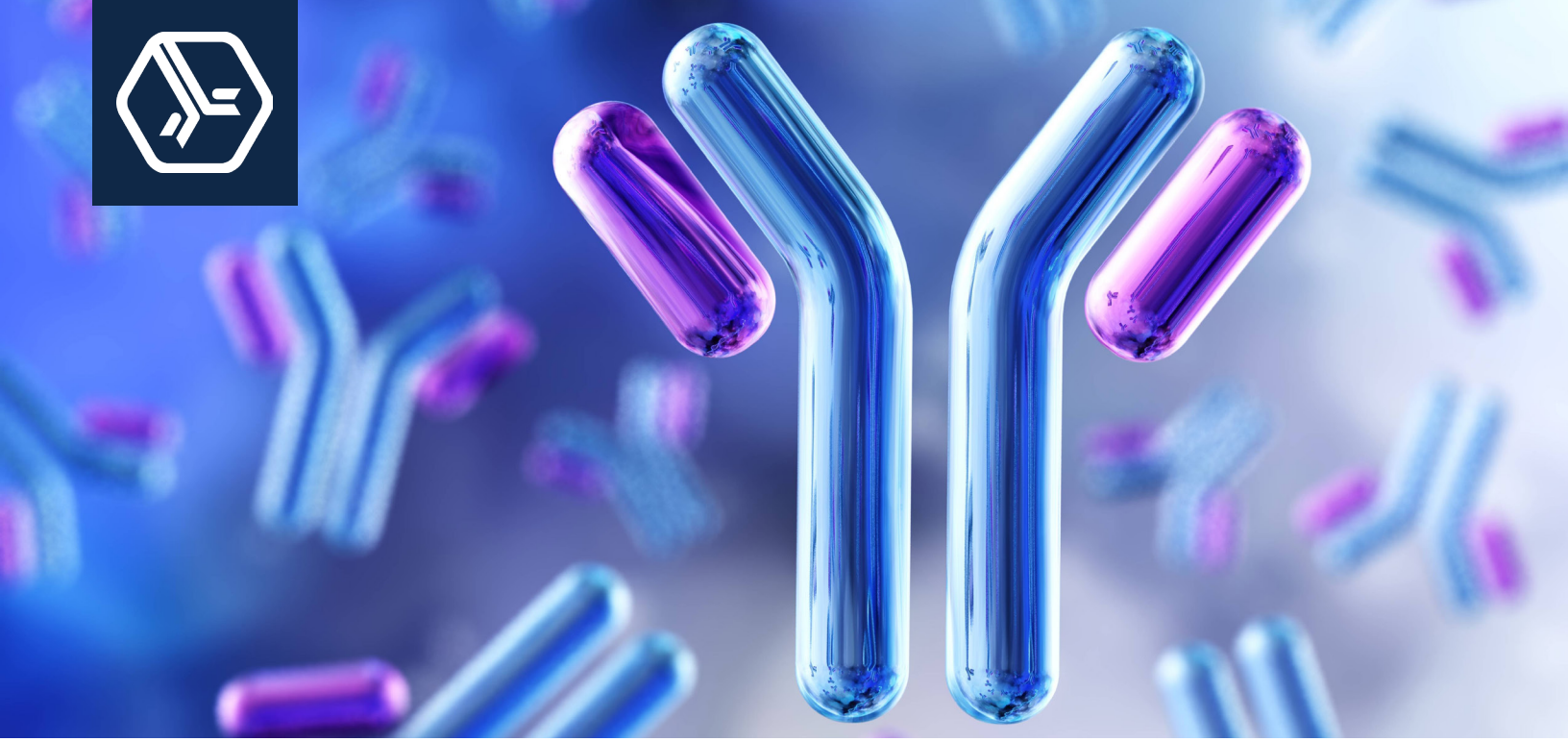

WHITE PAPER
ANTIBODY BIOMARKERS

Antibody Profiling: Decoding the Humoral Immune System

- Understand the current challenges in disease diagnosis and treatment
- Appreciate the role of antibody biomarkers in disease detection
- Explore the technical aspects of antibody screening for biomarker discovery

sengenics

Introduction

Chronic diseases such as autoimmune diseases, cancer, and neurological disorders are complex, difficult to diagnose early, and problematic to treat due to their inherent heterogeneity. As a result, patient responses to current therapeutics are highly variable; some patients may not benefit at all, while others could face serious side effects.

Certain health conditions like cancer and neurodegenerative disorders lead to the abnormal activation of proteins within the host, prompting the immune system to produce antibodies (see light blue insert for examples). Such antibodies that target self-proteins are known as autoantibodies.

