



Drug Repurposing for Human HER2 Positive Breast Cancer based on Gene Co-expression Data

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Abstract: Breast cancer is the most common cancer and the second leading cause of cancer-related death among women in the world [1]. This cancer is classified into four main subtypes including Luminal A, Luminal B, HER2 and triple negative (basal-like) [2]. Since the diagnosis and the treatment of breast cancers stay a challenging task, there is an essential need for discovering new breast cancer drugs with fewer side effects. Drug discovery is a long and onerous process, that made the major obstacles to the prompt development of medicine. Therefore, some strategies for improving the drug development are needed to provide efficient drugs. So in this study, we used drug repurposing to solve this problem. The aim of this approach is to find potential new applications for existing drugs and decrease the time and cost of the progress of commercial drugs [3]. The mRNA gene expression microarray data concerning breast invasive carcinoma, was retrieved from The Cancer Genome Atlas (TCGA). In this work, HER2 subtype has been investigated and separated by clinical dataset of rest samples. The normal and treatment samples have been analysed using Linear Models for Microarray Data (LIMMA) R package in order to find the top differentially expressed genes (DEG). Then the characteristic direction signatures search engine (L1000CDS) was used to obtain candidate drugs in order to eliminate the disorders caused by the detected DEGs in the normal function of tissues and signaling pathways. One of these proposed drugs was Alvocidib, a semisynthetic flavonoid that approved by FDA for chronic lymphocytic leukemia (CLL). This drug acts by inhibiting cyclin-dependent kinases (CDK2), stopping cell division and causing apoptosis in lung cancer cells [4]. Therefore, Alvocidib may be considered for the cancers treatment, such as breast cancer, due to its inhibitory function. Also, according to the studies conducted so far, Alvocidib has investigated in Phase 1 and 2 clinical trials for all types of breast cancer.

Keywords: Breast cancer; Drug repurposing; Gene expression; LINCS; Microarray Data

References

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