

Original Article

An update on the World Trade Center cancer tissue biobank: a scientific resource for molecular and mechanistic studies on WTC-related cancer

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Abstract

World Trade Center (WTC) responders were exposed to a complex mixture of toxins and carcinogens through dust, fumes, and smoke at ground zero. Since then, studies have indicated that WTC responders have elevated cancer rates compared with the general population. While studies have detailed the overarching connection between WTC exposure and cancer, a tissue biobank is needed to enable molecular and mechanistic studies on WTC-related cancers. The cohort includes responders involved in rescue, recovery, or cleanup enrolled in the World Trade Center Health Program (WTCHP) who consented to participate in research. Responders with cancer were identified through WTCHP certification. WTCHP provided data with patients' demographic information, contact details, and cancer diagnoses. Potential participants were contacted by mail, email, or phone for consent and procedure location. If consented, samples were requested from pathology departments. A biobank of cancer tissues from WTC responders has been established with 551 distinct primary cancers from 521 patients. Of these, prostate makes up 39.0%, thyroid 9.8%, melanoma 8.9%, kidney 6.5%, bladder 6.0%, colorectal 5.8%, breast 5.6%, lung 4.7%, head and neck 4.7%, and other cancers 9%. An additional 343 patients have consented for biobank projects and their samples are being requested. To date, we have created a valuable tissue biobank available to the scientific community for high-impact oncology studies in the unique population of WTC responders. By studying links between carcinogenic exposure and cancer sites, exposure signatures, and markers of cancer aggressiveness, this biobank offers an unprecedented opportunity to advance cancer research in an exposed population.

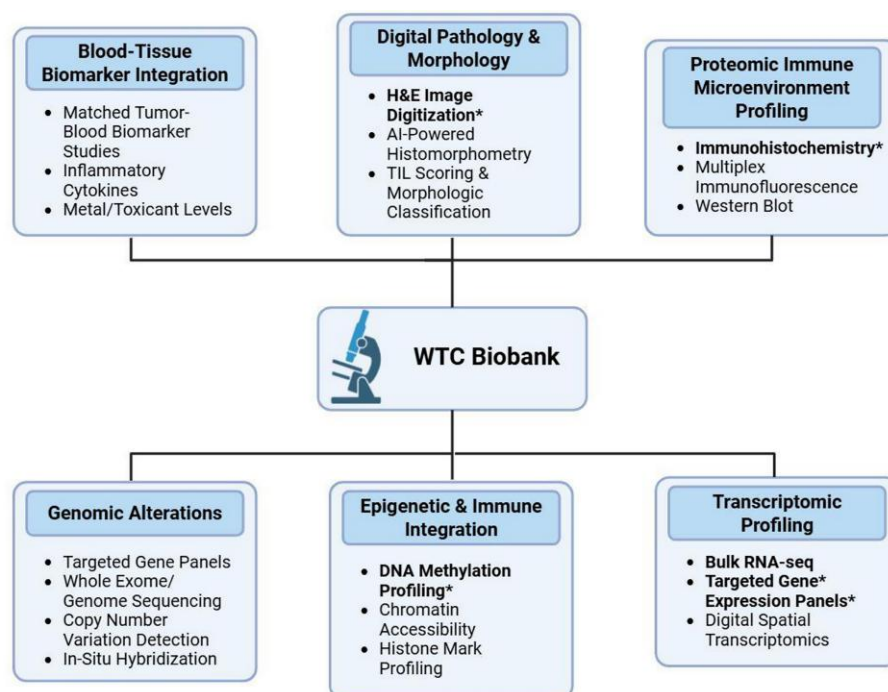
Lay summary

The creation of a tissue biobank for scientific use in oncology studies of WTC responders. It enables research on links between carcinogenic exposure and cancer sites, exposure signatures, and cancer aggressiveness, offering a unique opportunity to advance cancer research.

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Graphical Abstract



* Indicates the method has been performed using WTC biobank samples.

