

MORE THAN 500 BILLS RESTRICTING TRANS MEDICAL CARE THREATEN LGBTQ+ PEOPLE WITH CANCER

More than 500 legislative proposals in 49 states are targeting trans people—predominantly youths prompting fear among patients, healthcare providers, advocates, and legal experts that trans and gender nonconforming patients will be excluded from care. CANCER HISTORY PROJECT JOHN LASZLO'S DUAL ROLE: (1) WORKING TO CURE CHILDHOOD LEUKEMIA, AND (2) WRITING THE AUTHORITATIVE BOOK ON IT

 \rightarrow PAGE 15

BOOK REVIEW WHAT ARE YOU READING IN 2023?

 \rightarrow PAGE 29

BOOK REVIEW

WAFIK EL-DEIRY TOOK AN EXTRA SUITCASE ON VACATION— FOR THE BOOKS ON HIS 2023 READING LIST

 \rightarrow PAGE 46

CONVERSATION WITH THE CANCER LETTER STEVE ROSEN READS HIS POEMS—AND TELLS US WHY HE WRITES

 \rightarrow PAGE 57



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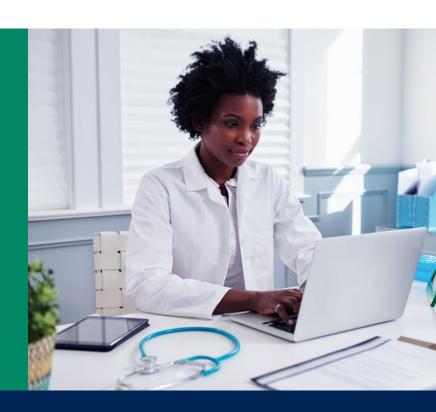
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In this issue

COVER STORY

6 More than 500 bills restricting trans medical care threaten LGBTQ+ people with cancer

CANCER HISTORY PROJECT

 John Laszlo's dual role:
(1) Working to cure childhood leukemia, and (2) Writing the authoritative book on it

BOOK REVIEW

- 29 What are you reading in 2023?
- **46** Wafik El-Deiry took an extra suitcase on vacation—for the books on his 2023 reading list

CONVERSATION WITH THE CANCER LETTER

57 Steve Rosen reads his poems and tells us why he writes

OBITUARY

62 Pioneering oncologist Irwin H. Krakoff dies at 100

IN BRIEF

- 66 Boris C. Pasche named president & CEO of Karmanos, chair of Wayne State Department of Oncology
- 66 Thomas J. Herzog named president of GOG Foundation
- 67 Alexander Price named assistant professor at Wistar
- 67 Yu "Sunny" Liu named assistant professor at Fox Chase
- 68 Michael G. Tecce named assistant professor at Fox Chase
- 68 City of Hope receives \$32.3M from CIRM
- 69 Baylor, Texas Children's awarded \$7.6M to study disparities for Latino survivors of childhood cancer
- **70** Gracell Bio enters into \$150M private financing deal to expand on CAR T therapies
- **70** DeGregorio Family Foundation awards \$87.500 to Howard University researcher to study immunotherapy in gastric cancer
- **70** Mount Sinai oncologist Krystal Cascetta, 40, and her infant daughter die in Somers, NY, home

FUNDING OPPORTUNITIES

- 71 DKMS 2024 John Hansen Research Grant accepting applications
- THE CLINICAL CANCER LETTER

CLINICAL ROUNDUP

- 73 City of Hope researchers develop a CAR T-cell therapy for advanced ovarian cancer, now in phase I
- 73 Analysis challenges hypothesis that depression and anxiety increase cancer risk
- 74 Researchers identify biological signature that may identify refractory ovarian cancer patients
- 74 Loss of gene releases mutationgenerating protein, rendering cancers resistant to treatment, UTSW researchers find
- 75 Study shows how Epstein-Barr transforms B cells

DRUGS & TARGETS

- 76 FDA grants accelerated approval to Talvey for R/R multiple myeloma
- 77 FDA approves Gavreto for NSCLC with RET gene fusions
- 77 FDA approves companion diagnostic to Ayvakit in gastrointestinal stromal tumors
- 77 FDA accepts Astellas's sNDA for Cresemba in children
- 78 C2i Genomics and Ichilov bring cancer detection and monitoring platform to Israel

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More than 500 bills restricting trans medical care threaten LGBTQ+ people with cancer

By Alexandria Carolan

More than <u>500 legislative proposals</u> in 49 states are targeting trans people—predominantly youths prompting fear among patients, healthcare providers, advocates, and legal experts that trans and gender nonconforming patients will be excluded from care.

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Illustrations by Cyrus Finegan

According to translegislation.com, a legislation tracker, 80 such state bills have been signed into law.

Studies show that transgender and gender nonconforming patients are reluctant to seek cancer care. And now, nearly identically worded pieces of legislation churned out by Alliance Defending Freedom, the Family Research Council, the Liberty Counsel, the American Principles Project, and other extreme right groups, threaten to deepen health disparities among these patients.

At a time when cancer centers are focused on reducing disparities, anti-trans legislation and court rulings are part of a concerted attack on gender-affirming care:

- In April, Missouri passed a <u>law</u> that essentially bans gender-affirming care for all transgender people, regardless of age.
- Florida recently passed a <u>law</u> that bans insurance companies from covering gender-affirming care in adults. The law, which was narrowly <u>blocked</u> by courts, is similar to legislation moving forward in other states.
- In Tennessee, ostensibly in an effort to investigate whether state funds went toward gender-affirming care, the Attorney General's Office successfully obtained, from Vanderbilt University Medical Center, the medical records of patients who are trans.
- 303 Creative LLC. v. Elenis, a recent ruling by the U.S. Supreme Court, allowed creative businesses to discriminate against LGBTQ+ people, a move that experts fear could lead to discrimination against sexual and gender minorities in the healthcare setting (*The Cancer Letter*, July 14, 2023).

