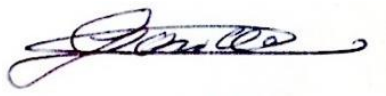
Exhibit 96

General Causation Expert Report of

Lukasz Gondek, MD, PhD

Leukemia

Prepared by:



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Contents

I am writing this report in my capacity as a scientist and practicing hematologist. In response to your request, I am providing a medical expert opinion on the following matters: (a) the causal relationship between exposure to trichloroethylene (TCE), tetrachloroethylene (PCE), benzene, and vinyl chloride in the water at Camp Lejeune and the development of leukemia; (b) assuming the aforementioned causal relationships exist, the likely dose-response relationship at low levels of exposure; and (c) the potential impact of combined exposure to TCE, PCE, benzene, and vinyl chloride. I hold all opinions to a reasonable degree of medical certainty.

I. EXPERT QUALIFICATIONS

I am a physician-scientist with a Ph.D. in cancer genomics and post-doctoral training in cancer biology and genetics of blood cancers. In addition to being a practicing hematologist/oncologist, I also lead a research laboratory studying cancer genomics, cancer biology, and the role of DNA mutations in cancer development and progression. I obtained my M.D. degree from the Medical University of Silesia in 2003, and my Ph.D. from the University of Warsaw. Following my graduation from medical school, I undertook a research fellowship at the Cleveland Clinic and studied the pathogenesis and genomics of leukemia. Following 4 years in the laboratory, I completed Internal Medicine Residency training at the Cleveland Clinic and Hematology Fellowship at Johns Hopkins. I joined the faculty of Johns Hopkins University in 2014. For the last decade, my academic career has focused on cancer genomics and the role of DNA aberrations in cancer development and progression. I have published over 60 original research manuscripts, 10 review articles and contributed to four book chapters as well as review articles and editorials. My research is frequently cited, with over 3900 citations in scientific literature. I also participate extensively in peer-review activities, serving as a reviewer for many cancer journals as well as study sections for both private and governmental funding organizations, including The European Hematology Association (EHA) and the National Institute of Health. I also served as a Scientific Session Chair for the American Society of Hematology and a Steering Committee Member for the Break Through Cancer initiative.

In addition to my research and clinical activities, I am actively involved in the education of future generations of physicians and scientists. At Johns Hopkins University, I serve as a clinical educator in the Oncology Department. I am a preceptor to internal medicine residents and hematology and oncology fellows. In addition to serving as a teacher in inpatient leukemia service, I am also an organizer of the weekly Leukemia Tumor Board for faculty and fellows. As an expert in leukemia biology and treatment, I have been leading the discussion on a particularly challenging leukemia case, where my specialized knowledge in molecular pathogenesis and advanced therapeutic strategies is critical to guiding prognosis and optimal patient management. I have been an active participant in medical student education on the topics of oncology, regenerative medicine, and cancer stem cells. Furthermore, I have served as an advisor for several postdoctoral fellows and undergraduate students. I have been the mentor for 12 postdoctoral fellows, internal medicine residents, as well as medical and graduate students. Several of my mentees successfully competed for prestigious awards such as the Molina-Grasmick Scholar Award and the American Society of Hematology HONORS Award.

My work has been recognized and supported by governmental and private funding agencies, including the National Institute of Health, Aplastic Anemia, and MDS International Foundation (AA&MDSIF), Edward P. Evan Foundation, Hopkins-Allegheny Health Network (AHN), and the Break Through Cancer Initiative.

Attached as exhibits are my CV, a list of publications from the past 10 years, a list of cases in which I testified in the past four years, and my fee schedule for this case.

II. METHODOLOGY

To reach my opinions, I performed a systematic search in the PubMed-Medline database using the terms: benzene + acute myeloid leukemia (318 results), benzene + acute lymphoblastic leukemia (62 results), perchloroethylene + leukemia (24 results), perchloroethylene + cancer (239 results), tetrachloroethylene + leukemia (20 results), tetrachloroethylene + cancer (194 results), trichloroethylene + leukemia (32 results), trichloroethylene + cancer (517 results), vinyl chloride + leukemia (31 results) and vinyl chloride + cancer (832 results) and Camp Lejeune + cancer (35 results), on May 15, 2024. I reviewed and considered all studies. I also reviewed IARC monographs and the ATSDR report 2017. All relevant data were considered; however, this report does not necessarily cite all the literature concerning the subject of an evaluation. Only those data considered to be necessary to making my evaluation were included in this report. Anecdotal evidence such as case reports and opinions without appropriate control groups are not included as they are not sufficient to demonstrate an association.

I followed the weight of the evidence approach to investigating and analyzing the data. I also drew upon the Bradford Hill considerations in moving from association to causation. Published as nine considerations in 1965, the Bradford Hill considerations are often used to determine if observed epidemiologic associations are causal. Those nine principles are: strength of association; consistency; specificity; temporality; biological gradient; plausibility; coherence; experiment; and analogy (Hill, 1965). According to Sir Bradford Hill himself, these viewpoints need not all be met to find causation.

Recent advances in understanding the mechanisms of disease now play a significant role in establishing causation, a level of insight that was not available 50 years ago when Sir Bradford Hill published his considerations. Thus, the weight of evidence from mechanistic studies may, in some cases, outweigh purely epidemiological data. The data should be interpreted in the context of a broader array of scientific evidence that includes experimental, mechanistic, and genetic data to conclusively establish causation. Thus, I also focused on the experimental evidence using laboratory studies and the mechanistic understanding of the biological pathway by which an exposure leads to cancer.

III. STANDARD APPLIED

Having reviewed the Camp Lejeune Justice Act (CLJA), it is my understanding that in order to prove causation, the evidence showing that the relationship between exposure to the water and the specified harm, for example, Leukemia, is sufficient to demonstrate that a causal relationship is at least as likely as not. In its 2017 Assessment of the Evidence for Camp Lejeune (2017 Assessment), the ATSDR utilized a classification method to evaluate the associations and causal relationships between various diseases and exposure to the water on base. One of the categories was that of "Equipoise and Above," which in my reading of the Assessment, would be equivalent to the "at least as likely as not" standard set forth in the CLJA. Based upon my education, training and experience as a practicing hematologist and cancer scientist, I am familiar with the term Equipoise, and it is my opinion that the causation standard under the CLJA is a lower standard than the "more likely than not," standard which is traditionally used in medical-legal cases. I have reviewed the ATSDR's guidance in the 2017 Assessment,

and it is my professional opinion that their explanation on how one could meet the "Equipoise and Above" standard is reasonable and scientifically valid.

IV. SUMMARY OF OPINIONS

Using the weight of the evidence approach for causation, there is sufficient evidence to opine that there is at least as likely as not a causal relationship between exposure to benzene, TCE, and PCE, both individually and cumulatively, in the contaminated water at Camp Lejeune and Leukemia. To a reasonable degree of scientific certainty, the levels of exposure at Camp Lejeune to benzene, TCE, and PCE are sufficient to create a significant risk for and cause Leukemia based upon analysis of epidemiological data, animal data, and mechanistic data.

V. DISCUSSION OF OPINIONS

A. CAMP LEJEUNE WATER CONTAMINATION

Between the 1950s and the 1980s, Camp Lejeune in North Carolina experienced extensive groundwater contamination due to improper disposal and handling of industrial chemicals. Key contaminants included benzene, TCE, PCE and VC, all known to persist in water and soil. Sources of contamination included leaking underground storage tanks, waste disposal practices, and spills at nearby industrial sites, including dry-cleaning facilities. These chemicals, some of them highly volatile organic compounds migrated through the soil into the groundwater, ultimately affecting multiple wells that supplied a portion of the base's water system. This contamination went undetected for decades, leading to prolonged periods of contamination within the water supply, and only began to receive public attention after water testing in the early 1980s revealed alarmingly high levels of toxic substances.

B. LEUKEMIA

Leukemia is a group of cancers that originate in the bone marrow, characterized by the uncontrolled growth of abnormal white blood cells. It includes several subtypes, primarily divided into acute and chronic forms, as well as lymphoid and myeloid lineages. Though leukemia is relatively rare, it remains a significant cause of cancer-related mortality. Leukemia occurs when white blood cells, acquire DNA damage, leading to uncontrolled growth and accumulation in the bone marrow and bloodstream. This DNA damage can disrupt normal cell functions, causing the cells to multiply rapidly and crowd out healthy blood cells, impairing the body's ability to fight infections, carry oxygen, and control bleeding. Certain substances, known as genotoxic compounds,-increase the risk of leukemia by directly damaging the DNA within these cells. Chemotherapy, radiation and chemicals like benzene and some industrial solvents as well are recognized as genotoxic agents, meaning they can alter the genetic material of cells and increase the likelihood of developing leukemia over time. This link between exposure to genotoxic substances and leukemia risk has been central to understanding the disease's origins and assessing risks for those exposed to harmful chemicals.

Acute myeloid leukemia (AML) is the most common type of acute leukemia. AML is relatively rare, and it accounts for approximately 1 percent of adult cancers in the United States, but nearly 2 percent of cancer-related deaths. The incidence of AML is approximately 4.1 per 100,000 population and over 20,000 new cases are diagnosed each year (SEER 12). The median age at diagnosis is 68 years and

the incidence increases with age. There is a modest predominance in men and a higher incidence in non-Hispanic White Americans than in other racial and ethnic groups.

AML arises from a single immature myeloid blood cell (stem cell) due to acquired defects in DNA. Specific chromosomal abnormalities, DNA mutations, gene duplications, gene deletions, or translocations can be identified in nearly all patients with AML. Thus, it is not surprising that AML has been associated with environmental factors that can damage DNA such as genotoxic chemicals (particularly benzene), radiation, and chemotherapy. In some patients, evolution to AML is preceded by other blood disorders such as myelodysplastic syndrome (MDS), myeloproliferative neoplasms, and aplastic anemia. In rare cases, AML is inherited.

1. ALL

Acute lymphoblastic leukemia (ALL) is another primary subtype of leukemia, typically affecting lymphoid cells and is also caused by DNA damage. Similarly to AML, ALL is rare and represents 0.3% of all new cancer cases. The incidence worldwide is 1-5 cases/100,000 population, and approximately 6,500 people are diagnosed with ALL in the USA each year (SEER 12). More than two-thirds of cases of ALL are arising from B cell precursors and one-third from T cells.

ALL is primarily a disease of children, with three-quarters of cases occurring in children <6 years old. There is however a second peak of incidence in adults >60 years old. B cell ALL occurs slightly more frequently in males than females. The incidence of B cell ALL is three times higher in White people than Black people. Hispanic populations have the highest incidence of any ethnic group.

The cause of B cell ALL is due to DNA damage and has been associated with ionizing radiation and DNA damaging chemicals. True familial ALL is rare.

C. PRINCIPLES OF CARCINOGENESIS

1. DNA Mutations

DNA stands for deoxyribonucleic acid, and it is like a manual for our body. DNA tells our cells when, how, and what kind of building blocks should be used for every part of the body such as the eyes, brain, heart, lungs, etc. Additionally, it provides the blueprint for all cells to do exactly what is necessary for every organ. DNA is made up of four different types of "building blocks," called bases. These are adenine (A), guanine (G), cytosine (C), and thymine (T). It is estimated that every cell in the human body contains 6 billion of these bases! There are 3,116,480 letters in the Bible, so the entire human DNA comprises as many DNA “letters” as 1,952 Bibles.

During the process of cell division and replication, these 6 billion letters must be copied verbatim to guarantee that the daughter cells inherit an accurate manual. The human body is composed of an estimated 30 to 40 trillion cells. That’s 30,000 more cells than stars in our galaxy. Some of these cells are lost or damaged and must be replaced by new cells from the special type of cells called “stem cells.” It is estimated that over 100 billion cell divisions happen per day in the adult human body. In general, the rate of cell division is carefully regulated by the body to maintain proper functioning and overall health, and the rate of cell division varies greatly in different organs. For example, skin, gut, and blood cells divide rapidly while bone, muscle, and brain cells divide slowly in adults.

Throughout this process, specialized proteins that copy and proofread DNA can sometimes make mistakes, introducing incorrect bases to the DNA strands. Although this system is highly accurate, errors, or "mutations can occur during cell division. These mutations can be thought of as "typos" in the manual, similar to if the architect made a mistake on a blueprint, and the contractor just blindly followed the instructions. This could result in an odd appearance and sometimes unstable construction. Mutations that accumulate over time can lead to the development of cancer, as these errors in DNA alter the genetic instructions, resulting in uncontrolled growth of mutated cells compared to healthy cells. These abnormal cells proliferate more quickly, accumulate additional mutations, and can ultimately form detectable cancer.

The rate of mutations is influenced by the frequency of cell divisions, making organs, including the blood, bone marrow and lymphatic system, with rapidly dividing cells more susceptible to cancer. Environmental factors, such as exposure to carcinogens, can further increase mutation rates by causing DNA damage that overwhelms cellular repair mechanisms. For example, exposure to chemicals like benzene, trichloroethylene, and vinyl chloride can introduce genotoxic stress to cells, leading to DNA mutations that may initiate cancer.

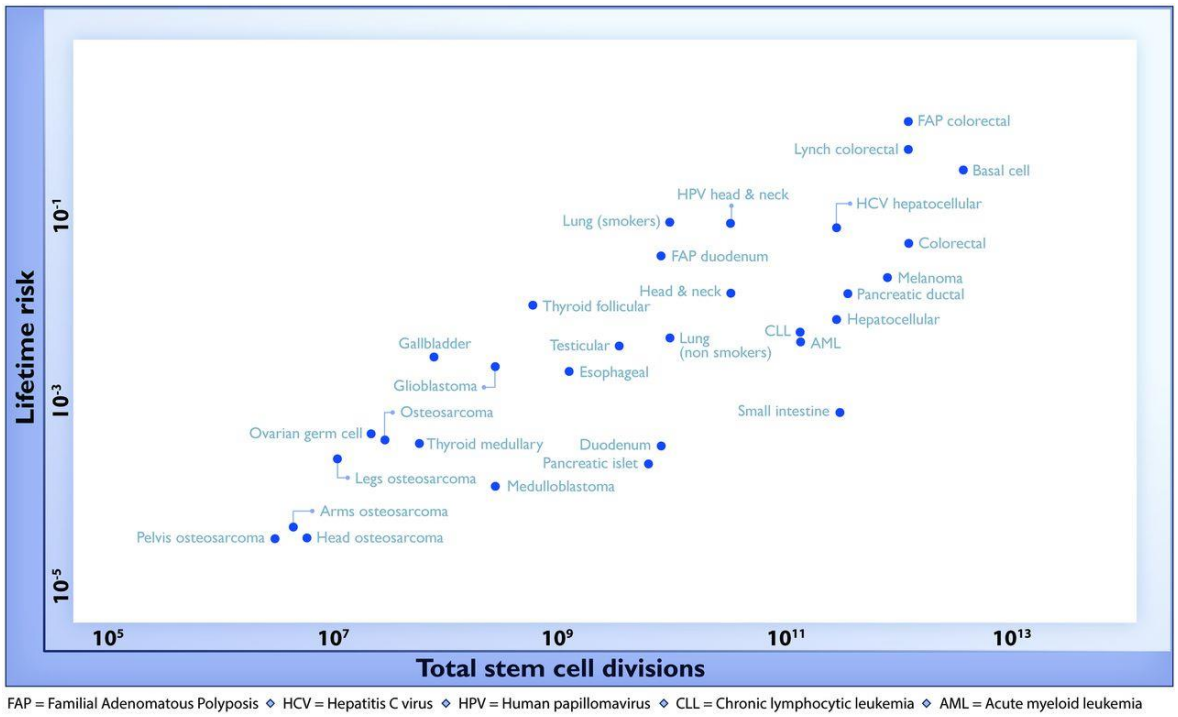


Figure 1. The relationship between the number of stem cell divisions in the lifetime of a given tissue and the lifetime risk of cancer in that tissue

Cancer incidences were determined from an analysis of 423 cancer registries that were made available by the International Agency for Research on Cancer (IARC). They observed a statistically significant correlation between the estimated number of cell divisions and the incidence of cancer (**Figure 1**).

2. Environmental Agents and Cancer

As discussed above, cancer often results from somatic mutations, or genetic changes acquired after birth, as a result of errors in DNA replication during cell division. Beyond natural DNA mutations and hereditary factors, this process can be accelerated by specific environmental, or exogenous factors. These environmental factors promote cancer development(oncogenesis) by increasing the rate of DNA mutations in two ways: 1) by directly damaging DNA, so-called carcinogens or mutagens, and 2) by promoting the division of cells that already contain cancer-promoting mutations, changing the microenvironment and weakening an immune system that is responsible for eliminating cancer cells.

The first group of factors, known as *initiators*, directly damage DNA. This group includes various chemical carcinogens that can interact directly with DNA, causing structural changes or "adducts," which lead to mutations during DNA replication. (Poirier 2004) For example, tobacco smoke contains over 60 known carcinogens, including benzene. Another example of a potent carcinogen is ionizing radiation. It can directly damage DNA via the introduction of erroneous DNA bases, deletion of certain bases, or induction of structural changes to the packaged DNA, also known as chromosomes (Little 2000).

The second group of environmental factors includes *promoters*. While they don't damage DNA directly, they accelerate the proliferation of cells with existing mutations, thereby increasing the likelihood of additional mutations and cancer formation (oncogenesis). Promoters create an environment favorable for the growth of abnormal cells.

D. MECHANISTIC EVIDENCE

1. Benzene and Cancer

Benzene is a widely recognized carcinogen extensively studied for its adverse effects on human health. The association between benzene exposure and carcinogenesis has been well-documented, and there is substantial evidence indicating that benzene can induce genotoxic effects, which contribute to its carcinogenic properties.

One of the main mechanisms through which benzene causes cancer is by damaging DNA, a process known as genotoxicity. This damage leads to mutations, or changes in the DNA sequence, which can result in the uncontrolled growth and division of cells, a hallmark of cancer.

Upon entering the body, benzene undergoes metabolic activation in the liver, where it is converted into reactive metabolites such as benzene oxide, phenol, hydroquinone, and catechol (Robert Snyder 2004; R Snyder and Hedli 1996). This reaction is mediated by a special protein called cytochrome P450 2E1 (CYP2E1). These metabolites are capable of forming reactive oxygen species (ROS), which are highly reactive molecules that can cause oxidative damage to cellular components, including DNA (Kawanishi et al. 2017). In addition to the generation of ROS, the metabolites can also bind directly to DNA, forming DNA adducts. These adducts can interfere with the normal base-pairing and replication of DNA, which leads to mutations and structural changes to DNA strands. The tissues involved in benzene metabolism are particularly prone to DNA damaging action of the benzene metabolites. Since bone marrow (an organ in the body located inside the bones where blood cells are produced) is actively involved in benzene metabolism, it is not surprising that blood cancers are the most common malignant consequences of benzene exposure (**Figure 2**).

Benzene-induced blood cancers are thought to be initiated when benzene metabolites target genes or pathways that are critical to hematopoiesis (blood production) (McHale, Zhang, and Smith 2012). These toxins impose their carcinogenic action via several mechanisms: 1) direct damage to DNA and breakage of the DNA molecule, and 2) oxidative stress mediated by ROS and error-prone DNA repair.

Direct DNA damage: Benzene is known to cause cytogenetic abnormalities in human lymphocytes (a type of immune cell some of). (M. T. Smith and Zhang 1998; Zhang et al. 2007). In a study of 47 workers and 27 unexposed controls, a statistically significant increase in the rates of abnormal chromosome numbers (monosomies or trisomies) was found to be exposure-dependently associated with benzene exposure (Zhang et al. 2011). Dozens of other studies in mice and humans confirm that benzene exposure results in structural chromosomal changes (McHale, Zhang, and Smith 2012).

Oxidative Stress: During benzene metabolism, oxygen radicals are produced which cause toxic effects, including DNA strand breaks and mutations. Several studies link benzene-induced ROS production to DNA Damages. (Ho and Witz 1997; Kolachana et al. 1993; Wiemels and Smith 1999). ROS causes oxidative DNA damage as described earlier.