Keywords: 9/11 exposure; WTC health program; biorepository; occupational health; cancer incidence

1. Background

In the aftermath of 11 September 2001, thousands of workers, including police officers, firefighters, paramedics, and volunteers, responded to the site of the World Trade Center (WTC) disaster. In addition to the acute physical risks, responders were also faced with long-term health hazards due to the inhalation of a wide variety of substances present from the plane crashes and ensuing collapse of the towers. Through this plume, responders were exposed to particulate matter such as glass fibers, asbestos, and cement dust from building remnants, toxic polycyclic aromatic hydrocarbons from burning fuel, and even heavy metals such as mercury or lead from destroyed lightbulbs and computers [1, 2]. Concerns were quickly raised about the dangers of having been exposed to such hazardous inhalants and an increased likelihood of getting cancer as a result [3–5].

Studies have since confirmed these concerns, showing that WTC responders experience a significantly elevated risk for cancer. A 2019 study examining cancer diagnoses of 28 729 WTC responders found significantly increased standardized incidence ratios (SIRs) for cancer at all sites compared with the general US population (SIR: 1.09; 95% CI: 1.02–1.16), and an increased incidence of thyroid and prostate cancers, as well as leukemia [6]. A more recent study using a sample of 57 402 WTC responders from a combination of the existing three cohorts, linked to 13 state cancer registries, found that responders who had a direct exposure to WTC dust had a significantly increased risk of cancer [HR_{adj} (hazards ratio): 1.21; 95% CI: 1.12–1.31] compared with those without dust exposure.

Specifically, the study found that workers arriving on September 11th had increased incidence of melanoma-skin, prostate, thyroid, and tonsil cancer compared with cancer incidence rates from the general population (SIR: 1.61, 95% CI: 1.29–1.99; SIR: 1.45, 95% CI: 1.31–1.59; SIR: 2.34, 95% CI: 1.86–2.91; SIR: 1.76, 95% CI: 1.08–2.72, respectively) [7]. Included in this broader analysis were patients from a 2021 study observing cancer incidence among a group of New York firefighters, comparing their rates to demographically similar US males and to non-WTC exposed firefighters from the Career Firefighter Health Study. The study found that WTC-exposed firefighters had higher SIRs for all cancer types (SIR: 1.09; 95% CI 1.02–1.16) compared with US males, and a higher relative rate of cancer at all sites than their non-WTC exposed firefighter counterparts [RR_{adj}: 1.13; 95% CI: 1.02–1.25]—in this study, secondary analyses taking into account surveillance bias confirmed the results [8]. The relevancy of these findings cannot be understated, as they account for the occupational cancer hazards that many responders underwent while still demonstrating an elevated cancer risk uniquely associated with WTC exposure, underscoring the long-term health impacts of the disaster and the importance of continued monitoring and support for this population. These represent only the beginning of establishing the link between cancer and dust exposure, as most WTC responders are still under the age of 65 years, and cancer risk in this group is likely to increase as they continue to age [9].

While epidemiological studies have been important in providing critical evidence for the association between WTC exposure and cancer, it is equally as important to conduct tissue-based research to determine the biological mechanisms

through which these cancers may be more prevalent, aggressive, or deadly. As each cancer is unique and may be impacted by WTC exposure in different ways, it is critical to build a large, diverse resource bank of cancers tissues that can be used to conduct mechanistic studies. This work outlines the development and maintenance of a tissue bank system specifically designed for WTC-related cancers, allowing for their study, and offering the potential to identify biomarker and exposure signatures that can inform how WTC responders are treated and surveyed in the future.

2. Materials and methods

The World Trade Center Health Program (WTCHP) was funded by the James Zadroga 9/11 Health and Compensation Act of 2010 and first established in 2011 as an effort to consolidate the various resources that were gathered to address the effects of the WTC disaster on the health and well-being of WTC responders and survivors [10–12]. The WTC responders who participated as employees or volunteers in the rescue, recovery, or cleanup efforts may enroll in one of the New York-based WTCHP Clinical Centers of Excellence (CCE). To qualify, responders must meet certain criteria related to their potential for exposure, such as activity, location within the WTC sites, timing of exposure, and duration of exposure [13]. This eligibility is described in more detail by the WTCHP [14]. For this tissue bank, individuals needed to be enrolled in the General Responder CCE at Mount Sinai.