"We know that there are delays in care within the LGBTQ community, and these

are likely to worsen that," said Don Dizon, director of the Pelvic Malignancies Program and Hematology-Oncology Outpatient Clinics at Lifespan Cancer Institute, director of medical oncology at Rhode Island Hospital, and founder of the Oncology Sexual Health First Responders Program.

These laws prevent doctors from having open, honest conversations with their patients, Dizon said.

"Take a transgender female who still has a prostate—if no one ever asks her, 'Do you have a prostate?' then there may never have been an opportunity to screen for prostate cancer, and she runs the risk of not only developing it, but not having it caught early," Dizon said to *The Cancer Letter*.

The laws will foster medical mistrust, said NFN Scout, executive director of the National LGBT Cancer Network.

"The biggest danger with all of this legislation is that it is rapidly accelerating the medical mistrust and eroding the basis of that dignified and high-trust relationship you want to have with your provider during your cancer treatment," Scout, who is nonbinary and trans, said to *The Cancer Letter*. "[These laws] have a disproportionately negative impact on people who have a cancer diagnosis," Kivel said. "I think that's important to recognize, and for healthcare providers to be very aware of this impact."

Though the laws primarily target youths, they have also begun affecting care for adults.

"There are definitely already ways in which we are hearing and seeing adults having their ability to access care restricted in ways that are often a ripple effect of the attempts to ban care for minors," Alexander Chen, founding director of the LGBTQ+ Advocacy Clinic at Harvard Law School, where he also teaches gender identity, sexual orientation, and the law, said to *The Cancer Letter*.

It's difficult to quantify the inequity that already beleaguers trans and gender nonconforming patients.

One study published in <u>JAMA Oncology</u> found that patients with breast cancer in sexual and gender minority groups "had delays in diagnosis, declined oncologist-recommended therapies more often, and experienced a 3-fold higher rate of breast cancer recurrence, compared with cisgender heterosexual patients."



Dana Kivel, a nonbinary patient with cancer and professor and director of recreation, parks and tourism administration at California State University, Sacramento, said trans and nonbinary patients with cancer are especially vulnerable.



Kiara St. James, co-founder and executive director of the New York Trans-

gender Advocacy Group, who is also a trans survivor of cancer, said she knows several trans women whose diagnoses of cancer have been delayed because of barriers to care.

She knows one woman of trans experience who noticed a bump on her scrotum, and held off on seeing a doctor.

"She was also embarrassed to tell her doctor about it, because she's like, 'I'm a woman of trans experience, and I'm talking about having a bump in my scrotum," St. James said to *The Cancer Letter.* "That kept her from getting an earlier diagnosis. By the time she got her diagnosis, the cancer had already spread. Now she's dealing with radiation necrosis because it spread to her brain."

Trans patients with cancers that affect their genitals are specifically vulnerable, St. James said.

"It keeps a lot of us from having these real honest conversations with our doctors because we don't really want people to touch us down there, especially if they're not our intimate partners," she said. "It also is a main reason why cancer goes untreated for so long in the trans community—because there's that fear of, I just can't go into the hospital and tell them I'm having these issues in my genital area, because it's going to feel awkward.

"You're going to have all these different strangers coming in and taking a look at your genitalia area, and you're going to feel really violated. That would be a barrier for me as well."

These laws could exacerbate issues that patients who are trans have faced their whole lives, oncologist Dizon said.

"What I fear with these laws enacted people will not be able or not willing to restart gender-affirming hormone therapy," Dizon said. "Which is just tragic because you are essentially in a position where you can impose gender on someone you are supposed to be in a therapeutic relationship with."

Receiving gender-affirming care as a minor reduces adverse health outcomes "because it just meant that they could not be forced to go through the puberty that traumatized them," Scout said to *The Cancer Letter.*

"Their longer term outcomes and health disparities much more resemble the non-trans population than the wildly unstable and beleaguered health issues in the trans community," they said.

Patients who began hormones as minors would not have to face that traumatizing puberty, Scout said.

"They are not going to have nearly the health disparities that my generation has," they said. "But of course, these laws have effectively stopped that from being the reality we can see for many years in the future."

Zul Surani, associate director of Community Outreach & Engagement at Cedars-Sinai Cancer, said anti-LGBTQ+ bills harm patients.

"The Supreme Court [303 Creative LLC. v. Elenis] decision, during a time when a wave of anti-LGBTQ+ bills is sweeping the country, is making a segment of our catchment area communities second-class citizens," he said. "Cancer centers are charged with ensuring equity in cancer prevention, control and care for all Americans, and this is the time when we have to step into our power and organize for inclusion and justice at all levels of our society."

Oncology leaders agree.

"There is evidence that people in general who face more social stress have greater overall illness burden and worse outcomes," Clifford Hudis, CEO of the American Society of Clinical Oncology, said to *The Cancer Letter.* "Any action, even broadly, that erodes anti-discrimination protections, has the potential to exacerbate those existing disparities and worsen a community's access to services."

Karen Knudsen, CEO of the American Cancer Society and its advocacy affiliate, the ACS Cancer Action Network, said ACS will continue to advocate for LGBTQ+ patients.

"We believe that every person, regardless of their race, color, national origin, gender identity, sexual orientation, age or disability deserves to be given equal access to timely, quality, comprehensive health care without discrimination," she said.

"Black trans women also are at risk of cancer"

New York Transgender Advocacy Group's Kiara St. James, a Black trans woman and New York City resident, was treated for stage 2 anal cancer at Mount Sinai.

New York doesn't have any laws that restrict gender-affirming care.

St. James said the side effects she experienced might have prevented someone who is trans from seeking the care that saved her life.

As a result of the chemotherapy, her face grew swollen.

"I didn't even recognize myself when I looked in the mirror," she said. "It made me feel sexless. I just felt like a monster."

St. James's hair, which she associates with her femininity, began to fall out in clumps.

"That was impacting me mentally," she said. "That was definitely traumatic for me."



