

World Trade Center responders at higher risk for blood cancer-associated mutations

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Scientists from Vanderbilt-Ingram Cancer Center (VICC) collaborated with researchers from New York to determine that 9/11 first responders to the World Trade Center have increased levels of mutations that escalate their risk for blood cancers or cardiovascular disease, according to a study published March 7 in *Nature Medicine*.

The researchers determined that a significantly higher percentage of

World Trade Center responders have an increased mutational burden when compared to blood sample data from BioVU, Vanderbilt's biorepository of DNA extracted from discarded blood collected during routine clinical testing. Among the World Trade Center firefighters, 10% had evidence of clonal hematopoiesis compared to 6.7% for firefighters who were not exposed to particulate matter from the burning skyscrapers. Clonal hematopoiesis is an age-associated phenomenon marked by mutations in commonly mutated genes within [blood cells](#) that provide those cells a competitive advantage and increases risk of [blood cancer](#) and [cardiovascular disease](#).

The VUMC team was able to access the DNA of 203 Nashville firefighters from BioVU. The Vanderbilt team was able to use the de-identified, annotated data within the Synthetic Derivative (SD) to locate over 200 firefighters who were age, sex and smoking-status matched to first responders at the World Trade Center disaster. Combined with 52 firefighters recruited at the annual convention of the International Association of Firefighters, this control group was compared to those exposed to particulate matter at the World Trade Center disaster.

The VICC researchers were led by Michael Savona, MD, holder of the Beverly and George Rawlings Directorship in Hematology Research, professor of Medicine and Head of Hematology, Cellular Therapy and Stem Cell Transplantation at VICC.

"This is the first publication that I am aware of that successfully leveraged BioVU to measure somatic genetic changes to study clonal hematopoiesis," said Savona, one of four corresponding authors on the study.

Alexander Silver, a MD/Ph.D. candidate working in the Savona Lab, is one of seven lead authors of the study.

The research team included scientists and physicians from Vanderbilt, Albert Einstein College of Medicine, Montefiore Medical Center, the Fire Department of the City of New York Bureau of Health Services, Rutgers Cancer Institute of New Jersey, Weill Cornell Medicine, Memorial Sloan Kettering Cancer Center, Sylvester Comprehensive Cancer Center, New York University School of Medicine, Genoptix, The Leukemia Lymphoma Society and Dana Farber Cancer Center.

Researchers also exposed mice to World Trade Center particulate matter thought to be equivalent to what the first responders absorbed. The scientists observed a significant expansion of hematopoietic stem cells 30 days after exposure.

The researchers concluded that [first responders](#) to the World Trade Center have an increased mutational burden that puts them at greater risk for [blood cancers](#) beyond what normally occurs with aging, and further studies of the [particulate matter](#) and the mechanism of [blood cancer](#) development are under way.

Other Vanderbilt authors on the study included Cosmin "Adi" Bejan, Ph.D., assistant professor of Biomedical Informatics, and clinical fellows in Hematology/Oncology, Shannon Stockton, MD, and Travis Spaulding, MD.

More information: Anna Nolan, High burden of clonal hematopoiesis in first responders exposed to the World Trade Center disaster, *Nature Medicine* (2022). [DOI: 10.1038/s41591-022-01708-3](https://doi.org/10.1038/s41591-022-01708-3).
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