Synergy network based inference for breast cancer metastasis

Abstract:

Breast cancer is a world wide leading cancer and it is characterized by its aggressive metastasis. In many patients, microscopic or clinically evident metastases have already occurred by the time the primary tumor is diagnosed. Chemotherapy or hormonal therapy reduces the risk of distant metastasis by one-third, but it is estimated that about 70% to 80% of patients receiving treatment would have survived without it. Therefore, being able to predict breast cancer metastasis can spare a significant number of breast cancer patients from receiving unnecessary adjuvant systemic treatment and its related expensive medical costs. Current studies have demonstrated the potential value of gene expression signatures in assessing the risk of post-surgical disease recurrence. However, most of these studies attempt to develop genetic marker-based prognostic systems to replace the existing clinical criteria, while ignoring the rich information contained in established clinical markers. Clinical markers, such as patient history and laboratory analysis, which are the basis of day-to-day clinical decision support, are often underused to guide the clinical management of cancer in the presence of microarray data. As a result, given the complexity of breast cancer prognosis, we proposed a novel strategy based on synergy network that utilize both clinical and genetic markers to identify the potential hybrid signatures and investigate their interactions which are associated with breast cancer metastasis. In this study, a computational method is performed on publicly available microarray and clinical data. A rigorous experimental protocol is used to estimate the prognostic performance of the hybrid signature and other prognostic approaches. The hybrid signature performs significantly better than other methods, including the 70-gene signature, clinical makers alone and the St. Gallen consensus criterion. At 90% sensitivity level, the hybrid signature achieves 77% specificity, as compared to 53% for the 70-gene signature and 43% for the clinical makers. The predicted results also showed a strong dependence of regulator genes that are related to cell death in cell development process. These significant gene regulators are useful to understand cancer biology and in producing new drug design.