The change in one's appearance is another barrier for trans people who are going through cancer treatment, she said.

"That's something else that was hard for me to deal with—not feeling attractive, not having my energy level up," she said. "It was very, very traumatic for me, even though I knew the chemo was to help me. I couldn't even look at myself in the mirror without feeling disgusted."

Still, St. James recognizes that people in red states might not receive the same quality of care that she did.

"When I speak to those trans folks who live in those states that are red states the type of care they get depends on if they're full-time employees as opposed to being unemployed," St. James said. "It's dependent on if they're working for a LGBTQ nonprofit organization that makes sure that they get health care provided as part of their insurance."

Insurance coverage can be a barrier anywhere, she said.

"All those are factors when you live in a red state, I should say, when you live outside of New York City," she said. "Even in New York State, even in New York City, actually, I've heard of community members who have been in other hospitals and have not had a good experience."

The most frustrating part of St. James's experience wasn't the side effects of treatment.

"My frustration comes because of my 20-plus years of being an activist, going to conferences—when I'm in these spaces, when they talk about Black trans women, the only thing they really talk about is Black trans women and HIV," she said. "Nobody talks about—'Black trans women also are at risk of cancer."

Along with her organization NYTAG, St. James is coordinating a trans wellness summit that will raise awareness about cancer risk in people who are trans.

"One of the things I want to make sure we're talking about at the trans women summit is not just HIV and PrEP, but cancer, stroke," she said. "All of these things are happening in my community right now, but the main focus is just HIV. The trans wellness summit is going to be to address that."

A new crop of laws

Bills banning gender-affirming care in minors started to appear in state legis-

latures in 2020, said Naomi G. Goldberg, deputy director and LGBTQ Program Director of the Movement Advancement Project (MAP), an independent, nonprofit think tank that <u>tracks anti-trans</u> <u>legislation</u>.

Since then, these laws have expanded in scope, Goldberg said.

"When you look specifically at the kinds of legislation that's being introduced, as well as some of the bills that have actually made it into law, you see a lot of expansion in what they ban," Goldberg said. "Some of the key themes that we see—we saw bills, thankfully, none of which passed, but we saw bills introduced over the last couple of years that expanded the age of the ban."

States like Florida are not alone in aggressive legislation against trans and gender-nonconforming patients. In 2023, nearly three in 10 (29%) bills introduced would ban or restrict care for both transgender children and transgender adults, according to a report published by MAP.

According to <u>MAP</u>, newer bills are more aggressive:

- Oklahoma's HB2177 would effectively ban best practice medical care for all transgender people in the state. The bill bans medical providers from providing such care for minors, and it also bans private insurers from covering this care regardless of age.
- Kentucky's 34-page HB470 seemingly combined almost every anti-transgender healthcare provision into one bill. It would have banned both best practice medical care for transgender youth, and even mental health care and social transition support. The bill banned

mental health providersincluding therapists, social workers, school counselors, and more—from providing "social transition services...including but not limited to affirming the person's name change, pronoun adoption, dress and grooming, and sex-role specific behaviors that vary from those behaviors typically associated with the person's sex." While the bans on social transition and mental health care were removed in committee, the amended bills would still ban medical care for minors and state funds from providing or reimbursing care for minors, among other provisions.

- Florida's S254 would allow the state to take custody of children "at risk of being subjected to" best practice, gender-affirming care, or even to take custody of children if they have a transgender sibling or parent. Even families who do not live in the state but who are visiting for work or perhaps to visit family or Disney World could have their children seized by the state. The bill would also allow the state to void, ignore, or change child custody agreements issued by courts in other states if Florida believes the child in question is "at risk" of receiving medically necessary transgender-related care.
- While not legislation, the unprecedented "emergency" regulation issued by Missouri's unelected attorney general in April 2023 represents the most extreme and comprehensive attack on transgender people's health care yet seen. The regulation effectively bans gender-affirming care for all transgender people regard-

less of age, though the rule will expire in February 2024 and will certainly be challenged in court before then.

Measures that seek to eliminate insurance coverage for trans care are becoming increasingly common, Goldberg said.

"We know for example, that there are states now that have passed laws that explicitly say state Medicaid can't cover [gender-affirming care]," Goldberg said. "That's true in Florida, for example, and in Texas, and in Missouri. We know that there are states that have explicitly said, state employees, even adults—'we're not going to cover this.'

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We need to stand there as beacons saying, we exist, and we are who we are, and we are a testament that you can overcome adversity and you can belong.

9

– Don Dizon

"[These laws] really tie the hands of insurers to continue to provide best practice medical care," Goldberg said. "It also ties the hands of employers, for example, who want to make sure that they are doing the best that they can for their employees and their employees' children."

The wording of these laws is vague and confusing on purpose, Chen said.

"If you read [the Florida law] and you said, 'I thought you marketed this as just being about minors, but now somehow it also affects all insurance. Is it supposed to do that?'" Chen said to *The Cancer Letter.* "The ambiguity is part of the point, because, in fact, that is their goal. They know that it's not politically saleable, and that the majority of Americans do not support that. And so they are trying to say it's only about kids, but they're trying to expand it."

Before introducing laws that ban care for trans youths, the organizations behind these bans had tried popularizing hot-button anti-trans policies that weren't popular—introducing bathroom bans and trans identification card bills.

"They've zeroed in on these micro-targeted areas, but the goal is ultimately to roll back care for everybody," Chen said.

The groups behind these bills are borrowing from methods they used to roll back reproductive rights when *Roe v*. *Wade* was overturned last year (*The Cancer Letter*, July 1, 2022), Chen said.

"Reproductive care access is a good place to look if you want a little bit of a understanding of the playbook of what's happening right now when it comes to LGBTQ+ healthcare, especially transgender care, and what the future of that's going to look like—because the connection is not just thematic, it's also concrete in the sense that the same groups are pivoting," Chen said. "The goal is ultimately to roll back care for everybody."

