Distinct peptide signatures for remodeling after myocardial infarction in a mouse heart

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Introduction

Myocardial infarction (MI) remains the main cause of death worldwide[1]. MI leads to ischemia and subsequent molecular changes, inflammatory pathway activation, and remodelling. In this work, a mouse model susceptible for cardiac ischemic injury is used to investigate the remodelling process after MI at the protein level. Using MALDI MSI in-depth information on involved components and pathways can be obtained, providing information on the pathophysiology after MI.

We aim to find specific peptide signatures, linked to cardiac remodelling in the mouse heart after myocardial infarction.

Method

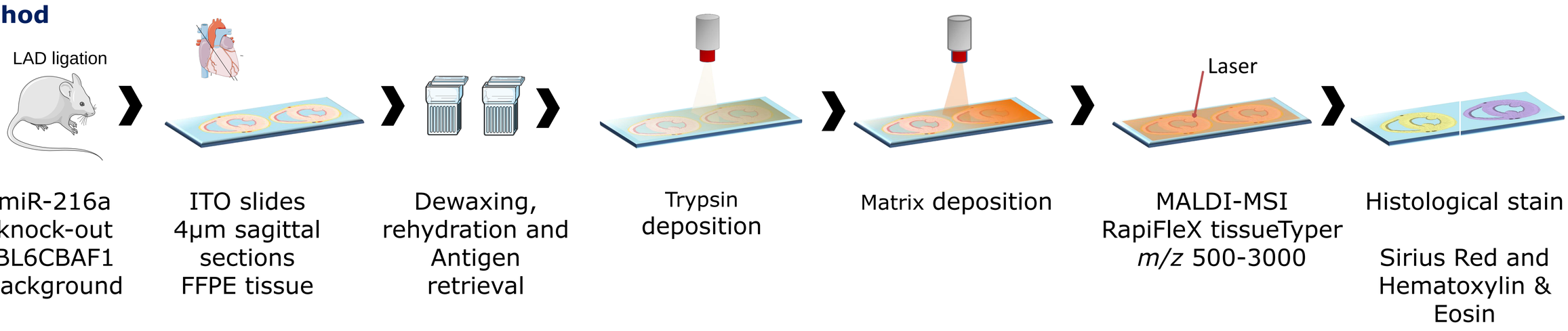


Figure 1. Schematic representation of the MALDI-MSI workflow. Tissue is collected four weeks after the LAD ligation and the hearts are formalin fixed paraffin embedded.

Results

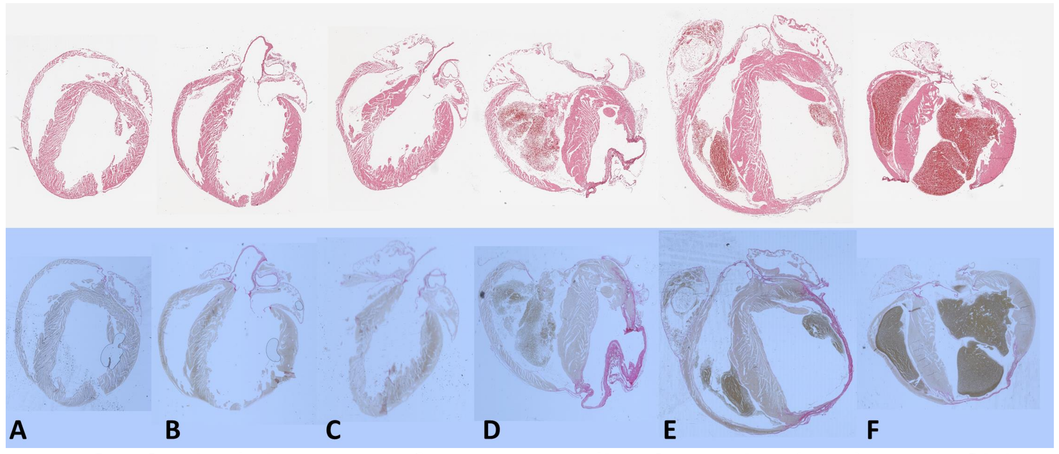


Figure 2. Optical images of Hematoxylin & eosin (top) and Sirius Red (bottom) stained sections, (*A-C*) sham hearts and (*D-F*) MI hearts, with the collagen rich areas in red.

