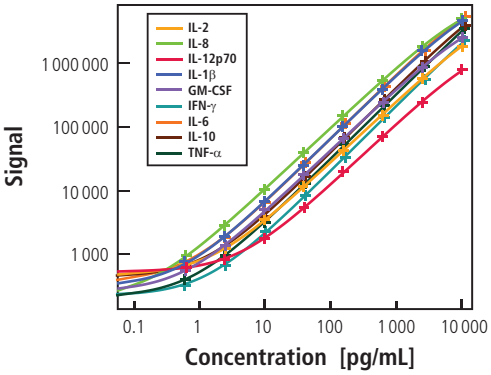
Measurement of Biomarkers in Complex Samples

Clinical samples push the limits of traditional methods for immunoassays (e.g. ELISA, RIA). Complex matrices (e.g. sputum, vaginal fluids, etc.), widely ranging concentations of analytes, and limited sample volume can make assays intractable. MSD's assays improve sensitivity, expand the dynamic range, enable measurement of multiple analytes from a single sample (i.e. multiplexing), and work well in difficult sample types. The MSD platform has also proven to be well-suited for use in regulated work environments with available packages for IQ/OQ/PQ validation and software designed to support 21 CFR Part 11 and GLP compliance. Visit www.mesoscale.com for a complete list of assays and reagents.

Catalog Numbers for Human ProInflammatory 9-Plex Ultra-Sensitive Kit

	Kit Size	Catalog Numbers
Human	1 Plate	K15007C-1
	5 Plate	K15007C-2
	25 Plate	K15007C-4

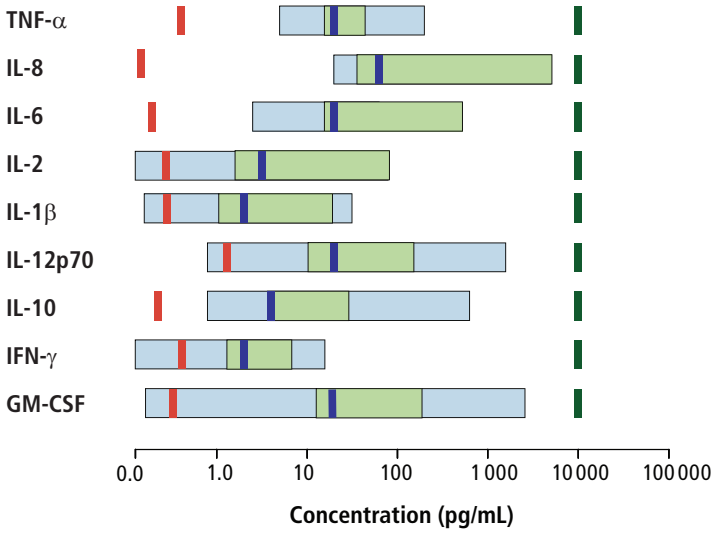
Representative Data from Clinical Samples using MSD Human ProInflammatory 9-Plex

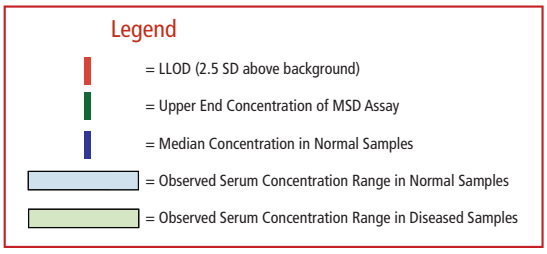


- **Wide dynamic range enables biomarker measurement in controls and diseased samples with minimal dilution**
- **Highly adaptable assays allow quantification of analytes in complex sample matrices**
- **High sensitivity and multiplexing capability facilitate analysis of several biomarkers in a single sample**

	Analyte								
Analyte	IL-2	IL-8	IL-12p70	IL-1β	GM-CSF	IFN-γ	IL-6	IL-10	TNF-α
LLOD (pg/mL)	0.35	0.090	1.4	0.36	0.34	0.53	0.27	0.21	0.50

LLOD (Lower Limit of Detection) is defined as 2.5 SD above the background.





