Nanostring Prognosis Panel for Progression of Persistent Bronchial Dysplasia to Squamous Cell Lung Cancer

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BACKGROUND

• To provide prognostic information for patients with premalignant airway disease in a clinical setting, it is important to classify whether patients will experience persistent or regressive behavior relative to baseline.

AIM

• Identify a prognostic panel of baseline gene ratios to predict whether patients will experience persistent or regressive bronchial dysplasia (BD).

METHODS

• 63 baseline biopsies from patients with BD were collected between 1997 and 2017 and followed over time to determine whether their BD persisted or regressed.

• Univariate associations between each baseline independent variable (age, sex, smoking status, etc.) and the outcome (persistent or regressive BD) were assessed with a logistic regression model.

• A multivariate model was selected to assess the association between the Nanostring gene ratios and persistence.

• The best-fitting model according to the Bayesian Information Criterion (BIC) was chosen as the final multivariate model.

RESULTS

Table: The univariate associations between each independent variable and persistence using a logistic regression model.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>BMP7_PPKCE</th>
<th>COL4A_3_PPKCE</th>
<th>ESRP2_SCCPDH</th>
<th>PTEN_IQGAP2</th>
<th>AFRR5A_MODEL</th>
<th>PTK2_RGL2</th>
<th>CYP4F3_PPKCE</th>
<th>AFRR6A_PPKCE</th>
<th>AFRR6B_PPKCE</th>
<th>ESRP2_ST3GAM1</th>
<th>ESPC1_PPKCE</th>
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</thead>
<tbody>
<tr>
<td>OR</td>
<td>1.64</td>
<td>1.01</td>
<td>1.26</td>
<td>1.56</td>
<td>1.03</td>
<td>1.15</td>
<td>1.23</td>
<td>1.01</td>
<td>1.16</td>
<td>1.01</td>
<td>1.07</td>
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<td>p-value</td>
<td>0.066</td>
<td>0.11</td>
<td>0.063</td>
<td>0.004</td>
<td>0.086</td>
<td>0.85</td>
<td>0.323</td>
<td>0.08</td>
<td>0.512</td>
<td>0.31</td>
<td>0.558</td>
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<td>PLK1_ELMO1</td>
<td>2.52</td>
<td>1.06</td>
<td>1.08</td>
<td>4.36</td>
<td>1</td>
<td>1.11</td>
<td>1</td>
<td>1</td>
<td>1.1</td>
<td>1.15</td>
<td>1.1</td>
</tr>
<tr>
<td>p-value</td>
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<td>0.246</td>
<td>0.154</td>
<td>0.075</td>
<td>0.889</td>
<td>0.732</td>
<td>0.342</td>
<td>0.136</td>
<td>0.383</td>
<td>0.03</td>
<td>0.552</td>
</tr>
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</table>

Figure: The Model ROC curve is plotted in blue with an Area under the ROC Curve (AUC) of 0.86 (95% CI: 0.75 to 0.98). The leave-one-out cross-validated ROC curve is presented in red and has an AUC of 0.77 (95% CI: 0.61 to 0.92). The sensitivity is 83.3% and the specificity is 80%.

CONCLUSIONS

• The following six gene ratios had significant (p<0.05) associations with persistence: CYP4F3_PPKCE, EPS8L1_ST3GAL6, ESRP2_SCCPDH, P2RY2_RGL2, PLK1_ELMO1, and PTK6_IQGAP2.

• The model AUC suggests that there is an 86 percent chance that the model will correctly distinguish between persistent and regressive patients. The sensitivity for this model is 83.3% and the specificity is 80%.

• The baseline gene ratios of patients with BD had an excellent ability to discriminate between persistent and regressive BD.

• These results are promising for the future prognostic ability of the Nanostring gene ratio panel.