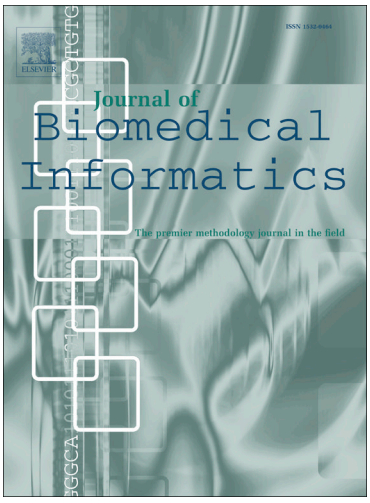

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Predict effective drug combination by deep belief network and Ontology Fingerprints

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ABSTRACT

The synergistic effect of drug combination is one of the most desirable properties for treating cancer. However, systematically predicting effective drug combination is a significant challenge. We report here a novel method based on deep belief network to predict drug synergy from gene expression, pathway and the Ontology Fingerprints—a literature derived ontological profile of genes. Using data sets provided by 2015 DREAM competition, our analysis shows that this integrative method outperforms published results from the DREAM website for 4999 drug pairs, demonstrating the feasibility of predicting drug synergy from literature and the –omics data using advanced artificial intelligence approach.

Keywords—drug combination, deep belief network, Ontology Fingerprint

I. INTRODUCTION

Combining drugs to treat cancer has significant benefit over single agent therapy. In combination therapy, using several drugs can significant boost the efficacy of the therapy, and the amount of drugs used can be reduced to alleviate the toxidity while maintaining the effectiveness to kill cancer cells. Effective drug combination relies on the synergy between drugs—the more than additive effect that cannot be predicted by well-established Loewe model (1, 2). Experimental detection of such synergy is time consuming and costly, especially for the extremely large search space of the combination of drugs, genes and cell lines. For this reason, computational methods have been playing a crucial role to predict drug synergy.

ANOVA (Analysis of variance) was the first computational method used to detect drug synergy (3-11). However, the approach was proven to be invalid by Robert M. Caudle and Gene M. Williams (12) because the condition to support the use of ANOVA is not meet. The assumption underlying the null hypothesis of ANOVA is that the dose-response curve for combined drugs should parallel to that of drug alone when the effects are additive, a condition that is not generally correct. Later on, a network and clustering analyses approach was used (13) to highlight common interactions of drugs to predict drug synergy. However, this network has limited application because it only used the most synergistic subsets of drug combinations based on Delta Bliss Summary metric. Machine learning methods, such as Random Forests and Support Vector Machines, are broadly used for drug synergy detection (14, 15). Recently,