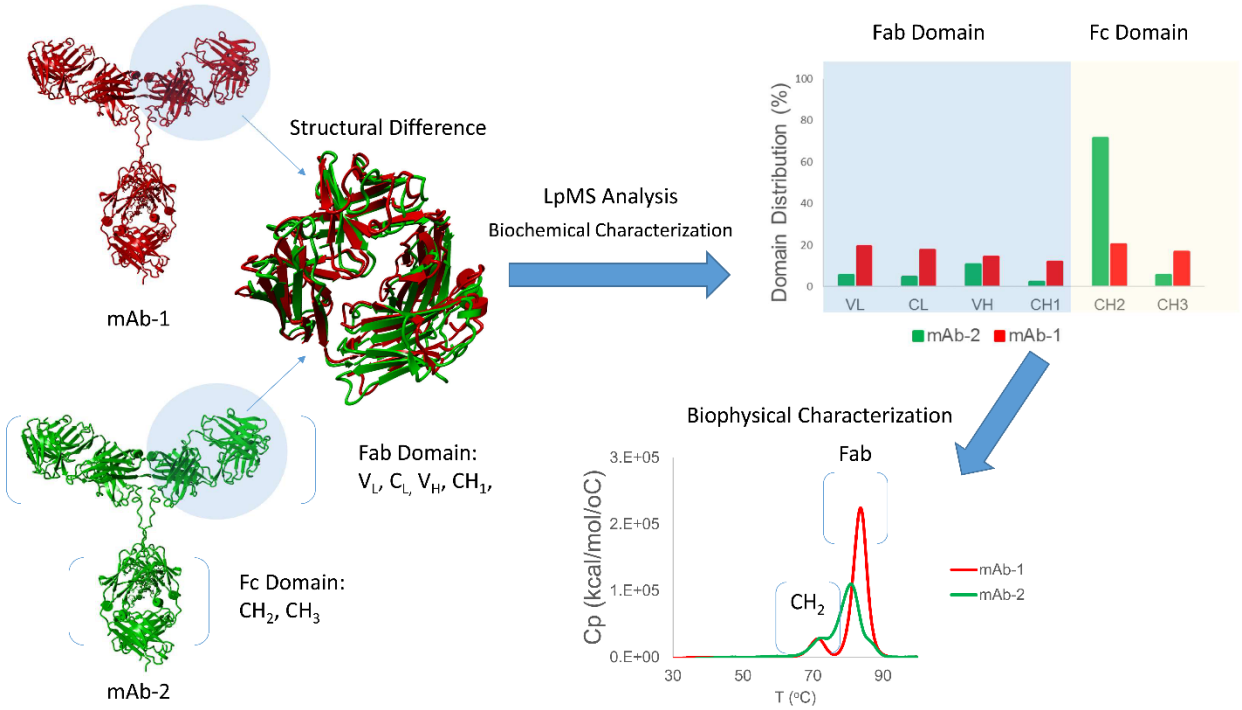
Structural Mapping of Various IgG-type monoclonal antibodies and Antibody-drug Conjugates: The Impact of Structural Features on Protein Colloidal and/or Thermal Stability.



The higher order structure (HOS) of protein biopharmaceuticals is key in delivering a biological function to its target. Modifications in the HOS of protein therapeutics can result in loss of biological function and thus alter product stability, efficacy, and immunogenicity. To ensure product quality, therefore, a variety of biophysical characterization methods is used in support of product characterization during product and process development. Structural proteomics methods based on mass spectrometry have recently gained attention for HOS characterization. MS data was found to supplement data obtained by conventional biophysical characterization techniques such as FUV-CD, NUV-CD, FT-IR, 2dUV and fluorescence spectroscopy, that are routinely used in the pharmaceutical industry to study structural features of the products

Recently, a limited-proteolysis-based mass spectrometry method for structural characterization of various mAb and ADC products was developed at Byondis. Preliminary research has showed that LpMS method can be used to detect the structural differences in various mAbs at the domain level, which enables the investigation of the impact of linker-drug conjugation on protein HOS, and to determine protein unfolding/aggregation pathways.

As we would like to further improve our understanding of how specific structural features (e.g. structural integrity of Fab and/or Fc domain) can alter structural attributes of our biopharmaceuticals (e.g. protein-ligand interactions, colloidal and/or thermal stability), the objective of an internship project would be to explore a relationship between the structural features and colloidal and/or thermal stability of various mAbs and ADCs by using conventional biophysical methods and limited-proteolysis-based mass spectrometry.