Comprehensive Proteomic Characterization Reveals Subclass-Specific Molecular Aberrations within Triple-negative Breast Cancer

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Proteomic dissection of TNBC heterogeneity: Kosok & Alli-Shaik et al.

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Abstract

Triple-negative breast cancer (TNBC) is the most aggressive subtype of breast cancer lacking targeted therapies. This is attributed to its high heterogeneity that complicates elucidation of its molecular aberrations. Here, we report identification of specific proteome expression profiles pertaining to two TNBC subclasses, basal A and basal B, through in-depth proteomics analysis of breast cancer cells. We observed that kinases and proteases displayed unique expression patterns within the subclasses. Systematic analyses of protein-protein interaction and co-regulation networks of these kinases and proteases unraveled dysregulated pathways and plausible targets for each TNBC subclass. Among these, we identified kinases AXL, PEAK1, and TGFBR2 and proteases FAP, UCHL1, and MMP2/14 as specific targets for basal B subclass, which represents the more aggressive TNBC cell lines. Our study highlights intricate mechanisms and distinct targets within TNBC and emphasizes that these have to be exploited in a subclass-specific manner rather than a one-for-all TNBC therapy.
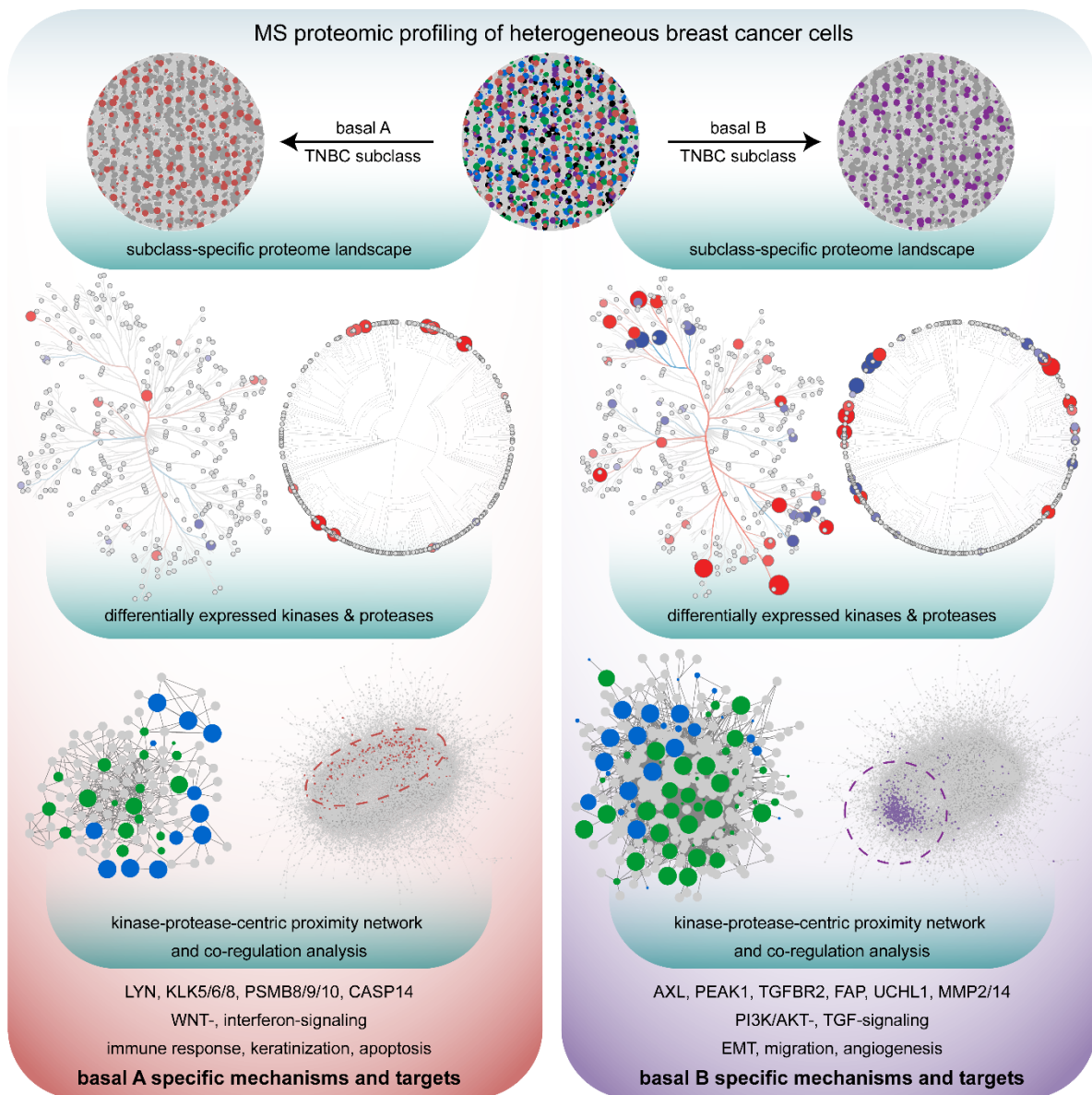
Figure

Figure Legend: Distinct subclass-specific mechanisms in breast cancer

The illustration showcases the potential of proteome-based subclassification in dissecting the intrinsic heterogeneity within breast cancer, particularly the highly aggressive TNBC, along with their subclass-specific functional associations, molecular vulnerabilities and pathway aberrations. Rationalizing therapies based on such unique dysregulated pathways and perturbed molecular targets, coupled with patient stratification, holds great promise for precision medicine and improved health outcomes in breast cancer.

For more information on Translational Biomedical Proteomics lab lead by Dr. Gunaratne, please click here.
https://www.a-star.edu.sg/imcb/science/scientific-programmes/technology-and-translation