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A new approach to quantification of mAb aggregates using peptide probes

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Molecular interactions that occur in high concentration formulations of monoclonal antibodies (mAbs) increase the propensity of antibody molecules to undergo aggregation. Aggregation is particularly concerning because of the suspected immunogenicity of antibody aggregates. Little is known about the morphology of these aggregates, which likely ranges from irregular or spherical particulates to ordered fibrils. Furthermore, analytical techniques to quantify aggregates with different morphologies in complex mixed samples do not currently exist. Ideally, an analytical method that could discern between different aggregate morphologies and provide quantitation of these aggregate morphologies in complex samples would be highly beneficial in both research and clinical settings. In the present work, we reasoned that protein-protein interfaces formed by mAb aggregation could be selectively recognized by short peptides with random amino acid sequence. We will present experimental data supporting a proof-of-concept for this new methodology. Assay development included using an aggregated mAb as bait for screening of phage display peptide library and identifying those peptides with random sequence which can recognize mAb aggregates. Once identified, the selected peptides can be used for developing quantitative methods to assess mAb aggregation. Results indicate that a peptide binding method coupled with mass spectrometric detection of bound peptide can quantify mAb aggregation and potentially be useful for monitoring aggregation propensity of therapeutic protein candidates. Further exploration of this idea is of interest to major arenas of antibody applications.

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