Molecular Signatures of Exposure in Cancer:
A Joint NIEHS and NCI Workshop
June 29-30, 2023

Resources and Key Publications

Session 1: Mutational Signatures of Exposure in Cancer

Alexandrov, L.B., et al., *Deciphering signatures of mutational processes operative in human cancer*. Cell Rep, 2013. 3(1): p. 246-259.

Alexandrov, L.B., et al., *Signatures of mutational processes in human cancer*. Nature, 2013. 500(7463): p. 415-421.

Alexandrov, L.B., et al., *The repertoire of mutational signatures in human cancer*. Nature, 2020. 578(7793): p. 94-101.

Kim, Y.A., et al., *Mutational Signatures as Sensors of Environmental Exposures: Analysis of Smoking-Induced Lung Tissue Remodeling.* Biomolecules, 2022. 12(10): p. 1384.

Kim, Y.A., et al., *Mutational Signatures: From Methods to Mechanisms.* Annu Rev Biomed Data Sci, 2021. 4: p. 189-206.

Wojtowicz, D., et al., *Hidden Markov models lead to higher resolution maps of mutation signature activity in cancer.* Genome Med, 2019. 11(1): p. 49.

Huang, X., D. Wojtowicz, and T.M. Przytycka, *Detecting presence of mutational signatures in cancer with confidence.* Bioinformatics, 2018. 34(2): p. 330-337.

Session 2: Other Data Types as Signatures of Exposure in Cancer

Johnson, K.J., et al., *A Transformative Vision for an Omics-Based Regulatory Chemical Testing Paradigm*. Toxicol Sci, 2022. 190(2): p. 127-132.

Corton, J.C., et al., *A Collaborative Initiative to Establish Genomic Biomarkers for Assessing Tumorigenic Potential to Reduce Reliance on Conventional Rodent Carcinogenicity Studies*. Toxicol Sci, 2022. 188(1): p. 4-16.

Gwinn, W.M., et al., *Evaluation of 5-day in vivo rat liver and kidney with high-throughput transcriptomics for estimating benchmark doses of apical outcomes*. Toxicol Sci, 2020. 176(2): p. 343–354.

Ramaiahgari, S.C., et al., *The power of resolution: contextualized understanding of biological responses to liver injury chemicals using high-throughput transcriptomics and benchmark concentration modeling*. Toxicol Sci, 2019. 169(2): p. 553–566.

Dekkers, K.F., et al., *An online atlas of human plasma metabolite signatures of gut microbiome composition.* Nat Commun, 2022. 13(1): p. 5370.

Bokulich, N.A., et al., *Multi-omics data integration reveals metabolome as the top predictor of the cervicovaginal microenvironment.* PLoS Comput Biol, 2022. 18(2): p. e1009876.

Hofseth, L.J., et al., *Early-onset colorectal cancer: initial clues and current views.* Nat Rev Gastroenterol Hepatol, 2020. 17(6): p. 352-364.

Ugai, T., et al., *Is early-onset cancer an emerging global epidemic? Current evidence and future implications.* Nat Rev Clin Oncol, 2022. 19(10): p. 656-673.

Bessonneau, V. and Rudel, R.A., *Mapping the Human Exposome to Uncover the Causes of Breast Cancer.* Int J Environ Res Public Health, 2019. 17(1): p. 189.

Sud, A., Turnbull, C., and Houlston, R, *Will polygenic risk scores for cancer ever be clinically useful?* NPJ Precis Oncol, 2021. 5(1): p. 40.

Yao, S., et al., *Proceedings of the fifth international Molecular Pathological Epidemiology (MPE) meeting.* Cancer Causes Control, 2022. 33(8): p. 1107-1120.

Advancing cancer research with genetic analysis tools. ThermoFisher Scientific, 2022.

Brockway-Lunardi, L., et al., *Early-onset colorectal cancer research: gaps and opportunities.* Colorect Cancer, 2020.

Wang, M., et al., *Strain dropouts reveal interactions that govern the metabolic output of the gut microbiome.* Cell, 2023. 186(13): p. 2839-2852.