In the above study*, the MSD Human ProInflammatory 9-plex Ultra-Sensitive Assay was used to analyze a total of 127 human sera samples, which included diseased pools and controls. The upper end of the calibrator curve for this panel was 10000 pg/mL for all cytokines and the lower limit of detection (LLOD) was determined as 2.5 standard deviations above the background.

* The Biomarker Reference Set for Cancers in Women (BRSCW) was provided by the National Cancer Institute on behalf of the Early Detection Research Network (EDRN).

Assessment of Toxic Effects

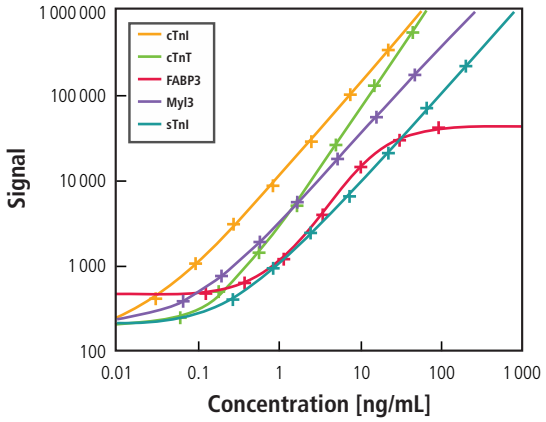
In toxicity studies, compound or disease-induced changes are typically evaluated using a combination of histochemical endpoints and a number of potential biomarkers, each of which can indicate toxic change in tissues and organs. The best biomarkers are specific to particular organs or tissue types. Toxicologists require an assay system with consistent performance, high sensitivity, and large dynamic range. MSD technology provides all of these characteristics plus multiplexing to save time and precious samples. Featured here is the MSD Muscle Injury Panel I (rat) which measures cardiac Troponin I, skeletal Troponin I, cardiac Troponin T, FABP3, and Myl3.

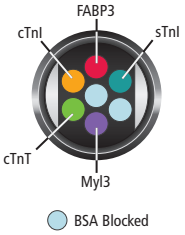
For more detail on these and other relevant markers please see our Toxicology Brochure online at www.mesoscale.com.

Catalog Numbers for Muscle Injury Panel 1 (rat)

	Kit Size	Catalog Numbers
Rat	1 Plate	K15181C-1
	5 Plate	K15181C-2
	25 Plate	K15181C-4

Muscle Injury Panel 1 (rat)



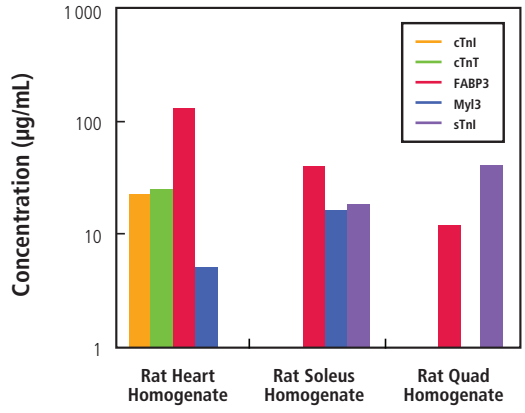


	Analyte				
	cTnI	cTnT	FABP3	Myl3	sTnI
LLOD (ng/mL)	0.0040	0.017	0.16	0.015	0.047

LLOD (Lower Limit of Detection) is defined as 2.5 SD above the background.

MSD has developed assays to rapidly screen for biomarkers of drug-induced toxicity in conjunction with the Critical Path Initiative (C-Path) and Health and Environmental Sciences (HESI) consortia.

Specificity



- **MSD assays for cardiac markers are positive for cardiac homogenates and negative for others, whereas skeletal marker assays are positive for skeletal muscle only**

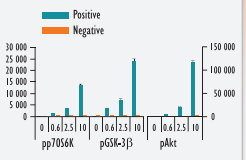
MSD offers robust assays for markers of kidney injury, cardiotoxicity, and acute phase inflammatory response. Please visit www.mesoscale.com for a comprehensive list of toxicology assay kits.

Rapid Quantification of Phosphoproteins

MSD

Simple and fast

In less than **4.5 hours,** up to 960 quantitative data points can be generated and analyzed.



