

Exploration of degradome with MALDI Imaging provides fingerprint that differentiates hepatocellular carcinomas from cirrhosis

J. Le Faouder(1,2) • M.Chapelle(3) • P. Bedossa(2) • J.-M. Camadro(3) • V. Paradis(2)

(1)Claude Bernard Institute, IFR2, Paris • (2)INSERM U773, CRB3 Bichat & Beaujon hospital, Clichy • (3)Mass spectrometry facility, J. Monod Institute, Paris, France

To improve hepatocellular carcinoma (HCC) diagnosis and prognosis, we need specific and sensitive tissue markers. Matrix-assisted laser desorption/ionization (MALDI) imaging is a powerful tool for investigating proteins through the direct analysis of tissue section. Liver sections (n = 30) corresponding to HCC and non tumoral cirrhosis were subjected to MALDI-IMS. We found specific protein/peptide expression whose changes correlated recurrently with the presence or absence of HCC. Of particular note, the differential expression of 14 peptides was able to accurately define cancer tissue from non-cancerous tissue.

Identification of the most powerful marker was performed by tissue micro-extraction and separation followed by bottom-up tandem mass spectrometry. This protein corresponding to the ubiquitin monomer was validated by immunohistochemistry on a large set of HCC sampled on Tissue Microarray. Identification of two other peptides was performed by tissue micro-extraction and fractionation followed by top-down tandem mass spectrometry. m/z 2753 corresponding to a fragment of albumin was over expressed in tumoral tissue, whereas m/z 3195 corresponding to a fragment of alpha globin was strongly expressed in cirrhotic non-tumoral parenchyma.

Our results underscore the potential of MALDI-IMS to discriminate tumor from non-tumor tissues and the role of degradome as a specific fingerprint differentiating HCC from peritumoral cirrhotic tissue.