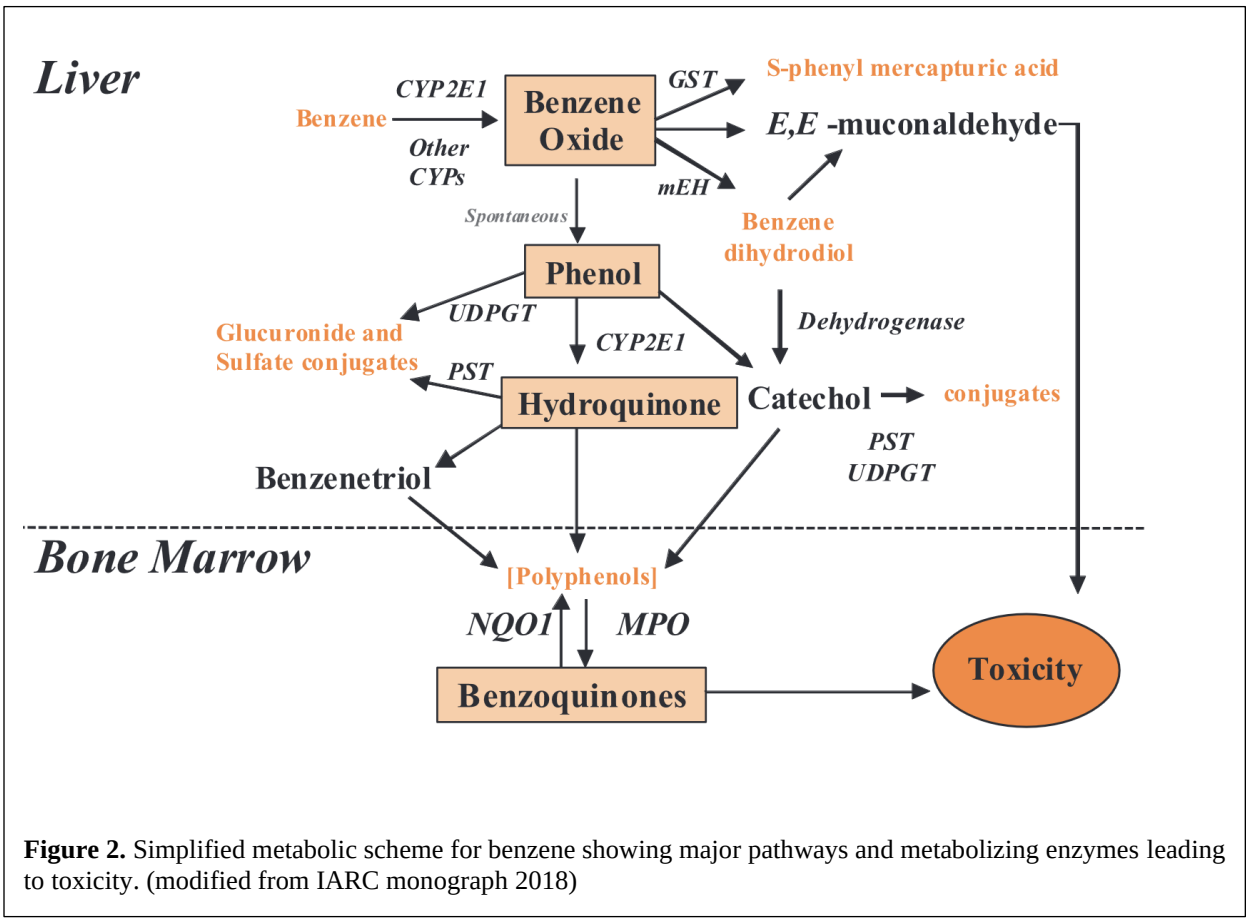


Figure 2. Simplified metabolic scheme for benzene showing major pathways and metabolizing enzymes leading to toxicity. (modified from IARC monograph 2018)

In addition to being a carcinogen, benzene can also act as a "*promoter*" (*see* "Environmental agents and cancer," *supra*) by weakening the immune system. The immune system is an important

guardian responsible for the elimination of cancer cells at the early stages of tumor formation. The importance of an intact immune system in many cancers has been well established. The toxic effects of benzene on the lymphocytes (professional killers of infected or cancer cells) have been reported (Guo, Ahn, and Zhang 2020).The effect of benzene on the number of immune cells has been observed at concentration levels below 1 part per million (ppm) (Lan et al. 2004). Such weakening of the immune system allows cancer cells to escape this surveillance mechanism and grow uncontrollably.

The significant heterogeneity in assessing cumulative benzene exposure complicates a precise and definitive assessment of the exposure-response curve. Additionally, most published studies have not evaluated continuous measures of benzene exposure. Several studies demonstrate an increased risk of AML at near-ambient benzene concentrations (Rushton et al. 2014; Glass et al. 2003; 2006; Martyn T. Smith 2010; Shallis et al. 2021). Some flawed conclusions of a "safe" benzene exposure threshold came from the studies that demonstrated a significant increase in AML risk when compared to the "control" population below an arbitrary exposure level. This is particularly true for older studies where the "control" population may have been exposed to more than ambient levels of benzene. This would result in a significant underestimation of the exposure effect on the incidence of AML.

The genotoxic effects of benzene are primarily mediated predominantly by its metabolites, produced by CYP2E1 (as described above). Most recently, studies using biomarkers of benzene toxicity demonstrated that albumin adducts (an indicator of toxicity) can be introduced with an ambient benzene concentration of much less than 1ppm and there is no "minimum threshold" to harm . Rappaport et al. 2002; 2005). Moreover, the same study reported that the human CYP2E1system becomes saturated at a benzene exposure of 1ppm resulting in a supralinear exposure-response curve. In other words, the exposure-response relationship is steepest at the lowest exposure levels. This indicates that the actual risks of AML after low-level benzene exposure can be substantially higher than initially predicted.

A study of Australian petroleum workers demonstrated that workers exposed only to Benzene, obviously different from the multiple exposures at Camp Lejeune, demonstrated an increased risk of leukemia at cumulative exposures above 2ppm – years (Glass et al. 2003). Importantly, that study found no evidence of a threshold level, below which there was no risk for cancer. The hazard ratio with cumulative exposure as a continuous measure was 1.65 (95% CI 1.25-2.17) (Glass et al. 2003). This risk was comparable to a Chinese study of workers exposed to benzene at average levels of less than 10ppm (RR 2.2 95% CI 1.1-4.2) (Hayes et al. 1997). Finally, a risk assessment study on low level benzene exposures utilizing a Chinese Benzene Cohort found that leukemia risks may occur at cumulative concentrations below 3mg/m3 year (Jin 2024).

A large case-control study of 250 workers exposed to low levels of benzene demonstrated statistically significant toxicity to hematopoietic cells (leukopenia and thrombocytopenia). Interestingly, blood precursors (the cells from which AML originates) were particularly sensitive to benzene exposure at a level below 1 ppm (Lan et al. 2004). Thus, the data suggest that exposure to low levels of benzene, including the levels at Camp Lejeune over the entire study period, pose a significant and increased risk for hematologic malignancies.

In conclusion, benzene is a potent carcinogen, and its ability to cause cancer is closely associated with either direct damage to DNA or indirectly through a weakening of the immune system. (Guo 2022). Benzene is metabolized in the bone marrow; thus, people exposed to benzene are

particularly at risk for blood cancers. Because of these mechanisms, and particularly because benzene is a tumor initiator, it is at least as likely as not that the levels of benzene in the water at Camp Lejeune are biologically significant and can lead to cancer, including leukemia. Given this overwhelming body of scientific evidence, the International Agency for Research on Cancer (IARC) has classified benzene as a Group 1 carcinogen (IARC's highest classification), indicating that there is sufficient evidence of its carcinogenicity in humans. The IARC classified benzene as a human carcinogen in 1979. In 2012, the Working Group confirmed the previous findings of sufficient evidence of carcinogenicity in humans and experimental animals and, for the first time, presented strong evidence of multiple genotoxic effects based on a review of extensive mechanistic data. In humans, the Working Group concluded that benzene causes AML (IARC Working Group on the Evaluation of Carcinogenic Risks to Humans 2012). It is a generally accepted practice in my field to rely on IARC classifications where available because IARC provides a robust and authoritative analysis of peer-reviewed scientific literature regarding potential carcinogens. In addition, I have independently reviewed the studies and data underlying the IARC Working Group's classification of benzene and agree with IARC's classification.

2. TCE and Cancer

TCE is a chlorinated solvent that has been produced commercially since the1920s. TCE was previously used as a stain-remover in dry-cleaning; an ingredient in paints, adhesives, cleaners; and more recently, for degreasing metal parts, and as a feedstock for producing chlorinated chemicals. TCE has been found in outdoor and indoor air, water, soil, food, and exposure from environmental sources (including hazardous-waste sites and contaminated water). It is common in the USA and elsewhere.

In 2014, an IARC Working Group classified TCE as carcinogenic to humans (Group 1) (IARC's highest classification). Biotransformation of TCE, well characterized in humans and animals, occurs primarily through oxidative metabolism by cytochrome P450 enzymes and also via glutathione conjugation by glutathione S-transferase enzymes (**Figure 3**). The main oxidative metabolites are dichloroacetic acid (DCA), trichloroacetic acid (TCA), and chloral hydrate (CH). Metabolites of TCE formed via cytochrome P450 enzymes or glutathione conjugation are genotoxic. Particularly S-(1,2-dichlorovinyl)-L-cysteine (DCVC), and to a lesser degree, DCVG and N-acetyl-S-(1,2-dichloroWvinyl)-L-cysteine (NAcDCVC), are genotoxic on the basis of consistent results in several studies (Dekant et al. 1986; Vamvakas et al. 1988; Jaffe et al. 1985; Vamvakas, Dekant, and Henschler 1989; Vamvakas, Richter, and Bittner 1996). Additionally, for oxidative metabolites of TCE, such as TCA, chloral (CHL) and CH, strong evidence is available to suggest that CH/CHL may be genotoxic and mutagenic. The evidence is from both *in vivo* and *in vitro* tests, in mammalian and other experimental systems, including studies with and without metabolic activation (Lash et al. 2014). The types of damage reported include mutations, chromosomal aberrations, micronuclei, and cell transformation. Importantly, micronuclei in peripheral blood lymphocytes isolated from infants administered CH crystals mixed in breast milk or formula were significantly increased, consistent with the conclusion that CH is genotoxic in humans (Ikbal et al. 2004).

Interestingly, because of its lipophilicity, TCE preferentially partitions to tissues with a high lipid content, such as fat. Bone marrow cavity has relatively high fat content that increases with age. This may result in a relative increase in local TCE concentration in bone marrow. Additionally, cytochrome P450 enzymes are essential for protection of hematopoietic cells from external toxin (Alonso et al. 2015). This "protective" mechanism may result in a local increase in the level of toxic metabolites such

as CHL/CH leading to DNA damage and blood-cancer development. Some reports utilizing *in vivo* animal models demonstrated increased cytotoxicity in bone marrow cells after TCE exposure.

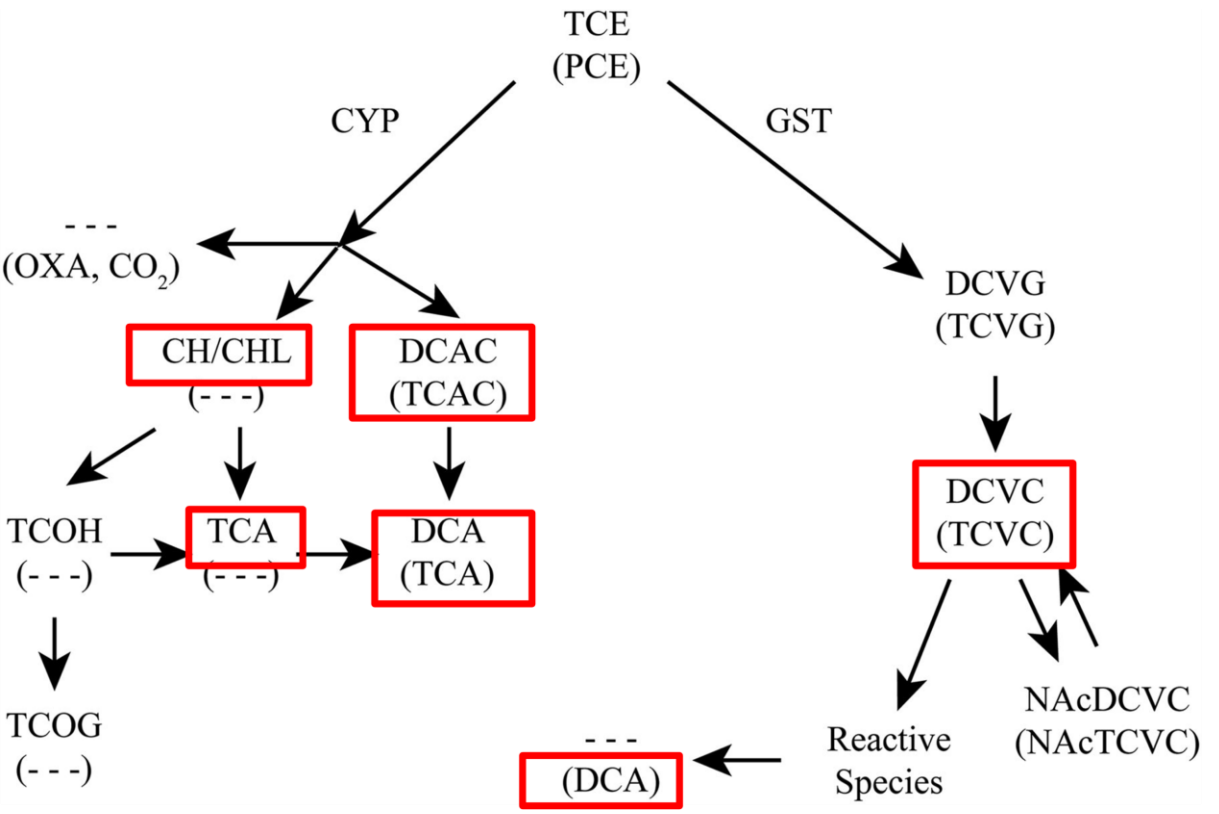


Figure 3. Metabolic pathways of TCE and PCE. Major metabolites of TCE (top) and PCE (bottom, in parentheses) are shown through P450-mediated oxidation and GSH conjugation. Toxic metabolites are highlighted in red rectangles (adapted from Joseph A. Cichocki et al. J Pharmacol Exp Ther 2016;359:110-123)

3. PCE and Cancer

Perchloroethylene (PCE), also known as tetrachloroethylene, is a synthetic chemical commonly used as a solvent. It is a colorless, nonflammable liquid with a distinctive, sharp odor and is chemically classified as a chlorinated hydrocarbon. PCE is primarily used in industries for degreasing metal parts and in dry cleaning processes due to its effective dissolving properties. It also finds application in manufacturing other chemicals and is sometimes present in consumer products like paint removers and stain removers.

The primary use of PCE is in the dry-cleaning industry, where it serves as a powerful cleaning agent for fabrics that cannot withstand water-based cleaning methods. In addition, it is used as a solvent in metal degreasing, especially in automotive and aerospace industries, due to its ability to dissolve oils, fats, and greases effectively. Beyond industrial applications, PCE is utilized in the production of fluorinated compounds, such as refrigerants, and in specific adhesives, coatings, and ink formulations. Its versatile solvent properties make it valuable in both specialized and common industrial processes.

PCE contamination in water, soil, and air is primarily the result of industrial activities, improper disposal, and leaks from storage tanks. Since PCE does not easily degrade in the environment, it can persist and accumulate over time, posing risks to environmental and human health.

PCE has been classified by the IARC as a Group 2A carcinogen, meaning it is "probably carcinogenic to humans." This classification is based on sufficient evidence from animal studies that have shown an association between PCE exposure and the development of certain cancers, including liver and kidney cancers, and limited epidemiological evidence in humans. Studies on occupational exposure, particularly among workers in the dry-cleaning industry, have suggested an increased risk of cancer associated with PCE exposure.

Similar to TCE, PCE is primarily metabolized via glutathione conjugation by glutathione S-transferase enzymes as well as oxidation by cytochrome P450 enzymes as well, with CYP2E1 being involved, but to a lesser extent than TCE (**Figure 3**). The main metabolites are TCA and other chlorinated compounds, though in smaller amounts than those from TCE. However, PCE is metabolized at a slower rate, with a larger fraction excreted unchanged through exhalation. PCE has been demonstrated to cause DNA toxicity, primarily through its metabolites showing evidence of genotoxic effects in both in vitro and in vivo studies.

Experimental studies on animals and cell lines exposed to PCE and its metabolites have reported DNA strand breaks and chromosomal aberrations. Metabolites like trichloroethylene and its derivatives have been implicated in causing chromosomal abnormalities including deletions, translocation and micronuclei formation (IARC 2020). More importantly and particularly pertinent to this case is the genotoxic effect of PCE and its impact on blood cells. Studies have investigated hematological alterations, oxidative stress, and DNA damage in blood cells due to exposure to PCE, particularly in occupational settings. The findings indicated that PCE exposure led to significant increases in structural chromosome aberrations and micronucleus formation, suggesting DNA damage (Kocaman and Asfuroğlu 2021). Another study involving dry cleaning workers exposed to PCE compared to unexposed laundry workers revealed a significant correlation between PCE levels and the percentage of cells with acentric fragments, a type of chromosomal damage (Tucker et al. 2011).

PCE is more lipophilic than TCE and exhibits greater sequestration and accumulation in fat than TCE. This would suggest potentially higher and prolonged exposure of cells in high fat organs such as bone marrow.

4. VC and Cancer

Vinyl chloride (VC), also known as chloroethene, is a synthetic chemical primarily used as an intermediate in the production of polyvinyl chloride (PVC), a versatile plastic widely utilized in construction, automotive, and consumer goods industries. It is a colorless gas at room temperature with a faint, sweet odor and is classified as a chlorinated hydrocarbon. Its primary use is in the polymerization process to manufacture PVC, which serves as the basis for products such as pipes, flooring, wiring insulation, and medical equipment. Additionally, VC is sometimes used in the production of other chemical intermediates, though its direct applications outside PVC manufacturing are limited.

VC contamination in the environment can result from industrial emissions, improper waste disposal, and leaks during manufacturing or storage. It is also a degradation product of other chlorinated

hydrocarbons, such as TCE and PCE, in anaerobic conditions. Because VC is highly volatile, it readily disperses in the air, but it can persist in groundwater, posing risks to both environmental and human health.

VC has been classified by the IARC as a Group 1 carcinogen, indicating it is "carcinogenic to humans." This classification is based on robust evidence from occupational and epidemiological studies showing a strong association between VC exposure and the development of angiosarcoma of the liver, a rare and aggressive cancer. In addition to liver cancer, vinyl chloride exposure has been linked to an increased risk of other cancers, including lung and brain cancer, as well as hematologic malignancies.

Metabolically, VC undergoes bioactivation primarily through the cytochrome P450 enzyme system, specifically CYP2E1, resulting in the formation of reactive intermediates, such as chloroethylene oxide and chloroacetaldehyde. These metabolites are responsible for DNA and protein adduct formation, contributing to genotoxic effects. Experimental studies have shown that VC exposure can induce DNA strand breaks, chromosomal aberrations, and mutations. Chloroethylene oxide and chloroacetaldehyde can form etheno adducts with nucleic acid bases in vitro (Guengerich 1992) (**Figure 4**). Interestingly, in experimental animals, exposure to VC resulted in increased rate of etheno adducts in lymphocytes (Barbin 1999). Hematologic studies in exposed workers have reported oxidative stress, DNA damage, and chromosomal instability, particularly in blood cells, which may contribute to its carcinogenic potential (Kumar et al. 2013).

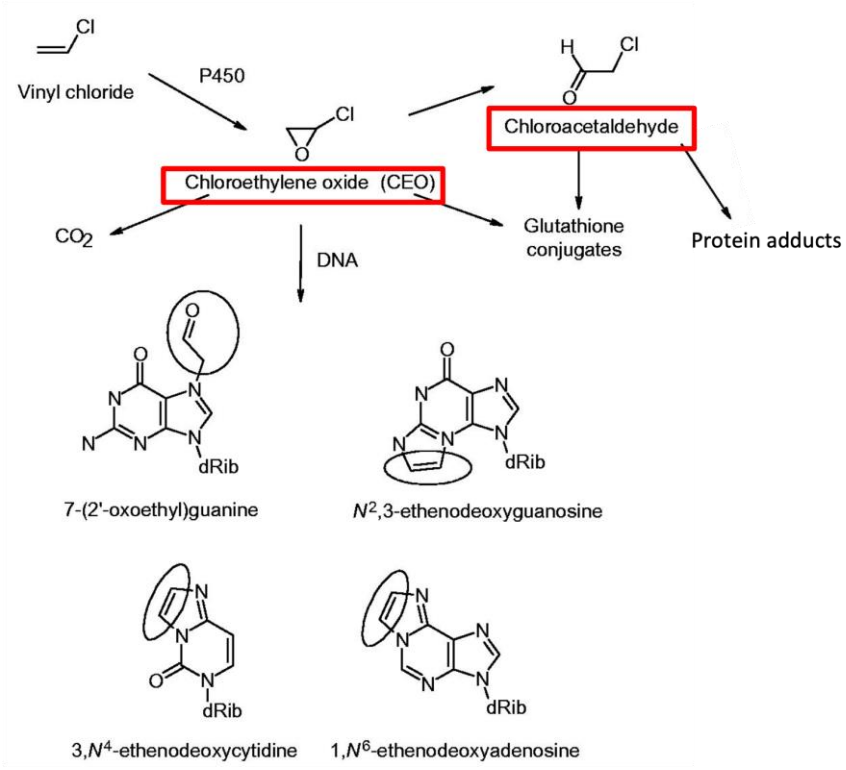


Figure 4. Vinyl chloride metabolism showing binding sites of identified DNA adducts. Toxic metabolites are highlighted in red rectangles (adapted from Pottenger LH, et al. Crit Rev Toxicol. 2014 Apr;44(4):348-91.)

