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Molecular portraits revealing the heterogeneity of breast tumor subtypes defined using immunohistochemistry markers

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Breast cancer is highly heterogeneous. The subtypes defined using immunohistochemistry markers and gene expression profilings (GEP) are related but not equivalent, with inter-connections under investigated. We revealed a set of diff-genes, containing 1015 mRNAs and 69 miRNAs, which characterize the immunohistochemistry-defined breast tumor subtypes at the GEP level. We further reduced the dimension of this gene set to remove redundancy or noisy information. Using hierarchical clustering and nearest-to-center principle, we identified 119 mRNAs and 20 miRNAs best explaining breast tumor heterogeneity with the most succinct number of genes. The final signature panelcontains the 119 mRNAs, whose superiority over diff-genes was replicated in two independent public datasets. The comparison of our signature with two pioneering signatures, the Sorlie'ssignature and PAM50, suggests a novel marker, FOXA1, in breast cancer classification. Subtype-specific feature genes are reported to characterize each immunohistochemistry-defined subgroup. Pathway and network analysis reveal the critical roles of Notch signalings in [ER+|PR+] HER2- and cell cycle in [ER+|PR+]HER2+ tumors. Our study reveals the primary differences among the four immunohistochemistry-defined breast tumors at the mRNA and miRNA expression levels, and proposes a novel signature for breast tumor subtyping given gene expression data.

Biography:

Dr. Xiaofeng Dai, Ph.D., now is an Associate Professor at the National Engineering Laboratory for Cereal Fermentation Technology, School of Biotechnology, JiangNan University, China. She has master degrees both in Molecular Biology and Bioinformatics, and two doctoral degrees, one in Computational System Biology, and one in Quantitative Methods in Economics. Currently Dr. Dai' researches focus on breast cancer subtyping and heterogeneity, cancer stem cell signaling network and its association with immune response in basal breast cancer. She has published 15 SCI papers as the first author in reputed journals.

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