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Using specific response towards environment as a selective marker for therapy in breast cancer cells

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Breast cancer heterogeneity occurs as a consequence of the dysregulation of oncogenic and non-genetic factors, including tumor microenvironmental stresses. Although the non-genetic factors are important, it is not clear how to integrate these factors within the genetic framework of cancer as the next step in understanding tumor heterogeneity. In the first part, series of gene expression signatures were developed to examine the influences of microenvironmental stresses. Through the integrative pathway analysis of microenvironmental stresses and oncogenic events in breast tumors, we identify many known and novel correlations. We further determine two subgroups, which have features consistent with basal and luminal breast tumors including patterns of oncogenic signaling pathways and cellular mechanisms that regulate the hypoxia response, in HER2 breast cancers. Although significant variations in the metabolic profiles exist among different cells, little is understood in genetic regulations of cell type-specific metabolism and nutrient requirements. While cancer cells depend on exogenous glutamine for survival, the mechanisms of glutamine dependence, the response and resistance of glutamine-targeting strategies among cancers are largely unknown. In the second part, we find a systematic variation in the glutamine dependence among breast tumor subtypes: basal- but not luminal-type breast cells are more glutamine-dependent and may be susceptible to glutamine-targeting therapeutics. The ability of glutamine synthetase to predict patterns of glutamine metabolism and dependency among tumors is also crucial in the rational design and application of glutamine targeted therapies. Taking two studies together, results demonstrate the potential of genetic and non-genetic factors to investigate the basis of tumor heterogeneity.

Biography

Hsiu-Ni Kung completed her PhD at National Taiwan University in 2008 and Postdoctoral fellow at Duke University in 2011. She joined the faculty member in Anatomy and Cell Biology in National Taiwan University, 2011-present.

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