E. EPIDEMIOLOGICAL STUDIES

1. Benzene and Leukemia

In 1987, a group of experts from the International Agency for Research on Cancer (IARC) analyzed four independent cohort studies that demonstrated an increased incidence of AML in workers exposed to benzene (Decoufle, Blattner, and Blair 1983; Bond et al. 1986; McCraw, Joyner, and Cole 1985; Yin et al. 1987).

In 2012 IARC Working Group analyzed numerous additional cohort studies in populations exposed to benzene, including updates of earlier reports, and new case–control studies of leukemia. Additional analyses of previously published cohort studies [(Crump 1994) and (O. Wong 1995)], and new cohort studies with quantitative data on benzene exposure have shown evidence of a dose–response relationship between exposure to benzene and risk for AML in various industries and in several countries (Hayes et al. 1997; Rushton and Romaniuk 1997; Divine, Hartman, and Wendt 1999; Guénel et al. 2002; Collins et al. 2003; Glass et al. 2003; Bloemen et al. 2004; Gun et al. 2006; Kirkeleit et al. 2008). Additionally, studies on benzene have revealed that it has a broad effect on lymphatic and hemapoetic cancers, including acute and chronic lymphocytic leukemia, not just AML alone. (Savitz 1997).

In the most recent 2018 IARC Monograph, occupational and general-population studies published since the previous IARC Monographs on benzene, including studies in occupational cohorts with careful assessment of benzene exposure, confirmed the association between AML and exposure to benzene.

a. Petroleum distribution workers

The previously published cohort studies from Australia (Glass et al. 2003), Canada (A. R. Schnatter et al. 1996), and the United Kingdom (Rushton and Romaniuk 1997) were updated with new hematologic malignancies cases. The pooled analysis was performed using a nested case-control study design, and 370 cases and 1587 controls were included in the analysis (A. Robert Schnatter et al. 2012). The study was characterized by the high quality of the assessment of benzene exposure and diagnostic classification. The study found that even low-level of cumulative benzene exposure (>2.93 ppm-year) was associated with the risk of myeloid malignancies, particularly MDS. In the further analysis of the same data, the risk of AML in terminal workers employed for at least 1 year was statistically significant (odds ratio (OR): 2.02, 95% CI: 1.08, 3.78) as was the risk for tanker drivers who had ever worked at a terminal (OR: 2.41, 95% CI: 1.21, 4.80) (Rushton et al. 2014). Moreover, the OR for leukemia increased with cumulative exposure when exposure was treated as a continuous variable in a matched analysis, OR 1.10 (95% CI: 1.04–1.16) per ppm year demonstrating a strong correlation between exposure level and leukemia risk (Glass et al. 2003).

b. Chinese workers study

The incidence of and mortality from blood cancers were studied in a large cohort of 74,828 Chinese workers exposed to benzene and 35,805 unexposed workers (National Cancer Institute-Chinese Academy of Preventive Medicine (NCI-CAPM) cohort). The initial cohort follow-up (Hayes et al. 1997) was extended to 1999 (Linet et al. 2015). Significantly elevated incidence of all myeloid disorders reflected excesses of MDS/AML (relative risk (RR) 2.7, CI 1.2, 6.6). A total of 26 AML cases were found

among exposed to benzene and 7 among the unexposed, resulting in an RR of 2.1 (95% CI, 0.9–5.2). A subsequent analysis in 2018 (Linet et al. 2019) found increased MDS/AML particularly in younger patients before age 30 years within 2-10 years of benzene exposure (*P* =0 .004) with rate ratios of 1.12 (CI, 0.27, 4.29), 5.58 (CI , 1.65, 19.68), and 4.50 (CI, 1.22, 16.68) for cumulative exposures of 0-40, 40-100 and >100 ppm-years, respectively, compared with no exposure. This is particularly important as the median age of AML diagnosis in the general population is 68 years.

c. Norwegian offshore oil industry workers.

Stenehjem and colleagues reported the incidence of hematologic cancers in nearly 25,000 offshore petroleum workers in Norway between 1965 and 1999 (Stenehjem et al. 2015). Most workers were exposed for < 15 years and were exposed to relatively low levels of benzene. A total of 112 cases of blood cancer were reported between 1999-2011. The hazard ratio (HR) of AML for exposed versus never exposed to benzene was 2.18 (CI, 0.41, 10.00). The risk estimate was substantially higher in the highest tertile of cumulative exposure (0.124–0.948 ppm-years) compared with the lowest tertile (< 0.001–0.037 ppm-years), with a hazard ratio of 4.85 (CI, 0.88, 27.00). There was evidence of dose-related risk patterns according to cumulative exposure for AML (p for trend 0.052).

d. Quantitative data and meta-analyses

In 2018 IARC Working Groups carried out meta-analyses of quantitative associations between occupational benzene exposure and several cancers of the hematopoietic tissues including AML. The data from 13 studies were included in the meta-analysis which examined the incidence of and mortality due to AML after benzene exposure. The OR for incidence was 1.45 (CI, 0.96, 2.17) for mortality was 1.71 (CI, 0.95, 3.08). The cumulative OR was 1.54 (CI, 1.16, 2.05) indicating a significant association between benzene exposure and incidence of and mortality due to AML (**Figure 3**).

A meta-regression analysis was also conducted by the same group of experts to better define the cumulative benzene exposure and the risk of AML and included six occupational cohort studies. The results indicated the association between cumulative benzene exposure and AML (**Figure 4**).

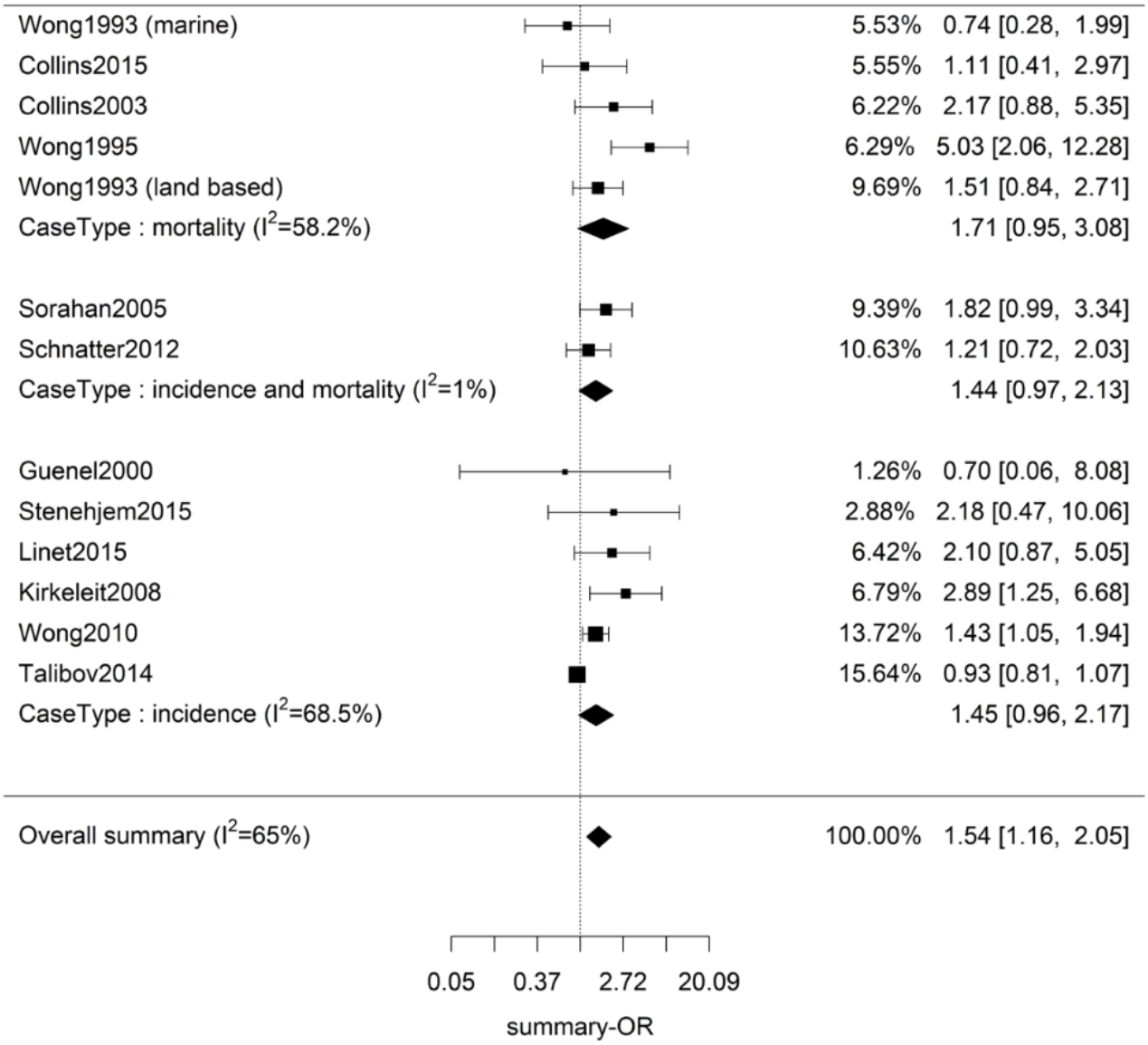
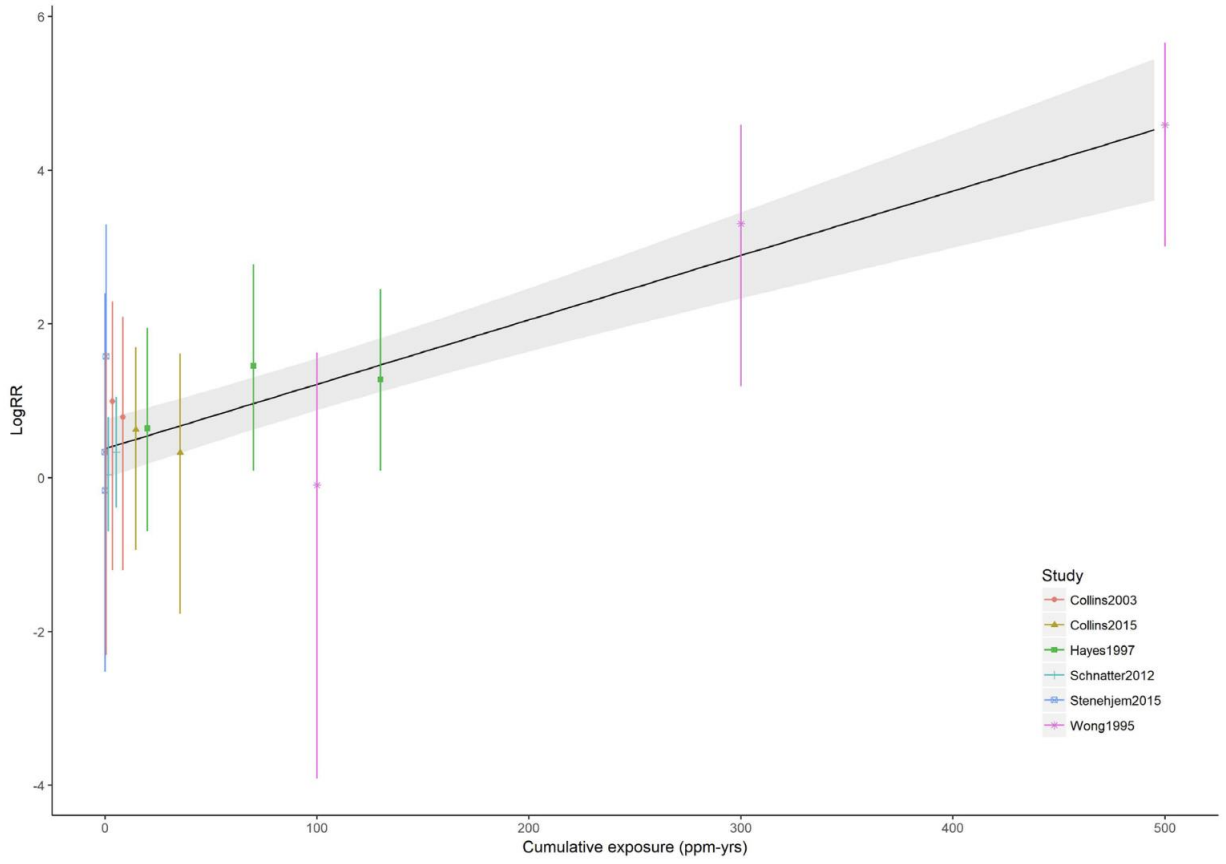


Figure 3. Forest plots of AML stratified by type of outcome (incidence or mortality, adopted from IARC 2018, volume 120)



AML, acute myeloid leukaemia
Compiled by the Working Group

Figure 4. Meta-regression model of cumulative benzene exposure and AML, including fitted curve and confidence intervals.

2. TCE and Leukemia

Multiple cohort, case-control studies and metanalysis addressed the association between AML and TCE exposure. In 2017 the Agency for Toxic Substances and Disease Registry (ATSDR) performed a meticulous analysis of available high-quality of epidemiological studies and concluded:

> "ATSDR concludes that the epidemiological evidence for TCE and leukemia from the occupational and drinking water studies is not strong but nevertheless sufficient to at least reach equipoise"

A large cohort study performed by Hansen et al. in Denmark examined the incidence of common cancer in among 803 Danish workers exposed to TCE, using historical files of individual air and urinary measurements of TCE metabolite. The standardized incidence ratio (SIR) was significantly increased for non–Hodgkin's lymphoma (SIR = 3.5, 1.5-6.9). Increase but not statistically significant SIR was observed in leukemia (SIR= 1.6, 0.6-4.4) as only 5 patients developed leukemia (Hansen et al. 2001). Thus, the lack

of statistical significane was very likely due to a low number of cases. Another Danish cohort study by Raaschou-Nielsen and colleague examined the cancer incidence between 1968 and 1997 in a cohort of 40,049 blue-collar workers in 347 Danish companies with documented TCE use. SIR for non-Hodgkin's lymphoma was similar to renal cell carcinoma [1.2 (95% CI: 1.0, 1.5) and 1.2 (95% CI: 0.9, 1.5), respectively] (Raaschou-Nielsen et al. 2003).

The epidemiological studies investigating the association between TCE exposure and hematologic malignancies resulted in equivocal findings. While some failed to demonstrate the statistically significant association between TCE exposure and hematologic malignancies. (Axelson et al. 1994; Anttila et al. 1995; Greenland et al. 1994; Zhao et al. 2005; Boice et al. 2006; Radican et al. 2008) several demonstrated significant association. While not given the same weight, even non-significant findings of an association are relevant to my analysis.

A case–control study that investigated 105 Swedish men diagnosed with NHL between 1974 and 1978 and 335 matched controls from a national population registry demonstrated more than a 700% increased risk of NHL in workers reporting exposure to TCE (OR, 7.2; 95% CI, 1.3–42.0) (Hardell, Eriksson, and Degerman 1994). Another case–control study from Germany included 710 patients with lymphoma and 710 matched controls from population registries. The exposure was determined by a physician based on an occupational exposure questionnaire. Workers with highest exposure to TCE (> 35 ppm-years) had significantly increased risk of lymphoma in general (OR, 2.1; 95% CI, 1.0–4.8) but also for various lymphoma subtypes including both B- and T-cell lymphomas (Seidler et al. 2007). A case-control study from the USA investigated the association between occupational exposure to solvents and NHL among 601 women in Connecticut recruited between 1996 and 2000 and 717 random controls. An increased risk of NHL in women ever exposed to TCE was noted (OR,1.2; 95% CI, 0.9–1.8), after adjustment for multipole potential confounder such as age, family history of hematopoietic cancers, alcohol consumption, and race. Compared with non-exposed subjects, the risk was elevated at a medium-to-high intensity of exposure (OR, 2.2; 95% CI, 0.9–5.4) (Wang et al. 2009).

The ATSDR also recognized that exposure to TCE was associated with acute lymphoid leukemia (ALL) and acute myeloid leukemia (AML). This conclusion was based on two studies. The first was a case-control study of 15,332 incident cases of AML diagnosed in Finland, Norway, Sweden and Iceland from 1961-2005 and 76,660 controls matched by year of birth, sex, and country (Talibov et al. 2014). Even though the association was not statistically significant, a meaningful trend and nearly statistically significant p-value of 0.08 was observed for the trend with various levels of exposure (**Figure 5**).

Agent [a] (ppm/year)	Cases	Controls	HR	95% CI	P-value for trend
Solvents					
Aliphatic and alicyclic hydrocarbon solvents					
≤17.5	353	1743	1.01	0.79–1.29	
17.5–300	283	1393	1.08	0.82–1.42	
>300	54	366	0.64	0.38–1.08	0.76
Aromatic hydrocarbon solvents [b]					
≤9.3	362	1661	1.10	0.98–1.25	
9.3–275	256	1362	0.99	0.80–1.24	
>275	63	342	1.18	0.76–1.86	0.56
Benzene					
≤3.7	430	1999	1.02	0.84–1.24	
3.7–13.6	310	1633	0.88	0.71–1.11	
>13.6	68	418	0.80	0.56–1.15	0.33
Toluene					
≤42.4	424	1954	1.17	0.94–1.45	
42.4–61	296	1602	1.01	0.79–1.30	
>612	76	400	1.35	0.74–2.46	0.49
Trichloroethylene					
≤16.2	302	1760	0.93	0.79–1.09	
16.2–121	275	1373	1.12	0.94–1.33	
>121	68	345	1.12	0.83–1.49	0.08

Figure 5. Hazard ratios (HR) and 95% confidence intervals (95% CI) of acute myeloid leukemia associated with exposure to solvents and other co-factors.

In a large cohort study of 34,494 workers employed at a microelectronics and business machine facility 1969–2001 in New York City, Silver and colleagues analyzed standardized mortality ratio (SMR) and standardized incidence ratios to evaluate relations between occupational exposures to various chemicals including TCE and outcomes. They found a significant association between non-CLL leukemia (77 cases), which also include myeloid and lymphoid leukemias such as ALL, and TCE exposure (HR, 1.31; CI, 0.98-1.75).

Additionally, two meta-analyses were performed. Alexander and colleagues examined seven studies and found a summary relative risk (RR) estimate to be 1.11 (CI, 0.93-1.32) (Alexander et al. 2006). The second meta-analysis was performed by Karami et al (Karami et al. 2013) and included nine

cohort studies and one case control study that included TCE exposure. The overall RR for all studies was 1.1 (CI, 0.9-1.3). Unfortunately, the type of leukemia was not further specified in this study.

An ecological study, which analyzed the effect of combined TCE/PCE exposure in the drinking water of 75 municipalities in New Jersey, revealed elevated associations between exposure to the drinking water and ALL, CLL, CML, as well as total leukemias (Cohn et al. 1994). More specifically and importantly, the levels of TCE in the drinking water in the New Jersey study were lower than those found and modeled in the Hadnot Point water supply at Camp Lejeune. The study looked at three specific exposure levels to TCE, including the lowest category with levels below 0.1 ppb, the middle category of 0.1 to 5 ppb, and the highest category of 5 ppb and above, although the highest assigned TCE level was 67 ppb.

The study revealed an elevation in total leukemias for women exposed to 0.1 to 5 ppb (RR = 1.13, 95% CI 0.93-1.37). For men and women exposed to drinking water with TCE levels at 5 ppb and above, the study showed increased associations to total leukemia at (RR = 1.10, 95% CI 0.84-1.43) and (RR = 1.43, 95% CI 1.07-1.90), respectively.