As of May 2025, 25 074 responders were enrolled in the WTCHP CCE at Mount Sinai. These patients are seen at an initial health evaluation as well as at annual monitoring visits that include blood tests, electrocardiograms, colonoscopies, urinalysis, and X-rays [15]. Through these monitoring visits, the WTCHP is able to track enrollee health over time and, if new conditions arise, determine whether they can be certified as WTC-related. These certifications were used to define our cohort of patients as any enrolled responder who has had a WTCHP certified case of cancer. The WTCHP CCE at Mount Sinai was contacted, and a data request form was submitted to obtain the demographic and contact information for those certified cancer patients from the General Responder Cohort at the Mount Sinai CCE who signed an informed consent to indicate that they were interested in participating in research.

Potential participants were first contacted by phone to explain the study and assess interest in discussing the consent process. If a patient expressed interest, the consent process was reviewed in detail and consent forms were sent out by mail or electronically, depending on patient preference. The purpose of the consent was to obtain written permission to request and receive patient tumor samples from the hospital or clinic where their WTC-certified cancers had been surgically removed, or in cases without surgery, biopsied. In the consent form, participants were also asked whether they were willing to allow for the storage and future use of samples in separate research studies outside of the Institute of Translational Epidemiology. If these consent forms were not returned, patients were called back to reassess interest. Once the forms were received, patients were contacted again by phone to collect information about their cancer treatment, any recurrences, and any

additional cases of cancer that they may have had. All contact and consenting data was collected and managed using REDCap (Research Electronic Data Capture) electronic data capture tools hosted at Mount Sinai [16, 17], a secure, web-based software platform designed to support data capture for research studies, providing (i) an intuitive interface for validated data capture; (ii) audit trails for tracking data manipulation and export procedures; (iii) automated export procedures for seamless data downloads to common statistical packages; and (iv) procedures for data integration and interoperability with external sources.

To procure patient tissue samples, relationships were established with the pathology departments of hospitals and clinic groups across the tri-state area. These departments were then contacted on a case-by-case basis to confirm that the patient's tumor tissue was in their possession. Once confirmed, a request form was sent out to these hospitals containing instructions about how to section the tissue, the area of malignancy that we were interested in, and what additional materials to include, such as pathology reports or blood test results. If samples were not received within 2 months, follow-up calls were placed to check on the status of the request. For patients who had their samples at Mount Sinai, requests were made to our pathology department and reports were retrieved through EPIC.

As pathology departments are generally reluctant to give out entire formalin-fixed paraffin-embedded (FFPE) tissue blocks due to concerns about contamination or loss, we chose to request our tissue in the form of slide samples, thin slices of FFPE blocks that are laid onto slides. We instructed pathology departments to section the blocks into fifteen 4 μ m unstained slides, one 4 μ m hematoxylin and eosin (H&E) stained slide, and, in cases where there was an excess of tissue, an additional 10 μ m tissue curl. All blocks were sectioned onto charged slides. Upon receiving the tissue material, it was deidentified and assigned a unique "B number" specific to the case of cancer. If a patient had multiple distinct cancers, each received its own B number. These B numbers were assigned sequentially and could be identified through REDCap.

In the event that a hospital sent an entire FFPE block rather than slides, the blocks were sectioned and stained by an in-house technician, and the block was returned to the original institution. Slides and tissue curls were enclosed in slide boxes kept in a lockable cabinet, away from any dust, moisture, and sunlight to prevent degradation of the material. Each tissue sample is accompanied by a relevant pathology and cytology reports and can be linked with the main WTCHP data set containing clinical, epidemiological, and exposure information, both at the time of inclusion in the WTCHP and during the regularly performed follow-up.

We have established a process for qualified applicants to submit requests for samples that are made available as de-identified and annotated with pathology and clinical information (stage, grade, and histology, etc.). These proposals are reviewed by the WTC cancer tissue biobank Research Evaluation Panel, with the aims of evaluating the scientific merit of the proposals, and balancing relevance with the availability of the samples and sustainability for future studies, and to ensure that requesters have appropriate IRB approvals. Interested parties can find more information as well as a Biorepository Request Form at <https://icahn.mssm.edu/research/epidemiology/capabilities/biorepository-wtc>.