Though the laws are relatively new, trans people have always faced difficulties accessing gender-affirming care, Chen said.

"People should not make the mistake of thinking that prior to these bans, the majority of transgender people had access to gender-affirming healthcare that was medically necessary, because that is unfortunately not true," he said.

The ideas behind the anti-trans bills proposed in states are not new, Chen said.

"In this country, we have for a long time had a two-tiered system where there are certain kinds of healthcare that everybody just agrees ought to be paid for—there's no question or contest about it—and then there are other kinds of healthcare that our country refuses to pay for, even when healthcare professionals agree that individuals need that care," he said.

Transitioning with a cancer diagnosis

California resident Dana Kivel was diagnosed with a granulosa cell ovarian tumor in 2011, receiving treatment at Kaiser Permanente in Sacramento, CA.

The tumor, which was removed laparoscopically, ruptured during the procedure.

"The doctors did come to tell me the next day, 'We washed the omentum, we're 99% sure we got everything," they said. 'We know we got it."

In 2015, the same year Kivel was scheduled to receive a double mastectomy so they could begin the process of medically transitioning, they doubled over in pain. The tumor, thought to have been removed, had metastasized.

The proposed treatment this time was aggressive surgery. In June 2015 doctors removed several tumors and Kivel's appendix. In fall 2015, Kivel received a bilateral mastectomy.

The tumors returned again in January 2017, this time to their lower intestine. After several surgeries, doctors proposed chemotherapy. Historically, chemotherapy is not an effective treatment for granulosa cell tumor, Kivel said, but they gave it a shot anyway.

Kivel received chemo in the spring and summer of 2017. As of February 2018, the tumor had returned. Subsequently, in 2019, scans showed tumor was growing in size and had spread further.

In early 2020, surgery again appeared to be the best option. A foot-long section of their colon was removed as well as a portion of their omentum.

"I had a CAT scan not long after, and it showed that I had another small tumor," Kivel said.

Nearly out of options, and after having been treated for a blood clot that resulted from one of the surgeries, Kivel had the tumor tested again in 2020. The cancer, which had been estrogen-negative at first, was now estrogen-positive. This opened the door for treatment with estrogen-blocking aromatase inhibitors.

The treatment was effective. The blood marker for their cancer, INHBB, also dropped dramatically.

In the middle of treatment, around 2016 or 2017, Kivel spoke with their primary care doctor about taking hormones to transition.

"Then they talked to an endocrinologist in San Francisco, and basically they reported back to me that there's just not enough research to show that this wouldn't have a negative impact," they said.

They hadn't been involved in the conversation with the endocrinologist, and weren't sure who that doctor was to begin with.

"I couldn't ask, really, for better doctors, but in this particular instance, it felt very disempowering," they said. "It would've been better if my primary care had said, 'Hey, Dana, what if we all got together, you, your gynecological oncologist, and the endocrinologist, and talked about it."

Given that there's a lack of data collection for LGBTQ+ patients with cancer, and given the rarity of Kivel's tumor, there is not much research on the impact of testosterone on people with granulosa cell tumor ovarian cancer.

"Nobody has said, 'Absolutely you can't do it," Kivel said. "I mean, I could do it, but their professional medical recommendation, given the kind of cancer I have and given the unknowns, has said, don't do it.

"But they must know something, because there are plenty of people assigned female at birth who have transitioned, who have had ovarian cancer—and I'm just wondering about the interactions of testosterone in their treatment," they said.

Kivel has recognized that they may not get the chance to take testosterone.

"If I got to a point where this medication resulted in no evidence of disease for five years, I might think about taking that," they said. "But I'm also getting older. I'm 62 now, but it's been so long since there's not been any evidence of disease."

For now, Kivel has come to terms with their gender identity.

"I was grateful that I had the bilateral mastectomy," they said. "I feel like I've had to do a lot of reconciling that this is who I am, this is how I present and, and really take in that I'm going to identify as non-binary."

Having grown up in Tyler, in Smith County, TX, Kivel can empathize with trans and gender nonconforming patients in states that are not welcoming to LGBTQ+ people. "We got threatened, we got harassed," they said. "I know those places. And it's horrible. I mean, it was horrible then. And then I felt like things were getting better, and now I feel like again, we are going backwards, and that is just so painful and hard to see."

Medical mistrust

"If you have a high level of medical mistrust, then when your doctor says, 'You really should do this,' your response may be suspicion instead of adherence," National LGBT Cancer Network's Scout said. "What we fear is that once we finally get enough data to research this across different types of cancer and different types of people—we will find medical mistrust has a huge negative impact in cancer outcomes."

The absence of data on sexual and gender minorities is a problem, too, oncologist Dizon said.

"Even the association between gender-affirming hormone therapy and endocrine-associated cancers is not clear," Dizon said. "I think part of the reason is going back to the biggest part of inequality—we're not even collecting sexual orientation and gender identity data in a standardized way, and so, our understanding of even that topic is limited."

Scout agrees.

"There are a lot of hormone-interactive cancers, and one of our ongoing challenges is that lack of data makes it hard to get research funded, which then means there's no guidance on how to treat those of us who have hormone-interactive cancers," they said.

How should an oncologist respond if a patient decides to medically transition? Anti-trans laws prevent informed decision-making, Dizon said.

"If someone is a trans man and develops ovarian cancer that you test and has androgen receptors on it, you might not only say it's not safe for you to start testosterone," Dizon said. "But biologically your sex at birth was female and we should realize your true sex because that's what, now, the state law requires."

Ideally, even in the face of the unknowns, the decision to go on hormones would be made in partnership between a doctor and patient, Dizon said.

"You can say, 'If you would like to restart testosterone, I don't know about the safety of this, but I'm totally willing to follow you as we move forward," Dizon said.

Basic steps

For all intents and purposes, St. James had a positive treatment experience at Mount Sinai, but there were uncomfortable moments.

Hospitalized for months after her red blood cell counts had grown dangerously low because of radiation, St. James interacted with plenty of doctors outside of her oncology care team.

