Research & Reviews: Medical and Clinical Oncology

Complexity of Cancer Proteomes: Insights from Cell Lines and Tumor Heterogeneity

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Opinion Article

Received: 28-Nov-2023, Manuscript No. MCO-23-122102; **Editor assigned:** 01-Dec-2023, PreQC No. MCO-23-122102(PQ); **Reviewed:** 14-Dec-2023, QC No. MCO-23-122102; **Revised:** 21-Dec-2023, Manuscript No. MCO-23-122102(R); **Published:** 28-Dec-2023, DOI: 10.4172/medclinoncol.7.3.007

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Citation: Ishii T. Complexity of Cancer Proteomes: Insights from Cell Lines and Tumor Heterogeneity. Med Clin Oncol. 2023;7:007.

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ABOUT THE STUDY

Cancer cells may be isolated from effusions or tumor tissue, or investigated as cancer cell lines in culture. Analyzing a collection of cell populations that reflect tumor heterogeneity is advantageous because it is unlikely that a single cell population will accurately reflect the range of alterations that may occur in a particular type of cancer. a method for analyzing the proteomes of cancer cells that combines information from the cell surface, secretome, and entire cell lysate for each compartment of interest.

These data can also be combined with pertinent information about gene-expression patterns, genomic alterations, or other features of the cells, like mesenchymal or epithelial characteristics, primary versus metastatic origin, or other clinical traits of the subjects from whom the cells were derived. A few representative results regarding breast and ovarian cancer are given.

Astatic fluid-enriched ovarian cancer cells and three cell lines OVCAR3, CaOV3, and ES2 were used to analyze the protein repertoire expressed in ovarian adenocarcinoma cells. Using total cell lysates as a reference, separate mass spectrometric analyses of proteins released into culture media and of proteins on the cell surface were carried out.

A high degree of confidence was used to identify about 6400 proteins. Data that are comparable or complimentary and exhibit significant concordance have been published for ovarian cell lines and ovarian ascitic fluid. WFDC2, MUC16, MDK, PROS1, and SLPI are among the secreted proteins that were found; these have all been linked to ovarian cancer in the past. There are many more candidates that have been found to be potential targets for molecular imaging, therapeutics, or diagnostics.

Mass spectrometry-based protein tyrosine phosphorylation profiling was applied to 15 breast cancer-cell lines in an effort to identify therapeutic targets and prognostic markers for basal breast cancers. Different tyrosine phosphorylation signatures were seen in luminal and basal breast cancer cells, according to unsupervised hierarchical clustering.

Elevated tyrosine phosphorylation of substrates for FAK, Src-Family Kinase (SFK), Met, Lyn, EphA2, and Epidermal Growth-Factor Receptor (EGFR) was observed in Basel breast cancer cells. Cell survival, motility, and proliferation were all reduced by SFK inhibition. Based on the degree of target phosphorylation, based breast cancer cell lines also showed varying sensitivity to EGFR and Met inhibition. In a different study, changes resulting from gene copy number were determined through comprehensive proteomic analysis of breast cancer cell lines.

A viable substitute is the use of stable-isotope-labelled peptides as internal standards in Multiple Reaction Monitoring (MRM) to track fragments of particular peptides and directly quantify corresponding proteins in serum. Alternative strategies, such as peptide, RNA, or DNA aptamers, may also be able to do away with the requirement for antibodies.

Proteomics technologies have advanced to the point where proteome interrogation can now be done with significant reliability and depth of analysis, which is useful for applications related to cancer. However, not many people have taken notice of these developments. The task of mining the cancer proteome is complicated by the proteome's many facets, complexity, and potential for changes at multiple levels in cancer. Furthermore, given the volume and complexity of cancer proteomic data currently being produced, efficient data mining would necessitate combining proteomic data from several sources, such as primary tissue, cells, biological fluids, and animal models, in addition to combining proteomic data with other kinds of data.