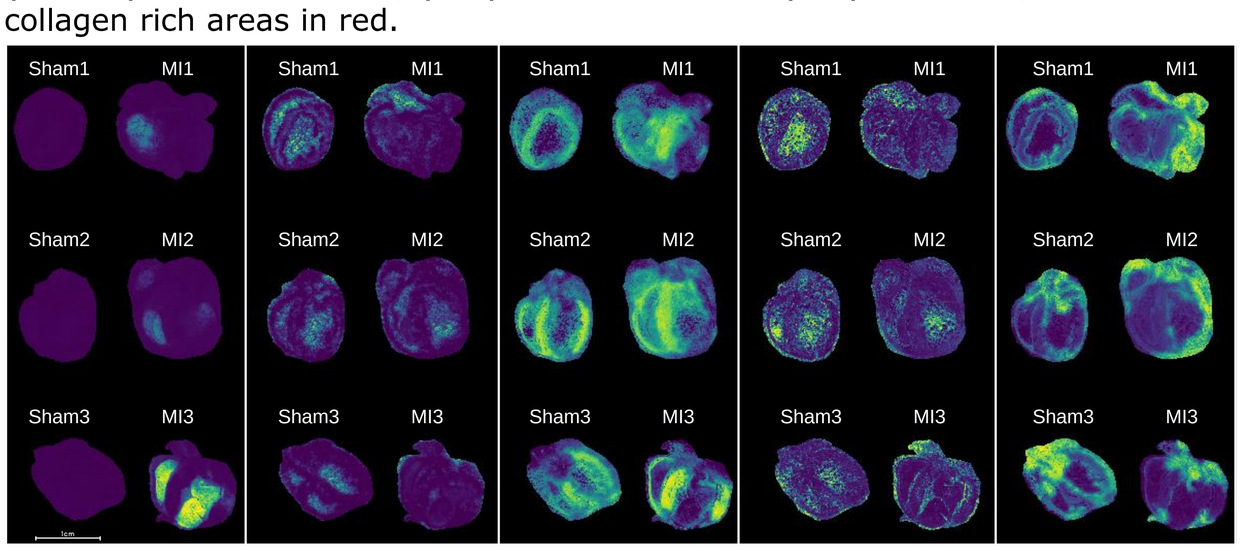


Figure 3. Probabilistic Latent Semantic Analysis with 5 components separating different area's. Components 1 represents blood, with the heme group (*m/z* 616.23) and peptides from hemoglobin *(m/z* 1529.73), while components 3 and 5 are represented by tissue related peptides, like actin (*m/z* 976.45 and 1198.70). Components 2 and 4 are trypsin autolysis peptides (*m/z* 842.57 and 1045.63) and matrix.

