Global DNA Methylation Analysis of Bronchial Epithelial Cells from Patients with Asthma, COPD With and Without Lung Cancer

E.A. Vucic, BSc[1], I.M. Wilson, BSc[1], B.P. Coe, PhD[1], D.D. Sin, MD[2], H. Coxson, PhD[3], W.L. Lam, PhD[1], S. Lam, MD[4]
[1]BC Cancer Research Centre - Vancouver/CA, [2]St. Paul´s Hospital - Vancouver, Bc/CA, [3]University of British Columbia - Vancouver/CA, [4]BC Cancer Agency - Vancouver/CA

INTRODUCTION: Emerging evidence suggests that aberrant epigenetic regulation is involved in the development and progression of malignant and non-malignant respiratory diseases. Although asthma, chronic obstructive pulmonary disease (COPD) and lung cancer have distinct phenotypes, patients with COPD may have a significant reversible component to their airflow obstruction. Also, patients with COPD have increased risk for lung cancer. Little is known about the global pattern of DNA methylation in bronchial epithelial cells associated with asthma, COPD and lung cancer. We hypothesize that changes to DNA methylation in airway epithelial cells play a key role in the pathogenesis of these respiratory diseases. We conducted a pilot study of the global DNA methylation changes in bronchial epithelial cells of patients with these three disorders to provide a better understanding of the molecular alterations that drive these diseases. As changes to methylation have been shown to be dependent on smoking history; we also evaluate DNA methylation changes associated with active smoking in current (CS) versus former (FS) smokers.

METHODS: Bronchial epithelial cells were obtained from brushings of small airways (< 2mm diameter) during bronchoscopy from FS with asthma (n=5), COPD (n=8) and patients with COPD as well as previous surgical resection of Stage I NSCLC (n=6 FS, n=12 CS). Illumina's Infinium Methylation (HM27) assay was used to assess DNA methylation status of 27,000 CpG sites associated with 14,000 genes.

RESULTS: COPD and Asthma can be distinguished based on their methylation profiles. Genes differentially methylated between COPD and asthma include: key modulators of inflammation and chronic inflammatory disease (matrix metalloproteinases, pro-inflammatory cytokines and chemokines) and pathogen recognition and innate immunity activation (toll like receptors). Additionally, a comparison of the airway epithelia methylation levels in CS and FS with NSCLC, identified genes involved in free radical savaging, xenobiotic metabolism, detoxification and immune signalling. These preliminary results imply a possible role for DNA methylation in the deregulation of previously identified disease-related genes.

CONCLUSION: We provide the first global DNA methylation analysis of airway epithelia in asthma, COPD and NSCLC patients. Knowledge of DNA methylation disruption in respiratory disease of both current and former smokers will provide rationale for further study of existing epigenetic drugs in treatment and prevention of these diseases.