3. Results

3.1. Biobank description

The biobank is comprised of 551 WTCHP certified tumor specimens, corresponding to 521 individual WTC responders. These samples represent patients that had biopsies or surgeries from 2004 to 2024. The mean year of diagnosis was 2013.7 ± 4.4 . Samples have been collected from over 100 institutions, ranging from large urban research hospitals to small rural clinics. Of the 521 patients for which we have samples in the biobank, 26 have two primary cancers, and 4 have three primary cancers. Across the patients, 38 distinct types of cancer are represented, ranging from highly prevalent epithelial tumors to rare hematologic malignancies. Ethnically, non-Hispanic patients make up 62.8% of the sample, Hispanic patients 8.4%, and patients of unknown ethnicity 28.8%. Racially, 62.0% of patients defined themselves as White, 6.5% as Black, 0.3% as Asian, 4.6% as multiracial; patients of unknown race make up 26.5% of the sample. The sample includes 12.1% female and 87.9% male cancer patients.

Prostate cancer was the most commonly represented malignancy, making up 39.0% ($n=216$) of the total samples. Other frequently collected tumor types included thyroid ($n=54$, 9.8%), melanoma ($n=49$, 8.9%), kidney ($n=36$, 6.5%), bladder ($n=33$, 6.0%), colorectal ($n=32$, 5.8%), breast ($n=31$, 5.6%), lung ($n=26$, 4.7%), head and neck ($n=26$, 4.7%), and hematologic cancers ($n=17$, 3.1%) (Table 1). In addition, there were smaller quantities collected of skin carcinomas ($n=6$) thymic ($n=5$), pancreatic ($n=4$), stomach ($n=4$), testicular ($n=4$), liver ($n=2$), and uterine ($n=2$) tumor samples. When examining the overall cohort of WTC responders eligible for biobank participation, non-melanoma skin was the most frequently diagnosed cancer (33.4%), followed by prostate (18.7%), melanoma (5.9%), kidney (5.2%), colorectal (4.8%), thyroid (4.7%), breast (4.3%), hematologic (3.4%), head and neck (3.3%), and other cancers (16.3%). There are an additional 343 patients who have already consented to the study. Work is ongoing to confirm sample availability and retrieve the corresponding tissue material.

3.2. Linkage to BioMe

BioMe is an electronic medical record-linked biobank of DNA and plasma that similarly enables genetic, epidemiologic, molecular, and genomic studies. To date, BioMe has enrolled more than 62 500 patients who have been treated at Mount Sinai or its affiliates. In 2019, our biobank was linked to this resource, linking a total of 53 responder tumor samples to their records and samples in BioMe [18]. Linkage is ongoing,

and provides access to plasma samples stored in BioMe, some of which may have been collected before the cancer occurred, thus allowing important temporal comparisons of biomarkers. BioMe has since been incorporated into the Mount Sinai Million Health Discoveries Program and future linkage will be done in collaboration with this program.

3.3. Biobank utilization

Since its creation, the biobank has also enabled numerous high-impact studies that have helped bridge the gap between epidemiological findings and molecular evidence (Table 2). While elevated rates of prostate cancer in WTC responders had already been established, the biological basis behind this increase remains largely unclear. A 2019 study using prostate cancer samples from the biobank ($n=30$, 15 WTC and 15 non-WTC) identified a significant upregulation in genes involved in DNA damage repair and G2-M cell cycle arrest among WTC responders, as well as a prostate-specific increase in Th17, a subset of pro-inflammatory T helper cells. These findings were mirrored in a parallel study involving rats being exposed to WTC dust, which showed a similar increase in Th17 cells in prostate tissue [19, 23]. A 2022 study also utilizing prostate cancer samples from the biobank ($n=28$, 13 WTC and 15 non-WTC) found significant dysregulation of DNA methylation for WTC-exposed patients, globally and site-specific, including genes involved in cancer-related TNFA signaling via NFkB, WNT signaling, and TGF beta signaling pathways; genes in the androgen response pathway showed decreased DNA methylation, and RNA-seq results confirmed this gene overexpression [20, 24].