One doctor asked her whether she was pregnant.

"I'm thinking, obviously he didn't read my medical report," she said. "He was like, 'Well, I just want to tell you the side effects of radiation that you might experience. You might experience the tightening of the vagina wall.' And I'm like, 'Is that a bad thing?"

St. James laughed it off—"Even while I was going through my radiation therapy, I still had a sense of humor."

"It was him and four others—they're all male doctors—and they're kind of with these smirks on their faces, because they don't know how to respond to that," she said. "I have other doctors who say 'I see that you are of trans experience."

When St. James first met her radiation oncologist, she told him about her background.

"'My name is Kiara St. James. I'm a founder, the director of New York Transgender Advocacy Group. I'm a Black woman of trans experience,'" she told him. "That's when he told me he was gay. 'I'm also part of the rainbow family,' that's how he put it.

"Just because someone's part of the rainbow family doesn't mean that they are inclusive of trans people, but he was very, very welcoming. His bedside manner is what you would want somebody to be—compassionate and sympathetic toward you."

Signage can be helpful, too. "There's a picture I remember from years ago and it was like—these people are trans," St. James said. "Some of them looked like, women of trans experience adhering to a binary, men of trans experience adhering to a binary. But there were women of trans experience who didn't look like the other women of trans experience, but they were still trans, likewise for the men."

It's crucial for cancer centers to have information for trans patients on their websites, Scout said. However, an analvsis conducted by the National LGBT Cancer Network in 2022 found that. during Pride Month, almost one third of all NCI-designated cancer center websites lacked any visible indication that they were welcoming of trans patients. And, according to an article published by Scout in the journal Cancer Discovery, more than 25% of NCI-designated cancer centers do not have sexual orientation or gender identity protected in their posted nondiscrimination statements or patient bills of rights.

"If you are not taking basic steps to show us that we're safe, putting something on your website, putting something in your physical environment, doing the data collection in a thoughtful way, having pronouns on your lanyards, respecting pronouns, respecting our real names, those basic steps—then right now, I'm sorry to say that you're contributing to our ongoing health disparities," Scout said.

The LGBT Cancer Advocacy Network offers a training, <u>Welcoming Spaces</u>, that fosters inclusion for LGBTQ+ patients.

For Dizon, being open about his identity helps combat medical mistrust and harm imposed by anti-LGBTQ+ bills.

Recently, he tweeted the following:

"I'm a non-Ivy League trained Pacific Islander, gay and proud, father of three, and a professor of medicine," he wrote.

"Those of us who are comfortable declaring our identities in an intersectional way—we should do that," Dizon said. "We need to stand there as beacons saying, we exist, and we are who we are, and we are a testament that you can overcome adversity and you can belong."

"I'm not saying that every person of the LGBT community in oncology needs to be public about it, but for those of us who are public, we need to provide ourselves as beacons, almost, in this society.

"And if I am here, then it means that we as a community matter. It means that we belong."

St. James has been open with her friends about her cancer treatment. "Trust me, you don't know what you have until you lose it," said St. James, who is now seven months out of treatment. "If you have your health, you're richer than a lot of people who are billionaires and millionaires."

Recently, she and a group of friends attended a conference in New Orleans. St. James brushed off the complaints some friends had about high temperatures in the Pelican State.

"I'm like, 'Baby, just go into the air conditioning, go back into your room," she said. "Like, I'm fine. I'm going to sit on this river boat and I'm going to take in this breeze."

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In this country, we have for a long time had a two-tiered system where there are certain kinds of healthcare that everybody just agrees ought to be paid for there's no question or contest about it—and then there are other kinds of healthcare that our country refuses to pay for, even when healthcare professionals agree that individuals need that care.

– Alexander Chen

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Laszlo spoke with Alexandria Carolan, a reporter with The Cancer Letter, and Paul Goldberg, editor and publisher of The Cancer Letter.





CONVERSATION WITH THE CANCER LETTER

CANCER HISTORY PROJECT

John Laszlo's dual role: (1) Working to cure childhood leukemia, and (2) Writing the authoritative book on it

His father, Daniel Laszlo, did early work on folate antagonists



Professor emeritus, Duke University Medical Center; Retired national vice president for research, American Cancer Society When John Laszlo joined the Acute Leukemia Service at NCI in 1956, the field of oncology was nascent—and the cure for childhood leukemia seemed beyond reach.

"It was a time that these children were just not going to do well. You knew that walking in," Laszlo, 92, professor emeritus at Duke University Medical Center and a retired national vice president for research at the American Cancer Society, said to *The Cancer Letter*. "It was very challenging to deal with children who were bleeding from the nose, who were bleeding from the rectum, who were vomiting—and parents were hovering about, very concerned about their children."

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It's very gratifying to think about all the progress that's been made since those early days of taking care of these tiny children who didn't know what was wrong, why they were there, why their parents were not with them.

Laszlo worked directly with Emil "Tom" Frei, and Emil J Freireich—early researchers and doctors of childhood leukemia at NCI. Their team tried as best they could to help children as young as three. They stopped the bleeding, gave them antibiotics, and packed their noses. "Most of them you couldn't help at that stage of the game," Laszlo said. "It's very gratifying to think about all the progress that's been made since those early days of taking care of these tiny children who didn't know what was wrong, why they were there, why their parents were not with them."

Laszlo's book, "The Cure of Childhood Leukemia: Into the Age of Miracles," is now available for free as a <u>digital download</u> on the Cancer History Project.

The Cure of Childhood Leukemia Into the Age of Miracles

John Laszlo, MD

The Cure of Childhood Leukemia: Into the Age of Miracles by John Laszlo

Available as a PDF or eBook

Based on taped interviews of doctors and scientists whose work led to the cure of childhood leukemia, Laszlo's book is an essential primary source for anyone interested in oncology and its history.

