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Big Data Training for Cancer Research

Special Lecture Series

Genomic Studies of Health Effects Following the Chernobyl Accident: Lessons Learned and Public Health Implications

Dr. Stephen Chanock

June 9, 2021, 1:30 – 3:00 PM (EDT)

Abstract: The talk will address two parallel studies using genomics to investigate important questions in radiation-related issues following the Chernobyl accident in 1986. In the first study, we report a large-scale integrated genomic landscape analysis of PTCs after the Chernobyl accident with detailed dose estimation points to DNA double-strand breaks as early carcinogenic events. Here, for the first time, the genomic landscape could eb carefully analyzed in relation to a specific, discrete environmental exposure of ionizing radiation, a known Class 1 IARC carcinogen. We observed that a parsimony of events subsequently enabled PTC growth after environmental radiation exposure. Based on detailed sequence analyses, non-homologous end-joining was consistently implicated as the key repair mechanism for the observed radiation dose-associated clonal DNA double-strand breaks, leading to more fusion drivers, small deletions, and structural variants as a result of increasing radiation dose. Tumor epigenomic and transcriptomic profiles reflected the PTC driver but were not associated with radiation dose. Because other mutagens can cause DNA double-strand breaks, a unique biomarker for radiation-induced carcinogenesis was not identified. Linear increases in radiation-associated damage, especially for exposure at younger ages, emphasize the potential deleterious consequences of ionizing radiation exposure.

The second study looked at the effects of radiation exposure from the Chernobyl nuclear accident which remain a topic of interest. We investigated whether children born to parents employed as cleanup workers or exposed to occupational and environmental ionizing radiation after the accident were born with more germline de novo mutations (DNMs). Whole-genome sequencing of 130 children (born 1987–2002) and their parents did not reveal an increase in the rates, distributions, or types of DNMs relative to the results of previous studies. We find no elevation in total DNMs, regardless of cumulative preconception gonadal paternal [mean = 365 milligrays (mGy), range = 0 to 4080 mGy] or maternal (mean = 19 mGy, range = 0 to 50 mGy) exposure to ionizing radiation. Thus, over this exposure range, evidence is lacking for a substantial effect on germline DNMs in humans, suggesting minimal impact from transgenerational genetic effects.

Speaker Bio: Dr. Stephen Chanock is a leading expert in the discovery and characterization of cancer susceptibility regions in the human genome. He has received numerous awards for his scientific contributions to our understanding of common inherited genetic variants associated with cancer risk and outcomes, including the Niehaus, Southorth, Weissenbach Award in Clinical Cancer Genetics, the 2015 Jeffrey M. Trent Lecture, and the 2021 NIH Clinical Center Contemporary Clinical Medicine: Great Teachers seminar. He is an elected member Research, the Association of American Physicians, and the American Epidemiological Dr. Chanock received his M.D. from Harvard Medical School in 1983 and completed clinical training in pediatrics, pediatric infectious diseases, and pediatric hematology/oncology and research training in molecular genetics at Boston Children's Hospital and the Dana-Farber Cancer Institute, Boston. Since 1995, Dr. Chanock has served as the Medical Director for Camp FantasticExit Disclaimer, a week-long recreational camp for pediatric cancer patients, which is a joint venture of the NCI and Special Love, Inc.

Register at: https://purdue-edu.zoom.us/webinar/register/WN_6nXmxHa7QU6sVNrrihs9Qg