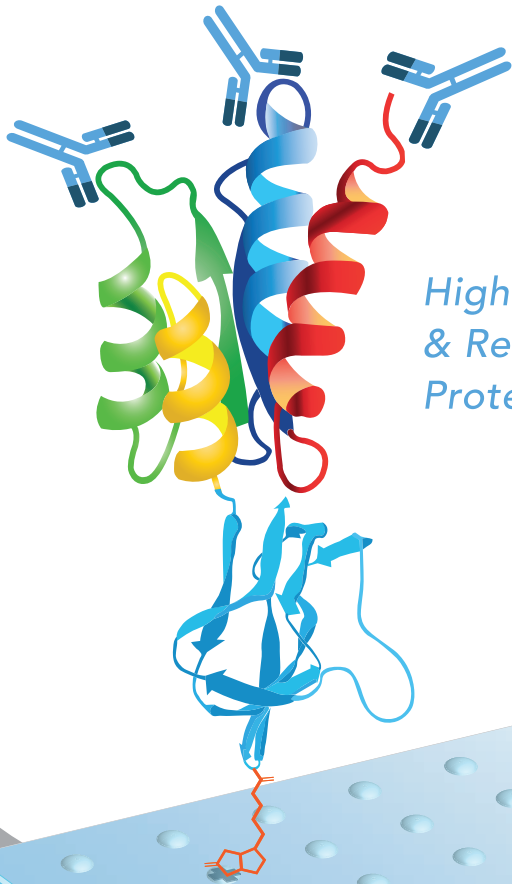


Autoantibody Biomarker Discovery

A precision medicine approach for patient stratification,
response prediction and development of companion diagnostics



*Highly Specific
& Reproducible
Protein Microarrays*

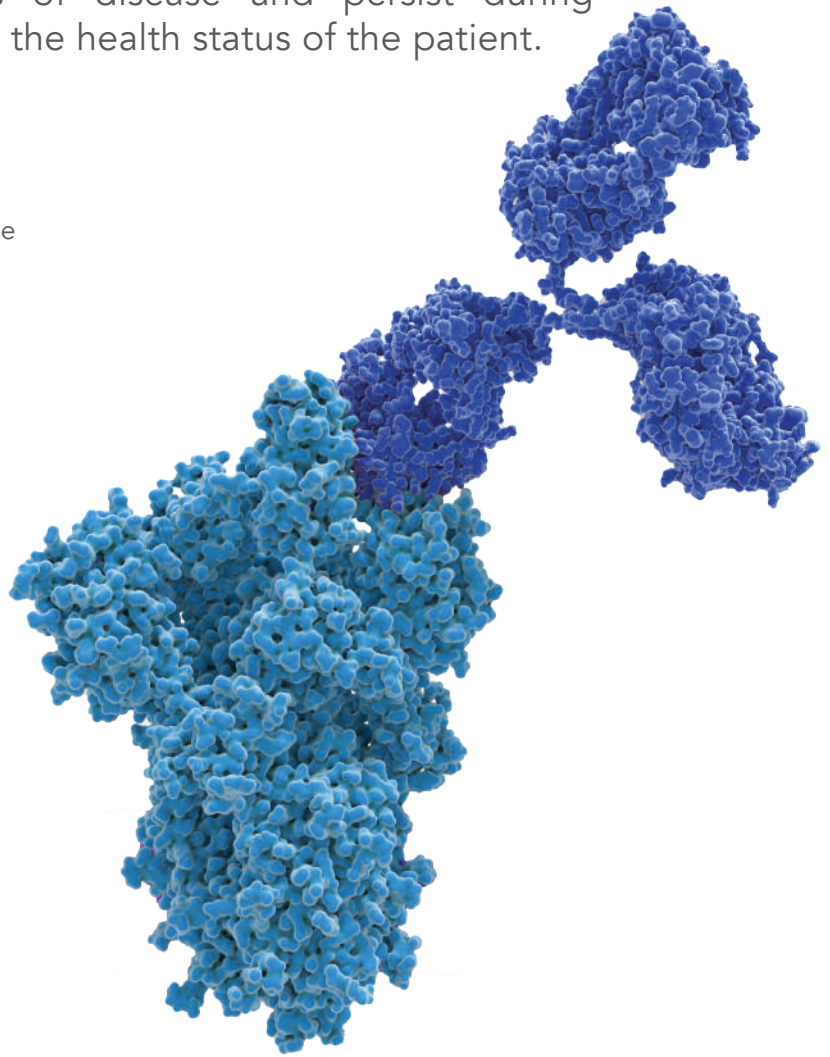
Sengenics patented KREX™ protein folding technology ensures all array proteins are correctly folded, full-length, and functional, giving you biologically meaningful results and actionable data.