Weeden, C.E., et al., *Impact of risk factors on early cancer evolution.* Cell, 2023. 186(8): p. 1541-1563.

Session 3: Computational Challenges and Integrating Multi-Omics to Identify Signatures

Campbell, J.D., et al., *Distinct patterns of somatic genome alterations in lung adenocarcinomas and squamous cell carcinomas.* Nat Genet, 2016. 48(6): p. 607-616.

Campbell, J.D., et al., *The Case for a Pre-Cancer Genome Atlas (PCGA).* Cancer Prev Res (Phila), 2016. 9(2): p. 119-124.

Campbell, J.D., et al., *Assessment of microRNA differential expression and detection in multiplexed small RNA sequencing data.* RNA, 2015. 21(2): 164-171.

Cancer Genome Atlas Research Network. *Comprehensive molecular profiling of lung adenocarcinoma.* Nature, 2014. 511(7511): p. 543-550.
-Roles: DNA-sequencing team and manuscript coordinator

Perdomo, C., et al., *MicroRNA 4423 is a primate-specific regulator of airway epithelial cell differentiation and lung carcinogenesis.* Proc Natl Acad Sci U S A, 2013. 110(47): p.18946-18951.

Campbell, J.D., et al., *A gene expression signature of emphysema-related lung destruction and its reversal by the tripeptide GHK.* Genome Med, 2012. 4(8): p. 67.

Li, S., F.W. Crawford, and M.B. Gerstein, *Using sigLASSO to optimize cancer mutation signatures jointly with sampling likelihood*. Nat Commun, 2020. 11(1): p. 3575.

Wojtowicz, D., et al., *RepairSig: Deconvolution of DNA damage and repair contributions to the mutational landscape of cancer.* Cell Syst, 2021. 12(10): p. 994-1003.

Wojtowicz, D., et al., *DNA Repair Footprint Uncovers Contributions of DNA Repair Mechanism to Mutational Signatures.* Pac Symp Biocomput, 2020. 25: p. 262-273.

Amgalan, B., et al., *Influence network model uncovers relations between biological processes and mutational signatures.* Genome Med, 2023. 15(1): p. 1-15.

Kim, Y.A., et al., *Network-based approaches eludicate differences within APOBEC and clock-like signatures in breast cancer.* Genome Med, 2020. 12(1): p. 52.

Chevalier, A., et al., *The Mutational Signature Comprehensive Analysis Toolkit (musicatk) for the Discovery, Prediction, and Exploration of Mutational Signatures.* Cancer Res, 2021. 81(23): p. 5813-5817.
Hill, W., et al., *Lung adenocarcinoma promotion by air pollutants.* Nature, 2023. 616(7955): p. 159-167.

Duclos, G.E., et al., *Characterizing smoking-induced transcriptional heterogeneity in the human bronchial epithelium at single-cell resolution.* Sci Adv, 2019. 5(12): p. eaaw3413.

Session 4: Challenges in Tracking Signatures of Exposures

Chawanthayatham, S., et al., *Mutational spectra of aflatoxin B_1 in vivo establish biomarkers of exposure for human hepatocellular carcinoma*. Proc Natl Acad Sci USA, 2017. 114(15): p. E3101-E3109.

Armijo, A.L., et al., *Molecular origins of mutational spectra produced by the environmental carcinogen N-nitrosodimethylamine and S_N1 chemotherapeutic agents*. NAR Cancer, 2023. 5(2).

Fedeles, B.I. and J.M. Essigmann, *Mutational spectra provide insight into the mechanisms bridging DNA damage to genetic disease*. DNA Damage, DNA Repair and Disease, Vol. 2, 2020. p. 214-253.

George, S., et al., *Epigenomic reprogramming in iAs-mediated carcinogenesis*. Adv Pharmacol, 2023. 96: p. 319-365.

Saintilnord, W.N., et al., *Chronic Exposure to Cadmium Induces Differential Methylation in Mice Spermatozoa*. Toxicol Sci, 2021. 180(2): p. 262-276.