Quantitative Result

- reduce cost and time
- gain sensitivity
- reduce cell culture volume
- analyze wide range of matrices
- conserve precious samples
- gain with MSD multiplexing
- gain in throughput

Sample Preparation
Lysate preparation in 96-well plate and direct transfer to MSD plate

- Multiple phosphoproteins as well as total pools can be accurately quantified in a single well from as few as 1000 cells
- % Phosphorylation of protein can also be calculated

Western Blot

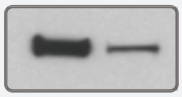
Laborious and time consuming

Sample Preparation

Gel Electrophoresis
6 gels ~ equivalent to one 96-well plate

Blotting and transfer to membrane

With Western blot, more than **10 hours, and up to 2 days** may be required to analyze 10-fold less data.



Non-quantitative Result

- Need expensive imaging system for semi-quantitative analysis
- Low throughput: stripping and reprobing are an inaccurate and undesirable approach for multiplexing

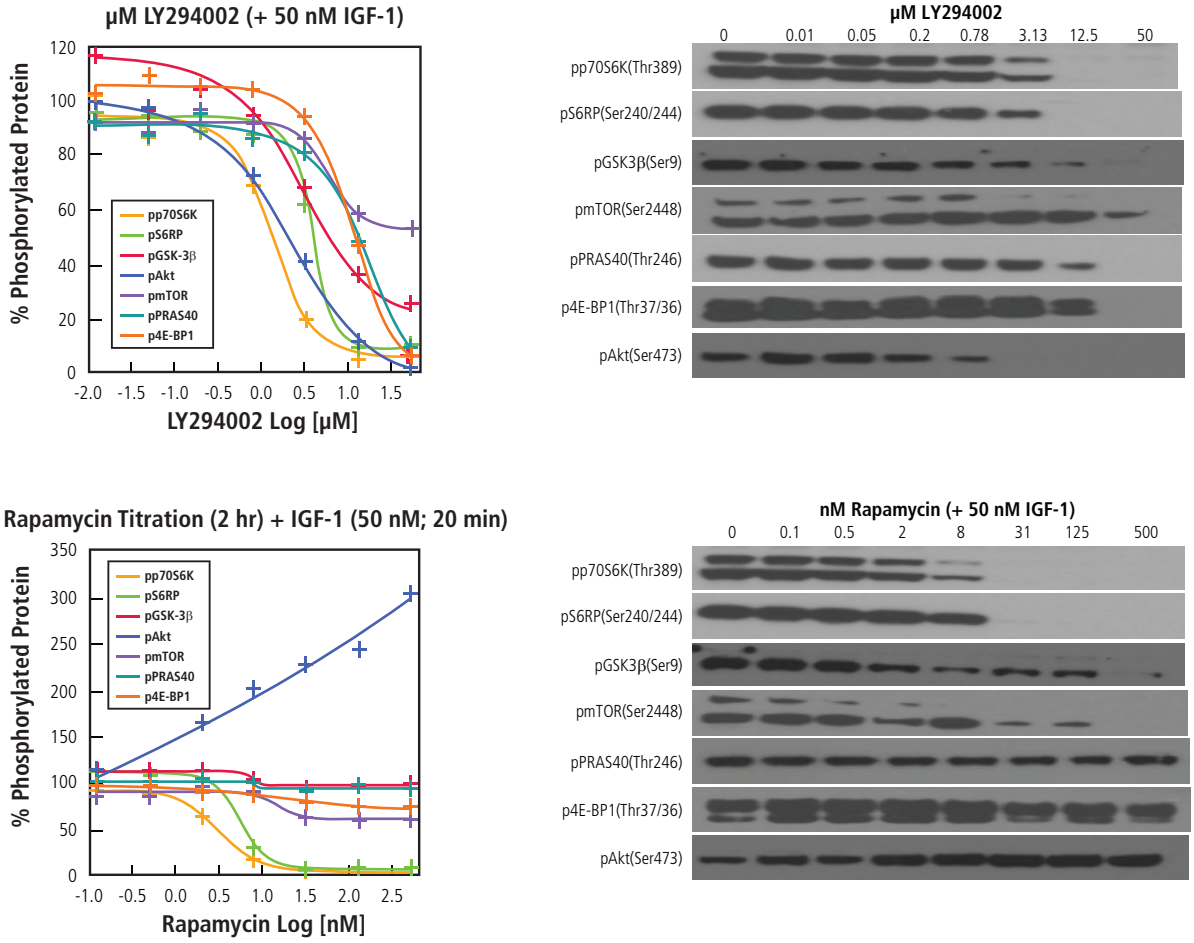
Study of Compound Inhibition

The discovery of potent and highly selective small molecule compounds has proven to be useful in targeted therapy of cancers, cardiovascular diseases, and neurodegenerative disorders. They serve as valuable tools for deciphering the functions of many cell signaling pathways. MSD assays can be used to rapidly evaluate the potency of an inhibitor against cell signaling targets such as Akt. The following example demonstrates the use of the MSD platform for dose response studies. LY294002 is a highly selective inhibitor of phosphatidylinositol 3-kinase and blocks Akt phosphorylation. This inhibitory effect of LY294002 has been demonstrated below. Rapamycin inhibits