Autoantibodies...

...are antibodies directed against self-antigens. They are the result of the immune response that is involved in the disease process.

...are excellent biomarkers

Traditional biomarkers such as DNA, RNA and proteins are macromolecules that provide a snapshot in time that may not correlate directly with disease. However, autoantibodies are manifestations of disease and persist during disease, giving valuable insight into the health status of the patient.



MANIFEST IN DISEASE

Produced as the result of an immune response

APPEAR EARLY

Produced early in disease progression

TARGET SPECIFIC

Highly specific antibody/epitope binding

STABLE

Easy to store and work with

ABUNDANT

Found at high concentrations in patient sera

ACCESSIBLE

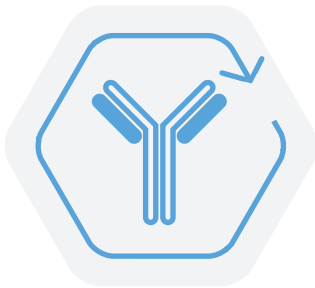
Blood sample

Autoantibodies are thought to arise in disease for several different reasons. Aberrant gene expression and mutation in disease tissues results in a unique set of proteins. These self-proteins can be immunogenic if they are over or inappropriately expressed, produced from variant genes, aberrantly post-translationally modified or proteolyzed or contain mutated epitopes. The result is mirrored in peripheral fluids because the humoral immune system is constantly surveilling and identifying disease-associated changes in the host proteome through the production of autoantibodies.

Applications

Biomarker Discovery, Patient Stratification, Drug Response Prediction and Development of Companion Diagnostics

Autoantibody biomarkers identified and validated using Sengenics protein arrays have shown utility in early disease detection, patient stratification, prediction of treatment outcomes and treatment monitoring, prediction of immune-related adverse events (irAE) as well as shedding light on underlying systems biology.



Biomarker Discovery

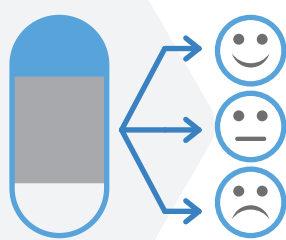
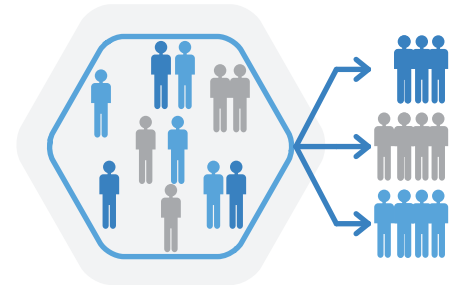
Identification of autoantibody biomarker signatures

High-throughput, quantitative array technology for discovering and validating autoantibody biomarkers that can be used to develop predictive signatures.

Patient Stratification

Intra-disease stratification, identification of cohorts and clinical trial patient enrichment

Predictive autoantibody signatures enable intra-disease stratification and identification of biologically relevant sub-cohorts that drive more efficient and economical study designs and clinical trial patient enrichment.