As to ALL, females exposed to levels of TCE in the range of 0.1 to 5 ppb and at 5 ppb and above demonstrated elevations in risk at (RR = 1.85, 95% CI 1.03-3.70) and (RR = 2.36, 95% CI 1.03-5.45). With regard to CLL, males and females exposed to TCE in drinking water at 5 ppb and above demonstrated an increased risk at (RR = 1.49, 95% CI 0.97-2.30) and (RR = 1.57, 95% CI 0.95-2.60), respectively.

This study, when considered in light of epidemiological data and mechanistic, helps answer the question as to the level(s) at which it is known that TCE causes leukemia in humans. Given that almost all epidemiological studies looking at the association between TCE and leukemia are occupational studies, the Cohn New Jersey study stands as the most similar to the exposures found at Camp Lejeune.

Based on the epidemiologic data ATSDR concluded that there was an equipoise and above evidence for causation for TCE and all adult leukemias, including AML, ALL, CML and CLL. Having independently reviewed the date underlying ATSDR's conclusions in this report, and having run searches in the scientific literature to supplement and update ATSDR's conclusions, I agree with ATSDR that it is at least as likely as not that exposure to TCE in the water at Camp Lejeune can cause AML and ALL.

3. PCE and Leukemia

In many workplaces where PCE is used, other chlorinated solvents can also be found. There is some overlap between exposures to PCE and TCE in studies evaluated which complicated the interpretation of study findings, but it should be remembered that nearly all workplaces have multiple exposures.

The association between PCE and hematologic malignancies has been evaluated in several case-control studies. However most studies focused on either hematologic malignancies as a whole or lymphomas. Additionally, the majority of studies investigated the effect of PCE on cancer incidence among dry cleaning workers who were exposed to volatile PCE in air. In humans, measured exposure via inhaled air demonstrated that nearly 85% of inhaled PCE was actively eliminated by exhaled air and only 15% was metabolized (Chiu et al. 2007). The data on oral route of exposure are missing but given the

fact that PCE is highly lipid soluble it is estimated that nearly 100% of PCE is absorbed after oral ingestion.

In addition to New Jersey water contamination study discussed above (Cohn et al. 1994) a population-based case-control study was used to evaluate the relationship between an exposure to tetrachloroethylene from public drinking water in Cape Cod, Massachusetts and the incidence of leukemia (Aschengrau et al. 1993). An elevated risk of leukemia was observed among ever exposed subjects (OR = 1.96, 95% CI 0.71-5.37) that increased further among subjects whose exposure level was over the 90th percentile (OR = 5.84, 95% CI = 1.37-24.91).

Based on the limited number of epidemiologic data, ATSDR concluded that there was below equipoise evidence for causation for PCE and leukemias.

Having independently reviewed the biological and mechanistic data as well as epidemiological studies, I concluded that it is at least as likely as not that exposure to PCE in the water at Camp Lejeune can cause AML and ALL.

4. VC and Leukemia

Several epidemiologic studies investigated the association between VC and hematologic malignancy. The cohort study from West German investigated 7,021 men exposed to VC and 8,917 controls. There was a significant association between exposure to VC and mortality due to hematologic malignancies (RR 2.14, CI 1.12–3.53) (Weber, Reinl, and Greiser 1981).

Another cancer mortality study from the former Soviet Union evaluated cancer mortality among 3,232 production workers (2,195 men, 1,037 women) employed in the production of VC, and PVC between 1939 and 1977. A significant increase in deaths from NHL and multiple myeloma (RR 4.17, $p < 0.05$) and leukemia (RR= 5, $p < 0.05$) were reported (Smulevich, Fedotova, and Filatova 1988). The risk of cancer was highest among the workers exposed to concentrations of VC of 300 mg/m3 and more who had worked at the plant for 15 to 19 years.

Finally, an extended follow up retrospective cohort study of the original report (R.-H. Wong et al. 2002) investigated the incidence of hematologic cancers caused by occupational exposure to VC among workers from PVC manufacturing factories in Taiwan, with follow-up of the cohort extended by 15 years, from 1980 to 2007 (Hsieh et al. 2011). The study included 3,336 male and the general Taiwanese male population served as control. Leukemia mortality significantly increased during 1984-1989 (SMR 6.06, CI 1.24 to 17.53), and reached a peak during 1985-1990 (SMR 7.56,CI 2.06 to 19.35) The mortality trend for other lymphopoietic cancer showed a similar pattern to that of leukemia.

Several studies (Mundt et al. 2000; Ward et al. 2001; Thériault and Allard 1981) did not show the significant association between VC and leukemia. Also a meta-analysis was performed to investigate association between VC and various cancer. However, a meta-analysis could not be performed on a subset of hematologic malignancies given significant heterogeneity of the published cohorts. The analysis was limited only to two multicenter cohorts showed nonsignificant meta-SMR (meta-SMR 0.90, CI 0.75–1.07) (Boffetta et al. 2003).

Because of the conflicting findings between the latter study and the meta-analysis, ATSDR concluded that there was below equipoise evidence for causation for vinyl chloride and leukemias.

F. CAMP LEJEUNE STUDIES

The initial retrospective cohort studies investigating the mortality among military personnel (Bove et al. 2014a) and civilians (Bove et al. 2014) at Camp Lejeune compared to Camp Pendleton were published in 2014.

The first study was a retrospective cohort mortality study of Marine and Naval personnel who began service during 1975-1985 and were stationed at Camp Lejeune or Camp Pendleton with a mortality follow-up from 1979 until 2008. Compared to Camp Pendleton, Camp Lejeune had elevated mortality for all cancers (HR = 1.10, 95% CI: 1.00, 1.20), kidney cancer (HR = 1.35, 95% CI: 0.84, 2.16), liver cancer (HR = 1.42, 95% CI: 0.92, 2.20), esophageal cancer (HR = 1.43 95% CI: 0.85, 2.38), cervical cancer (HR = 1.33, 95% CI: 0.24, 7.32), Hodgkin lymphoma (HR = 1.47, 95% CI: 0.71, 3.06), and multiple myeloma (HR = 1.68, 95% CI: 0.76, 3.72). Acute leukemia cases, specifically, were not studied.

In the second study elevated HRs in the Camp Lejeune cohort was found for several causes of death including cancers of the kidney (HR = 1.92, 95% CI: 0.58, 6.34), leukemias (HR = 1.59, 95% CI: 0.66, 3.84), multiple myeloma (HR = 1.84, 95% CI: 0.45, 7.58), rectal cancer (HR = 1.65, 95% CI: 0.36, 7.44), oral cavity cancers (HR = 1.93, 95% CI: 0.34, 10.81). However, 14% of the Camp Lejeune cohort died by end of follow-up, producing small numbers of cause-specific deaths and wide CIs (Bove et al. 2014b).

To address the short follow-up which was the major limitation of the previous studies, Bove and colleagues reported an updated retrospective cohort study (Bove, Greek, Gatiba, Boehm, et al. 2024). They investigated the cause of death of military personnel and civilian workers at Camp Lejeune. Compared to Camp Pendleton Marines/Navy personnel, Camp Lejeune had aHRs ≥ 1.20 for cancers of the kidney (aHR = 1.21, 95% CI: 0.95, 1.54), esophagus (aHR = 1.24, 95% CI: 1.00, 1.54) and female breast (aHR = 1.20, 95% CI: 0.73, 1.98). Causes of death with aHRs ≥ 1.20 and CIR > 3, included Parkinson disease, myelodysplastic syndrome, and cancers of the testes, cervix and ovary. The major limitation of cancer mortality studies is that they may underestimate the risk for curable cancers such as leukemias and lymphomas and rely on limited data from death certificates.

A cancer incidence study using individual-level data from US population-based cancer registries has a greater capability than a mortality study of evaluating the association between exposure and the incidence of cancer. Cancer registry data also provide more granular information about the individual cancer taking into account cancer classifications and histology. Thus, in 2024 Bove and colleagues performed the analysis of cancer incidence among Camp Lejeune Marines/Navy personnel and civilian workers, totaling 12,083 and 1,563, respectively (Bove, Greek, Gatiba, Kohler, et al. 2024). Compared with Camp Pendleton, Camp Lejeune Marines/Navy personnel had significantly higher incidence of all myeloid cancers (HR=1.24; 95% CI: 1.03, 1.49), acute myeloid leukemia (HR=1.38; 95% CI: 1.03, 1.85), myelodysplastic and myeloproliferative syndromes (HR=1.68; 95% CI: 1.07, 2.62), polycythemia vera (HR=1.41; 95% CI: 0.94, 2.11) in addition to several solid tumor cancers.

VI. BRADFORD HILL CONSIDERATIONS

As part of my analysis, I evaluated the Bradford Hill considerations to assess the level of support for causality. These considerations, proposed by Sir Bradford Hill in 1965, were developed at a time when scientific investigations into cancer risk were still in their early stages. It is important to note that the nine considerations outlined by Hill are not strict criteria; not all need to be satisfied for a causal relationship to be established. Instead, they serve as a flexible framework for evaluating the evidence for causation and not all are equally applicable to every scenario. For instance, criteria like specificity may not be relevant in complex diseases like cancer, which often have multifactorial causes, and many carcinogens cause more than one type of cancer. Importantly, these criteria were proposed over half a century ago, when the biology and mechanism of cancer development were unknown, and the proof of causal inference relied heavily on epidemiological studies. Thus, biological plausibility—the understanding of mechanisms through which an exposure leads to cancer—is often more critical than epidemiological associations. Epidemiological studies can demonstrate correlations but may be confounded by biases, incomplete data. They often fail to detect association in rare diseases (such as leukemia). In contrast, biological evidence provides direct mechanistic insights, supporting the causal inference in observable and reproducible pathways, such as genetic mutations or cellular changes caused by the exposure.

An extensive body of literature, drawing on various cohorts from multiple countries, provides strong evidence that exposure to benzene, TCE, and PCE is associated with an increased risk of leukemia. Furthermore, the studies reviewed align with the Bradford Hill considerations for causation, including strength of association, consistency, specificity, temporality, biological gradient, plausibility, coherence, experiment, and analogy. Collectively, these factors strongly support the conclusion that benzene, TCE, and PCE exposure can cause leukemia.

A. BENZENE

***Strength*:** Numerous studies, including large meta-analyses, indicated a strong, statistically significant, positive association between exposure to benzene and leukemia.

***Consistency*:** This association was consistent across cohort and case-control study designs.

***Specificity*:** This consideration is not fully met because benzene is associated with several diseases in addition to leukemia, including other bone marrow diseases such as aplastic anemia and multiple myeloma. However, the strong evidence linking benzene to leukemia remains compelling. Please also see the discussion on the limitation of certain Bradford Hill criteria above.

***Biological Gradient*:** There was evidence of dose-related risk patterns according to cumulative exposure for leukemia. Some studies demonstrated supra-linear relationships between benzene exposure and leukemia.

***Temporality*:** These studies were well-powered and sufficiently established an appropriate temporal relationship between benzene exposure and the onset of leukemia.

***Plausibility*:** The unquestionable effects of benzene on DNA damage and the immune system have been discussed above. Both effects were confirmed in experimental models.

***Coherence*:** The evidence aligns with current understanding of AML biology, including clonal evolution driven by mutations and chromosomal alterations often seen in benzene-related AML cases.

***Experiment*:** Animal studies, in vitro experiments and study is humans confirm benzene's leukemogenic potential, providing further evidence of its causal role.

***Analogy*:** Other chemicals with similar genotoxic properties, such as chemotherapeutic agents that result in DNA damage, are also known to induce AML, supporting the analogy criterion.

B. TCE

***Strength*:** Numerous studies, including epidemiological data, animal studies, and mechanistic analyses, demonstrate a statistically significant, positive association between exposure to TCE and leukemia.

***Consistency*:** This association was observed across a range of epidemiological study designs, as well as in animal and mechanistic research, reinforcing its reliability.

***Specificity*:** This consideration is not fully met because TCE has been shown to cause several different cancers, including leukemia, NHL, and others. However, the evidence linking TCE to leukemia remains robust. Please also see the discussion on the limitation of certain Bradford Hill criteria above.

***Biological Gradient*:** There was evidence of dose-response patterns, with some studies even demonstrating supra-linear relationships between TCE exposure and leukemia. This is consistent with the understanding that cancers do not always behave in a linear dose-response manner.

***Temporality*:** These studies were sufficiently powered and established an appropriate temporal relationship between TCE exposure and the onset of leukemia.

***Plausibility*:** The genotoxic and immunotoxic effects of TCE, as demonstrated in experimental models and mechanistic data, strongly support its role in causing leukemia.

***Coherence*:** TCE and its genotoxic metabolites are known to affect blood cells which was confirmed in humans. These DNA defect alter hematopoietic cell leading to leukemic transformation.

***Experiment*:** The genotoxic and immunotoxic effects of TCE strongly support its role in causing leukemia.

***Analogy*:** Other chemicals including benzene with similar genotoxic properties, are also known to induce AML, supporting the analogy criterion.

C. PCE

***Strength*:** Studies demonstrated a positive association between exposure to PCE and leukemia, although this association is not as strong as that observed for benzene or TCE.

***Consistency*:** While evidence for an association was observed across different study designs, it is less consistent compared to the data for benzene or TCE.

***Specificity*:** This consideration is not met because PCE has been linked to several diseases other than leukemia. However, the evidence for its role in causing leukemia remains significant. Please see discussion above.

***Biological Gradient*:** Some studies provided evidence of dose-response patterns between PCE exposure and leukemia, though these patterns are less robust compared to benzene or TCE.

***Temporality*:** These studies sufficiently established an appropriate temporal relationship between PCE exposure and the onset of leukemia.

***Plausibility*:** PCE, as a structurally similar compound to TCE, shares some of the same genotoxic metabolites and has been shown to contribute to cancer through genotoxicity. Its effects on the immune system further support its plausibility as a cause of leukemia.

***Coherence*:** Similarly to TCE, PCE and its genotoxic metabolites are known to affect blood cells which was confirmed in humans. These DNA defect alter hematopoietic cell leading to leukemic transformation

***Experiment*:** Experimental studies in vitro and in animals demonstrated that PCE and its metabolites induce DNA strand breaks and chromosomal aberrations, particularly blood cells.

***Analogy*:** Other DNA damaging agents such as benzene, are also known to induce AML, supporting the analogy criterion.

VII. CONCLUSIONS

Acute leukemias, both AML and ALL are a rare blood cancers arising from a single hematopoietic stem cell. Certain environmental factors such as ionizing radiation, chemotherapy and genotoxic chemicals such as benzene play an important role in the pathogenesis of this disease. Some cases of acute leukemias may arise as a result of inherited predisposition syndromes and several genes have been implicated in this process. Benzene is a potent carcinogen and multiple in vitro and in vivo data in laboratory animals and humans demonstrated the significant DNA-damaging activity of this agent, predominantly in blood cells. This may be partially because bone marrow, in addition to the liver and lungs, is an active site of benzene metabolism and certain enzymes responsible for the production of genotoxic byproducts are highly expressed in hematopoietic cells (e.g. myeloperoxidase, MPO). In addition to mechanistic studies demonstrating the mutagenic role of benzene, numerous epidemiological studies demonstrated a significant association between benzene exposure and hematologic malignancies including AML and ALL. Given this overwhelming body of evidence, benzene was classified as a Group I carcinogen by IARC and the causative agent of myeloid leukemia. Thus, the association between benzene exposure and blood cancer, including ALL, is undeniable. The mean

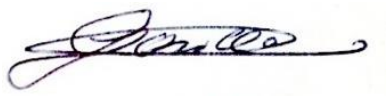
concentration of benzene in the water at Camp Lejeune is at least as likely as not capable of causing acute leukemias in Marines and civilian workers exposed to the water. Indeed, while not necessary for my causation opinion, I note that there is currently no established and agreed-upon safe level of benzene exposure. Recent studies using new biomarkers of benzene toxicity demonstrated that harmful effects of benzene can be observed with the level of exposure much less than 1ppm (cumulative exposure >2.93 ppm-year). For the comparison the level of benzene concentration in water at Camp Lejeune was around 10 ug/l (equals to 0.01 ppm).

Trichloroethylene (TCE) and perchloroethylene (PCE) are volatile organic compounds that are known to have significant genotoxic potential and have been implicated in the pathogenesis of various malignancies, including hematologic cancers. The evidence from both *in vivo* and *in vitro* tests, in mammalian and other experimental systems demonstrated that metabolites of TCE and PCE are highly genotoxic and lead to mutations, chromosomal aberrations, micronuclei, and cell transformation. Importantly, this type of damage was detected in peripheral blood lymphocytes of humans exposed to TCE and PCE metabolites. Thus, biological evidence of carcinogenic potential of these chemicals is indisputable. Moreover, studies in humans exposed to water contaminated with TCE, similar to Camp Lejeune exposure, demonstrated significantly increased incidence of leukemia at levels of exposure as low as 0.1 part per billion (ppb). For comparison, the maximum level of TCE and PCE in contaminated water at Camp Lejeune reached 1,400 ppb and 39 ppb for TCE and PCE, respectively.

While most aforementioned studies have examined the effects of exposure to benzene, trichloroethylene (TCE), and perchloroethylene (PCE) individually, the unique scenario at Camp Lejeune involved simultaneous exposure to all three mutagenic agents. Each of these chemicals has been well-documented as a potent genotoxin capable of inducing DNA damage, chromosomal aberrations, and other mutagenic effects that contribute to leukemogenesis. However, the combined exposure to benzene, TCE, and PCE creates an additive—or potentially synergistic—effect, amplifying the overall genotoxic burden on hematopoietic cells. The cumulative impact of these agents is expected to be significantly greater than the effects observed with exposure to any one toxin individually. This type of additive effect of offending agents is well known in other cancers (for example, asbestos exposure and smoking in mesothelioma, UV radiation and immunosuppressive therapy in skin cancer). This combined exposure at Camp Lejeune presents a far higher risk for the development of leukemias as the mutagenic pressures converge to accelerate the pathogenesis of these diseases.

While numerous studies have independently established the carcinogenic effects of benzene, TCE, and PCE, we do not need to rely solely on extrapolations from these data when evaluating the risks at Camp Lejeune. Research specifically examining Camp Lejeune residents has demonstrated a statistically significant increase in the incidence of blood cancers, including leukemia, among individuals exposed to the contaminated water. This provides strong evidence for the causal relationship between the combined exposure to benzene, TCE, and PCE and the development of hematologic malignancies in this population.

All my opinions and conclusions are held to a reasonable degree of medical certainty. I reserve the right to modify or supplement this report if additional information becomes available.



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VIII. REFERENCES

Alexander, Dominik D., Pamela J. Mink, Jeffrey H. Mandel, and Michael A. Kelsh. 2006. "A Meta-Analysis of Occupational Trichloroethylene Exposure and Multiple Myeloma or Leukaemia." *Occupational Medicine (Oxford, England)* 56 (7): 485–93. https://doi.org/10.1093/occmed/kql083.

Alonso, Salvador, Meng Su, Jace W. Jones, Sudipto Ganguly, Maureen A. Kane, Richard J. Jones, and Gabriel Ghiaur. 2015. "Human Bone Marrow Niche Chemoprotection Mediated by Cytochrome P450 Enzymes." *Oncotarget* 6 (17): 14905–12. https://doi.org/10.18632/oncotarget.3614.

Anttila, A., E. Pukkala, M. Sallmén, S. Hernberg, and K. Hemminki. 1995. "Cancer Incidence among Finnish Workers Exposed to Halogenated Hydrocarbons." *Journal of Occupational and Environmental Medicine* 37 (7): 797–806. https://doi.org/10.1097/00043764-199507000-00008.

Aschengrau, A., D. Ozonoff, C. Paulu, P. Coogan, R. Vezina, T. Heeren, and Y. Zhang. 1993. "Cancer Risk and Tetrachloroethylene-Contaminated Drinking Water in Massachusetts." *Archives of Environmental Health* 48 (5): 284–92. https://doi.org/10.1080/00039896.1993.9936715.

Axelson, O., A. Seldén, K. Andersson, and C. Hogstedt. 1994. "Updated and Expanded Swedish Cohort Study on Trichloroethylene and Cancer Risk." *Journal of Occupational Medicine.: Official Publication of the Industrial Medical Association* 36 (5): 556–62.

Barbin, A. 1999. "Role of Etheno DNA Adducts in Carcinogenesis Induced by Vinyl Chloride in Rats." *IARC Scientific Publications*, no. 150, 303–13.