mammalian target of rapamycin (mTOR), which is downstream of Akt in the cascade. The following plot illustrates the inhibition of mTOR signaling by rapamycin, which in turn leads to an increase of Akt phosphorylation by a negative feedback inhibition process.[22] MCF7 cells were used for the study.

Catalog Numbers for Akt Signaling Panel II

	Kit Size	Catalog Numbers
Human/ Mouse/ Rat	1 Plate	K15177D-1
	5 Plate	K15177D-2
	20 Plate	K15177D-3

Akt Signaling: Percent Activated Protein Normalized to Total Protein



- Faster and more quantitative measurements than Western blot
- High throughput analysis enables a large number of samples to be tested in 96- and 384-well formats

Custom Assays

MSD supports you in every step of the research and drug development process. If you are studying a special combination of analytes, we can provide a multiplex panel to meet your needs. We will work with you to prepare a custom kit according to your preferences and provide you with a protocol for the assay. If you need help, our field application scientists and scientific support team are available to support you.

Design your multiplex in 3 easy steps

STEP 1
Identify your analytes of interest.

STEP 2
Look at the extensive menu of assays offered by MSD and pick your analytes from the assay list at www.mesoscale.com.

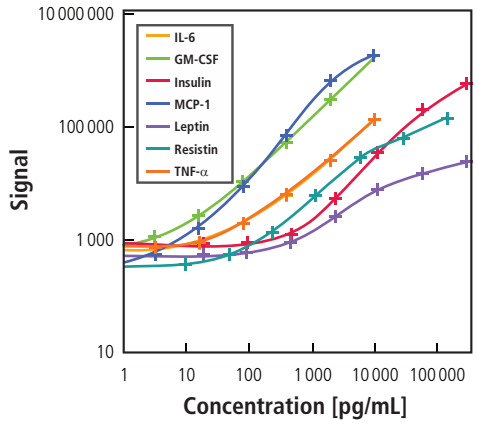
STEP 3
Contact MSD Customer Service to order your custom multiplex assay.

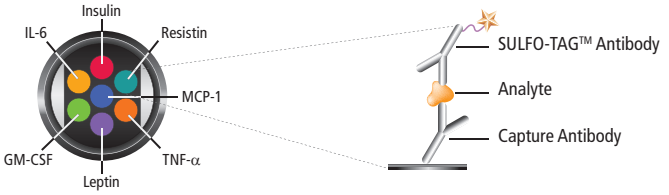
TEL: 1.240.314.2795
EMAIL: customerservice@mesoscale.com

If you cannot find your assay in the MSD assay list, then tell us the antibody pairs you use in your ELISA, and we'll coat them for you through Prototype Printing Services.

