Towards a web-based environment which assists physicians in guiding ARV resistance treatment

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Objective

The aim of this study is the development of a web-based environment that offers various bioinformatics tools to assist physicians in determining the optimal highly active anti-retroviral therapy for individual antiretroviral resistant patients. The clinical environment will facilitate the analysis of the collated output from different interpretation gold standards and predicting the future resistance profile of a patient.

Keywords:

Forecasting, Artificial intelligence, HIV, Drug resistance

Introduction

Interpretation algorithms for predicting resistance to antiretrovirals (ARVs) are disparate. There are instances where the same resistance profile can produce different resistance interpretations causing difficulty for physician to make a decisive intervention on behalf of the patient.

The aim of this study is the development of a web-based environment to assist physicians in determining the optimal highly active antiretroviral therapy for individual ARV resistant patients.

Methods

The algorithm to assist physicians in determining the optimal therapy will consist of numerous bioinformatics tools and its creation will be done in stages. These include the development of an HIV drug resistance interpretation algorithm capable of providing a single interpretation of genomic analysis, the development of support vector machines and neural networks that will create a mathematical model that can predict future CD_4 measures given the current genome, drug therapy and viral load etc., and to investigate the means of predicting the patient specific evolution of HIV with the aim of determining future HIV drug resistance mutations.

Single interpretation to genomic analysis

Three of the most widely accepted interpretations algorithms are HIV-db, REGA and ANRS. The latest versions of these algorithms will be applied to a single, publicly available, anonimised dataset. The outputs of these gold standard algorithms will be collated by using a weighted output approach, machine learning to try to find mappings between the outputs of the gold standards and the actual resistance measure, and by creating a simulated boosted dataset by modeling the strengths and weaknesses of the gold standards. This will be done by determining the data elements of the dataset that can not be correctly identified by the gold standards and increase their weightings. Machine learning techniques will then be applied to this new dataset.

Web-based prediction tool

The web-based prediction tool will be created to analyze the outputs of the above mention algorithms and will take into account toxicities, adherence, ARV concentrations attained etc. By determining the current resistance profile of a patient and his future resistance profile given different treatments, the prediction tool will determine a treatment that maximizes CD_4 and minimizes the effect of resistance.

Results

Algorithms that take as input genome, time and viral load and predict the current CD_4 count or if CD_4 count is less than 200 have been created and they produced an $r = 0.9$ and accuracy of 95% during testing respectively.

An algorithm that predicts drug resistance from genome has also been created using machine learning algorithms which produces an accuracy of 89% and which has shown to outperform many international interpretation gold standards.

Conclusion

The strengths of previously published and clinically used, seemingly disparate individual tools need to be harnessed to develop an application that aids physicians in determining the optimal therapy for HIV patients. Such a tool needs to take into account current and future resistance profiles of a patient when determining optimum therapy.