Top Down Tandem Mass Spectrometric Analysis of a Chemically Modified Rough-type Lipopolysaccharide Vaccine Candidate

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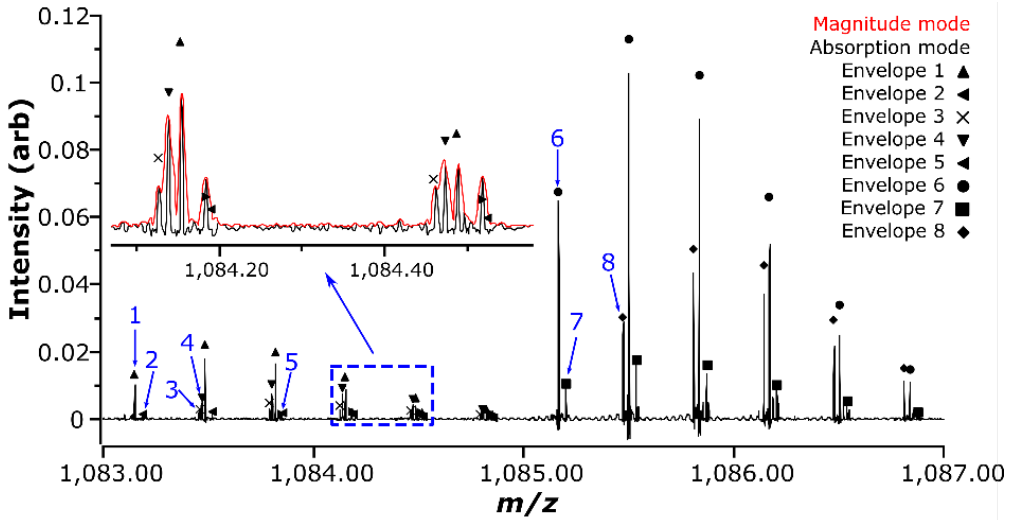
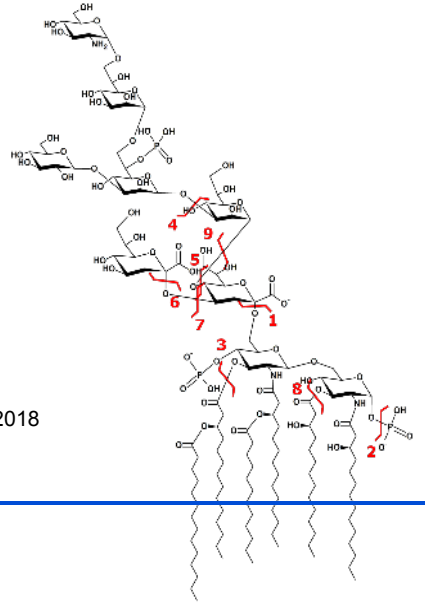
Lipopolysaccharide (LPS) host-microbe biology has made its use possible in vaccine and adjuvant discovery pipelines. Deep structural characterization of most LPS extracts is not performed routinely; hence, prediction of their biological activities is inaccurate. Also, the most common LPS structure elucidation workflow utilizes nonspecific chemical decomposition steps before analyses, making biological relevance less clear.

Novel mass spectrometry workflows were employed in this work for top down LPS primary structure elucidation, specifically for a rough-type mutant (J5) *E. coli* - derived LPS component of a vaccine candidate. Ultra-high mass resolving power and mass accuracy of the 21T FT-ICR mass spectrometry generated data enabling assignment of unequivocal precursor and product ion empirical formulae. Previous knowledge about LPS dissociation phenomena was used to show that MS^3 analyses in an ion trap instrument generate data that allow top down sequencing.



Top: Zoom mass spectrum illustrating lipopolysaccharide extract complexity, with eight potential isotopic distributions in an m/z window from 1083 to 1087.

Right: Tandem mass spectrometry provides sufficiently detailed spectra to make a structural characterization.



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Facility used: 21 T magnet system in the FT-ICR User Facility

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