Up to 10 assays in 96-well plates

Mouse Metabolkine Multiplex Panel



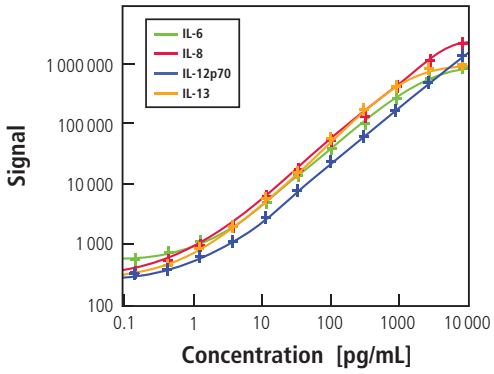


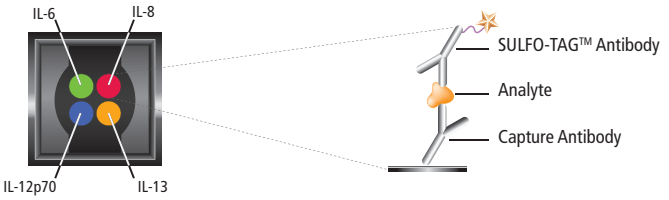
	Analyte						
	IL-6	GM-CSF	Insulin	MCP-1	Leptin	Resistin	TNF-α
LLOD (pg/mL)	4.3	1.1	125	1.3	83	10	6.1

LLOD (Lower Limit of Detection) is defined as 2.5 SD over the background signal.

Up to 4 assays in 384-well plates

Human Cytokine Multiplex





Prototype Printing Services

MSD offers Prototype Printing Services to facilitate assay development by customers. Prototype Printing Services provide the customer with a rapid and convenient way to get MSD plates coated with materials of their choice.

How to Order

STEP 1: Obtain a quote from MSD for your analyte of interest by contacting MSD Customer Service.

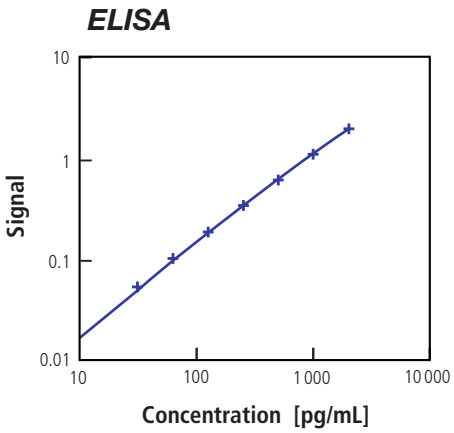
STEP 2: Place your order Reference the quote number on your order.

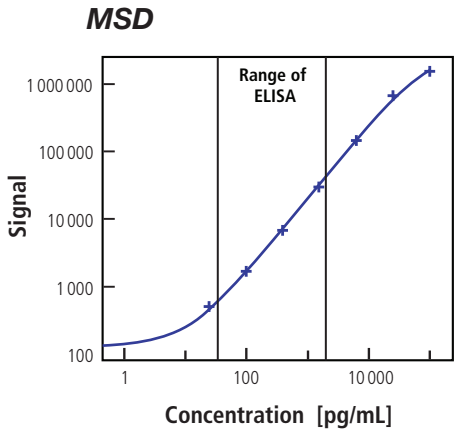
STEP 3: Receive your prototype assay.

Types of Capture Materials coated on MSD plates

1. Antibodies

Antibodies are readily coated on MSD plates. Customers routinely see significant improvements in assay performance when ELISAs are converted to the MSD format.

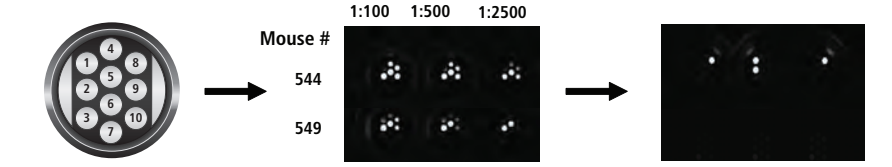




- **High sensitivity**
- **Multiplexing capability**
- **Time efficient**
- **Large dynamic range results in minimal sample dilution**
- **Saves sample volume**
- **Cost effective**

2. Proteins and Peptides

The following example demonstrates the use of an MSD 10-Spot plate for antibody screening. Titration of hybridoma supernatants identifies the high binding clones, which are subsequently tested for cross-reactivity as well as specificity.



