

# Advanced HDX-MS Approaches for Target Binding Analysis in Biologics Development

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A Protagen Protein Services Company

## Introduction

Target engagement is a critical factor in drug efficacy. Understanding and controlling how drug candidates interact with their expected targets can be enhanced using combined profiling approaches, specifically high-resolution analyses that provide details about the interaction. Hydrogen-Deuterium Exchange Mass Spectrometry (HDX-MS) and Native Mass Spectrometry (Native MS) are powerful, information-rich approaches that are increasingly used for binding site profiling and analysis of stoichiometry.

With interrogation and more accurate profiling of these properties, there is opportunity to de-risk and advance early development of biologic drugs by assessing target engagement and kinetics, particularly at different dose levels, and correspondingly, to leverage the understanding obtained to more reliably select and optimize candidates with greater probability of success. When combined with other well-established analytical techniques, there is further opportunity to utilize such detailed binding site profiling to better inform decisions and increase controls in CMC program development, to enhance clinical development success rates overall.

## Highlights

We apply advanced MS approaches for enhanced development of complex biologics:

- ✓ Epitope Mapping
- ✓ Paratope Mapping
- ✓ Identification of Binding Regions and Assessment of Binding Mode
- ✓ Distinguish Regions Where Binding Induces Conformational Changes
- ✓ Complete Coverage of Highly Glycosylated Proteins
- ✓ Determine Stoichiometry

**Heat Map of H/D Exchange  
Determined by HDX-MS**