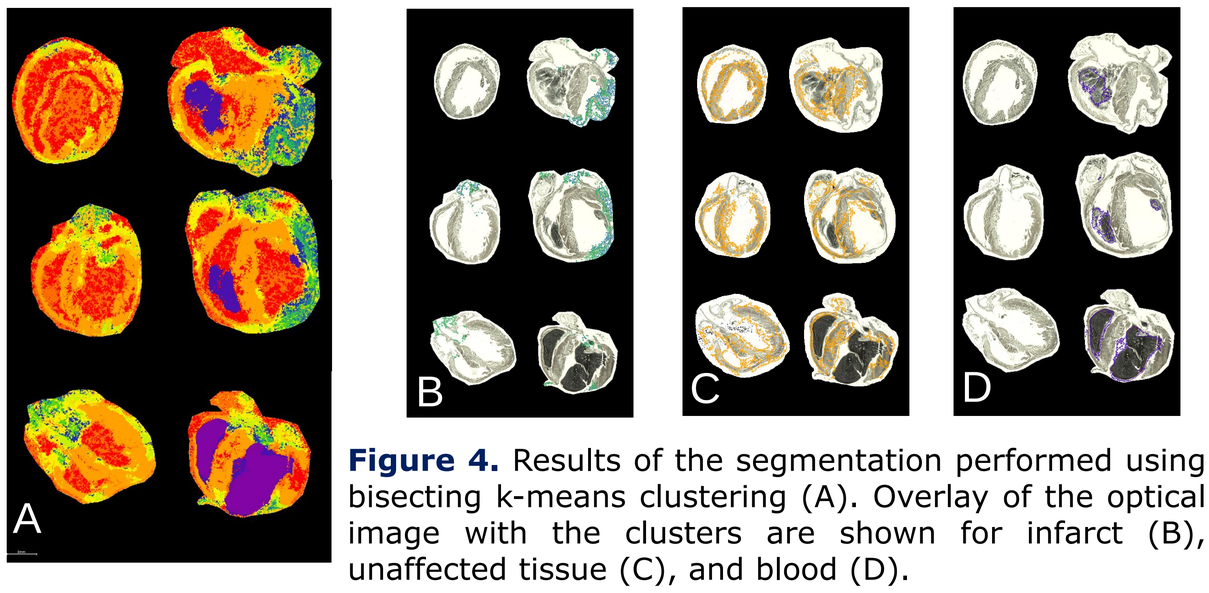


Figure 4. Results of the segmentation performed using bisecting k-means clustering (A). Overlay of the optical image with the clusters are shown for infarct (B), unaffected tissue (C), and blood (D).

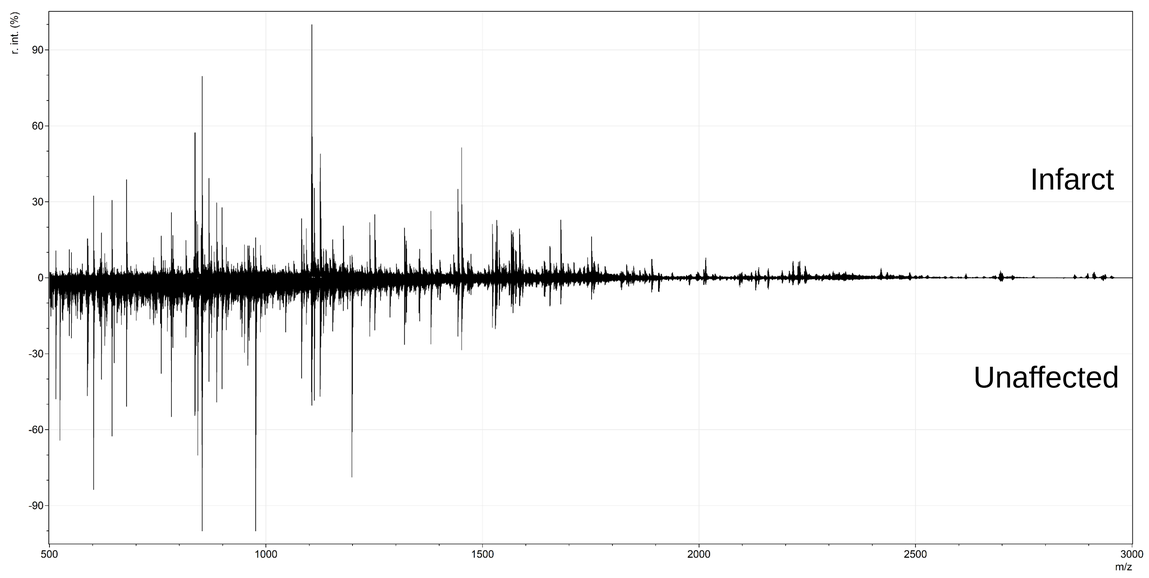


Figure 5. Average spectra from the infarct (top) and unaffected tissue (bottom) with *m/z* vales on the x-axis and relative peak intensities along the y-axis.

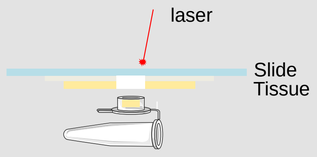
Future Direction

-MSI clustering data will be used to guide tissue laser microdissection.

-Bottom-up LC-MS/MS protocol optimized for very small tissue samples

-Analysis with nanoLC coupled to QExactiveTM HF Orbitrap.

-Data processing using Proteome Discoverer 2.2.



Acknowledgements

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References

[1]Benjamin *et al.* Heart Disease and Stroke Statistics-2018 update: a report from the American Heart Association. Circulation. 2018;137(12):e67–e492

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