Response Prediction

Predict responders, non-responders and those at risk for adverse events

Autoantibody biomarkers can be used to establish signatures for predicting if patients are likely to respond to treatment. Predictive signatures can also be used to identify patient populations likely to experience adverse events.

CDx Development

Establish biomarker signatures for companion diagnostic development

Develop companion diagnostics for new or existing drugs. Our technology can be used to identify predictive signatures that play an important role in ensuring patients receive the right treatments.



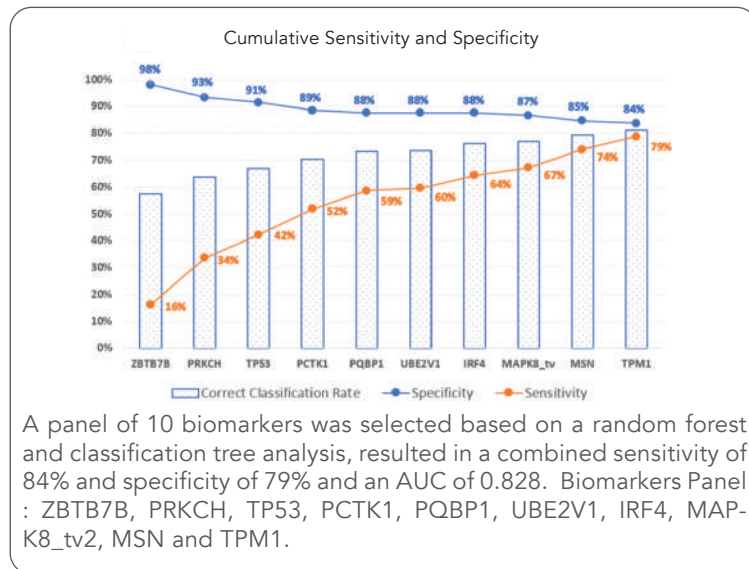
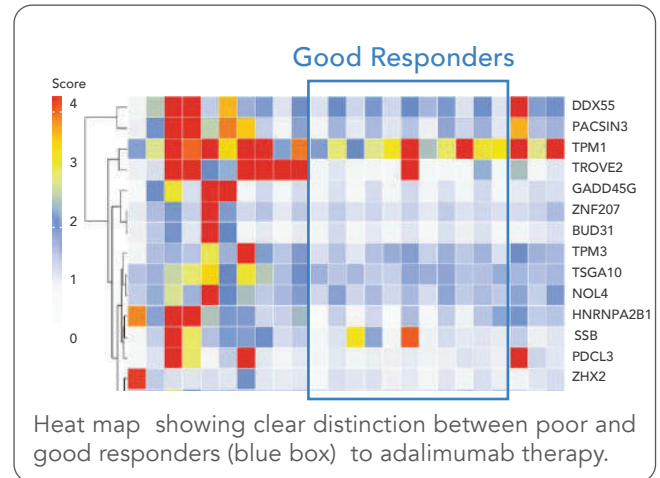
Case Studies

Predicting Response to Treatment in Rheumatoid Arthritis Patients

- Sengenics protein arrays were used to profile rheumatoid arthritis patients treated with Adalimumab.
- The aim was to find biomarkers that would be predictive of the therapeutic response.
- Results showed a panel of 8 autoantibody biomarkers, including anti-TROVE2, were able to distinguish therapeutic responses in this patient cohort with 77% sensitivity and 81% specificity.



Chen, Po-Ku, et al. 2021. "Anti-TROVE2 Antibody Determined by Immune-Related Array May Serve as a Predictive Marker for Adalimumab Immunogenicity and Effectiveness in RA." *Journal of Immunology Research* 2021 (March): 1–13.



Cancer Diagnostics in Melanoma

- Early stage melanoma patient samples were profiled using Sengenics protein arrays.
- A melanoma-specific signature consisting of a panel of 10 biomarkers with 84% sensitivity and 79% specificity was identified.
- The discovery of this autoantibody biomarker signature may prove valuable for the development of a diagnostic blood test.



