

Bronchial dysplasia (BD) is a recognized precursor of squamous cell carcinoma (SCC) of the lung. We have recently shown that the presence of multiple sites within the airway that persist as or progress to high grade dysplasia (moderate dysplasia or worse) portends a greater than 7-fold increase in risk for the development of SCC as compared to cases where this feature of persistence is not observed. Furthermore, array based global gene expression analyses have provided preliminary data that have identified alterations that distinguish persistent from regressive BD. These new findings provide rationale for the development of a prognostic marker panel that could be used to assess risk in patients with premalignant disease. While a number of publications have identified molecular alterations that can be correlated with progression of BD to invasive carcinoma, none of these are observed in a broad enough manner to be useful as prognostic markers. In this semi-prospective cohort study, we quantified gene expression ratios from bronchial specimens from the Colorado SPORE Lung Cancer dysplasia bank using Nanostring technology. We then assessed the accuracy of the prognostic gene panel in predicting persistence of BD by performing univariate and multivariate analyses between the gene expression ratios and the outcome (persistent or regressive BD). We found that six gene pairs (CYP4F3_PRKCE, EPS8L1_ST3GAL6, ESRP2_SCCPDH, P2RY2_RGL1, PLK1_ELMO1, and PTK6_IQGAP2) are statistically significant ($p < 0.5$) for predicting BD persistence. The best-fitting multivariate model suggests that there is an 86 percent chance that the gene panel will correctly distinguish between persistent and regressive patients. The sensitivity for this model is 83.3% and the specificity is 80%. These findings suggest that the selected gene ratios of patients with bronchial dysplasia can discriminate between persistent and regressive bronchial dysplasia and are promising for the future prognostic ability of the Nanostring gene ratio panel.