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MALDI-imaging: Identification of protein signatures of genomic instability in colorectal cancers

Timo Gemoll[a,*], Oliver Klein[b], Elena Miroll[a], Christoph Thorns[c], Jens Habermann[a]

[a] *University of Lübeck*
[b] *Charité, Berlin*
[c] *University Medical Center Schleswig-Holstein*

[*] *Corresponding author, email: timo.gemoll@uni-luebeck.de*

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Background: Matrix-assisted laser desorption/ionization (MALDI) imaging mass spectrometry (IMS) has improved over the years and is increasingly being used for biomarker discovery directly from human tissue. Since DNA aneuploidy has been identified as a prognostic factor for epithelial malignancies, we compared diploid and aneuploid colon cancer tissues of the colorectum by IMS.

Material and Methods: DNA image cytometry determined the ploidy status of tissue samples that were subsequently subjected to MALDI-IMS. After obtaining protein and peptide profiles through direct analysis of both, fresh frozen and FFPE tissue sections, a discovery and a validation set were used to predict ploidy and disease status by applying proteomic classification algorithms. Identification of m/z values were performed by using nUPLC mass spectrometry from an adjacent tissue section. Clinical target validations were performed by immunohistochemistry using in-house compiled tissue microarrays (TMA).

Results: Classification algorithms categorized normal mucosa and colon carcinoma as well as diploid and aneuploid colon cancers correctly. Proteins could be identified to be differentially expressed between diploid and aneuploid samples that showed expression differences also in clinical samples using a tissue microarray of normal mucosa, diploid and aneuploid colorectal carcinomas.

Conclusion: Our data underscore the potential of MALDI-IMS proteomic algorithms for individualized medicine to reveal significant molecular details from distinct tumor subtypes such as different ploidy types.