Estimating the Predictive Power of Silent Mutations on Cancer Classification and Prognosis

Tal Gutman¹, Tamir Tuller¹²

¹ Department of Biomedical Engineering, Tel-Aviv University, ² The Sagol School of Neuroscience, Tel Aviv University

Introduction

Silent mutations are DNA variations that do not cause a change in the linear sequence of amino-acids in the translated protein. These mutations could occur in introns, UTRs, flanking regions and even within the coding region, and yet they are often overlooked when performing cancer research. Nonetheless, these mutations could affect gene expression regulation and thus impact cancer development and fitness. This study aims to quantify the predictive ability of various silent mutations over cancer classification and prognosis.

Objectives

1. Use silent mutations to classify patients’ cancer types
2. Use silent mutations to estimate patients’ survival probabilities over time after the initial diagnosis
3. Perform both above-mentioned tasks using other types of mutations as well, and compare their predictive power to the power of silent mutations

Methods

THE DATA

Obtained from TCGA²
9915 Patients
33 cancer types
≈3.3M mutations

CANCER TYPE CLASSIFICATION

6 predictors per cancer type

<table>
<thead>
<tr>
<th>Mutation A</th>
<th>Segment B</th>
<th>Gene C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient 1</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Patient 2</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Patient 3</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Fig. 2 A demonstration of the classification algorithm

SURVIVAL ANALYSIS

Random Survival Forest

Conclusions

1. In both tasks, the use of silent mutations alone was enough to outperform the null models and under some circumstances also outperform models that used other types of mutations.
2. The ability to perform these tasks using silent mutations alone suggests that they do have an important effect on cancer fitness. Thus, silent mutations may hold unique and essential information and should not be discarded when performing cancer research.

References