Abstract

Motivation. Identifying chemotherapy combinations with the highest efficacy is instrumental for the accurate treatment of patients with cancer. Recently, approaches using genomics analysis to assess mutations and instability have been approved for clinical use. However, these approaches provide limited access to the metabolic plasticity and heterogeneity of cancers. This ability of cancers to diversify their metabolism contributes to chemotherapy resistance.

Solution. We developed METABOSCOPE, a machine learning based algorithm for the efficient and unbiased identification of the metabolic dependencies of a patient’s tumor. METABOSCOPE enables high-resolution and high-sensitivity exploration while using predictive analytics to determine the sensitivity of the tumoral metabolic profile to chemotherapeutics. METABOSCOPE is also equipped with robust statistical tools and diverse analytical profiles different from existing clinical options. METABOSCOPE introduces a unique advantage to clinicians by equipping them with patient-personalized metabolic profiles and chemotherapeutic sensitivities.

Introduction

METABOSCOPE provides a unique solution to chemotherapy selection by providing clinicians access to the metabolic profile of a patient’s tumor. This arms clinicians with improved information to guide their therapeutic selection given that an increasing number of FDA approved chemotherapeutics are metabolic inhibitors. Recently, genomic profiling methods have been approved by the FDA for use in cancer therapy with these genomic profiles providing clinicians guiding evidence for chemotherapy selection. While these pharmacogenomics methods unequivocally play an important role in cancer treatment, it is important to note that genetic dispositions are not always predictive of metabolic phenotypes, the ultimate target point of a number of chemotherapeutics. Furthermore, many patient tumors exhibit intratumoral heterogeneity which is a problem often underexamined in genomic profiling methods. Thus, our approach using a metabolomics platform provides a potential solution for the problem of chemotherapy selection and provides key insight into the patient’s tumor.

Workflow /

METABOSCOPE Workflow. The first two steps of the workflow outline the extraction of the tumor and the analysis of the tumor through LC-MS/MS. These steps are performed by the laboratory technician and then analyzed either within the oncology center or via a third-party platform. METABOSCOPE utilizes input data taken from the absolute and relative concentrations of the measured metabolites and proteins in parallel with other clinical data including genomics and surgical pathological data to create a network association map of overly active and therapeutically targetable metabolic pathways (Step 3). These pathways will also be cross-listed with probable pathways databases such as KEGG, Reactome, and HMDB and the resulting networks will be aligned against FDA approved drugs.

Framework /

METABOSCOPE uses experimental metabolomics data of a patient’s tumor to optimize clustering, classification, development, and verification of correlated models that can be used to predict the most apt chemotherapy. METABOSCOPE uses supervised and unsupervised learning related to other methods [1,2].

Conclusions

METABOSCOPE is an efficient and unbiased machine learning platform which utilizes aspects of a cancer’s metabolism to guide clinicians to the appropriate therapeutic. Specifically, METABOSCOPE incorporates metabolomics assessments with predictive analytics to quickly generate a library array of metabolic associations for a specific patient’s cancer. These associations are then cross-referenced with existing FDA approved therapeutics to simultaneously generate an automatic report containing a ranked list of the metabolic tendencies of the patient’s cancer.

References