Thyroid tumor samples from the biobank have also been studied to better understand the etiology of WTC-associated thyroid cancer. Initially, a 2019 study compared biobank samples with non-WTC samples ($n=60$, 30 WTC and 30 non-WTC) and used biomarkers of malignancy to rule out the possibility that physician misdiagnosis of benign nodules was contributing to the observed increase in thyroid cancer [21]. It was confirmed that WTC screenings are identifying true cases of thyroid cancer [21]. Building off of this finding, a 2023 study ($n=43$, 20 WTC and 23 non-WTC) identified a significant increase in the presence of TERT promoter mutations in WTC-related thyroid cancers [OR_{adj} : 7.11; 95% CI: 1.21–41.83]. TERT promoter mutations have been shown to be associated with higher recurrence risk, disease-specific mortality, and risk of distant metastasis for thyroid cancer as TERT abnormalities can lead to infinite malignant cell proliferation by stabilizing telomere length [22, 25, 26]. As a result of these projects, both prostate and thyroid cancers are over-represented in our samples, as significant time was solely dedicated to collecting samples for these funded projects. In addition to these published studies, unpublished work has also been done in collaboration with NYU and Johns

Table 1 A summary of the cancer cases in the WTC biobank.

Cancer type	Sample count (n)	Percentage of total (%)
Prostate	216	39.2%
Thyroid	54	9.8%
Melanoma	49	8.9%
Kidney	36	6.5%
Bladder	33	6.0%
Colorectal	32	5.8%
Breast	31	5.6%
Lung	26	4.7%
Head and Neck	26	4.7%
Hematologic	17	3.1%
Other cancers	27	4.9%

Table 2 Summary of studies that the WTC biobank has enabled

Study publication	Cancer type	Biobank samples used
Gong et al. [19]	Prostate	15
Yu et al. [20]	Prostate	13
van Gerwen et al. [21]	Thyroid	30
van Gerwen et al. [22]	Thyroid	20
Unpublished Study 1	Head and Neck	20
Unpublished Study 2	Melanoma	20

Hopkins on WTC-exposed patients who have diagnoses of melanomas and head and neck cancers, respectively.

4. Discussion

This project remains the first and only effort to maintain a dedicated bank of WTC-related cancer tissue samples. With over 500 samples representing a wide range of cancers, the biobank allows for molecular, genomic, and mechanistic studies to be carried out in conjunction with existing epidemiological research. By integrating data from the WTCHP, the biobank enables multidimensional analyses that account for clinical outcomes, biological mechanisms, and demographic factors. Studies using these samples have already identified new patterns, markers, and indicators associated with WTC exposure. These findings do not only shine light on the factors that make WTC responders more likely to be diagnosed with cancer, but also provide insight into potential therapeutic strategies that may benefit this population in the future.

Despite the success of building this tissue bank, the process presented several challenges, from consenting patients to sample acquisition. One of the major difficulties has been contacting patients. Much of the WTCHP contact information dated back to initial patient enrollment and was no longer accurate. In many cases, phone numbers were out of service, preventing direct calls to establish interest. When this happened, alternative methods (email, mail) were used to initiate contact and, once successful, updated information was entered into REDCap. Even when accurate phone numbers were available, phone contact itself was often difficult. To confirm a patient unreachable, at least three contact attempts were made at different times across separate days. Even upon contact and consent forms being mailed out, there was still confusion about the process. To address this, we mailed consent forms with a FAQ sheet and a phone number for any further questions.

Obtaining tumor samples came with its own set of challenges. Though samples stored in-house at Mount Sinai or at other large hospital systems such as Northwell or Memorial Sloan Kettering were generally straightforward to acquire, smaller regional hospitals and clinics were more hesitant to send slides out for research purposes. In these situations, the head of the pathology department was sent the IRB approval, a study overview, and the patient-specific consent form. These documents helped clarify that we had the necessary authorization to acquire the sample. This was especially the case for skin cancers, as many of the procedures were performed at local dermatology offices rather than hospitals. In certain cases, as some procedures were performed over ten years ago, pathology departments had to be notified to look at their archived records, as the procedures were not visible in newer EHR systems. In some rare instances, the cancer tissue sample had been destroyed, or the cancer procedure had happened at a hospital that is no longer active, making sample retrieval impossible; thus, timely requesting of WTC cancer samples is an ongoing and urgent priority.