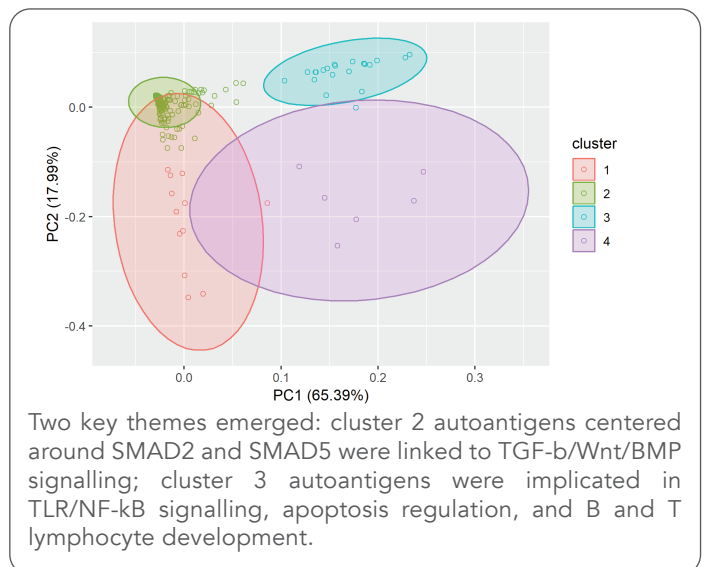
Zaenker, Pauline, et al. 2018. "A Diagnostic Autoantibody Signature for Primary Cutaneous Melanoma." *Oncotarget* 9 (55): 30539–51.

Autoimmune Patient Stratification in Lupus

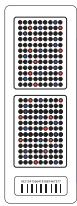
- Sengenics protein arrays were used to identify 4 different lupus cohorts.
- Autoantibody profiles stratified patients into clinically meaningful groups.
- The identified clusters hint at different pathogenic mechanisms and possible treatments for the different lupus subgroups.



Lewis, Myles J., et al. 2018. "Autoantibodies Targeting TLR and SMAD Pathways Define New Subgroups in Systemic Lupus Erythematosus." *Journal of Autoimmunity* 91 (July): 1–12.



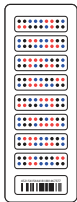
Products & Services



i-Ome Protein Array

High-throughput
sero-profiling platform

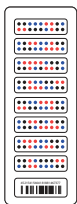
There are over 1600 autoimmune- and cancer-related proteins on this protein array including many known autoantigens.



CTA Protein Array

Screening of
cancer-testis autoantibodies

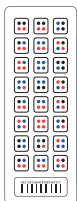
Cancer Testis Antigens (CTA) are a group of antigens that are commonly expressed by tumor cells. This protein array contains over 200 CT antigens.



OncoREX p53 Cancer Array

Cancer drug
screening and discovery

P53 is a tumor suppressor protein. This protein array offers high-throughput quantitation of autoantibodies to over 100 wild-type and mutant p53 variants.

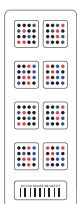


ImmusaFE Protein Array

Antibody screening
in COVID-19

COVID-19 protein array that captures 3 different results:

- Levels of antibody to the virus
- Ab neutralizing capability
- Levels of autoantibodies to immune modulators like INF γ and TNF α



CUSTOM Protein Array

Flexible formats for
high-throughput screening

Sengenics can create custom protein arrays with any protein, any layout and multiplicity as well as a variety of expression system options. Get in touch to discuss your project.