Bloemen, L. J., A. Youk, T. D. Bradley, K. M. Bodner, and G. Marsh. 2004. "Lymphohaematopoietic Cancer Risk among Chemical Workers Exposed to Benzene." *Occupational and Environmental Medicine* 61 (3): 270–74. https://doi.org/10.1136/oem.2003.007013.

Boffetta, Paolo, Linda Matisane, Kenneth A. Mundt, and Linda D. Dell. 2003. "Meta-Analysis of Studies of Occupational Exposure to Vinyl Chloride in Relation to Cancer Mortality." *Scandinavian Journal of Work, Environment & Health* 29 (3): 220–29. https://doi.org/10.5271/sjweh.725.

Boice, John D., Donald E. Marano, Sarah S. Cohen, Michael T. Mumma, William J. Blot, A. Bertrand Brill, Jon P. Fryzek, Brian E. Henderson, and Joseph K. McLaughlin. 2006. "Mortality among Rocketdyne Workers Who Tested Rocket Engines, 1948-1999." *Journal of Occupational and Environmental Medicine* 48 (10): 1070–92. https://doi.org/10.1097/01.jom.0000240661.33413.b5.

Bond, G G, E A McLaren, C L Baldwin, and R R Cook. 1986. "An Update of Mortality among Chemical Workers Exposed to Benzene." *British Journal of Industrial Medicine* 43 (10): 685–91.

Bove, Frank J., April Greek, Ruth Gatiba, Rona C. Boehm, and Marcie M. Mohnsen. 2024. "Evaluation of Mortality among Marines, Navy Personnel, and Civilian Workers Exposed to Contaminated Drinking Water at USMC Base Camp Lejeune: A Cohort Study." *Environmental Health: A Global Access Science Source* 23 (1): 61. https://doi.org/10.1186/s12940-024-01099-7.

Bove, Frank J., April Greek, Ruth Gatiba, Betsy Kohler, Recinda Sherman, Gene T. Shin, and Aaron Bernstein. 2024. "Cancer Incidence among Marines and Navy Personnel and Civilian Workers Exposed to Industrial Solvents in Drinking Water at US Marine Corps Base Camp Lejeune: A Cohort Study." *Environmental Health Perspectives* 132 (10): 107008. https://doi.org/10.1289/EHP14966.

Bove, Frank J., Perri Zeitz Ruckart, Morris Maslia, and Theodore C. Larson. 2014a. "Evaluation of Mortality among Marines and Navy Personnel Exposed to Contaminated Drinking Water at USMC Base Camp Lejeune: A Retrospective Cohort Study." *Environmental Health: A Global Access Science Source* 13 (1): 10. https://doi.org/10.1186/1476-069X-13-10.

———. 2014b. "Mortality Study of Civilian Employees Exposed to Contaminated Drinking Water at USMC Base Camp Lejeune: A Retrospective Cohort Study." *Environmental Health: A Global Access Science Source* 13 (August):68. https://doi.org/10.1186/1476-069X-13-68.

Chiu, Weihsueh A., Sandrine Micallef, Aart C. Monster, and Frédéric Y. Bois. 2007. "Toxicokinetics of Inhaled Trichloroethylene and Tetrachloroethylene in Humans at 1 Ppm: Empirical Results and Comparisons with Previous Studies." *Toxicological Sciences* 95 (1): 23–36. https://doi.org/10.1093/toxsci/kfl129.

Cohn, P., J. Klotz, F. Bove, M. Berkowitz, and J. Fagliano. 1994. "Drinking Water Contamination and the Incidence of Leukemia and Non-Hodgkin's Lymphoma." *Environmental Health Perspectives* 102 (6–7): 556–61. https://doi.org/10.1289/ehp.94102556.

Collins, J. J., B. Ireland, C. F. Buckley, and D. Shepperly. 2003. "Lymphohaematopoeitic Cancer Mortality among Workers with Benzene Exposure." *Occupational and Environmental Medicine* 60 (9): 676–79. https://doi.org/10.1136/oem.60.9.676.

Crump, Kenny S. 1994. "Risk of Benzene-induced Leukemia: A Sensitivity Analysis of the Pliofilm Cohort with Additional Follow-up and New Exposure Estimates." *Journal of Toxicology and Environmental Health* 42 (2): 219–42. https://doi.org/10.1080/15287399409531875.

Decoufle, Pierre, William A. Blattner, and Aaron Blair. 1983. "Mortality among Chemical Workers Exposed to Benzene and Other Agents." *Environmental Research* 30 (1): 16–25. https://doi.org/10.1016/0013-9351(83)90161-5.

Dekant, W., S. Vamvakas, K. Berthold, S. Schmidt, D. Wild, and D. Henschler. 1986. "Bacterial Beta-Lyase Mediated Cleavage and Mutagenicity of Cysteine Conjugates Derived from the Nephrocarcinogenic Alkenes Trichloroethylene, Tetrachloroethylene and Hexachlorobutadiene." *Chemico-Biological Interactions* 60 (1): 31–45. https://doi.org/10.1016/0009-2797(86)90015-3.

Divine, B. J., C. M. Hartman, and J. K. Wendt. 1999. "Update of the Texaco Mortality Study 1947-93: Part II. Analyses of Specific Causes of Death for White Men Employed in Refining, Research, and Petrochemicals." *Occupational and Environmental Medicine* 56 (3): 174–80. https://doi.org/10.1136/oem.56.3.174.

Glass, Deborah C., Christopher N. Gray, Damien J. Jolley, Carl Gibbons, and Malcolm R. Sim. 2006. "The Health Watch Case–Control Study of Leukemia and Benzene." *Annals of the New York Academy of Sciences* 1076 (1): 80–89. https://doi.org/10.1196/annals.1371.024.

Glass, Deborah C., Christopher N. Gray, Damien J. Jolley, Carl Gibbons, Malcolm R. Sim, Lin Fritschi, Geoffrey G. Adams, John A. Bisby, and Richard Manuell. 2003. "Leukemia Risk Associated with Low-Level Benzene Exposure." *Epidemiology (Cambridge, Mass.)* 14 (5): 569–77. https://doi.org/10.1097/01.ede.0000082001.05563.e0.

Greenland, S., A. Salvan, D. H. Wegman, M. F. Hallock, and T. J. Smith. 1994. "A Case-Control Study of Cancer Mortality at a Transformer-Assembly Facility." *International Archives of Occupational and Environmental Health* 66 (1): 49–54. https://doi.org/10.1007/BF00386579.

Guénel, Pascal, Ellen Imbernon, Anne Chevalier, Anne Crinquand-Calastreng, and Marcel Goldberg. 2002. "Leukemia in Relation to Occupational Exposures to Benzene and Other Agents: A Case-Control Study Nested in a Cohort of Gas and Electric Utility Workers." *American Journal of Industrial Medicine* 42 (2): 87–97. https://doi.org/10.1002/ajim.10090.

Guengerich, F. Peter. 1992. "Roles of the Vinyl Chloride Oxidation Products 2-Chlorooxirane and 2-Chloroacetaldehyde in the in Vitro Formation of Etheno Adducts of Nucleic Acid Bases." *Chemical Research in Toxicology* 5 (1): 2–5. https://doi.org/10.1021/tx00025a001.

Gun, R. T., N. Pratt, P. Ryan, and D. Roder. 2006. "Update of Mortality and Cancer Incidence in the Australian Petroleum Industry Cohort." *Occupational and Environmental Medicine* 63 (7): 476–81. https://doi.org/10.1136/oem.2005.023796.

Guo, Helen, Stacy Ahn, and Luoping Zhang. 2020. "Benzene-Associated Immunosuppression and Chronic Inflammation in Humans: A Systematic Review." *Occupational and*

Environmental Medicine, September, oemed-2020-106517. https://doi.org/10.1136/oemed-2020-106517.

Hansen, J., O. Raaschou-Nielsen, J. M. Christensen, I. Johansen, J. K. McLaughlin, L. Lipworth, W. J. Blot, and J. H. Olsen. 2001. "Cancer Incidence among Danish Workers Exposed to Trichloroethylene." *Journal of Occupational and Environmental Medicine* 43 (2): 133–39. https://doi.org/10.1097/00043764-200102000-00012.

Hardell, L., M. Eriksson, and A. Degerman. 1994. "Exposure to Phenoxyacetic Acids, Chlorophenols, or Organic Solvents in Relation to Histopathology, Stage, and Anatomical Localization of Non-Hodgkin's Lymphoma." *Cancer Research* 54 (9): 2386–89.

Hayes, Richard B., Mustafa Dosemeci, Sholom Wacholder, Lois B. Travis, Nathaniel Rothman, Robert N. Hoover, Martha S. Linet, Song-Nian Yin, Gui-Lan Li, and Chin-Yang Li. 1997. "Benzene and the Dose-Related Incidence of Hematologic Neoplasms in China." *JNCI: Journal of the National Cancer Institute* 89 (14): 1065–71. https://doi.org/10.1093/jnci/89.14.1065.

Ho, T. Y., and G. Witz. 1997. "Increased Gene Expression in Human Promyeloid Leukemia Cells Exposed to Trans,Trans-Muconaldehyde, a Hematotoxic Benzene Metabolite." *Carcinogenesis* 18 (4): 739–44. https://doi.org/10.1093/carcin/18.4.739.

Hsieh, Hui-I., Pau-Chung Chen, Ruey-Hong Wong, Chung-Li Du, Yu-Yin Chang, Jung-Der Wang, and Tsun-Jen Cheng. 2011. "Mortality from Liver Cancer and Leukaemia among Polyvinyl Chloride Workers in Taiwan: An Updated Study." *Occupational and Environmental Medicine* 68 (2): 120–25. https://doi.org/10.1136/oem.2010.056978.

IARC Working Group on the Evaluation of Carcinogenic Risks to Humans. 2012. "Chemical Agents and Related Occupations." *IARC Monographs on the Evaluation of Carcinogenic Risks to Humans* 100 (Pt F): 9–562.

Ikbal, Mevlit, Ayhan Tastekin, Hasan Dogan, Ibrahim Pirim, and Rahmi Ors. 2004. "The Assessment of Genotoxic Effects in Lymphocyte Cultures of Infants Treated with Chloral Hydrate." *Mutation Research/Genetic Toxicology and Environmental Mutagenesis* 564 (2): 159–64. https://doi.org/10.1016/j.mrgentox.2004.08.007.

Jaffe, D. R., C. D. Hassall, A. J. Gandolfi, and K. Brendel. 1985. "Production of DNA Single Strand Breaks in Rabbit Renal Tissue after Exposure to 1,2-Dichlorovinylcysteine." *Toxicology* 35 (1): 25–33. https://doi.org/10.1016/0300-483x(85)90129-5.

Karami, Sara, Bryan Bassig, Patricia A. Stewart, Kyoung-Mu Lee, Nathaniel Rothman, Lee E. Moore, and Qing Lan. 2013. "Occupational Trichloroethylene Exposure and Risk of Lymphatic and Haematopoietic Cancers: A Meta-Analysis." *Occupational and Environmental Medicine* 70 (8): 591–99. https://doi.org/10.1136/oemed-2012-101212.

Kawanishi, Shosuke, Shiho Ohnishi, Ning Ma, Yusuke Hiraku, and Mariko Murata. 2017. "Crosstalk between DNA Damage and Inflammation in the Multiple Steps of Carcinogenesis." *International Journal of Molecular Sciences* 18 (8): 1808. https://doi.org/10.3390/ijms18081808.

Kirkeleit, Jorunn, Trond Riise, Magne Bråtveit, and Bente E. Moen. 2008. "Increased Risk of Acute Myelogenous Leukemia and Multiple Myeloma in a Historical Cohort of Upstream Petroleum Workers Exposed to Crude Oil." *Cancer Causes & Control* 19 (1): 13–23. https://doi.org/10.1007/s10552-007-9065-x.

Kocaman, Ayşe Yavuz, and Kübra Asfuroğlu. 2021. "The Genotoxic Effects of Perchloroethylene in Human Peripheral Blood Lymphocytes and the Possible Ameliorative Role of α-Tocopherol." *Environmental Science and Pollution Research* 28 (29): 39576–86. https://doi.org/10.1007/s11356-021-13523-3.

Kolachana, P., V. V. Subrahmanyam, K. B. Meyer, L. Zhang, and M. T. Smith. 1993. "Benzene and Its Phenolic Metabolites Produce Oxidative DNA Damage in HL60 Cells in Vitro and in the Bone Marrow in Vivo." *Cancer Research* 53 (5): 1023–26.

Kumar, Alagamuthu Karthick, Vellingiri Balachandar, Meyyazhagan Arun, Shafi Ahammed Khan Mustaq Ahamed, Shanmugam Suresh Kumar, Balasubramanium Balamuralikrishnan, Kathannan Sankar, and Keshavarao Sasikala. 2013. "A Comprehensive Analysis of Plausible Genotoxic Covariates Among Workers of a Polyvinyl Chloride Plant Exposed to Vinyl Chloride Monomer." *Archives of Environmental Contamination and Toxicology* 64 (4): 652–58. https://doi.org/10.1007/s00244-012-9857-1.

Lan, Qing, Luoping Zhang, Guilan Li, Roel Vermeulen, Rona S. Weinberg, Mustafa Dosemeci, Stephen M. Rappaport, et al. 2004. "Hematotoxicity in Workers Exposed to Low Levels of Benzene." *Science* 306 (5702): 1774–76. https://doi.org/10.1126/science.1102443.

Lash, Lawrence H., Weihsueh A. Chiu, Kathryn Z. Guyton, and Ivan Rusyn. 2014. "Trichloroethylene Biotransformation and Its Role in Mutagenicity, Carcinogenicity and Target Organ Toxicity." *Mutation Research. Reviews in Mutation Research* 762:22–36. https://doi.org/10.1016/j.mrrev.2014.04.003.

Linet, Martha S, Ethel S Gilbert, Roel Vermeulen, Graça M Dores, Song-Nian Yin, Lutzen Portengen, Richard B Hayes, et al. 2019. "Benzene Exposure Response and Risk of Myeloid Neoplasms in Chinese Workers: A Multicenter Case–Cohort Study." *JNCI: Journal of the National Cancer Institute* 111 (5): 465–74. https://doi.org/10.1093/jnci/djy143.

Linet, Martha S., Song-Nian Yin, Ethel S. Gilbert, Graça M. Dores, Richard B. Hayes, Roel Vermeulen, Hao-Yuan Tian, et al. 2015. "A Retrospective Cohort Study of Cause-Specific Mortality and Incidence of Hematopoietic Malignancies in Chinese Benzene-

Exposed Workers." *International Journal of Cancer* 137 (9): 2184–97. https://doi.org/10.1002/ijc.29591.

Little, John B. 2000. "Radiation Carcinogenesis." *Carcinogenesis* 21 (3): 397–404. https://doi.org/10.1093/carcin/21.3.397.

McCraw, D. S., R. E. Joyner, and P. Cole. 1985. "Excess Leukemia in a Refinery Population." *Journal of Occupational Medicine.: Official Publication of the Industrial Medical Association* 27 (3): 220–22.

McHale, Cliona M., Luoping Zhang, and Martyn T. Smith. 2012. "Current Understanding of the Mechanism of Benzene-Induced Leukemia in Humans: Implications for Risk Assessment." *Carcinogenesis* 33 (2): 240–52. https://doi.org/10.1093/carcin/bgr297.

Mundt, K. A., L. D. Dell, R. P. Austin, R. S. Luippold, R. Noess, and C. Bigelow. 2000. "Historical Cohort Study of 10 109 Men in the North American Vinyl Chloride Industry, 1942-72: Update of Cancer Mortality to 31 December 1995." *Occupational and Environmental Medicine* 57 (11): 774–81. https://doi.org/10.1136/oem.57.11.774.

Poirier, Miriam C. 2004. "Chemical-Induced DNA Damage and Human Cancer Risk." *Nature Reviews. Cancer* 4 (8): 630–37. https://doi.org/10.1038/nrc1410.

Raaschou-Nielsen, Ole, Johnni Hansen, Joseph K. McLaughlin, Henrik Kolstad, Jytte M. Christensen, Robert E. Tarone, and Jørgen H. Olsen. 2003. "Cancer Risk among Workers at Danish Companies Using Trichloroethylene: A Cohort Study." *American Journal of Epidemiology* 158 (12): 1182–92. https://doi.org/10.1093/aje/kwg282.

Radican, Larry, Aaron Blair, Patricia Stewart, and Daniel Wartenberg. 2008. "Mortality of Aircraft Maintenance Workers Exposed to Trichloroethylene and Other Hydrocarbons and Chemicals: Extended Follow-Up." *Journal of Occupational and Environmental Medicine* 50 (11): 1306–19. https://doi.org/10.1097/JOM.0b013e3181845f7f.

Rappaport, Stephen M., Suramya Waidyanatha, Qingshan Qu, Roy Shore, Ximei Jin, Beverly Cohen, Lung-Chi Chen, et al. 2002. "Albumin Adducts of Benzene Oxide and 1,4-Benzoquinone as Measures of Human Benzene Metabolism1." *Cancer Research* 62 (5): 1330–37.

Rappaport, Stephen M., Suramya Waidyanatha, Karen Yeowell-O'Connell, Nathaniel Rothman, Martyn T. Smith, Luoping Zhang, Qingshan Qu, Roy Shore, Guilan Li, and Songnian Yin. 2005. "Protein Adducts as Biomarkers of Human Benzene Metabolism." *Chemico-Biological Interactions*, Proceedings of the International Symposium on Recent Advances in Benzene Toxicity, 153–154 (May):103–9. https://doi.org/10.1016/j.cbi.2005.03.014.

Rushton, L., and H. Romaniuk. 1997. "A Case-Control Study to Investigate the Risk of Leukaemia Associated with Exposure to Benzene in Petroleum Marketing and

Distribution Workers in the United Kingdom." *Occupational and Environmental Medicine* 54 (3): 152–66. https://doi.org/10.1136/oem.54.3.152.

Rushton, L., A. R. Schnatter, G. Tang, and D. C. Glass. 2014. "Acute Myeloid and Chronic Lymphoid Leukaemias and Exposure to Low-Level Benzene among Petroleum Workers." *British Journal of Cancer* 110 (3): 783–87. https://doi.org/10.1038/bjc.2013.780.

Schnatter, A. R., T. W. Armstrong, M. J. Nicolich, F. S. Thompson, A. M. Katz, W. W. Huebner, and E. D. Pearlman. 1996. "Lymphohaematopoietic Malignancies and Quantitative Estimates of Exposure to Benzene in Canadian Petroleum Distribution Workers." *Occupational and Environmental Medicine* 53 (11): 773–81. https://doi.org/10.1136/oem.53.11.773.

Schnatter, A. Robert, Deborah C. Glass, Gong Tang, Richard D. Irons, and Lesley Rushton. 2012. "Myelodysplastic Syndrome and Benzene Exposure Among Petroleum Workers: An International Pooled Analysis." *JNCI: Journal of the National Cancer Institute* 104 (22): 1724–37. https://doi.org/10.1093/jnci/djs411.

Seidler, Andreas, Matthias Möhner, Jürgen Berger, Birte Mester, Evelin Deeg, Gine Elsner, Alexandra Nieters, and Nikolaus Becker. 2007. "Solvent Exposure and Malignant Lymphoma: A Population-Based Case-Control Study in Germany." *Journal of Occupational Medicine and Toxicology (London, England)* 2 (April):2. https://doi.org/10.1186/1745-6673-2-2.

Shallis, Rory M., Julian J. Weiss, Nicole C. Deziel, and Steven D. Gore. 2021. "A Clandestine Culprit with Critical Consequences: Benzene and Acute Myeloid Leukemia." *Blood Reviews* 47 (May):100736. https://doi.org/10.1016/j.blre.2020.100736.

Smith, M. T., and L. Zhang. 1998. "Biomarkers of Leukemia Risk: Benzene as a Model." *Environmental Health Perspectives* 106 Suppl 4 (Suppl 4): 937–46. https://doi.org/10.1289/ehp.98106s4937.

Smith, Martyn T. 2010. "Advances in Understanding Benzene Health Effects and Susceptibility." *Annual Review of Public Health* 31 (1): 133–48. https://doi.org/10.1146/annurev.publhealth.012809.103646.

Smulevich, V. B., I. V. Fedotova, and V. S. Filatova. 1988. "Increasing Evidence of the Rise of Cancer in Workers Exposed to Vinylchloride." *British Journal of Industrial Medicine* 45 (2): 93–97. https://doi.org/10.1136/oem.45.2.93.

Snyder, R, and C C Hedli. 1996. "An Overview of Benzene Metabolism." *Environmental Health Perspectives* 104 (Suppl 6): 1165–71.

