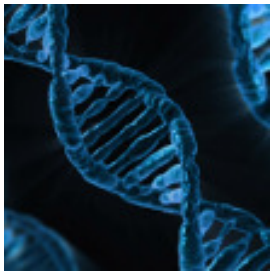

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INTERACTION STUDIES OF MONOCLONAL ANTIBODIES AT HIGH CONCENTRATIONS

Therapeutic monoclonal antibodies (MAbs) have been found to be highly effective agents in the treatment of immunological disorders with a high level of success due to their structural specificity and low toxicity. In formulation of protein therapeutics, one of the main concerns is the physical stability of the drug molecule. Proteins at high concentrations tend to self-associate, potentially leading to phase separation, opalescence and high viscosity solutions or aggregation, where highly concentrated protein solutions are required to meet patient dose requirements.

As the intermolecular solution structure of proteins is the controlling factor in determining the formulation attributes, we aim to study these interactions using small-angle X-ray scattering (SAXS) and static light scattering (SLS). Protein-protein interaction models have been used to study the solution structure of 5 MAbs and their protein-protein interactions at high concentrations under specific formulation conditions where they remain soluble.

SAXS experiments provide information about the spatial protein density distribution in terms of the static structure factor, S(q), which is a measure of the inter-particle interaction, because of attraction or repulsion. SLS measurement relates the intensity of scattered light, which is proportional to the excess Rayleigh ratio, to the weight-averaged molar mass and the osmotic second virial coefficient, B22, and has been used as an alternative approach for measuring S(q=0). B22 is also directly related to the protein-protein interaction potential U(r), which are extracted by modeling S(q) using a DLVO model.

S(0)s determined using SAXS and SLS for the different MAbs are then compared, based on the individual isoelectric point and net charge distribution over the surface for each MAb, to gain a deeper understanding of how these parameters affect protein-protein interactions at high concentrations.

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