Working with Sengenics

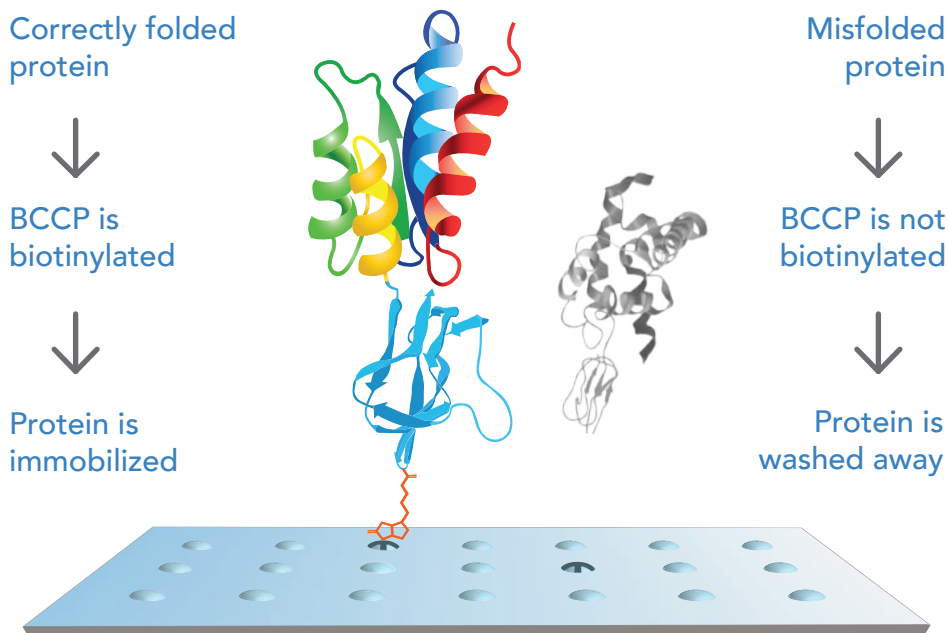
- Purchase off-the-shelf protein arrays in kit format.
- We can run our established arrays for you, including assistance with experimental design and data analysis.
- Choose to create custom protein arrays for your research program utilizing our expertise in protein expression and bioinformatics.

KREX™ Technology

Sengenics patented KREX™ protein folding technology enables the high-throughput expression of hundreds or even thousands of different proteins where the folding and functionality of the protein is controlled throughout expression, purification and immobilization.

How does it work?

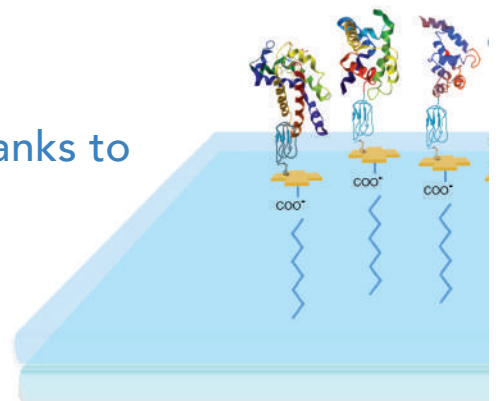
- Proteins are co-expressed with a biotin carboxyl carrier protein (BCCP).
- If the protein of interest is correctly folded, it co-translationally drives the correct folding of BCCP which, when correctly folded, has a biotin binding site. Exogenous biotin is added to the media during protein expression.
- When proteins are spotted on the array, biotinylated BCCP binds to the streptavidin coated surface.
- If the protein of interest folds incorrectly, the BCCP also folds incorrectly, obscuring the biotin binding site and preventing attachment to the surface of the array.
- This ensures that only correctly folded proteins remain, as incorrectly folded proteins cannot bind and are washed away.