Charles Gordon Zubrod, head of the NCI Division of Cancer Treatment (appointed in 1956), who became NCI's scientific director (1961-1974), described the book as authoritative. "[Laszlo] decided to write up what happened in the cure of leukemia, and I'd suggest you obtain this book from the library," Zubrod said in an oral history conducted by NCI and made available by the Cancer History Project.

In "<u>Stairway of Surprise</u>," Zubrod's previously unpublished memoir made available by the Cancer History Project, he writes:

We chose to try a modified IBM style task force and after obtaining the blessings of Drs. Farber and Ravdin, I began calling together the scientists and physicians whom I thought might give the most help, most were willing to give it a try.

We met every month or two at NCI and the results were spectacular. These are detailed in John Laszlo's book "The Cure of Childhood Leukemia," and I refer the reader to his fine history for the details and for the contribution and for the contributions of the individual members.

In brief, my role as chairman was to prepare meaningful agenda, keep the discussions on target, write the minutes, and then use the considerable budget of NCI to carry out the recommendations.

At that time, deaths (almost one hundred percent) of children with acute leukemia, came from hemorrhage and infection, because both the disease and intensive chemotherapy sharply reduced the protective platelets and white cells.

Dr. Freireich from NCI and George Judson of IBM, and later Dr. Seymour Perry, perfected a blood cell separator that harvested from a single donor, enough platelets to stop bleeding. Meticulous care in stopping hospital bacteria and fungi from causing infections, and massive antibiotics to treat those that occurred, sharply reduced infectious deaths.

These combined improvements permitted the trial of intensive chemotherapy, not previously possible because of early deaths, due to the absence of these protections.

In a conversation with *The Cancer Letter*, Laszlo also focused on discoveries made by his father, Daniel Laszlo, an oncology pioneer who conducted basic research on folate antagonists.

In 1937, Laszlo's family fled Vienna as Jewish refugees. His mother, a psychiatrist who trained with Anna Freud, discovered she had breast cancer on the <u>SS</u> <u>Île de France</u> while the family journeyed to America. She died two years later.

His father, Daniel Laszlo, a physician who specialized in cardiovascular physiology, found a job in cancer research at Mount Sinai Hospital.

Daniel Laszlo studied folate antagonists in mice—though folate antagonists hadn't been characterized yet. One <u>study</u> showed regressions of spontaneous breast cancer in 38 of 89 mice (43%) when treated with folic acid.

"They were working on derivatives of that molecule and were finding some anti-cancer effects in mice," Laszlo said. "I would go in on weekends and help to change the cages, put the mice in fresh cages, feed them, change the water bottles, and do that kind of thing as a child—in the laboratories at Mount Sinai Hospital."

The researchers had discovered what seemed to be a vitamin derivative that would inhibit the growth of cancer, "something that they were surprised at," Laszlo said. Daniel Laszlo's team took the information about folates to experts at Memorial Sloan Kettering Cancer Center.

"They were very interested in it, but didn't quite believe it, so they asked Dr. Sidney Farber from Harvard to comment on it," Laszlo said.

Farber's response?

"He pooh-poohed the whole idea," Laszlo said. "And then took it over himself."

Daniel Laszlo's boss, Richard Lewisohn, a surgeon and director of the laboratory, approached Laszlo one day with a proposal.

Babe Ruth had been admitted to Mount Sinai Hospital with symptoms of throat cancer (later determined to be naso-pharyngeal cancer), and Lewisohn was planning to treat Ruth with drugs that had been shown to reduce cancer in mice. Daniel Laszlo worried about the ethical implications of treating someone with drugs that had not been tested in humans.

"My father said he couldn't do that because it had never been given to patients," Laszlo said. "They didn't know what the dose was, how much to give, how long to give it, and so on. However, the hospital director wouldn't take no for an answer, even though my father thought it was unethical to do that."

And so, Babe Ruth received the drug teropterin, according to <u>The New York</u> <u>Times</u>—resulting in a brief remission. The drug was closely related to methotrexate, which became standard of care for certain cancers.

"The tumor disappeared, and Ruth had come in miserable shape, when he went home feeling just fine, and he stayed in remission for a time," Laszlo said.

"My father was very unhappy about being ordered to do something that he felt was unethical, and so he chose to leave Mount Sinai Hospital and was offered an opportunity...to start a new program at Montefiore Hospital in New York, where they had a lot of patients sitting around, taking up hospital beds, and they weren't doing much for these people," he said.

In a 1998 news story, a reporter at *The New York Times*, Lawrence K. Altman, connects the dots in the development of chemotherapy:

[Ruth] joined the often-unaware group of anonymous patients who ushered in the modern era of anti-cancer treatment, which grew out of American research into chemical warfare agents during World War II. In 1942, researchers at Yale University tested one such agent, nitrogen mustard, in a human for the first time. But Government secrecy restrictions prevented publication until 1946, after several hundred patients had been treated.

At the time, a team headed by Dr. Richard Lewisohn, a surgeon at Mount Sinai Hospital in New York City, was experimenting with an anti-cancer drug, teropterin, in mice. There were different teropterins, all extracted from brewers' yeast, and their effects on mice varied widely with the preparation.

After leaving Mount Sinai, the elder Laszlo started the Neoplastic Disease Division at Montefiore Hospital.

"He took many of these patients and sent them home, because many of them were locals from the Bronx—they could go home and be taken care of at home," he said. "I occasionally joined my father in making visits to these brownstone houses, and we would walk up two or three or four flights of stairs to see a patient who'd previously occupied a hospital bed, but was now being taken care of at home, and administer what medicine they needed." Laszlo spoke with Alexandria Carolan, a reporter with *The Cancer Letter*, and Paul Goldberg, editor and publisher of *The Cancer Letter*.





This conversation is also available on the Cancer History Project <u>podcast</u>, and as a <u>video</u>.

Paul Goldberg: Thank you very much for agreeing to talk with us, Dr. Laszlo. We were hoping you would walk us through your early career, and NCI, and childhood leukemia—and we'll take it from there. I should ask you about your parents, their decision to come to America.

