

POSTER PRESENTATION

Open Access

Lung tumors and non-malignant airways from patients with chronic lung inflammatory disease bear distinct genetic and epigenetic disruptions corresponding to metabolic processes involved in senescence and methylation

Emily Vucic^{1*}, Kelsie Thu¹, Victor Martinez¹, Chiara Pastrello², John Yee³, Igor Jurisica^{2,4}, Stephen Lam¹, Wan Lam¹

From *Metabolism, Diet and Disease 2014: Cancer and metabolism*
Washington DC, USA. 28-30 May 2014

Background

Chronic obstructive pulmonary disease (COPD) is an inflammatory lung disease associated with a 10-fold increased risk of lung cancer (LC), independent of smoking-status. Together these diseases contribute tremendously to mortality worldwide. Based on the notion that chronic inflammation forms a specific cancer-promoting environment; we hypothesized that COPD and non-COPD related lung tumors are molecularly distinct, and that these differences may yield promising diagnostic and therapeutic targets. Since genes that sustain high-level DNA and RNA alterations are likely selectively altered in tumor systems, we applied an integrative multi-omics analysis to lung tumors from COPD and non-COPD patients. To assess the potential clinical application of these findings, we examined the methylation status of COPD+LC specific genes in non-malignant airways from COPD patients w/LC.

Materials and methods

Multi-omics profiling (copy number, DNA methylation and gene-expression) was performed on 76 tumor and non-malignant lung tissues using genome-wide array platforms. To identify genes/pathways which sustain high DNA and RNA level changes in tumors, we developed an algorithm to generate "Integrated Scores" for each gene based on magnitude of concomitant DNA and mRNA

alterations. Integrated Scores were applied to all downstream analyses. COPD+LC specific genes were further assessed at the level of DNA methylation in airways from 25 COPD patients w/ and w/out LC.

Results

Gene set and pathway enrichment analyses of genes frequently and differentially disrupted at both DNA and RNA levels in COPD tumors revealed enrichment of transcription factor gene sets involved in inflammation-related cancer, oxidative stress and smoking response; the most significant being *PITX2* - a putative methylation biomarker in LC, previously associated with senescence gene networks in COPD.

Pathways specifically disrupted in COPD tumors included those involved in inflammation (atherosclerosis, fibrosis and IL-17 signalling), DNA damage (14-3-3 σ signalling) and synthesis of the methyl-donor, S-Adenosyl-methionine (SAM) - a critical cofactor involved in DNA and histone methylation. Five COPD+LC specific genes were also altered at the DNA methylation level in non-cancerous airways of COPD patients w/LC, including putative cancer epigenetic diagnostic biomarkers (*CCNDBP1*, *HPGD*), genes associated with oxidative response and COPD progression (*PPARGC1A*) and biosynthesis of SAM (*MAT2B*).

Conclusions

Genetic and epigenetic disruptions in lung tumors and small airways of patients with COPD and LC are distinct from those in corresponding tissues from patients

¹Department of Integrative Oncology, British Columbia Cancer Research Centre, Vancouver, BC, Canada
Full list of author information is available at the end of the article

w/COPD or LC alone. Genes altered in airways and involved in lung tumorigenesis in COPD patients may serve as clinically relevant markers for predicting LC or as targets for chemoprevention therapies.

Authors' details

¹Department of Integrative Oncology, British Columbia Cancer Research Centre, Vancouver, BC, Canada. ²Princess Margaret Cancer Centre, University Health Network, Toronto, ON, Canada. ³Department of Surgery, Vancouver General Hospital, Vancouver, BC, Canada. ⁴Departments of Computer Science and Medical Biophysics, University of Toronto, Toronto, ON, Canada.

Published: 28 May 2014

doi:10.1186/2049-3002-2-S1-P82

Cite this article as: Vucic *et al.*: Lung tumors and non-malignant airways from patients with chronic lung inflammatory disease bear distinct genetic and epigenetic disruptions corresponding to metabolic processes involved in senescence and methylation. *Cancer & Metabolism* 2014 **2**(Suppl 1):P82.

**Submit your next manuscript to BioMed Central
and take full advantage of:**

- Convenient online submission
- Thorough peer review
- No space constraints or color figure charges
- Immediate publication on acceptance
- Inclusion in PubMed, CAS, Scopus and Google Scholar
- Research which is freely available for redistribution

Submit your manuscript at
www.biomedcentral.com/submit