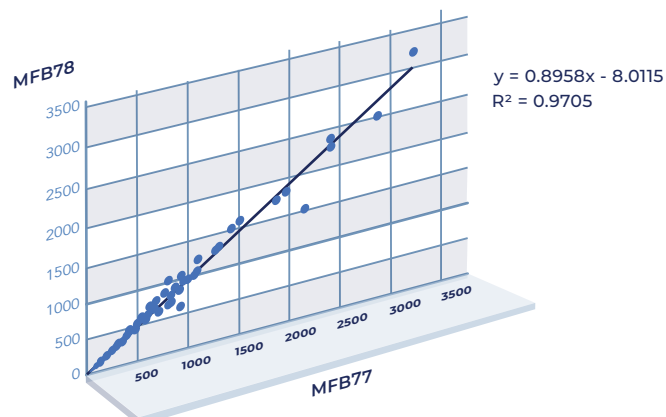
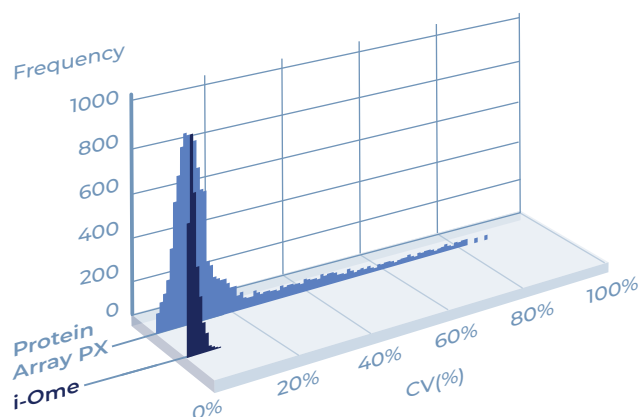
Check out our explainer video to see the technology in action

Proteins behave as if they are in free solution thanks to propriety surface chemistry

- Proteins are immobilized onto a streptavidin-coated hydrogel.
- Proteins retain their folded structure and function in the aqueous environment.
- Proteins are projected from the glass surface and attach at a single point ensuring consistent orientation on every array.



Technical Performance



Exceptional Consistency

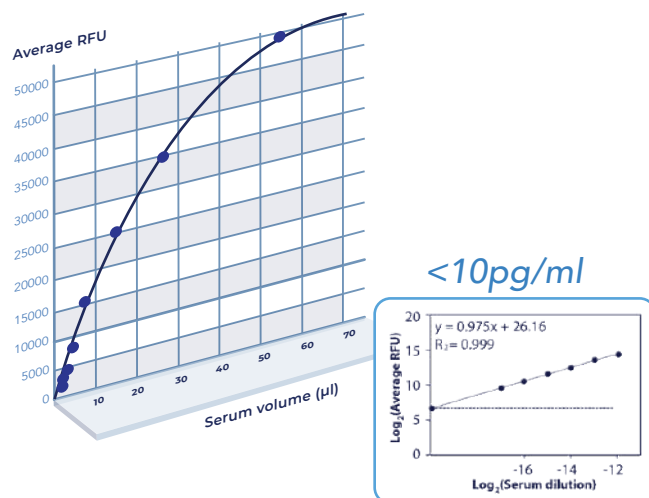
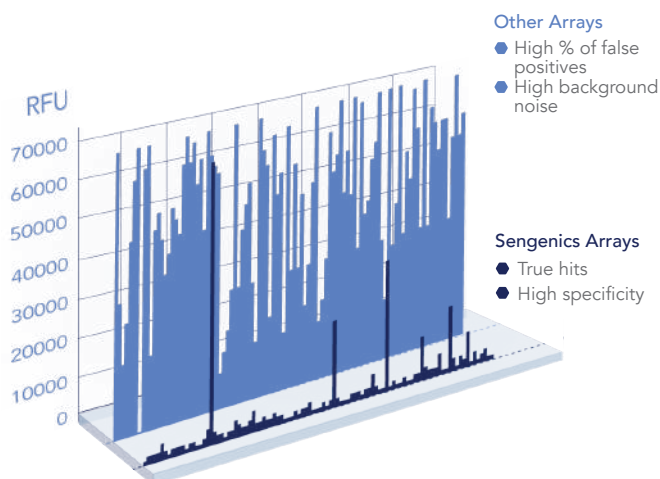
Sengenics KREX™ protein folding technology is used to create protein arrays with exceptional consistency.