John Laszlo: Well, I graduated from Columbia College, went to Harvard Medical School, and then took a rotating internship at the University of Chicago, because, although I knew I wanted to go into internal medicine, I needed to know more about surgery and how patients did after surgery, and the preoperative preparations. For that reason, I took a rotating internship.

After my internship, I went immediately to the National Cancer Institute for my next assignment, which was a two-year assignment in the Public Health Service at the National Cancer Institute.

And after being on the emergency room at the University of Chicago for two days in a row, I drove from there to New York to see my family, and then immediately down to Washington, DC, where I arrived a little bit rattled, not knowing my way around the city, not having a place to stay just yet.

However, I had to start right away at the National Cancer Institute.

I was given my assignment, which was to work on the Acute Leukemia Service. Here I am, having worked with adult patients for years prior, and not having worked with children in a setting like they had at the Cancer Institute.

It was a real challenge, and what was especially challenging was a ward full of children with acute leukemia who were bleeding at the time, who had high fevers, who had headaches, and were generally very uncomfortable.

I was given some orientation by Dr. [Emil]] Freireich and Dr. [Emil "Tom"] Frei, and then left to my own devices on the children's leukemia ward.

That was pretty challenging thing for a pretty green doctor who had just finished a rotating internship.

I dove right in. And it was very challenging to deal with children who were bleeding from the nose, who were bleeding from the rectum, who were vomiting—and parents were hovering about, very concerned about their children. We did what we could by stopping the bleeding in the nose, packing the nose, giving antibiotics to children with high fevers, and so on, as best we could. But it was a time that these children were just not going to do well. You knew that walking in.

You could help some of them, but most of them you couldn't help at that stage of the game. So, as I look back on it so many years later and think about how 80 plus percent, maybe higher, maybe closer to 90% of these children live a long time after their treatment, presumably cured, it's very gratifying to think about all the progress that's been made since those early days of taking care of these tiny children who didn't know what was wrong, why they were there, why their parents were not with them.

It was very challenging.

PG: Well, I wonder if we could go back a little bit to—not a little bit—a lot, to your parents—because your father did the folate studies and worked with some of the treatments that were used in childhood leukemia.

JL: That's right.

PG: I've read your book many times. You were born in 1931. Where? In Vienna?

JL: Well, actually, I was born in Cologne, because my father—although he studied in Vienna and trained in Vienna was on a postdoctoral fellowship in cardiovascular physiology in Cologne. So, in 1931, I was dropped off there, and lived there for the first two years of my life before my parents moved back to Vienna. I left Vienna in 1938—just in time with my parents, and came to the United States, where my father took a job in cancer research at Mount Sinai Hospital in New York City, where we lived for a period of time.

He was asked to do cancer research, which he had not done before, but he was good in chemistry, and he worked with some wonderful chemists, I believe, at Lederle who were working on folate derivatives, although folic acid had yet to be officially discovered at that time.

But they were working on derivatives of that molecule and were finding some anti-cancer effects in mice. I would go in on weekends and help to change the cages, put the mice in fresh cages, feed them, change the water bottles, and do that kind of thing as a child—in the laboratories at Mount Sinai Hospital.

By the way, the same laboratory area where my father originally worked with mice became Dr. James Holland's offices years later, when he became director of cancer at Mount Sinai Hospital.

PG: Oh, that's fascinating. But your family decided to leave Vienna because—were they anti-Nazi? Were they Jewish? What's the reason?

JL: No, as Jews, we were not welcome to stay.

PG: I didn't realize you're Jewish, because "Laszlo," is a Hungarian name.

JL: Right. All Laszlos are Hungarian, don't let them tell you any differently. But yes, I was kicked out of school because I was Jewish, and it was a real struggle for my parents to get the necessary papers to immigrate to the United States.

The U.S. State Department was very, very tough in those days—extremely exclusionary—and a lot of people who would've liked to have come were unable to do so. You had to have promise of a job in the United States in order to get papers to come, and then you had to have a backup family who would say, "Yes, we'll take care of Laszlos, or whoever, in case they lose their job."

Imagine trying to work from a foreign country, not knowing the language, to get a job, and yet to find another family who would vouch for you and take you in in case of emergency. All of that had to be done before we were able to come to the United States.

PG: What was the passage like?

JL: Well, the passage was interesting, everything was fine until we got to Manhattan, and then the storm moved in. The biggest hurricane ever to hit New York City prior to that time was on, I think it was September [21], 1938.

There was a famous hurricane that shut down the city, shut down everything in New York. We were not able to land at Ellis Island because the seas were so rough. We were taken in by tugboats and put into a slip in Manhattan.

I had to be carried off the gangplank, with a sailor on either arm who carried me across. And at that time, I asked my parents, "Why would you come to a place like this, with a storm like this?" And, of course, the next morning when I awoke and went downstairs, it was a beautiful sunny day, as though nothing had ever happened.

AC: Where in New York did your family end up?

JL: We were living with this family that agreed to take us in. They were on the Lower East Side, I believe about 12th Street and Second Avenue, and we had a room or so in their apartment, and that's where we lived probably for two or three weeks until my father was able to locate other arrangements on East 97th Street.

AC: And around that time is when he got involved in cancer research?

JL: Well, my father immediately went into his job at Mount Sinai. I was only seven years old at the time that we came to the United States.

PG: So, he was a clinician in Vienna and then, suddenly, he's in the basement, working with mice in a different profession?

JL: Absolutely.

But he was incredibly clever and talented, and he made so many contributions to medicine and having found these nutritional aspects of cancer, and this particular kind of substance, which seemed to be a vitamin derivative that would inhibit the growth of cancer, was something that they were very surprised at.

They took the information to other experts at Memorial Sloan Kettering Hospital. They were very interested in it, but didn't quite believe it, so they asked <u>Dr. Sidney Farber</u> from Harvard to comment on it.

He pooh-poohed the whole idea and then took it over himself.

PG: Nice. So, were you expected to become a physician? How did that work?

