

Western Pennsylvania (WPA) Environmental Risk Factors for Lung Cancer Brainstorming Mini-Workshop on Mutational Signatures of Exposures

February 9, 2021

Background

A multi-disciplinary team meets monthly at the Hillman Cancer Center with the goal of developing projects to address western Pennsylvania (WPA) environmental risk factors for lung cancer. We have identified three primary environmental concerns in the catchment areas for lung cancer: tobacco use, radon, and air pollution. This mini-workshop is a prelude to a larger workshop to address this topic. The overall goals are to establish projects that address environmental risk factors for lung cancers in our catchment area, and to develop multidisciplinary research with basic, translational and education outreach components.

Next generation sequencing has led to the identification of somatic mutations in cancer genomes, caused by multiple mutational processes and exposures which generate characteristic mutational signatures. Harnessing these data can provide valuable information on cancer etiology, exposure history, and therapeutic strategies.

References

[Ludmil Alexandrov et al., The repertoire of mutational signatures in human cancer, *Nature*, 2020.](#)

[Jill Kucab et al., A compendium of mutational signatures of environmental agents, *Cell*, 2019.](#)

Specific Goals

To explore use of mutational signatures in clinical samples to (1) inform cancer etiology and contribution of environmental exposures, (2) develop hypotheses for increase in non-smoking-related lung tumors, (3) inform strategies for precision medicine, and (4) determine other potential uses and applications.

Agenda

12:30 pm – 1:30 pm: Keynote lecture: *The Repertoire of Mutational Signatures in Human Cancer*

Ludmil Alexandrov, PhD

Assistant Professor, Cellular and Molecular Medicine, University of California San Diego

<https://alexandrov.cloud.ucsd.edu/home>

Note: The keynote lecture is also the UPMC Hillman Cancer Center Basic and Translational Research Seminar for Feb 9, 2021.

1:30 pm – 1:45 pm: *The Pittsburgh Lung Screening Study (PLuSS)*

Laura Stabile, PhD

Associate Professor, Pharmacology and Chemical Biology

1:45 pm – 2:00 pm: *Panel Questions*

- How can we leverage and/or expand existing cohorts and studies to inform about environmental risk factors of cancer in WPA?
- Can home addresses be linked to exposures?
- Can we obtain smoking status from all patients – what are the IRB requirements?

- What tumor sequencing data is available?

Panel Members:

Laura Stabile, PhD

James Herman, MD, Professor of Medicine

Timothy Burns, MD, PhD, Assistant Professor of Medicine

2:00 pm – 2:15 pm: *Radon exposure in Pittsburgh and WPA*

Shaina Stacy, PhD, Postdoctoral Fellow

2:15 pm – 2:45 pm: *Panel Questions*

- Can we determine whether residential radon exposure contributes to lung cancer incidence or prognosis?
- Can we obtain information on smoking status?
- Are there mutational signatures of radon exposure?
- Does radon exposure alter the mutations signatures associated with tobacco smoke?

Panel Members:

Shaina Stacy, PhD

Jian-Min Yuan, MD, PhD, Professor of Epidemiology

2:45 pm – 3:00 pm: *NGS facility and capabilities at UPMC Hillman Cancer Center*

Adrian Lee, PhD, Director of the Institute for Precision Medicine, Professor of Pharmacology and Chemical Biology

3:00 pm – 3:30 pm: *Panel Questions*

- What sequencing is ongoing here at UPMC-HCC; what has become routine and part of clinical care?
- Can we leverage existing exome of sequencing data?
- Can we link mutational signatures of environmental exposures to lung cancer?
- Can sequencing lung cancer specimens reveal mutational signatures of radon, pollution, or tobacco exposure? How deep do the reads need to be?
- What is the number of clinical samples to yield statistical power?
- Can mutational signature inform therapeutic strategy?

Panel Members:

Ludmil Alexandrov, PhD, Assistant Professor, Cellular and Molecular Medicine UCSD

Annerose Bernt, PhD, DVM, Co-Director of Hillman Cancer Genomics Facility

Yuri Nikiforov, MD, PhD, Professor of Pathology, Co-Director of the Hillman Cancer Genomics Facility

Xiaosong Wang, MD, PhD, Professor of Pathology