The graph above shows the coefficient of variation percentage (CV%) of intra-protein replicates on the Sengenics i-Ome protein array compared to another marketed protein array. The mean CV% for i-Ome was 7.2% whereas the CV% for Protein Array PX was 37%.

Highly Reproducible

Sengenics protein arrays use multiple positive and negative controls to measure reproducibility within, and across, studies and batches.

The graph above shows an almost perfect Pearson correlation of above 0.97 when comparing autoantibody levels across 6,524 protein data points in two different batches.

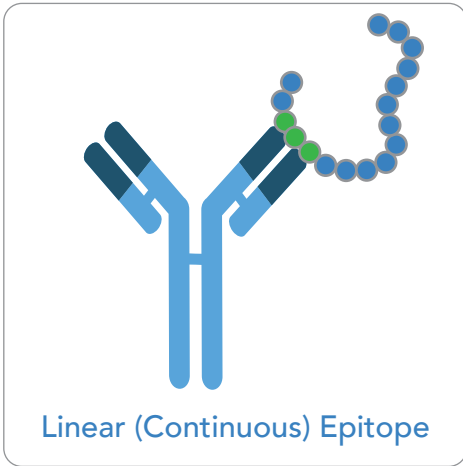


Superior Specificity

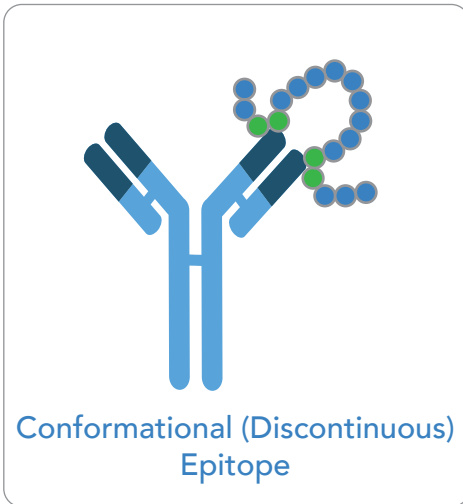
The correct folding of proteins on Sengenics protein arrays ensures that conformational epitopes are available for autoantibody binding (90% of antibody epitopes are non-linear). This results in specific hits and low background noise compared to other arrays that display a low signal-to-noise ratio.

Picomolar Sensitivity

Sengenics protein arrays can be used to detect autoantibodies at very high sensitivity, only 1 - 10 µl of serum is required. The detection limit is in the 10 pg/ml range, with a linear dynamic range of at least 5 orders of magnitude.



Linear (Continuous) Epitope



Conformational (Discontinuous) Epitope

Assays Run on Arrays with Correctly Folded, Full-Length, Functional Proteins are More Biologically Relevant.

Protein functionality relies on three-dimensional structure. Drug-binding interactions, protein-protein interactions and protein-ligand interactions all require the correctly folded structure of the protein. This is critical to autoantibody-based assays, where interactions between antibody and antigen are highly specific.

Antibodies primarily recognize discontinuous, 3-dimensional shapes and charges on a protein surface, rather than a linear peptide sequence. The discontinuous epitopes that provide the physiological selectivity and the specificity of antibody recognition are only present when the protein is folded correctly.

About Sengenics

Sengenics is a functional proteomics company that leverages its patented KREX™ protein folding technology to discover autoantibody biomarker signatures for drug response prediction, patient stratification and development of companion diagnostics. Our technology ensures that all microarray proteins are full-length, correctly folded and functional, enabling specific and quantitative antibody binding to conformational epitopes.

The company has a global footprint with multiple corporate and research sites across the world with customers and collaborators that include top pharma, biotech and Ivy League academic institutions in North America, Europe, and Asia.

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