Eckstein, M., M. Rea, and Y.N. Fondufe-Mittendorf, *Transient and permanent changes in DNA methylation patterns in inorganic arsenic-mediated epithelial-to-mesenchymal transition*. Toxicol Appl Pharmacol, 2017. 331: p. 6-17.

Rea, M., T. Gripshover, and Y.N. Fondufe-Mittendorf, *Selective inhibition of CTCF binding by iAs directs TET-mediated reprogramming of 5-hydroxymethylation patterns in iAs-transformed cells*. Toxicol Appl Pharmacol, 2018. 338: p. 124-133.

Eleazer, R., et al., *PARP1 Regulates Circular RNA Biogenesis though Control of Transcriptional Dynamics*. Cells, 2023. 12(8): p. 1160.

Chang, Z., et al., *The relationship between co-exposure to multiple heavy metals and liver damage*. J Trace Elem Med Biol, 2023. 77: p. 127128.

Dye, C.K., et al., *Maternal DNA methylation signatures of arsenic exposure is associated with adult offspring insulin resistance in the Strong Heart Study.* Environ Int, 2023. 173: p. 107774.

Chernoff, M.B., et al., *Sequencing-based fine-mapping and in silico functional characterization of the 10q24.32 arsenic metabolism efficiency locus across multiple arsenic-exposed populations.* PLoS Genet, 2023. 19(1): p. e1010588.

Zacher, T., et al., *Evaluation of a water arsenic filter in a participatory intervention to reduce arsenic exposure in American Indian communities: The Strong Heart Water Study.* Sci Total Environ, 2023. 862: p. 160217.

Lieberman-Cribbin, W., et al., *Epigenetic Biomarkers of Lead Exposure and Cardiovascular Disease: Prospective Evidence in the Strong Heart Study.* J Am Heart Assoc, 2022. 11(23): p. e026934.

Domingo-Relloso, A., et al., *Arsenic Exposure, Blood DNA Methylation, and Cardiovascular Disease.* Circ Res, 2022. 131(2): p. e51-e69.

Kuo, C.C., et al., *The association of arsenic exposure and arsenic metabolism with all-cause, cardiovascular and cancer mortality in the Strong Heart Study.* Environ Int, 2022. 159: p. 107029.

Session 5: Population-Based Cancer Studies

Goodrich, J.A., et al., *Exposure to perfluoroalkyl substances and risk of hepatocellular carcinoma in a multiethnic cohort*. JHEP Rep, 2022. 4(10): p. 100550.

Shearer, J.J., et al., *Serum Concentrations of Per- and Polyfluoroalkyl Substances and Risk of Renal Cell Carcinoma*. J Natl Cancer Inst, 2021. 113(5): p. 580-587.

Goodrich, J.A., et al., *Metabolic Signatures of Youth Exposure to Mixtures of Per- and Polyfluoroalkyl Substances: A Multi-Cohort Study*. Environ Health Perspect, 2023. 131(2): p. 27005.

Kucab, J.E., et al., *A Compendium of Mutational Signatures of Environmental Agents*. Cell, 2019. 177(4): p. 821-836.

Maitre, L., et al., *Multi-omics signatures of the human early life exposome*. Nat Commun, 2022. 13(1): p. 7024.

Ladd-Acosta, C., *Epigenetic Signatures as Biomarkers of Exposure*. Curr Environ Health Rep, 2015. 2(2): p. 117-125.

Huber, A.R., A.V. Hoeck, and R.V. Boxtel, *The Mutagenic Impact of Environmental Exposures in Human Cells and Cancer: Imprints Through Time*. Front Genet, 2021. 12: p. 760039.

Xue F. and Michels K.B., *Intrauterine factors and risk of breast cancer: a systematic review and meta-analysis of current evidence*. Lancet Oncol, 2007. 8(12): p. 1088-1100.

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Michels, K.B., et al., *Recommendations for the design and analysis of epigenome-wide association studies*. Nat Methods, 2013. 10(10): p. 949-955.

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Yoon, L.S., et al., *Variability in urinary phthalates, phenols, and parabens across childhood and relation to adolescent breast composition in Chilean girls.* Environ Int, 2022. 170: p. 107586.