Snyder, Robert. 2004. "Xenobiotic Metabolism and the Mechanism(s) of Benzene Toxicity." *Drug Metabolism Reviews* 36 (3–4): 531–47. https://doi.org/10.1081/DMR-200033445.

Stenehjem, J. S., K. Kjærheim, M. Bråtveit, S. O. Samuelsen, F. Barone-Adesi, N. Rothman, Q. Lan, and T. K. Grimsrud. 2015. "Benzene Exposure and Risk of Lymphohaematopoietic Cancers in 25 000 Offshore Oil Industry Workers." *British Journal of Cancer* 112 (9): 1603–12. https://doi.org/10.1038/bjc.2015.108.

Talibov, Madar, Susanna Lehtinen-Jacks, Jan Ivar Martinsen, Kristina Kjærheim, Elsebeth Lynge, Pär Sparén, Laufey Tryggvadottir, et al. 2014. "Occupational Exposure to Solvents and Acute Myeloid Leukemia: A Population-Based, Case–Control Study in Four Nordic Countries." *Scandinavian Journal of Work, Environment & Health* 40 (5): 511–17. https://doi.org/10.5271/sjweh.3436.

Thériault, G., and P. Allard. 1981. "Cancer Mortality of a Group of Canadian Workers Exposed to Vinyl Chloride Monomer." *Journal of Occupational Medicine.: Official Publication of the Industrial Medical Association* 23 (10): 671–76. https://doi.org/10.1097/00043764-198110000-00009.

Tucker, James D., Karen J. Sorensen, Avima M. Ruder, Lauralynn Taylor McKernan, Christy L. Forrester, and Mary Ann Butler. 2011. "Cytogenetic Analysis of an Exposed-Referent Study: Perchloroethylene-Exposed Dry Cleaners Compared to Unexposed Laundry Workers." *Environmental Health* 10 (1): 16. https://doi.org/10.1186/1476-069X-10-16.

Vamvakas, S., W. Dekant, and D. Henschler. 1989. "Assessment of Unscheduled DNA Synthesis in a Cultured Line of Renal Epithelial Cells Exposed to Cysteine S-Conjugates of Haloalkenes and Haloalkanes." *Mutation Research* 222 (4): 329–35. https://doi.org/10.1016/0165-1218(89)90108-0.

Vamvakas, S., A. A. Elfarra, W. Dekant, D. Henschler, and M. W. Anders. 1988. "Mutagenicity of Amino Acid and Glutathione S-Conjugates in the Ames Test." *Mutation Research* 206 (1): 83–90. https://doi.org/10.1016/0165-1218(88)90144-9.

Vamvakas, S., H. Richter, and D. Bittner. 1996. "Induction of Dedifferentiated Clones of LLC-PK1 Cells upon Long-Term Exposure to Dichlorovinylcysteine." *Toxicology* 106 (1–3): 65–74. https://doi.org/10.1016/0300-483x(95)03166-d.

Wang, Rong, Yawei Zhang, Qing Lan, Theodore R. Holford, Brian Leaderer, Shelia Hoar Zahm, Peter Boyle, et al. 2009. "Occupational Exposure to Solvents and Risk of Non-Hodgkin Lymphoma in Connecticut Women." *American Journal of Epidemiology* 169 (2): 176–85. https://doi.org/10.1093/aje/kwn300.

Ward, E., P. Boffetta, A. Andersen, D. Colin, P. Comba, J. A. Deddens, M. De Santis, et al. 2001. "Update of the Follow-up of Mortality and Cancer Incidence among European Workers Employed in the Vinyl Chloride Industry." *Epidemiology (Cambridge, Mass.)* 12 (6): 710–18. https://doi.org/10.1097/00001648-200111000-00021.

Weber, H., W. Reinl, and E. Greiser. 1981. "German Investigations on Morbidity and Mortality of Workers Exposed to Vinyl Chloride." *Environmental Health Perspectives* 41 (October):95–99. https://doi.org/10.1289/ehp.814195.

Wiemels, J., and M. T. Smith. 1999. “Enhancement of Myeloid Cell Growth by Benzene Metabolites via the Production of Active Oxygen Species.” *Free Radical Research* 30 (2): 93–103. https://doi.org/10.1080/10715769900300101.

Wong, O. 1995. “Risk of Acute Myeloid Leukaemia and Multiple Myeloma in Workers Exposed to Benzene.” *Occupational and Environmental Medicine* 52 (6): 380–84. https://doi.org/10.1136/oem.52.6.380.

Wong, R.-H., P.-C. Chen, C.-L. Du, J.-D. Wang, and T.-J. Cheng. 2002. “An Increased Standardised Mortality Ratio for Liver Cancer among Polyvinyl Chloride Workers in Taiwan.” *Occupational and Environmental Medicine* 59 (6): 405–9. https://doi.org/10.1136/oem.59.6.405.

Yin, S N, G L Li, F D Tain, Z I Fu, C Jin, Y J Chen, S J Luo, P Z Ye, J Z Zhang, and G C Wang. 1987. “Leukaemia in Benzene Workers: A Retrospective Cohort Study.” *British Journal of Industrial Medicine* 44 (2): 124–28. https://doi.org/10.1136/oem.44.2.124.

Zhang, Luoping, Qing Lan, Weihong Guo, Alan E. Hubbard, Guilan Li, Stephen M. Rappaport, Cliona M. McHale, et al. 2011. “Chromosome-Wide Aneuploidy Study (CWAS) in Workers Exposed to an Established Leukemogen, Benzene.” *Carcinogenesis* 32 (4): 605–12. https://doi.org/10.1093/carcin/bgq286.

Zhang, Luoping, Nathaniel Rothman, Guilan Li, Weihong Guo, Wei Yang, Alan E. Hubbard, Richard B. Hayes, Songnian Yin, Wei Lu, and Martyn T. Smith. 2007. “Aberrations in Chromosomes Associated with Lymphoma and Therapy-Related Leukemia in Benzene-Exposed Workers.” *Environmental and Molecular Mutagenesis* 48 (6): 467–74. https://doi.org/10.1002/em.20306.

Zhao, Yingxu, Anusha Krishnadasan, Nola Kennedy, Hal Morgenstern, and Beate Ritz. 2005. “Estimated Effects of Solvents and Mineral Oils on Cancer Incidence and Mortality in a Cohort of Aerospace Workers.” *American Journal of Industrial Medicine* 48 (4): 249–58. https://doi.org/10.1002/ajim.20216.

Appendix A

CURRICULUM VITAE
The Johns Hopkins University School of Medicine

Lukasz P. Gondek, M.D., Ph.D. 10/23/2024

DEMOGRAPHIC AND PERSONAL INFORMATION

Current Appointments

University

2023 – present Associate Professor of Oncology, The Johns Hopkins University School of Medicine

Hospital

2014 – present Attending Physician, The Johns Hopkins Hospital

Education and Training

Undergraduate

European School system

Doctoral/graduate

2003	MD/Medical University of Silesia, Poland	Medicine
2013	PhD/University of Warsaw, Poland	Hematology

Postdoctoral

2003-2004	Intern, Medicine, VA Hospital, Katowice, Poland
2004-2007	Postdoctoral Fellow, Hematology, Cleveland Clinic
2008-2011	Resident, Internal Medicine, Cleveland Clinic
2011-2014	Fellowship, Hematology, Johns Hopkins

Professional Experience

2007-2008	Research Associate, Cleveland Clinic
2014-2016	Instructor of Oncology, Johns Hopkins
2016-2023	Assistant Professor of Oncology, Johns Hopkins

PUBLICATIONS:

Original Research [OR]

1. Beck RC, Wlodarski M, **Gondek L**, Theil KS, Tuthill RJ, Sobeck R, Bolwell B, Maciejewski JP. Efficient identification of T-cell clones associated with graft-versus-host disease in target tissue allows for subsequent detection in peripheral blood. *Br J Haematol.* 2005;129(3):411-419. *Performed experiments.*
2. Wlodarski MW, **Gondek LP**, Nearman ZP, Plasilova M, Kalaycio M, Hsi ED, Maciejewski JP. Molecular strategies for detection and quantitation of clonal cytotoxic T-cell responses in aplastic anemia and myelodysplastic syndrome. *Blood.* 2006;108(8):2632-2641. *Performed experiments, analyzed data and wrote the manuscript.*
3. Babel N, Vergopoulos A, Trappe RU, Oertel S, Hammer MH, Karaivanov S, Schneider N, Riess H, Papp-Vary M, Neuhaus R, **Gondek LP**, Volk HD, Reinke P. Evidence for genetic susceptibility towards development of posttransplant lymphoproliferative disorder in solid organ recipients. *Transplantation*. 2007;84(3):387-391. *Performed experiments.*
4. **Gondek LP**, Dunbar AJ, Szpurka H, McDevitt MA, Maciejewski JP. SNP array karyotyping allows for the detection of uniparental disomy and cryptic chromosomal abnormalities in MDS/MPD-U and MPD. *PLoS One.* 2007;2(11):e1225.
5. **Gondek LP**, Haddad AS, O'Keefe CL, Tiu R, Wlodarski MW, Sekeres MA, Theil KS, Maciejewski JP. Detection of cryptic chromosomal lesions including acquired segmental uniparental disomy in advanced and low-risk myelodysplastic syndromes. *Exp Hematol.* 2007;35(11):1728-1738.

6. **Gondek LP**, Tiu R, Haddad AS, O'Keefe CL, Sekeres MA, Theil KS, Maciejewski JP. Single nucleotide polymorphism arrays complement metaphase cytogenetics in detection of new chromosomal lesions in MDS. *Leukemia*. 2007;21(9):2058-2061.
7. Maciejewski JP, O'Keefe C, **Gondek L**, Tiu R. Immune-mediated bone marrow failure syndromes of progenitor and stem cells: molecular analysis of cytotoxic T cell clones. *Folia Histochem Cytobiol*. 2007;45(1):5-14. *Analyzed data.*
8. O'Keefe CL, **Gondek L**, Davis R, Kuczkowski E, Sobecks RM, Rodriguez A, Narvaez Y, McIver Z, Tuthill R, Laughlin M, Bolwell B, Maciejewski JP. Molecular analysis of alloreactive CTL post-hemopoietic stem cell transplantation. *J Immunol*. 2007;179(3):2013-2022. *Performed experiments and analyzed data.*
9. O'Keefe CL, Tiu R, **Gondek LP**, Powers J, Theil KS, Kalaycio M, Lichtin A, Sekeres MA, Maciejewski JP. High-resolution genomic arrays facilitate detection of novel cryptic chromosomal lesions in myelodysplastic syndromes. *Exp Hematol*. 2007;35(2):240-251. *Analyzed data.*
10. Tiu R, **Gondek L**, O'Keefe C, Maciejewski JP. Clonality of the stem cell compartment during evolution of myelodysplastic syndromes and other bone marrow failure syndromes. *Leukemia*. 2007;21(8):1648-1657. *Designed and performed experiments, analyzed data and wrote the manuscript.*
11. Dunbar AJ, **Gondek LP**, O'Keefe CL, Makishima H, Rataul MS, Szpurka H, Sekeres MA, Wang XF, McDevitt MA, Maciejewski JP. 250K single nucleotide polymorphism array karyotyping identifies acquired uniparental disomy and homozygous mutations, including novel missense substitutions of c-Cbl, in myeloid malignancies. *Cancer Res*. 2008;68(24):10349-10357. *Designed and performed experiments, analyzed data and wrote the manuscript.*
12. **Gondek LP**, Tiu R, O'Keefe CL, Sekeres MA, Theil KS, Maciejewski JP. Chromosomal lesions and uniparental disomy detected by SNP arrays in MDS, MDS/MPD, and MDS-derived AML. *Blood*. 2008;111(3):1534-1542.
13. Jankowska AM, **Gondek LP**, Szpurka H, Nearman ZP, Tiu RV, Maciejewski JP. Base excision repair dysfunction in a subgroup of patients with myelodysplastic syndrome. *Leukemia*. 2008;22(3):551-558. *Designed and performed experiments, analyzed data and wrote the manuscript.*
14. Babel N, Brestrich G, **Gondek LP**, Sattler A, Wlodarski MW, Poliak N, Bethke N, Thiel A, Hammer MH, Reinke P, Maciejewski JP. Clonotype analysis of cytomegalovirus-specific cytotoxic T lymphocytes. *J Am Soc Nephrol*. 2009;20(2):344-352. *Performed experiement.*
15. Jiang Y, Dunbar A, **Gondek LP**, Mohan S, Rataul M, O'Keefe C, Sekeres M, Saunthararajah Y, Maciejewski JP. Aberrant DNA methylation is a dominant mechanism in MDS progression to AML. *Blood*. 2009;113(6):1315-1325. *Performed experiments and analyzed data.*
16. Szpurka H, **Gondek LP**, Mohan SR, Hsi ED, Theil KS, Maciejewski JP. UPD1p indicates the presence of MPL W515L mutation in RARS-T, a mechanism analogous to UPD9p and JAK2 V617F mutation. *Leukemia*. 2009;23(3):610-614. *Analyzed genomics data and wrote the manuscript.*
17. Tiu RV, **Gondek LP**, O'Keefe CL, Huh J, Sekeres MA, Elson P, McDevitt MA, Wang XF, Levis MJ, Karp JE, Advani AS, Maciejewski JP. New lesions detected by single nucleotide polymorphism array-based chromosomal analysis have important clinical impact in acute myeloid leukemia. *J Clin Oncol*. 2009;27(31):5219-5226. *Designed and performed experiments, analyzed data and wrote the manuscript.*
18. Ye Y, McDevitt MA, Guo M, Zhang W, Galm O, Gore SD, Karp JE, Maciejewski JP, Kowalski J, Tsai HL, **Gondek LP**, Tsai HC, Wang X, Hooker C, Smith BD, Carraway HE, Herman JG. Progressive chromatin repression and promoter methylation of CTNNA1 associated with advanced myeloid malignancies. *Cancer Res*. 2009;69(21):8482-8490. *Performed experiments and analyzed data.*
19. Huh J, Tiu RV, **Gondek LP**, O'Keefe CL, Jasek M, Makishima H, Jankowska AM, Jiang Y, Verma A, Theil KS, McDevitt MA, Maciejewski JP. Characterization of chromosome arm 20q abnormalities in myeloid malignancies using genome-wide single nucleotide polymorphism array analysis. *Genes Chromosomes Cancer*. 2010;49(4):390-399. *Performed experiments and analyzed data.*
20. Jasek M, **Gondek LP**, Bejanyan N, Tiu R, Huh J, Theil KS, O'Keefe C, McDevitt MA, Maciejewski JP. TP53 mutations in myeloid malignancies are either homozygous or hemizygous due to copy number-neutral loss of heterozygosity or deletion of 17p. *Leukemia*. 2010;24(1):216-219. *Designed and performed experiments, analyzed data and wrote the manuscript*
21. Makishima H, Rataul M, **Gondek LP**, Huh J, Cook JR, Theil KS, Sekeres MA, Kuczkowski E, O'Keefe C, Maciejewski JP. FISH and SNP-A karyotyping in myelodysplastic syndromes: improving cytogenetic detection of del(5q), monosomy 7, del(7q), trisomy 8 and del(20q). *Leuk Res*. 2010;34(4):447-453. *Analyzed data and wrote the manuscript*
22. Paquette RL, Nicoll J, Chalukya M, **Gondek L**, Jasek M, Sawyers CL, Shah NP, Maciejewski J. Clonal hematopoiesis in Philadelphia chromosome-negative bone marrow cells of chronic myeloid leukemia patients receiving dasatinib. *Leuk Res*. 2010;34(6):708-713. *Analyzed genomics data*
23. Tiu RV, **Gondek LP**, O'Keefe CL, Elson P, Huh J, Mohamedali A, Kulasekararaj A, Advani AS, Paquette R, List AF, Sekeres MA, McDevitt MA, Mufti GJ, Maciejewski JP. Prognostic impact of SNP array karyotyping in myelodysplastic

syndromes and related myeloid malignancies. *Blood.* 2011;117(17):4552-4560. *Performed experiments, analyzed data, wrote the manuscript*

24. Jerez A, **Gondek LP**, Jankowska AM, Makishima H, Przychodzen B, Tiu RV, O'Keefe CL, Mohamedali AM, Batista D, Sekeres MA, McDevitt MA, Mufti GJ, Maciejewski JP. Topography, clinical, and genomic correlates of 5q myeloid malignancies revisited. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology*. 2012;30(12):1343-1349. *Performed experiments, analyzed data, wrote the manuscript*
25. Lim Y, **Gondek L**, Li L, Wang Q, Ma H, Huso DL, Foerster S, Marchionni L, McGovern K, Watkins DN, Peacock CP, Levis M, Smith BD, Merchant AA, Small D, Matsui W. The Hedgehog pathway enhances aberrant FLT3 signaling in myeloid leukemia. Sci Transl Med. 2015 Jun 10;7(291):291. *Performed experiments, analyzed data, wrote the manuscript*
26. **Gondek LP**, Zheng G, Ghiaur G, DeZern A, Matsui W, Yegnasubramanian S, Lin M, Levis M, Eshleman, Varadhan R, Tucker N, Jones RJ, Gocke C. Donor cell leukemia arising from clonal hematopoiesis after bone marrow transplantation. Leukemia. 2016 Sep;30(9):1916-20. *Corresponding and co-first author*
27. Pallazola VA, Murray JC, Al Harthy M, Zimmerman SL, Webster J, **Gondek LP**. Anthracycline-induced acute myocarditis and ventricular fibrillation arrest. Am J Hematol. 2017 Dec 1. *Senior author*
28. Lau BW, Huh K, Madero-Marroquin R, De Marchi F, Lim Y, Wang Q, Lobo F, Marchionni L, Smith BD, DeZern A, Levis MJ, Aplan PD, Matsui W, **Gondek LP**. Hedgehog/GLI1 activation leads to leukemic transformation of myelodysplastic syndrome in vivo and GLI1 inhibition results in antitumor activity. Oncogene. 2019 Jan;38(5):687-698. *Senior author*
29. Hambley BC, Norsworthy KJ, Jasem J, Zimmerman JW, Shenderov E, Webster JA, Showel MM, **Gondek LP**, Dalton WB, Prince G, Gladstone DE, Streiff MB, Pratz KW, Gojo I, Ghiaur G, Levis MJ, Smith BD, DeZern AE. Fibrinogen consumption and use of heparin are risk factors for delayed bleeding during acute promyelocytic leukemia induction. Leuk Res. 2019 Aug;83:106174. *Analyzed data.*
30. Zheng G, Chen P, Pallavajjalla A, Haley L, **Gondek L**, Dezern A, Ling H, De Marchi F, Lin MT, Gocke C. The diagnostic utility of targeted gene panel sequencing in discriminating etiologies of cytopenia. Am J Hematol. 2019 Oct;94(10):1141-1148. *Analyzed data*
31. Dalton WB, Helmenstine E, Walsh N, **Gondek LP**, Kelkar DS, Read A, Natrajan R, Christenson ES, Roman B, Das S, Zhao L, Leone RD, Shinn D, Groginski T, Madugundu AK, Patil A, Zabransky DJ, Medford A, Lee J, Cole AJ, Rosen M, Thakar M, Ambinder A, Donaldson J, DeZern AE, Cravero K, Chu D, Madero-Marroquin R, Pandey A, Hurley PJ, Lauring J, Park BH. Hotspot SF3B1 mutations induce metabolic reprogramming and vulnerability to serine deprivation. J Clin Invest. 2019 Aug 8;130. *Performed experiments, analyzed data, wrote the manuscript*
32. Zeidner JF, Knaus HA, Zeidan AM, Blackford AL, Montiel-Esparza R, Hackl H, Prince GT, **Gondek LP**, Ghiaur G, Showel MM, DeZern AE, Pratz KW, Douglas Smith B, Levis MJ, Gore S, Coombs CC, Foster MC, Streicher H, Karp JE, Luznik L, Gojo I. Immunomodulation with pomalidomide at early lymphocyte recovery after induction chemotherapy in newly diagnosed AML and high-risk MDS. Leukemia. 2020 Jan 3. *Enrolled patients, wrote the manuscript*
33. Dalton WB, Helmenstine E, Pieterse L, Li B, Gocke CD, Donaldson J, Xiao Z, **Gondek LP**, Ghiaur G, Gojo I, Smith BD, Levis MJ, DeZern AE.The K666N mutation in SF3B1 is associated with increased progression of MDS and distinct RNA splicing. Blood Adv. 2020 Apr 14;4(7):1192-1196. *Analyzed data*
34. Webster JA, Luznik L, Tsai HL, Imus PH, DeZern AE, Pratz KW, Levis MJ, Gojo I, Showel MM, Prince G, Bolaños-Meade J, **Gondek LP**, Ghiaur G, Dalton WB, Jain T, Fuchs EJ, Gladstone DE, Gocke CB, Ali SA, Huff CA, Borrello IM, Swinnen L, Wagner-Johnston N, Ambinder RF, Jones RJ, Smith BD. Allogeneic transplantation for Ph+ acute lymphoblastic leukemia with posttransplantation cyclophosphamide. Blood Adv. 2020 Oct 27;4(20):5078-5088. *Analyzed data*
35. Wang S, Zbib NH, Skaist A, Gui J, Madero-Marroquin R, De Marchi F, **Gondek LP**, Matsui W, Lau BW. Whole-exome sequencing identifies functional classes of gene mutations associated with bone marrow failure in pediatric Fanconi Anemia patients. Eur J Haematol. 2021 Aug;107(2):293-294. *Analyzed data.*
36. Sidhom JW, Siddarthan IJ, Lai BS, Luo A, Hambley BC, Bynum J, Duffield AS, Streiff MB, Moliterno AR, Imus P, Gocke CB, **Gondek LP**, DeZern AE, Baras AS, Kickler T, Levis MJ, Shenderov E. Deep learning for diagnosis of acute promyelocytic leukemia via recognition of genomically imprinted morphologic features. NPJ Precis Oncol. 2021 May 14;5(1):38. *Analyzed data.*
37. Karantanos T, **Gondek LP**, Varadhan R, Moliterno AR, DeZern AE, Jones RJ, Jain T. Gender-related differences in the outcomes and genomic landscape of patients with myelodysplastic syndrome/myeloproliferative neoplasm overlap syndromes. Br J Haematol. 2021 Jun;193(6):1142-1150. *Designed experiment, analyzed data, wrote the manuscript.*
38. Ambinder A, Smith M, Tsai HL, Varadhan R, DeZern A, Dalton W, Gocke C, Webster J, **Gondek L**, Gojo I, Ali SA, Huff CA, Swinnen L, Wagner-Johnston N, Showel M, Prince G, Borrello I, Bolaños-Meade J, Luznik L, Jain T, Imus P, Fuchs E, Ambinder R, Gladstone DE, Levis M, Jones R, Ghiaur G, Smith BD. Nonmyeloablative Allogeneic Transplantation with Post-Transplant Cyclophosphamide for Acute Myeloid Leukemia with IDH Mutations: A Single Center Experience. Clin Lymphoma Myeloma Leuk. 2021 Oct 9;S2152-2650(21)02071-1. *Analyzed data.*

