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ISSN: 2153-2435
Pharmaceutica Analytica Acta

Opinion Article

Multi-Drug Combinations in Breast Cancer Treatment

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ABOUT THE STUDY

The greatest challenge in recent years in cancer treatment has been drug screening. Few platforms presented reliable solutions for personalized drug validation and safety testing. Here, we constructed a drug combination protocol as the primary input to such platforms. We used public data from whole-genome expression profiles of 6173 breast cancer patients, 312 healthy individuals, and 691 drugs. We developed an individual pattern of perturbed gene expression (IPPGE) for each patient. A protocol was designed to extract personalized drug combinations by comparing the IPPGE and drug signatures. We tried to use the concept of drug repurposing, which searches for the new benefits of the existing medicines that may perturb the desired genes. The potential for treatment effectiveness was more significant for drug combinations extracted from specialized and nonspecialized cancer medicines than specialized medicines. Thus, effective treatments can be provided through the approach of drug repurposing and combination drug therapy.

The gene expression involved in diseases typically shows a unique pattern, which can be detected when studying patient populations. Drug repurposing studies aim to identify the most appropriate medicines that can regulate the genes involved in perturbed expression patterns in disease. Moreover, studies have shown that combination drug therapy can be more efficient in reducing drug resistance due to the control of parallel biological pathways. Heterogeneity of cancer leads to different responses to similar treatments. Therefore, it is essential to identify the gene expression pattern of each patient to determine the most effective combination drug therapy

The IPPGEs of the abovementioned four patients and connectivity map (CMAP) data were used as input to our designed protocol to extract personalized drug combinations. The CMAP database reports the effect of drugs on gene expression. Any drug or drug combination that could affect several IPPGE oncogenes to bring their expression back into the health interval was extracted, forming a personalized drug combination. Given the possibility of obtaining better comparisons between breast cancer-specific drugs and between nonspecific drugs, drug combinations were extracted from these two major drug groups. The first group consisted of drugs approved for breast cancer, called the Alpha group. The second group included the Alpha group drugs and all other FDA-approved drugs and was called the Beta group. Overall, 27 combinations of drugs were extracted across the two groups for the four patients. The protocol extracted personalized drug combinations from the Alpha group for the first, second, third, and fourth patients, respectively.

Several drug repurposing studies have reported significant anticancer efficacy for non-specialized drugs. One of the first drug repurposing studies showed that the anti-ulcer drug cimetidine to be a therapeutic candidate for the treatment of adenocarcinoma of the lung. Subsequent studies have found that combination drug therapy increases the success of drug repurposing

The combinations extracted included both specialized and non-specialized cancer medications. These drug combinations can be used as the primary input for personalized medicine platforms. The protocol can be used as a methodological interface between drug repurposing activities and combination drug therapy.

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Received: 02-Feb- 2022, Manuscript No. PAA-22-16105; **Editor assigned:** 04-Feb-2022, PreQC No. PAA-22-16105 (PQ); **Reviewed:** 18-Feb-2022, QC No. PAA-22-16105; **Revised:** 25-Feb-2022, Manuscript No. PAA-22-16105 (R); **Published:** 02-Mar-2022. DOI: 10.35248/2153-2435.22.13.656.

Citation: Haan E (2022) Multi-Drug Combinations in Breast Cancer Treatment. Pharm Anal Acta. 13:656.