MSD 10 Spot Plate Coated with Different Proteins

Titration and Screening of hybridoma on MSD plate

Cross-reactivity and Specificity Testing of Clones

By screening antibodies against multiple antigens, cross-reactivity and specificity can be determined in the same well.

3. Carbohydrates and Polysaccharides

Carbohydrates have been successfully coated on MSD plates, which have enabled the testing of different Pneumococcal vaccines by Marchese, et al.[5] MSD plates coated with lipopolysaccharides have been used by Thompson, et al. for serodiagnosis of Brucellosis in ruminants.[6]

In addition to the above mentioned materials, MSD plates are highly amenable to coating with viral proteins, cell lysates, etc.

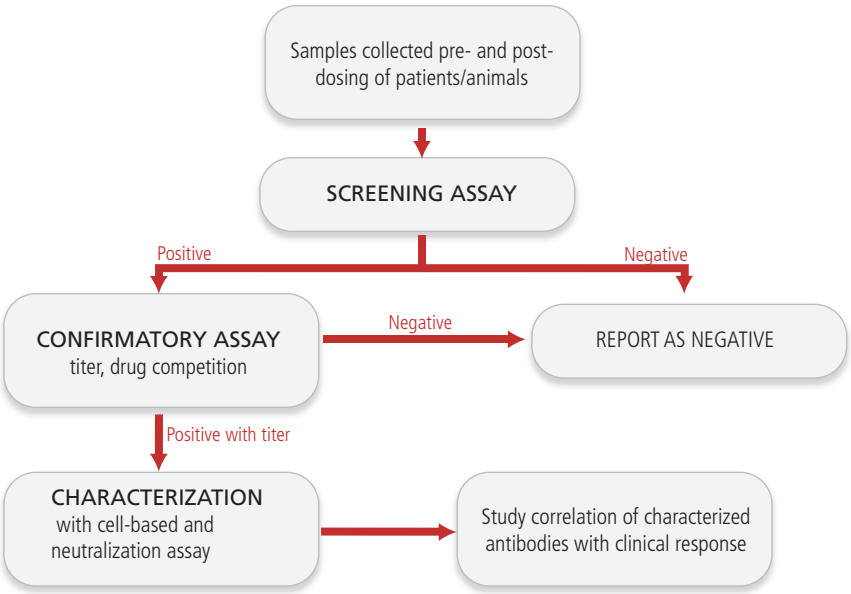
Request a Quote
Contact customer service to request a quote. TEL: 1.240.314.2795 EMAIL: customerservice@mesoscale.com

Evaluation of Protein Therapeutics

Immunogenicity testing is a crucial part of biopharmaceutical development. The EMA and FDA have mandated immunogenicity testing for biotherapeutics. More stringent recommendations regarding immunogenicity assay performance necessitates the development of more robust and tolerant assays. MSD has worked with leaders in the biotherapeutics field to fine-tune its technology to meet the needs of the immunogenicity community. MSD offers a suite of assay development materials and kits that provide superior solutions for each stage of drug development process. The typical steps in testing immunogenicity of therapeutic antibodies have been shown below. The development of cell-based neutralization assays on the MSD platform has also been featured below. Visit www.mesoscale.com for more information on immunogenicity assay development and a complete listing of materials and reagents.

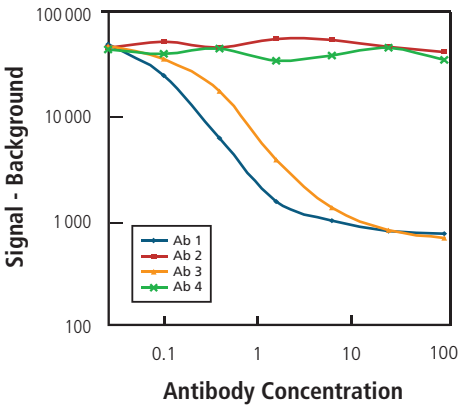
Catalog Numbers for Immunogenicity Development Pack