39. Gibson CJ, Kim HT, Zhao L, Murdock HM, Hambley B, Ogata A, Madero-Marroquin R, Wang S, Green L, Fleharty M, Dougan T, Cheng CA, Blumenstiel B, Cibulskis C, Tsuji J, Duran M, Gocke CD, Antin JH, Nikiforow S, DeZern AE, Chen YB, Ho VT, Jones RJ, Lennon NJ, Walt DR, Ritz J, Soiffer RJ, **Gondek LP**, Lindsley RC. Donor Clonal Hematopoiesis and Recipient Outcomes After Transplantation. J Clin Oncol. 2022 Jan 10;40(2):189-201. doi: 10.1200/JCO.21.02286.; *Co-senior author.*
40. Schaefer EJ, Wang HC, Karp HQ, Meyer CA, Cejas P, Gearhart MD, Adelman ER, Fares I, Apffel A, Lim K, Xie Y, Gibson CJ, Schenone M, Murdock HM, Wang ES, **Gondek LP**, Carroll MP, Vedula RS, Winer ES, Garcia JS, Stone RM, Luskin MR, Carr SA, Long HW, Bardwell VJ, Figueroa ME, Lindsley RC. BCOR and BCORL1 mutations drive epigenetic reprogramming and oncogenic signaling by unlinking PRC1.1 from target genes. Blood Cancer Discovery. 2021 Dec 17; *Enrolled patients, wrote the manuscript*
41. Jain T, Tsai HL, DeZern AE, **Gondek LP**, Elmariah H, Bolaños-Meade J, Luznik L, Fuchs E, Ambinder R, Gladstone DE, Imus P, Webster J, Prince G, Ghiaur G, Smith BD, Ali SA, Ambinder A, Dalton WB, Gocke CB, Huff CA, Gojo I, Swinnen L, Wagner-Johnston N, Borrello I, Varadhan R, Levis M, Jones RJ. Post-Transplantation Cyclophosphamide-Based Graft- versus-Host Disease Prophylaxis with Nonmyeloablative Conditioning for Blood or Marrow Transplantation for Myelofibrosis. Transplant Cell Ther. 2022 Feb; *Enrolled patients, wrote the manuscript*
42. Karantanos T, Teodorescu P, Perkins B, Christodoulou I, Esteb C, Varadhan R, Helmenstine E, Rajkhowa T, Paun BC, Bonifant C, Dalton WB, **Gondek LP**, Moliterno AR, Levis MJ, Ghiaur G, Jones RJ. The role of the atypical chemokine receptor CCRL2 in myelodysplastic syndrome and secondary acute myeloid leukemia. Sci Adv. 2022 Feb 18;8(7); *Analyzed data, wrote the manuscript*
43. Murdock HM, Kim HT, Denlinger N, Vachhani P, Hambley BC, Manning BS, Gier S, Cho C, Tsai HK, McCurdy SR, Ho VT, Koreth J, Soiffer RJ, Ritz J, Carroll MP, Vasu S, Perales MA, Wang ES, **Gondek LP**, Devine SM, Alyea EP, Lindsley RC, Gibson CJ. Impact of diagnostic genetics on remission MRD and transplantation outcomes in older AML patients. Blood. 2022 Mar 14. *Enrolled patients, analyzed data, wrote the manuscript*
44. Karantanos T, Tsai HL, **Gondek LP**, DeZern AE, Ghiaur G, Dalton WB, Gojo I, Prince GT, Webster J, Ambinder A, Smith BD, Levis MJ, Varadhan R, Jones RJ, Jain T. Genomic landscape of myelodysplastic/myeloproliferative neoplasm can predict response to hypomethylating agent therapy. Leuk Lymphoma. 2022 Apr 4:1-7. doi: 10.1080/10428194.2022.2057488. *Analyzed data, wrote the manuscript*
45. Tsai HK, Gibson CJ, Murdock HM, Davineni PK, Harris M, Wang ES, **Gondek LP**, Kim AS, Nardi V, Lindsley RC. Allelic Complexity of KMT2A Partial Tandem Duplications in Acute Myeloid Leukemia and Myelodysplastic Syndromes. Blood Adv. 2022 May 18:bloodadvances.2022007613. doi: 10.1182/bloodadvances.2022007613. *Enrolled patients, analyzed data, wrote the manuscript*
46. Wang S, Pasca S, Post WW, Langan S, Pallavajjalla A, Haley L, Gocke C, Budoff M, Haberlen S, Brown T, Ambinder RF, Margolick LB, **Gondek LP**. Clonal hematopoiesis in men living with HIV and association with subclinical atherosclerosis. AIDS. 2022 Sep 1;36(11):1521-1531. doi: 10.1097/QAD.0000000000003280. *Senior author*
47. Karantanos T, Teodorescu P, Arvanitis M, Perkins B, Jain T, DeZern AE, Dalton WB, Christodoulou I, Paun BC, Varadhan R, Esteb C, Rajkhowa T, Bonifant C, **Gondek LP**, Levis MJ, Yegnasubramanian S, Ghiaur G, Jones RJ. CCRL2 affects the sensitivity of myelodysplastic syndrome and secondary acute myeloid leukemia cells to azacitidine. Haematologica. 2022 Dec 15. doi: 10.3324/haematol.2022.281444. Online ahead of print. *Analyzed data, wrote the manuscript*
48. Braunstein EM, Imada E, Pasca S, Wang S, Chen H, Alba C, Hupalo DN, Wilkerson M, Dalgard CL, Ghannam J, Liu Y, Marchionni L, Moliterno A, Hourigan CS, **Gondek LP**. Recurrent germline variant in ATM associated with familial myeloproliferative neoplasms. Leukemia. 2022 Dec 21. doi: 10.1038/s41375-022-01797-6. Online ahead of print. *Senior author*
49. Webster JA, Reed M, Tsai HL, Ambinder A, Jain T, Dezern AE, Levis MJ, Showel MM, Prince GT, Hourigan CS, Gladstone DE, Bolanos-Meade J, **Gondek LP**, Ghiaur G, Dalton WB, Paul S, Fuchs EJ, Gocke CB, Ali SA, Huff CA, Borrello IM, Swinnen L, Wagner-Johnston N, Ambinder RF, Luznik L, Gojo I, Smith BD, Varadhan R, Jones RJ, Imus PH. Allogeneic Blood or Marrow Transplantation with High-Dose Post-transplantation Cyclophosphamide for Acute Lymphoblastic Leukemia in Patients Aged ≥55. Transplant Cell Ther. 2022 Dec 29:S2666-6367(22)01866-8. doi: 10.1016/j.jtct.2022.12.018. Online ahead of print. *Enrolled patients, analyzed data, wrote the manuscript*
50. Sanber K, Ye K, Tsai HL, Newman M, Webster JA, Gojo I, Ghiaur G, Prince GT, **Gondek LP**, Smith BD, Levis MJ, DeZern AE, Ambinder AJ, Dalton WB, Jain T. Venetoclax in combination with hypomethylating agent for the treatment of advanced myeloproliferative neoplasms and acute myeloid leukemia with extramedullary disease. Leuk Lymphoma. 2023 Feb 6:1-10. doi: 10.1080/10428194.2023.2173523. Online ahead of print. PMID: 36744656. *Enrolled patients, analyzed data, wrote the manuscript*
51. Pasca S, Guo MZ, Wang S, Stokvis K, Shedeck A, Pallavajjala A, Shams C, Pallavajjala R, DeZern AE, Varadhan R, Gocke CD, Jones RJ, **Gondek LP**. Cell-free DNA measurable residual disease as a predictor of postallogeneic hematopoietic cell transplant outcomes. Blood Adv. 2023 Aug 22;7(16):4660-4670. doi: 10.1182/bloodadvances.2023010416. *Senior author*

52. Jain T, Ware AD, Dalton WB, Pasca S, Tsai HL, Gocke CD, **Gondek LP**, Xian RR, Borowitz MJ, Levis MJ. Co-occurring mutations in ASXL1, SRSF2, and SETBP1 define a subset of myelodysplastic/ myeloproliferative neoplasm with neutrophilia. Leuk Res. 2023 Aug;131:107345. doi: 10.1016/j.leukres.2023.107345. Epub 2023 Jun 21. *Enrolled patients, analyzed data, wrote the manuscript*
53. Teodorescu P, Pasca S, Choi I, Shams C, Dalton WB, **Gondek LP**, DeZern AE, Ghiaur G. An accessible patient-derived xenograft model of low-risk myelodysplastic syndromes. Haematologica. 2023 Jul 6. doi: 10.3324/haematol.2023.282967. Online ahead of print. *Perform sequencing, analyzed data, wrote the manuscript*
54. Jain T, Tsai HL, Elmariah H, Vachhani P, Karantanos T, Wall SA, **Gondek LP**, Bashey A, Keyzner A, Tamari R, Grunwald MR, Abedin S, Nadiminti KV, Iqbal M, Gerds AT, Viswabandya A, McCurdy SR, Al Malki MM, Varadhan R, Ali H, Gupta V, Jones RJ, Otoukesh S. Haploidentical donor hematopoietic cell transplantation for myelodysplastic/myeloproliferative overlap neoplasms: results from a North American collaboration. Haematologica. 2023 Jul 6. doi: 10.3324/haematol.2023.283426. Online ahead of print. *Enrolled patients, analyzed data, wrote the manuscript*
55. Pasca S, Haldar SD, Ambinder A, Webster JA, Jain T, Dalton WB, Prince GT, Ghiaur G, DeZern AE, Gojo I, Smith BD, Karantanos T, Schulz C, Stokvis K, Levis MJ, Jones RJ, **Gondek LP**. Outcome heterogeneity of TP53-mutated myeloid neoplasms and the role of allogeneic hematopoietic cell transplantation. Haematologica. 2023 Sep 21. doi: 10.3324/haematol.2023.283886. Online ahead of print. *Senior author*
56. Hong YS, Battle SL, Shi W, Puiu D, Pillalamarri V, Xie J, Pankratz N, Lake NJ, Lek M, Rotter JI, Rich SS, Kooperberg C, Reiner AP, Auer PL, Heard-Costa N, Liu C, Lai M, Murabito JM, Levy D, Grove ML, Alonso A, Gibbs R, Dugan-Perez S, **Gondek LP**, Guallar E, Arking DE. Deleterious heteroplasmic mitochondrial mutations are associated with an increased risk of overall and cancer-specific mortality. Nat Commun. 2023 Sep 30;14(1):6113. doi: 10.1038/s41467-023-41785-7. *Analyzed data, wrote the manuscript*
57. Klausner M, Phan B, Morsberger L, Parish R, Shane A, Park R, Gocke CD, Xian RR, Jones RJ, Bolaños-Meade J, **Gondek LP**, Phan M, Zou YS. Donor cell-derived genetic abnormalities after sex mismatched allogeneic cell transplantation: a unique challenge of donor cell leukemia. Blood Cancer J. 2023 Nov 6;13(1):163. doi: 10.1038/s41408-023-00938-z. *Analyzed data, wrote the manuscript*
58. Ravindra N, Dillon LW, Gui G, Smith M, **Gondek LP**, Jones RJ, Corner A, Hourigan CS, Ambinder AJ. Persistent IDH mutations are not associated with increased relapse or death in patients with IDH-mutated acute myeloid leukemia undergoing allogeneic hematopoietic cell transplant with post-transplant cyclophosphamide. Bone Marrow Transplant. 2024 Jan 5. doi: 10.1038/s41409-023-02189-9. Online ahead of print. *Analyzed data, wrote the manuscript*
59. Saadatagah S, Uddin MM, Weeks LD, Niroula A, Ru M, Takahashi K, **Gondek L**, Yu B, Bick AG, Ebert BL, Platz EA, Natarajan P, Ballantyne CM. Clonal Hematopoiesis Risk Score and All-Cause and Cardiovascular Mortality in Older Adults. JAMA Netw Open. 2024 Jan 2;7(1):e2351927. doi: 10.1001/jamanetworkopen.2023.51927. *Analyzed data, wrote the manuscript*
60. Imus PH, Pasca S, Tsai HL, Aljawai Y, Cooke KR, Walston JD, Gocke CD, Varadhan R, Jones RJ, **Gondek LP**. Recipient clonal hematopoiesis in allogeneic bone marrow transplantation for lymphoid malignancies. Blood Adv. 2024 Apr 19:bloodadvances.2023011761. doi: 10.1182/bloodadvances.2023011761. *Senior author*
61. Marshall CH, **Gondek LP**, Daniels V, Lu C, Pasca S, Xie J, Markowski MC, Paller CJ, Sena LA, Denmeade SR, Luo J, Antonarakis ES. Association of PARP inhibitor treatment on the prevalence and progression of clonal hematopoiesis in patients with advanced prostate cancer. Prostate. 2024 Jul;84(10):954-958. doi: 10.1002/pros.24712. Epub 2024 Apr 20.. PMID: 38641986. *Designed the project, performed experiments, analyzed data, wrote the manuscript*
62. Hong YS, Pasca S, Shi W, Puiu D, Lake NJ, Lek M, Ru M, Grove M, Prizment A, Joshu CE, Platz EA, Guallar E, Arking DE, Gondek LP. Mitochondrial heteroplasmy improves risk prediction for myeloid neoplasms. medRxiv doi: https://doi.org/10.1101/2024.04.07.24305454. *Senior author*
63. Jitaru C, Peters MC, Aggarwal L, Bancos A, Tigu AB, Cenariu D, Selicean C, Pasca S, Moisoiu V, Rotariu P, Santa M, Iluta S, Drula R, Kegyes D, Kurtus A, Zdrenghea M, **Gondek L**, Tomuleasa C, Ghiaur G. Single low-dose decitabine as frontline therapy of acute myeloid leukaemia, with venetoclax salvage. J Cell Mol Med. 2024 Oct;28(20):e18592. doi: 10.1111/jcmm.18592. PMID: 39435884 *Designed the project, analyzed data, wrote the manuscript*

Review Articles [RA]

1. **Gondek LP**, Spivak J. Somatic mutations in polycythaemia vera and other Philadelphia chromosome negative myeloproliferative neoplasms. John Wiley & Sons, Ltd. 2012 Dec;
2. **Gondek LP**, DeZern AE., I walk the line: how to tell MDS from other bone marrow failure conditions. Curr Hematol Malig Rep. 2014 Dec;9(4):389-399
3. **Gondek LP**, DeZern AE. Assessing clonal haematopoiesis: clinical burdens and benefits of diagnosing myelodysplastic syndrome precursor states. Lancet Haematol. 2019 Dec 3.
4. DeZern AE, **Gondek LP**. Stem cell donors should be screened for CHIP. Blood Adv. Feb 25;4(4):784-788

5. Pasca S, **Gondek LP**. Clonal hematopoiesis and bone marrow failure syndromes. Best Pract Res Clin Haematol. 2021 Jun;34(2):101273.
6. **Gondek LP**. CHIP: is clonal hematopoiesis a surrogate for aging and other disease? Hematology Am Soc Hematol Educ Program. 2021 Dec 10;2021(1):384-389. doi: 10.1182/hematology.2021000270
7. **Gondek LP**, Sheehan VA, Fitzhugh CD. Clonal Hematopoiesis and the Risk of Hematologic Malignancies after Curative Therapies for Sickle Cell Disease. J Clin Med 2022 Jun 2;11(11):3160.
8. Marshall CH, **Gondek LP**, Luo J, Antonarakis ES. Clonal hematopoiesis of indeterminate potential in patients with solid tumor malignancies. Cancer Res. 2022 Aug 30:CAN-22-0985.
9. Ktena YP, Dionysiou M, **Gondek LP**, Cooke KR. The impact of epigenetic modifications on allogeneic hematopoietic stem cell transplantation. Front Immunol. 2023 May 31;14:1188853. doi: 10.3389/fimmu.2023.1188853. eCollection 2023.
10. Gibson CJ, Lindsley RC, **Gondek LP**. Clonal hematopoiesis in the setting of hematopoietic cell transplantation. Semin Hematol. 2024 Feb 1:S0037-1963(24)00012-X. doi: 10.1053/j.seminhematol.2024.01.011.

Book Chapters, Monographs [BC]

1. Maciejewski, JP, **Gondek, LP**, Selleri, C, & Risitano, AM (2010). Molecular Diagnostics in Hematology. In G.P. Rodgers, N.S. Young (Ed.), *The Bethesda Handbook of Clinical Hematology*. Philadelphia, PA. Wolters Kluwer Health/Lippincott William & Wilkins.
2. **Gondek LP**, Ghiaur G (2017) micro-RNAs: Network in Acute Leukemia. In Emadi, A, Karp, JE (Ed.), *Acute Leukemia: An Illustrated Guide to Diagnosis and Treatment*. New York: Demos
3. **Gondek LP** (2018). Epigenetic Modulators. In Emadi, A, Karp, JE (Ed). *Illustrative Oncopharmacology*.
4. Pasca S, **Gondek LP**(2023). Epigenetic Modulators. In Emadi, A, Karp, JE (Ed). *Cancer Pharmacology: An Illustrated Manual of Anticancer Drugs, Second Edition*

Editorials [ED]

1. **Gondek LP**. Hitting the bullseye with a nonlethal payload: resistance in CD123-positive malignancies. *J Clin Invest. 2019 Oct 14.*
2. **Gondek LP.** High Prevalence of Clonal Hematopoiesis in the Blood and Bone Marrow of Healthy Volunteers. *PracticeUpdate 2020*
3. **Gondek LP.** Donor Clonal Hematopoiesis and Outcomes After Transplantation. *PracticeUpdate 2021*
4. **Gondek LP.** Refining CHIP in population datasets. *Blood.* 2023 May 4;141(18):2163-2164. doi: 10.1182/blood.2023019801..

