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Type	Oral communication
Session	Systems Biology
Title	The New Paradigm of Network Medicine to Analyze Breast Cancer Phenotypes
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Motivation

Breast cancer (BC) is a heterogeneous and complex disease as witnessed by the existence of different subtypes and clinical characteristics that poses significant challenges in disease management. The complexity of this tumor may rely on the highly interconnected nature of the various biological processes as stated by the new paradigm of Network Medicine [1]. Despite the remarkable increase in the depth of understanding of BC, the disease is still a major public health problem worldwide and poses significant open challenges.

Methods

Searching for molecular signatures underlying different subtypes of BC, we applied one of the most promising network-medicine-based algorithms, named SWItch Miner (SWIM) [2], on The Cancer Genome Atlas (TCGA)-Breast Invasive Carcinoma (BRCA) dataset. Specifically, SWIM methodology builds upon the structural properties of gene co-expression networks to mine key genes (called switch genes) likely associated with drastic physiological changes in many biological settings. In this study, the transcriptomic profiles of TCGA-BRCA patients were stratified into different BC subtypes according to the well-established immunohistochemistry and PAM50 genetic classifications, to identify both switch genes shared among different subtypes and those specific for each subtype.

Results

We identified 266 and 372 switch genes from immunohistochemistry and PAM50 classifications, respectively. The identified switch genes were functionally characterized to select an interconnected pathway of disease genes. By intersecting the common switch genes of the two classifications, we selected a unique signature of 28 disease genes that were BC subtype-independent and classification subtype-independent. Data were validated both in vitro (10 BC cell lines) and ex vivo (66 BC tissues) experiments [3]. Results showed that four of these hub proteins (AURKA, CDC45, ESPL1, and RAD54L) were over-expressed in all tumor subtypes. Moreover, the inhibition of one of the identified switch genes (AURKA) similarly affected all BC subtypes. In conclusion, using a network-based approach, we identified a common BC disease module which might reflect its pathological signature, suggesting a new vision to face with the disease heterogeneity.

Info

Reference
[1] Barabási, A. L., Gulbahce, N., & Loscalzo, J. (2011). Network medicine: a network-based approach to human disease. Nature reviews genetics, 12(1), 56-68.
[2] Paci, P., Colombo, T., Fiscon, G., Gurtner, A., Pavesi, G., & Farina, L. (2017). SWIM: a computational tool to unveiling crucial nodes in complex biological networks. Scientific reports, 7(1), 1-16.
[3] Grimaldi, A. M., Conte, F., Pane, K., Fiscon, G., Mirabelli, P., Baselice, S., ... & Incoronato, M. (2020). The new paradigm of network medicine to analyze breast cancer phenotypes. International journal of molecular sciences, 21(18), 6690.

Figure

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Availability	-

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