MALDI-2-MS, chemical derivatization and Ion Mobility on the timsTOF-fleX-MS for enhanced MSI to assess Vit-D metabolism and androgen intracrinology

Diego Cobice, Jens Soltwisch, Bram Heijs, Karl Smith, Annika Koch, Klaus Dreisewerd and C. Logan Mackay. 1

1 Mass Spectrometry Centre, Ulster University, Coleraine, Northern Ireland, UK; 2 Institute of Hygiene, University of Münster, Münster, NRW, Germany; 3 Interdisciplinary Centre for Clinical Research (IZKF), Münster, NRW, Germany; 4 National High Magnetic Field Laboratory (NHFML), Tallahassee, FL, USA; 5 Bruker Daltonics, Bremen, Germany; 6 SIRCAMS, EastChem School of Chemistry, University of Edinburgh, Scotland, UK. Corresponding author: lmackay@ed.ac.uk

INTRODUCTION

• Growth of many prostate cancer tumors are dependent on active androgens such as testosterone (T) and dehydroepiandrosterone (DHEA).
• Vitamin D's active metabolite (1,25-(OH)2-D3), modulates the androgen intracrine pathway

Aims of the study

• To evaluate the application of ion mobility and MALDI-2 on a timsTOF fleX for determining the spatial distribution of derivatized androgens and vitamin D metabolites to improve sensitivity, and separate biological active isobaric species.

MATERIALS AND METHODS

• Instrument was a MALDI-2-IM-MSI using a timsTOF-fleX in-house modified with a 1 kHz, frequency-quadrupled Nd:YAG post-ionization laser (266 nm).
• Several derivatization reagents for both androgens (Girard-T and Dansyl Hydrazine) and VitD metabolite (PTAD and DMEQ-TAD) were screened to assess ionization enhancement and mobility separation on standards and tissue sections
• On-tissue chemical derivatization (OTCD) was performed by the Bruker ImagePrep using prostate tumour (10µm) tissue and matrix was applied using a modified 3D printer
• The source and TIMS pressures, as well as the CCS were calibrated using a low-molecular weight tune-mix.

RESULTS

• Isobaric androgens resolved by TIMS as hydrazones derivatives
• Dansyl derivatives achieved better resolution and signal enhanced by post-ionization

CONCLUSIONS

• Increase in ionization efficiency and isobaric separation of Dansyl DHEA/T derivatives achieved using MALDI-2-TIMS
• MALDI-2-MS shown an increase in sensitivity for azodicarbonyls VitD derivatives and C3-epimers successfully resolved using TIMS.
• First time spatial distribution of isobaric androgens achieved at tissue level by OTCD-MALDI-2-IM-MSI.

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