Media Release of Interviews [MR]

1. https://www.youtube.com/watch?v=pceG4k4bBxo
2. https://www.youtube.com/watch?v=4LlYYKwZXCE

FUNDING

EXTRAMURAL FUNDING

Research Extramural Funding

Current

1/15/21 – 1/31/26	The Biological Consequences of Age-related Clonal Hematopoiesis R01 HL156144-01A1 NIH/NHLBI $2,000,005 Role: PI, 30% effort
2/1/23 – 1/31/26	Identifying, Understanding, and Eradicating Measurable Residual Disease (MRD) in Patients with Acute Myeloid Leukemia (AML). Break Through Cancer $1,599,453 Role: co-PI, 5% effort
2/1/23 – 1/31/26	Targeting Clonal Hematopoiesis (CH) to Prevent Acute Myeloid Leukemia (AML). Break Through Cancer $1,877,429 Role: co-PI, 3% effort

Pending

07/01/24 – 06/30/29
Mitochondrial heteroplasmy and risk of myeloid malignancies
R01
NIH/NCI
$4,093,735.00
Role: PI, 20% effort

Previous

2006 – 2008
A Novel Approach for the Study of Genetic Predisposition in AA and PNH Using High-Density Arrays
Young Investigator Award/AA&MDS
$60,000
Role: PI, 50% effort

7/1/12 – 6/30/14
Self-renewal mechanisms in myeloid leukemias
5T32HL007525
NIH
$110,360
PI: Robert Brodsky
Role: Trainee, 80% effort

7/1/14 – 6/30/15
Hedgehog signaling in MDS progression
90056518
Aplastic Anemia & MDS International Foundation (AA&MDSIF)
$90,090
PI: Amy DeZern
Role: Project Leader, 20% effort

7/1/14 – 6/30/16
Edward P. Evan Fellowship
90056518
Aplastic Anemia & MDS International Foundation (AA&MDSIF)
$74,700
PI: Amy DeZern
Role: Project Leader, 35% effort

9/1/18 – 8/31/20
The prevalence and molecular characteristics of age-related clonal hematopoiesis in HIV-positive patients.
P30 Cancer Centers Support Grants
NIH/NCI
$133,335
Role: PI, 10% effort

7/15/18 – 5/31/21
Personalized molecular approaches to disease monitoring and maintenance therapies for Myelodysplastic Syndromes (MDS) and Acute Myeloid Leukemia (AML) patients undergoing allogeneic bone marrow transplantation.
R21 HL143096-01
NIH/NHLBI
$245,626
Role: PI, 10% effort

4/5/17 – 3/31/22
Hedgehog Signaling in the Progression of Myelodysplastic Syndromes
K08 HL136894-01
NIH/NHLBI
$856,600
Role: PI, 75% effort

INTRAMURAL FUNDING

Research Intramural Funding

Current

4/1/22 – 3/31/24
The role of clonal hematopoiesis in solid tumor malignancies: The Atherosclerosis Risk in Communities (ARIC) Study
Allegheny Health Network-Johns Hopkins Cancer Research Fund

	$200,000 Role: PI, 20% effort
Pending	None
Previous	
4/1/16 – 3/31/18	Age-related clonal hematopoiesis and the mechanism of leukemic transformation using allogeneic bone marrow transplantation model Hopkins-Allegheny Health Network (AHN) Cancer Research Fund $200,000 Role: PI, 10% effort
7/1/17 – 6/30/19	Clinician Scientist Award Johns Hopkins University, School of Medicine $80,000 Role: PI, 75% effort
6/1/19 – 5/31/20	The prevalence, molecular characteristics and clinical consequences of clonal hematopoiesis of indeterminate potential (CHIP) in HIV positive and HIV-negative men. Faculty Development Award, Johns Hopkins University Center for AIDS Research (JHU CFAR) Developmental Core. NIH/NIAID $50,000 Role: PI, 10% effort
1/1/20 – 12/31/22	The Pathogenesis, Prognosis and Treatment of Clonal Hematopoiesis and Myelodysplastic Syndromes Hematologic Malignancies and Bone Marrow Transplantation CCSG Program $150,000 Role: PI, 10% effort
1/1/20 – 12/31/22	Hematologic Malignancies and their Precursors in HIV: Applications of Advanced Molecular Techniques. Hematologic Malignancies and Bone Marrow Transplantation CCSG Program $150,000 Role: co-PI, 10% effort
1/1/21 – 12/31/22	Plasma-based minimal residual disease detection and allogeneic bone marrow transplantation outcome in patients with myeloid malignancies $50,000 Role: PI, 5% effort

CLINICAL ACTIVITIES

Clinical Focus

Care of patients with hematological malignancies on adult leukemia service.

Certification

Medical, other state/government licensure

2011 – present State of Maryland (D72150)

Boards, other specialty certification

2008 – present Advanced Cardiac Life Support
2011 – 2021 American Board of Internal Medicine
2013 – present American Board of Hematology

Clinical (Service) Responsibilities

2014 – present Hematology/Oncology - Leukemia 15% effort (8 weeks per year)
2014 – present Hematology/Oncology and Surgery – Bone marrow harvest 5% effort
2014 – present Hematology/Oncology and Pathology – Interpretation of bone marrow aspirations 5% effort

Clinical Productivity

2014 – present My targeted clinical effort assignment is 25%.

Total RVUs

FY15	FY16	FY17	FY18	FY19	FY20	FY21	FY22	FY23	FY24
1764	2104	1735	1792	1836	1628	1551	1470	1093	1829

Clinical Draw from outside local/regional area none
Membership in or examiner for specialty board none
Clinical Program Building / Leadership none

Clinical Demonstration Activities to external audience, on or off campus
2024 – present Clinical Program in Clonal Hematopoiesis and myeloid precursor states.

Development of nationally/internationally recognized clinical standard of care none

EDUCATIONAL ACTIVITIES
Educational Focus
My educational focus is on the biology, diagnostic approaches, and treatment of myeloid malignancies, in particular, Myelodysplastic Syndrome and Clonal Hematopoiesis.

Teaching
Classroom Instruction
JHMI/Regional
2015 – 2022 Instructor, medical students, Genes to Society – Hematology Course, Johns Hopkins SOM, Baltimore, MD
2024 – present Instructor, medical students, Genes to Society – Hematologic Malignancies Course, Johns Hopkins SOM, Baltimore, MD
2015 – present Instructor, medical students, Topics in Interdisciplinary Medicine - Introduction to Regenerative Medicine, Johns Hopkins SOM, Baltimore, MD
National None
International None

Clinical Instruction
JHMI/Regional
2014 – present Instructor, Internal Medicine residents and Medical Oncology fellows, Clinical skills instruction for on the Leukemia Inpatient Service, Johns Hopkins SKCCC, Johns Hopkins University, Baltimore, MD
National None
International None

CME Instruction
See Invited Talks.

Mentoring
Pre-doctoral Advisees /Mentees
2016 – 2019 Samantha Kegel; college student, Johns Hopkins; currently medical student at University of Maryland SOM
2020 – present Matthew Gao; medical student, Johns Hopkins; recipient of American Society of Hematology HONORS Award (2021)

Post-doctoral Advisees
2015 – 2018 Bonnie Lau, MD, PhD; hematology/oncology fellow, currently Assistant Professor at the Geisel School of Medicine, Dartmouth; co-authored articles OR 28, OR35
2016 – 2018 Rafael Madero-Marroquin, MD; postdoctoral fellow; currently hematology/oncology fellow at the University of Chicago; co-authored OR28, OR31, OR35, OR39
2016 – 2017 Federico De Marchi, MD; postdoctoral fellow; currently PhD student at Juntendo University Graduate School of Medicine, Tokyo, Japan; co-authored OR28, OR30, OR35
2018 – 2019 Lin Zhao, MD; visiting scholar; currently Chief Physician, Shanghai University of Traditional Chinese Medicine, China; co-authored OR31, OR39
2019 – 2022 Daniel Haldar, MD; internal medicine resident, John Hopkins; currently hematology/oncology fellow at Johns Hopkins University; recipient of Molina/Grasmick Scholar (2021); co-authored OR 56

2020 – present Sergiu Pasca, MD, PhD; postdoctoral fellow; recipient of the Romanian Society of Bone Marrow Transplantation Award; co-authored OR46, OR48, OR53, OR56, OR60, OR61, OR62, OR63, RA5
2021 – 2023 Michael Hochman, MD; postdoctoral hematology fellow, currently Assistant Professor at Department of Hematology and Medical Oncology, Emory University School of Medicine
2022 – present Jiajun Xie, MD; postdoctoral fellow. co-authored OR56, OR61.
2023 – present Anna Bereznicka, PhD; postdoctoral fellow
2024 – present Shirley Mo, MD; postdoctoral fellow

Thesis committees
None

Educational Program Building / Leadership None
Institutional Administrative Appointments None
Educational Demonstration Activities to external audiences None

RESEARCH ACTIVITIES

Research Focus
I am an Associate Professor of Oncology in the Division of Hematologic Malignancies, Leukemia Program at the Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins. My career goal is to develop novel insights into the pathogenesis of myelodysplastic syndromes (MDS) and acute myeloid leukemia (AML) and translate these findings into new treatments for patients with these diseases. My research focuses on the genetic mechanisms responsible for MDS development and events leading to disease progression and leukemic transformation. We have recently utilized the allogeneic bone marrow transplantation platform to study the natural history of clonal hematopoiesis of indeterminate potential (CHIP) and the mechanism leading to clonal evolution and expansion. The experience in AML and MDS genetics will allow me to functionally characterize the genetic alteration identified in patients during disease development and progression. Since my appointment as an Assistant Professor, my laboratory research has been continuously founded by the National Institute of Health (K08, R21, R01) as well as several foundation grants. I envision my laboratory and clinical effort the centerpiece of the translational research program in MDS and clonal hematopoiesis.

Research Program Building / Leadership
2024 – present Clonal Hematopoiesis clinical and research program.

Research Demonstration Activities None
Inventions, Patents, Copyrights None
Technology Transfer Activities None

SYSTEM INNOVATION AND QUALITY IMPROVEMENT ACTIVITIES

None

ORGANIZATIONAL ACTIVITIES

Institutional Administrative Appointments
2013 – 2014 Member, Hematology/Oncology Fellowship- Tracks Committee
2016 – present Member, Medical School Admissions Committee, Johns Hopkins School of Medicine
2017 – present Member, Internal Medicine Residency Admissions Committee, Johns Hopkins School of Medicine

Editorial Activities

Editorial Board Appointments None

Journal peer review activities
2011 – present Reviewer for The British Journal of Haematology
2014 – present Reviewer for Case Reports in Hematology
2017 – present Reviewer for Journal of Clinical Investigation
2017 – present Reviewer for Biology of Blood and Marrow Transplantation
2018 – present Reviewer for Haematologica
2019 – present Reviewer for Clinical Cancer Research

2019 – present Reviewer for Blood Advances
2019 – present Reviewer for Blood
2020 – present Reviewer for American Journal of Transplantation
2021 – present Reviewer for Lancet Haematology
2021 – present Reviewer for Frontiers in Oncology
2022 – present Reviewer for Circulation
2023 – present Reviewer for Journal of Clinical Oncology
2024 – present Reviewer for American Journal of Hematology

Other peer review activities

2019 American Society of Hematology, Abstract Reviewer, Clonal Hematopoiesis: Aging and Inflammation.
2020 American Society of Hematology, Coordinating Abstract Reviewer, Clonal Hematopoiesis: Aging and Inflammation.

Advisory Committees, Review Groups/Study Sections

2020 The European Hematology Association, Grant Reviewer
2021 Stichting Kinderen Kankervrij' (Foundation Children Cancerfree) or 'KiKa' Foundation, Netherlands, Grant Reviewer
2022 Special Emphasis Panel for R21 Study Section, NIH/NHLBI, ad hoc Grant Reviewer
2023 Biology of Blood, Heart and Vasculature Study Section, NIH, ad hoc Grant Reviewer
2023 Special Emphasis Panel for R21 Study Section, NIH/NHLBI, ad hoc Grant Reviewer
2023-2024 Break Through Cancer- AML Measurable Residual Disease Steering Committee
2024 Hemostasis, Thrombosis, Blood Cells and Transfusion Study Section, NIH, ad hoc Grant Reviewer
2024 MPN Foundation, 2024 MPN Challenge Grant Reviewer

Professional Societies

2011 – present Member, American Society of Hematology
2011 – present Member, American Society of Clinical Oncology

Conference Organizer

None

Session Chair

JHMI/Regional None
National
12/2019 Session Chair, American Society of Hematology Annual Meeting, Clonal Hematopoiesis: Aging and Inflammation. Orlando, FL
12/2020 Session Chair, American Society of Hematology Annual Meeting, Clonal Hematopoiesis: Aging and Inflammation. Virtual event
12/2021 Session Chair, American Society of Hematology Annual Meeting, ASH Education Program, Clonal Hematopoiesis. Atlanta, GA
International None

Consultantships

2018 – present GLG consulting, medical consulting for GLG clients/ consultant
2020 – present VeraMedica LLC., medical/oncology consulting for legal cases/ expert witness
2021 – present Bristol Myers Squibb, MDS advisory board/ member
2022 – present Bluebird Bio, cell therapy advisory board/ member

RECOGNITION

Awards, Honors

1997 – 2003 Full academic scholarship, Medical University of Silesia

2005, 2006, 2007 Travel Award, American Society of Hematology
2014 – 2016 Edward P. Evans Fellowship, AA & MDS International Foundation
2017 – 2019 Clinician Scientist Award, Johns Hopkins School of Medicine

2019 – 2020 Faculty Development Award, Johns Hopkins University Center for AIDS Research (JHU CFAR)

Invited Talks

JHMI/Regional

5/26/15 Genetics and Society, Clinical application of genetics research, Annual Science Outreach Event, Project Bridge, Baltimore, MD.2/2016 Myelodysplastic Syndromes: From Metaphase Karyotyping to Molecular DNA Profiling, JHMI Division of Hematology, Hematology Grand Rounds, Baltimore, MD

8/17/16 Molecular Profiling in MDS, Assistant Professor Summer Lecture Series, SKCCC, Baltimore, MD

8/7/19 The Clinical Consequence of Age-related Clonal Hematopoiesis, Assistant Professor Summer Lecture Series, SKCCC, Baltimore, MD

5/27/20 Clonal Hematopoiesis: Biology and Clinical Consequences, Translational Research Conference, SKCCC, Baltimore, MD

1/15/21 Clinical Consequences of Age-related Clonal Hematopoiesis, JHH Medical Grand Rounds, Baltimore, MD

2/2/21 Age-related Clonal Hematopoiesis – Biology and Clinical Consequences, Biology of Healthy Aging Lecture Series, Baltimore, MD

5/7/21 Clonal Hematopoiesis in Cancer and Beyond, JHU SKCCC Oncology Grand Rounds, Baltimore, MD

3/29/22 Clonal Hematopoiesis in Aging and Cancer, JHU SKCCC Novel Approaches to Therapy and Prevention Course, Baltimore, MD

4/22/22 Clinical Consequences of Clonal Hematopoiesis, JHU SKCC Sibley Memorial Hospital, Grand Rounds, Washington DC.

11/02/23 Fundamentals of hematologic malignancies/stem cells/clonal evolution, JHU SKCCC Fundamentals of Cancer, Cause to Cure Course

National

12/6/19 Clinical Management of Myeloid Malignancies: The Coming of Age of Targeted Therapies, American Society of Hematology, Friday Scientific Symposia, Orlando, FL

3/2/21 Age-related clonal hematopoiesis – biology and clinical consequences. Norris Cotton Cancer Center, Dartmouth, Oncology Grand Rounds, Lebanon, NH

10/3/21 Impact of Clonal Hematopoiesis on Hematopoietic Cell Transplantation Outcome. Global Cure for SCD Virtual Conference.

11/20/21 Rationale for screening stem cell donors for clonal hematopoiesis. Association for Molecular Pathology Meeting, Philadelphia, PA.

12/12/21 ARCH: Is Clonal Hematopoiesis a Surrogate for Age and Other Disease? American Society of Hematology, ASH Education Program, Atlanta, GA

3/24/22 Clonal hematopoiesis and its implications for hematopoietic stem cell transplantation. Cellular and Molecular Therapeutics Branch and the Sickle Cell Branch at the NHLBI Scientific Meeting, Bethesda, MD

5/4/22 Clonal Hematopoiesis in Cancer and Beyond. Herbert Irving CCC, Columbia University, Hematology/Oncology Grand Rounds, New York, NY

6/10/22 Allogenic Transplant and Clonal Hematopoiesis in Sickle Cell Disease. 5th Annual Sickle Cell Disease Access to Care Summit, Fort Lauderdale, FL.

12/9/22 The Biological Consequences of Age-Related Clonal Hematopoiesis. Scientific Workshop on Hematology and Aging, American Society of Hematology, New Orleans, LA.

2/9/23 Clonal hematopoiesis and hematopoietic stem cell transplant outcomes. Division of Hematology & Oncology Cutter Lecture Series, Vanderbilt University, Nashville, TN

10/11/23 Post-curative Malignancies Risk. 16th Annual Sickle Cell in Focus Conference, NIH, Bethesda, MD.

03/13/24 Clonal hematopoiesis and the risk of myeloid neoplasms. Molecular Therapeutics Lecture, Karmanos Cancer Institute, Detroit, MI

03/19/24 Mitochondrial heteroplasmy and the risk of myeloid malignancies. Translational Hematology & Oncology Research Lecture Series, Cleveland Clinic Cancer Center, Cleveland, OH.

06/21/24 Improving outcome of patients after allogeneic hematopoietic cell transplantation, Oncology Grand Rounds, Case Western Reserve University, Cleveland, OH.

08/16/24 Novel NGS approaches to single-cell analysis and measurable residual disease detection, Food and Drug Administration, Bethesda, MD.

10/2/24 Improving outcome of patients after allogeneic hematopoietic cell transplantation, Translation Research Conference, University of Pennsylvania, Philadelphia, PA.

International

10/30/15	MDS: Clinical Application of Molecular Techniques, IV Ibero-American Symposium on Myelodysplastic Syndromes, Puerto-Vallarta, Mexico
10/04/18	MDS: Clinical Application of Molecular Techniques, V Ibero-American Symposium on Myelodysplastic Syndromes, Cancun, Mexico
10/11/18	Molecular testing in myeloid diseases – diagnostic and therapeutic implications, XXV Romanian Society of Hematology National Meeting, Sinaia, Romania
9/17/22	Donor Clonal Hematopoiesis and HSC Recipient Outcomes, Insights in Hematology, 7th Edition, Cluj, Romania.
10/28/22	Keynote Speaker, Diagnostic and clinical implications of clonal hematopoiesis, Laboratory Medicine Congress & Exhibition & KSLM 63rd Annual Meeting (LMCE 2022), Seoul, South Korea
1/4/23	Clonal Hematopoiesis, Post-New Orleans ASH 2022: Novità dal Meeting della Società Americana di Ematologia, Milan, Italy.

Appendix B

4 Year Expert Testimony List of Lucasz Gondek, MD, PhD

Date	Case Name	Case Number	Deposition or Trial
29-Jul-2024	Godfrey, Patricia v. Union Pacific Railroad Company		Deposition
7-Aug-2024	Bonar, Jason v. Norfolk Southern Railway		Deposition

Appendix C

Fee Schedule
The VeraMedica Institute, LLC

LUCASZ GONDEK, MD, PHD.
Instructor of Oncology, The Johns Hopkins University School of Medicine.
Assistant Professor of Oncology, The Johns Hopkins University School of Medicine.
Attending Physician, The Johns Hopkins Hospital.

Baseline billable rate ……. $600.00 per hour

Travel time…….....…….. $600.00 per hour

Travel Policy:

> ***Travel Policy:*** The client agrees to compensation for minimum commitment equivalent to a half day of the doctor's time when the client schedules the physician to travel more than 60 miles from home or office, for a meeting.

Deposition (Minimum 4 hours) and Trial (Minimum 8 hours) …….. $900.00 per hour

****Please note for projects requiring expedited service due to late submission of materials or announcement of deadlines that will require Expert's adjusting of schedules and staff overtime within three weeks of deadline dates will thus require a rate premium increase of 50% across the board. Thank you for your understanding.***

Cancellation/Rescheduling Policy (meeting, deposition, or testimony):

- Within 1 week of travel to a deposition or trial appearance, the client agrees to minimum commitment equivalent to a full day of the doctor's time when the client cancels or reschedules physician's time……$4,800 per calendar day
- The client assumes responsibility for travel fees, penalties, or supplemental costs resulting from change in travel plans.

Laboratory and Equipment Fees ……Advance quote prepared as needed

<u>Physician's Support Staff</u>:

Associate Scientist ……. $185 to $225 per hour

Staff MD/PhD Epidemiologist……$235 to $335 per hour

Nurse Practitioner (advance practice) …..…….…….…. $205 to $235 per hour