Recent publications

Following you find a brief abstract of a scientific publication concerning LEUKOCARE's technologies. Please find the full text article at the given reference.

Biotechnology Journal 2012, March, Volume 7, Issue 8

A protein-stabilizing technology for enhanced antibody stability and antibody-binding profiles in a microchip array

MARTIN SCHOLZ[1] AND ANGELIKA LÜKING[2]

[1]Leukocare AG, München, Martinsried, Germany
[2]Protagen AG, Dortmund, Germany
*E-mail: martin.scholz@leukocare.com; angelika.lueking@protagen.de

The stability of therapeutic antibodies during downstream processing and storage is important for functionality and quality. To determine functional antibody performance, the UNIchip® high-density protein microarray with 384 recombinant antigenic targets was developed; this allows characterization of antibody specificity by generating standardized quantitative binding profiles. In this study, we used UNIchip® to test the efficacy of a novel protein stabilizing and protecting solution (SPS) to preserve the binding specificity and binding strength of a therapeutic anti-TNF-α antibody (Adalimumab; Humira). Our results show that reconstituted SPS-formulated and lyophilized Adalimumab elicits significantly less off-target activity after reconstitution and preserves binding strength even after six weeks of storage at 40°C compared with Adalimumab that underwent the same treatment with the original formulation. By means of UNIchip®, we were able to confirm the protein stabilizing effects of SPS as shown by preserved antibody functionality.

Although many studies were conducted in the past to better understand the links between protein structure, protein aggregation, protein misfolding, and immunogenicity, no information on how to prevent changes in antibody binding profiles during stress is available. Therefore, major challenges in the screening of antibody binding profiles are modifications of the 3D protein structure due to misfolding and aggregation of the test antibody during storage and/or under stress conditions.
A novel technology has recently been reported that stabilized biomolecules such as therapeutic antibodies and vaccines. For example, immobilized IgG antibodies against TNF-α were transiently coated with a protecting layer (stabilizing and protecting solution [SPS]) that allowed lyophilization, sterilization (irradiation at 25–40 kGy; EtO), and rehydration without relevant loss of function. The specific composition of SPS, consisting of five to seven different small molecule type excipients, including a rigid amphiphilic molecule, is free from proteins, sugars, and salts known to have limited stabilizing properties and can be adjusted to the

specific requirements of the biologic. Even though primarily developed for dry formulations, SPS may also stabilize biologics and even viruses during liquid storage.

The aim of the study was to determine the influence of the stabilizing and protecting solution (SPS) on the therapeutic antibody (Humira/Adalimumab) by applying protein microarrays as an easy and fast tool. UNIchip® high-density protein microarrays are designed for the quantitative analysis of antibody binding profiles and characteristics. The UNIchip® microarray contains 384 predefined and His-tag purified recombinant human proteins on a nitrocellulose-coated glass slide. Sets of membrane proteins, intra- and extra-cellular proteins, are available. The screening of antibody binding profiles is, for example, an important tool to characterize the specificity of therapeutic antibodies, to avoid side effects due to antibody cross-reactivity, or to detect autoimmune antibodies in patient blood.