Along with these logistical challenges, there is a potential for selection bias among the current cohort. Since outreach is required before samples can be requested, tumor tissue is difficult to obtain, even though our IRB allows for its use. Determining where a deceased patient was treated has proven difficult. Additionally, it is possible that certain demographic

groups are more likely to respond to our outreach. For instance, those in the cohort of a higher socioeconomic status may be more engaged, more health-conscious, and more open to consenting to the study. These individuals would be likely to have healthier lifestyles, fewer comorbidities, better access to care, and thus earlier cancer detection. As a result, the biobank may over represent cancers that are less aggressive or more treatable, which could limit how broadly findings from our biobank can be applied to the full WTC population. However, we conduct periodic quality checks to assess if the assembled cohort differs in terms of demographics from those whose samples are not in the biobank. Another aspect to consider is the discrepancy between the percentage of non-melanoma skin cancer diagnoses of the cohort and the percentage of non-melanoma skin cancers in the biobank: given the high frequency of this cancer, and the fact that the diagnoses are often conducted at small doctors' offices, we have not yet focused our attention on collecting it, but have given priority to the other solid cancers.

Given these limitations, it is critical to continue expanding the biobank with a focus on both cancer type and participant diversity. While the large number of prostate cancer samples reflects its high prevalence among WTC responders, it is important to collect tissue from other types of cancer to enable similar molecular epidemiology studies across a broader range of diseases [15]. Additionally, although most WTC responders are white males, efforts should be made to improve outreach to understudied groups, including females, minorities, and individuals with lower socioeconomic status. This would help reduce selection bias and improve the relevance of future findings. We hope to expand this study to include WTCHP firefighters and survivors, whose data is stored at different WTCHP CCEs. WTC Survivors, those who were not general responders or firefighters but may have had similar exposures to WTC debris, may represent a comparably more racially and socio-economically diverse group, and include a higher proportion of females with WTC exposure.

Collaboration with other researchers interested in WTC exposure is a key priority, as we wish to maximize the scientific impact of this resource. We aim to expand access to a larger number of scientists and institutions, with the purpose of allowing high-impact studies on environmental exposures and cancer etiology, cancer outcomes, and gene-environment interaction in the unique population of WTC responders. As the WTC cancer tissue biobank continues to expand, we anticipate a larger number of samples collected per cancer type, allowing for larger studies, as well as studies focused on rarer cancers, or on multiple primaries.

The WTC cancer tissue biobank represents a landmark resource for investigating the long-term health effects of WTC disaster response. By moving forward with the collection and diversification of the tissue bank, significant advances can be made in understanding WTC exposure-related carcinogenesis, leading to improved treatments and outcomes for WTC responders and survivors.

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Bellevue Hospital, Northwell Health, Rutgers University, and the State University of New York, Stony Brook.

Author contributions

W.M.T. assisted in manuscript writing, contacted, and consented participants, and requested, processed, and stored samples. A.Z. assisted with project administration. T.I.-P. contacted and consented participants, and requested, processed, and stored samples. S.T. assisted with manuscript writing and data organization. R.B. provided support for obtaining samples and expertise as a pathologist. E.T. was responsible for the conception and design of the study, study progress, and assisted with manuscript writing. All authors read and approved the final manuscript. National Institute for Occupational Safety and Health.

Ethics statement

Approval for this study was provided by the Institutional Review Board at the Icahn School of Medicine at Mount Sinai. Consent was provided by participants for this study.

Conflict of interest

The authors declare that they have no competing interests.

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Data availability

Data is available upon request from the WTCHP at Mount Sinai. Samples are available to researchers and more information as well as a Biorepository Request Form can be found at <https://icahn.mssm.edu/research/epidemiology/capabilities/biorepository-wtc>.

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