Self-proteins can become targets for the immune system when they are altered by disease-related factors like genetic mutations or ectopic expression. Similarly, unusual post-translational modifications, splice variants, and neoantigens, among other changes, can also cause self-proteins to become autoantigenic.

Antibody biomarkers hold the potential to transform patient care. They can help facilitate early detection, subtype diseases more accurately, predict who will (or won't) respond to treatments, foresee possible negative reactions, and improve patient stratification for clinical trials.

By analyzing the vast array of humoral antibodies through a process called immunoprofiling, scientists can gain a clear understanding of a patient's disease state, offering guidance in the complex landscape of chronic illnesses.

Autoantibody Biomarkers in Disease

Antibody generation is linked to the formation of TDP-43 protein aggregates that occurs in amyotrophic lateral sclerosis (ALS) (1).

Tumor-associated proteins in cancer elicit an autoimmune response (2,3).

Antibody biomarkers of lupus in the blood samples of military personnel were detected up to nine years before their diagnosis (4).

Antibodies have shown significant potential in predicting disease outcomes (5-7).

Researchers identified and validated a signature of 13 antibodies predictive of a lower five-year survival in non-small cell lung cancer (8).

Antibodies Are Ideal Biomarkers

Antibodies are direct manifestations of disease, appearing often before any symptoms arise and remaining detectable throughout the course of illness.

Unlike commonly used biomarkers such as RNA and proteins — which might change due to a variety of bodily processes — antibody levels in serum are typically unaffected by common stimuli like diet or exercise. They change primarily in response to disease or treatment.

Antibodies are also less prone to degradation than RNA and proteins. They remain stable for one month at room temperature and 200 days when stored at -20 °C on dried blood spot collection cards, enabling population screening in rural and low-income areas (9). Antibodies are also suitable for retrospective and longitudinal studies.

The humoral immune system acts as a vigilant guardian, continuously monitoring the entire body and generating antibodies associated with disease that often impact multiple organs. In other words, autoantibodies obtained from blood samples represent the full repertoire of antibodies from various tissues, as

they circulate system-wide. In contrast, proteins profiled in blood using technologies like mass spectrometry represent only those proteins that have been secreted or released into the bloodstream.

Moreover, antibodies can reveal disease-associated proteins and protein pathways, providing valuable insights for unraveling the complexities of diseases and aiding in the development of new medications.

The Importance of Protein Folding in Antibody Screening

Antibodies are highly specific, with 90% of antibodies generated by the immune system recognizing and binding to small conformational epitopes that contain six to eight amino acid residues (10,11). Thus, accurately profiling antibodies requires screening against full-length, correctly folded proteins that display specific, biologically relevant epitopes.

Sengenics employs its patented KREX® technology to ensure that only full-length proteins with proper folding are immobilized on functional protein arrays for antibody screening (Figure 1). Various screening options are available, from custom arrays to the comprehensive i-Ome® Discovery array with over 1800 human proteins.

Concluding Remarks

Immunoprofiling with the right tools can provide crucial and direct insights into the immune response to disease, help identify disease-specific and disease-associated changes at the protein level, and serve as an important source of biomarkers for diagnosis, patient stratification, monitoring, and drug development.

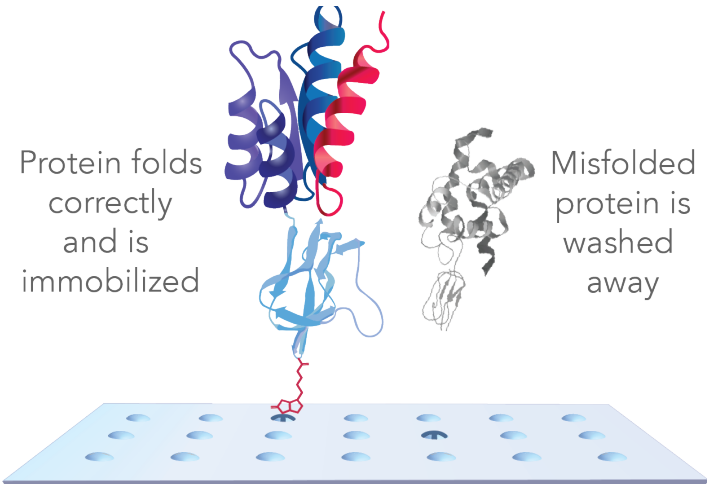

Figure 1. KREX technology for precise antibody profiling

Contact us

Sengenics develops key solutions for biological research, specializing in the discovery and validation of autoantibody biomarker signatures. For more information on how Sengenics can advance your research, email us at enquiries@sengenics.com or visit our website at sengenics.com.

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