Insulin Dependent Diabetes Mellitus Rats and Autoimmune Diabetes

Rainer SCHMIDT\textsuperscript{a,1}, Georg FUELLEN\textsuperscript{a}
\textsuperscript{a}Institute for Biostatistics and Informatics in Medicine and Aging Research, University of Rostock, Germany

Abstract. The investigation of the mechanism of tolerance induction by the modulatory anti CD4 monoclonal antibody RIB 5/2 in insulin dependent diabetes mellitus rat is the aim of our study. Decision trees and some other classification methods have been applied on data sets of just twelve specifically breded rats.

Keywords. Bioinformatics, Machine Learning, Autoimmune Diabetes

1. Introduction

Type 1 diabetes is an autoimmune disease in which beta cells are exclusively destroyed by the interaction of antigen presenting cells, T cells, and environmental triggers such as nutrients and viral infection [1]. Biomarkers related to mechanisms of T cell mediated beta cell destruction and induction of self-tolerance are missing. In this project it was the intention
- To elucidate the mechanisms of the modulating anti CD4 antibody RIB5/2 on prevention of autoimmune destruction of beta cells in the insulin dependent diabetes mellitus (IDDM) rat model.
- To analyse immune cell (bio-) markers in peripheral blood during progression of autoimmunity and/or induction of self-tolerance.

2. Methods

In our recent experiment we used just twelve rats. They were monitored for gene expression data in blood immune cells for functional gene clusters on the days 30, 35, 40, 45, 50, 55, 60, 65, 70, 80, and 90 of their life. However, just the days between 45 and 60 are assumed to be important for the prediction whether a rat will develop diabetes. Six of the twelve rats developed diabetes, three did not, and another three rats (background strain) were diabetes resistant because of the way they had been bred.

The attributes are eighteen preselected genes and biomarkers. Since we wanted to get attributes (genes) that are most decisive for the classification, decision trees (C4.5 [2] implemented as J48 in WEKA) were chosen. Later on, other classification algorithms provided in WEKA were used.

\textsuperscript{1} Corresponding Author.
3. Results

The results for the days 45, 50, and 55 are shown in figure 1. There are three trees depicted, the left one is for day 45, the right one is for day 55. At the beginning of infiltration (day 45) the RT6 gene expression, responsible for the correct thymic development of T-cells, may decide whether autoimmunity could develop. At a stage of islet infiltration (day 50) selectin and neuropilin gene expression decides whether primed T-cells will infiltrate the endocrine pancreas for beta cell destruction. During progression of beta cell destruction (day 55) IL-4 as a T cell stimulating cytokine is crucial for the progression of beta cell infiltration.

Next some standard classification methods were applied. In table 1, the results are shown just for day 50 as an example.

Table 1. Accuracy and Area Under the Curve for day 50.

<table>
<thead>
<tr>
<th>Methods</th>
<th>Accuracy (%)</th>
<th>Area Under the Curve</th>
</tr>
</thead>
<tbody>
<tr>
<td>Naïve Bayes</td>
<td>58.3</td>
<td>0.52</td>
</tr>
<tr>
<td>Nearest Neighbor</td>
<td>75.0</td>
<td>0.75</td>
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<tr>
<td>Random Forest</td>
<td>66.7</td>
<td>0.80</td>
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<tr>
<td>J48 (Decision tree)</td>
<td>66.7</td>
<td>0.76</td>
</tr>
<tr>
<td>SMO (SVM)</td>
<td>58.3</td>
<td>0.65</td>
</tr>
</tbody>
</table>

References
