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Rauser, S; Marquardt, C; Balluff, B; Deininger, SO; Albers, C; Belau, E; Hartmer, R; Suckau, D; Specht, K; Ebert, MP; Schmitt, M; Aubele, M; Hoßfler, H; Walch, A

Titel des Beitrags: Classification of HER2 receptor status in breast cancer tissues by MALDI imaging mass spectrometry.

Abstract:
Clinical laboratory testing for HER2 status in breast cancer tissues is critically important for therapeutic decision making. Matrix-assisted laser desorption/ionization (MALDI) imaging mass spectrometry (IMS) is a powerful tool for investigating proteins through the direct and morphology-driven analysis of tissue sections. We hypothesized that MALDI-IMS may determine HER2 status directly from breast cancer tissues. Breast cancer tissues ($n = 48$) predefined for HER2 status were subjected to MALDI-IMS, and protein profiles were obtained through direct analysis of tissue sections. Protein identification was performed by tissue microextraction and fractionation followed by top-down tandem mass spectrometry. A discovery and an independent validation set were used to predict HER2 status by applying proteomic classification algorithms. We found that specific protein/peptide expression changes strongly correlated with the HER2 overexpression. Among these, we identified m/z 8404 as cysteine-rich intestinal protein 1. The proteomic signature was able to accurately define HER2-positive from HER2-negative tissues, achieving high values for sensitivity of $83\%$, for specificity of $92\%$, and an overall accuracy of $89\%$. Our results underscore the potential of MALDI-IMS proteomic algorithms for
morphology-driven tissue diagnostics such as HER2 testing and show that MALDI-IMS can reveal biologically significant molecular details from tissues which are not limited to traditional high-abundance proteins.

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