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J Proteomics Bioinform 2016, 9:11(Suppl)
http://dx.doi.org/10.4172/0974-276X.C1.092

Multi-omics profiling of tumor interstitial fluid of breast cancer patients: A novel resource to identify cancer biomarkers for prognostic classification and detection

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Breast cancer (BC) is one of the most common cancers with millions of cases each year world-wide. Recent studies have revealed extensive genetic diversity and intra-tumor heterogeneity even within the same BC subtype. BC heterogeneity that is determined by complex clonal and spatial tumor organization severely affects key biological pathways thus challenging BC diagnostic classification and treatment. Despite tremendous efforts, no robust blood markers for BC patients have been identified so far, mainly due to current underestimation of BC complexity and high dilution factor in blood. The levels of disease biomarkers in local tumor microenvironment are estimated to be several orders higher than in blood and thus, the analysis of lesion-proximal fluids have become one of the most promising strategies for identification of potential candidates for non-invasive biomarkers. In this respect, tumor interstitial fluid (TIF), watery phase that is formed largely in solid tumor interstitium, comprising all biocompounds externalized from tumor mass is a novel, unique and valuable source for biomarker discovery. In the course of the study, we applied multiple–omics technologies, such as different proteomics platforms and glycomics screening, for the profiling of biomolecules externalized directly from the tumor and its microenvironment. Representative sets of tumors of multiple BC subtypes, matched TIFs, and blood samples obtained from high risk breast cancer patients with complete clinical and histopathological records including characterization of immune-infiltrates were analyzed. Such integrative approach allows revealing interconnection of BC biomarkers and their associated specific subtypes depending on the spatial tumor organization.

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