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Large scale breast cancer clinical proteomics using high-resolution mass spectrometry and super-SILAC

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Tissue proteomics is one of the most challenging tasks of the proteomic field due to its heterogeneity, the small sample amounts and the inability to metabolically label human tissues for quantification. Here we combined advanced proteomic technologies to identify protein signatures of breast cancer subtypes and stages. We used the recently developed super-SILAC mix, which is a mixture of lysates of five SILAC-labeled cell lines that serves as an internal standard for accurate tissue quantification. We analyzed formalin-fixed paraffin-embedded (FFPE) human breast cancer tissue samples from various subtypes and stages. High-resolution mass spectrometric analysis was performed with the Q-Exactive mass spectrometer, and data analysis was performed with MaxQuant. Deep proteomic analysis identified and quantified in total more than 12,000 proteins, and more than 8,000 proteins in each tumor sample. We then classified the tumors and created proteomic signatures that distinguish between breast cancer subtypes and stages with high accuracy using machine learning techniques. The signatures highlight differences in cell proliferation, cell adhesion and metabolism between the different groups. This signature is distinct from the signatures that are based on transcriptomics studies and is therefore highlighting novel aspects of each of the breast cancer groups.

This work shows that accurate quantification with super-SILAC enables establishment of robust breast cancer signatures, with the potential to alter breast cancer diagnosis and classification.

Biography

Tamar Geiger completed her PhD in biochemistry at the Hebrew University of Jerusalem, Israel, and her post-doctoral studies in the laboratory of Prof. Matthias Mann at the Max Planck Institute of Biochemistry. During her post-doc she specialized in proteomics technology and applied it to cancer research. In October 2011 Tamar has moved back to Israel and opened her own research laboratory at the Sackler Faculty of Medicine at the Tel Aviv University. She is proceeding with clinical proteomic research of breast cancer progression with emphasis on the metabolic changes that occur in this process.

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