DESI™ Cyclic IMS Enables the Detection and Spatial Distribution of Proteins in Tuberculosis Granulomas

Hernando Olivos[1]; Emmanuelle Claude[2]; Veronique Dartois[3]; Ning Wang[3]; Claire Carter[3]
[1]Waters Corporation Milford, MA; [2]Waters Corporation, Wilmslow, UK; [3]Center for Discovery and Innovation, Nutley, NJ

Waters
THE SCIENCE OF WHAT'S POSSIBLE.™

Introduction

Despite the use of antibiotics to treat tuberculosis (TB), *Mycobacterium tuberculosis* (Mtb), remains a serious global health threat. Due to lengthy treatments for TB, and drug resistance in some cases, new solutions are needed to shorten the therapy and eradicate the disease. A prominent pathological feature of TB is the formation of granulomas. Understanding the drivers of granuloma formation will enable the identification of new host-directed therapeutics.

We show the preliminary experiments done on MS Imaging of granulomas on rabbit lung tissues to focus on peptides and proteins. The complementary analysis on lipids is presented in this conference as well(1).

Experimental

The tissue slides were washed, based on a published protocol(2). DESI™ XS source was coupled to a SELECT SERIES™ Cyclic™ IMS system equipped with a heated transfer line at 450 ºC and a high-performance sprayer (Figure 1). Solvent (acetonitrile/water 80:20, 0.1% formic acid, 200 ng/mL LeuEnk) was delivered at 3 µL/min. Datasets were processed with Driftscope™ 3.0, High Definition Imaging (HDI™) 1.6 and MassLynx™. 4.2.

Figure 1. DESI™-XS source with Cyclic IMS.

Results

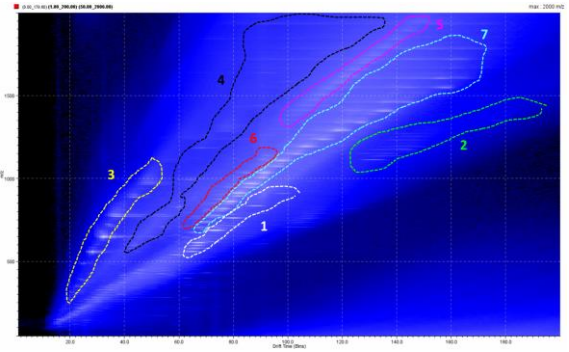

Figure 2. Driftscope™ view (Drift time vs. m/z) of the different regions that were selected for analysis.

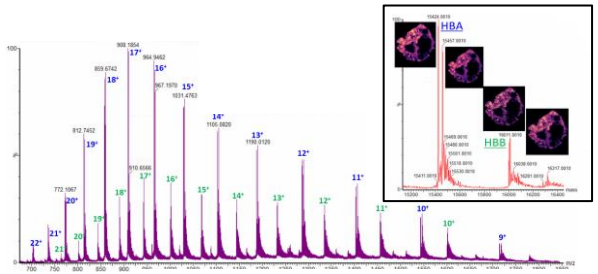

Figure 3. Spectrum from band 7, showing the charge states and, in the inset, the deconvoluted spectrum and MS image distribution.

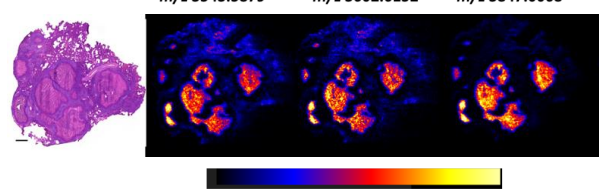

Figure 4. Image distribution of peptides from band 3 along with the histology image of an adjacent section

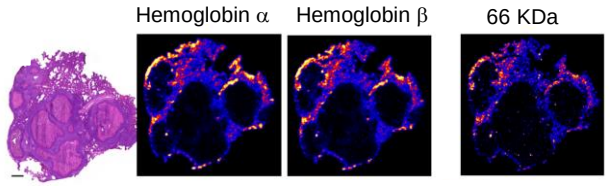

Figure 5. Image distribution of proteins along with the histology image of an adjacent section

Discussion/Conclusions

Figure 2 shows the Driftscope™ 2D-plot with the different regions observed that were grouped in bands. Bands labeled 1 and 2 showed singly charged species such as monomers and dimers of LeuEnk (used for normalization and mass accuracy corrections) and remaining lipids that were not completely washed off the tissue. The remaining bands have shorter drift time compared to these bands and are consistent with multiply-charge species of the peptides and protein species. For example, in Figure 3, the band 7 matched up with the charge envelope corresponding to hemoglobin α and β, with the deconvoluted spectra in the inset.

Figure 4 shows histology image of an adjacent section and the MS image distribution of some peptides with the quickest drift time from band 1 in the caseum and normal lung parenchyma. In Figure 5, we show the MS image distribution of hemoglobin α and β, and a protein at 66 KDa, tentatively assigned to albumin.

We are showing that we can use DESI™ coupled to Ion Mobility MS to detect multiple charged species corresponding to peptides and proteins of granulomas in lung tissues. Additional experiments need to be performed to confirm the identification of these peptides and proteins.

Reference

1. C Carter et al, "DESI™ Cyclic IMS imaging enhances the lipid class and chain length coverage detected from immune cells that comprise tuberculosis granulomas", ASMS 2021, oral presentation, TOD
2. MW Towers, T Karancsi, EA Jones, SD Pringle, E Claude, J. Am. Soc. Mass Spectrom. (2018) 29:2456-2466