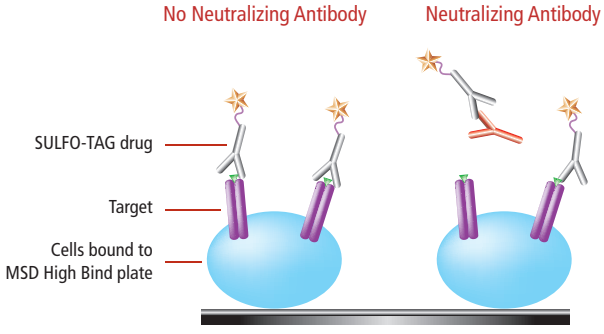
Instrument	Catalog Numbers
SECTOR Imager	K15A04-1
SECTOR PR	K13A04-1



- **MSD assays allow for higher free drug tolerance**
- **Fewer washes permits the detection of low affinity antibodies**
- **Flexible assay formats enable testing of many drug types including antibodies, proteins and peptides**
- **Rapid assay development makes the assay cost- and time-efficient**

Cell-based Neutralization Assay





SECTOR Instruments

The SECTOR Imager 6000 and the SECTOR Imager 2400 offered by MSD are ideal for users seeking high information content and high throughput. Both instruments use ultra-low noise CCD cameras for ultimate sensitivity, wide dynamic range, and rapid read times.

MSD SECTOR PR® readers offer users a choice of multiplex and single readout capabilities in our popular and compact benchtop platform. These affordable readers provide a combination of speed, simplicity, and performance that makes them perfect for target validation, assay development, immunogenicity testing, and basic research applications. Assays developed on the SECTOR PR readers are fully portable to the SECTOR Imagers.

All the instruments use MSD DISCOVERY WORKBENCH software, which offers one-click assays, enhanced data export tools, partial-plate reading features, and supports 21 CFR Part 11 compliance.

Catalog Numbers for SECTOR Instruments

Instrument	Catalog Numbers
SECTOR Imager 6000	I10AA
SECTOR Imager 2400	I30AA

SECTOR Imager Features

- Single and multiplex assay formats
- Highly sensitive imaging systems
- No complicated fluidics
- Rapid read times (~1 minute/plate for SI6000, and ~3 minutes/plate for SI2400)
- Six logs dynamic range
- Non-washed assay formats
- Simple operation
- Workstation or automated operation
- Simultaneous bar code label reading on short and long sides of microplates

SECTOR PR Features

- Photodiode array for fast and efficient detection
- No complicated fluidics
- Integrated barcode readers
- Multiplex and single array readouts
- Simple operation
- Five logs dynamic range
- Non-washed assay formats

Model	Detection Technology	Plate Read Time	Multiplex Capability	Automation Integration
SECTOR Imager 6000	CCD Camera	70 seconds	Yes	Yes
SECTOR Imager 2400	CCD Camera	3.5 minutes	Yes	Yes
SECTOR PR 400 Reader	Photodiode array	2-5 minutes	Yes	Optional
SECTOR PR 100 Reader	Photodiode array	2 minutes	No	Optional

MSD Resources at Your Service

Customer Support

Phone: 1-240-314-2795
Fax: 1-301-990-2776
Email: CustomerService@mesoscale.com
Web: www.mesoscale.com/support
Hours of Operation: 5:00 AM to 8:00 PM, Monday – Friday, U.S. Eastern Time

Scientific Support

Phone: 1-240-314-2798
Email: ScientificSupport@mesoscale.com
Web: www.mesoscale.com/support
Hours of Operation: 8:30 AM to 5:30 PM, Monday – Friday, U.S. Eastern Time

- Contract Assay Development Services
- Custom Assays and Prototype Printing Services
- On-Site Assistance

Field Service Engineers

Phone: 1-301-947-2057
Email: InstrumentService@mesoscale.com
Hours of Operation: 8:30 AM to 5:30 PM, Monday – Friday, U.S. Eastern Time
After Hours: 1-301-767-5682

Literature

Browse our online library of product literature, technical application notes, and FAQs as well as an extensive list of research studies citing MSD technology.

- Brochures
- Customer Presentations
- Posters
- Product Inserts
- Publications

Publications using MSD MULTI-ARRAY Technology

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