JL: Well, I didn't have any expectation to become a physician at that point. I was interested in agricultural science and thought maybe I'd make a career in that. But, somewhere along the way, I guess I was already in college at Columbia, that I decided to go into pre-med, and made a career of it.

PG: Where did you go to medical school? Yale, you said?

JL: Harvard.

PG: Harvard. This would be very much of a quota situation then. So that must have been very interesting, the antisemitism, and the quotas.

JL: Well, it was helped by the fact that I also applied to Yale, and they sent me a telegram that said that they would accept me, but I had to answer in 10 days that I wish to attend Yale.

And so, I contacted Harvard and said, "I'd like a rapid answer as to whether you'll take me or not," and they said, "No, we can't do that," but then they called me back and said, "Well, we will take you."

So, the knowledge that Yale was pressing for an answer may have influenced Harvard, I don't know.

PG: But Yale, too, famously, had the same quotas; right?

JL: I would presume so.

PG: It was like 10 to 15%, and medical school was even more rigid. That's less, right? That must have been quite a time for you to do this.

JL: As a student, you never know what's on the other side of that curtain that's called the admitting committee.

AC: I'm curious, when did you first find that you were drawn to oncology?

JL: When I was an intern, I didn't know what I was going to do the year after I finished my internship, I didn't think I wanted to stay at the University of Chicago.

And then a former classmate of mine had called me and said, "There's this thing called the National Institutes of Health, and that counts as time in the service, because you're a member of the Public Health Service, and it's a twovear position, and they have a number of institutes at the National Institutes of Health." He said, "I'm going into tropical medicine, I want to study tropical medicine. How about you?" And I said, "Well, I'd like to study internal medicine, I'm sort of interested in cardiology." He said, "Well, go and apply." I contacted the Heart Institute and they were full for the next year-so what else?

And there was a Cancer Institute and I decided to try that. The nice thing about working in the field of oncology—the word, "Oncology," hadn't been invented yet, by the way—my father had, by this time moved to Montefiore Hospital and had started a service called, "Neoplastic diseases," which was the first ward in a general hospital devoted to patients with cancer.

Anyhow, I applied to the Cancer Institute at the National Institutes of Health, and had an opportunity to speak with <u>Dr. [Charles Gordon] Zubrod</u>, and he said they only had one position left for the following year that I could possibly apply for.

He knew that my father, at this time, was working on breast cancer and anti-hormone therapy, and he had met my father. So, I guess, he liked my credentials and decided to take a gamble on me.

Somehow in the middle of my internship I ended up getting the last position at the National Cancer Institute for July 1.

PG: Wow. Can we go back a little bit? UChicago, which, of course, did not play the quotas game at all... didn't care. <u>Charlie Huggins</u> was there with—

JL: Yes.

PG: He got the Nobel Prize for [his research into] hormones.

JL: Yeah, he had just gotten the Nobel Prize a year or two earlier, and I had an opportunity to visit with him in his lab. What an interesting fellow he was. You walk into his lab and he said, "Look, Laszlo, there's a Nobel Prize here."

He was not a modest man, shall we say, but he was very accomplished, obviously.

I learned a bit from him, although I was not in the laboratory, I was an intern seeing patients. I was inspired by him and also a lot of good doctors who were interested in oncology. I can't remember them all. [Leon O.] Jacobson was the head of the cancer program there. He had done a lot of work on radiation therapy.

PG: John Ultmann was there.

JL: Yes. John Ultmann, I didn't know there. He might have been a year or so behind me. But you're right, he was there.

PG: He went there maybe later because he was in New York for a while. And so, your father; can we go back to him again? He becomes a clinician again in the United States after the war; right?

JL: Yes. He had done some work on the folate antagonists, which he didn't know what folate antagonist exactly was, because it hadn't been characterized just at that time, it would be in a year or so. At any rate, the work that they did on experimental cancer in mice led to an interesting event. A man was admitted to Mount Sinai Hospital with—I believe it was laryngeal cancer.

AC: Babe Ruth?

JL: Babe Ruth. Thank you. It was Babe Ruth. He was admitted to Mount Sinai Hospital in bad shape. He had been there before, and the hospital director wanted to do something for this famous patient, and they went to the laboratory director who was my father's boss and said, "I hear you've got some interesting chemicals that might be useful."

Dr. Richard Lewisohn, who was the director of the laboratory, was a surgeon. He said, "Well, Laszlo has these drugs that are doing some things in animals."

The director called my father in and said, "I want you to give this medicine to Mr. Ruth," and my father said he couldn't do that because it had never been given to patients. They didn't know what the dose was, how much to give, how long to give it, and so on. However, the hospital director wouldn't take no for an answer, even though my father thought it was unethical to do that.

So, he was ordered to give this to Babe Ruth, who had a brilliant remission. The tumor disappeared, and Ruth had come in miserable shape, when he went home feeling just fine, and he stayed in remission for a time.

At any rate, without divulging his name, he was the subject of a paper given to the *Medical Journal of North America*—I have to think of the name of it—and there was a meeting in Chicago of a society every year, and this paper was included there, never naming the patient himself.

My father was very unhappy about being ordered to do something that he felt was unethical, and so he chose to leave Mount Sinai Hospital and was offered an opportunity—I don't know how this came about really—to start a new program at Montefiore Hospital in New York, where they had a lot of patients sitting around, taking up hospital beds, and they weren't doing much for these people.

They [had] advanced prostate cancer, but they had nothing to do with them, to do for them, so they were lounging there. So, my father went to Montefiore Hospital and started this program for patients with advanced cancer and called it the Neoplastic Disease Division.

And he did something really quite remarkable there, he took many of these patients and sent them home, because many of them were locals from the Bronx—they could go home and be taken care of at home. And he developed his residents to make house calls on them at least on a weekly basis, and he himself made house calls, and I occasionally joined my father in making visits to these brownstone houses, and we would walk up two or three or four flights of stairs to see a patient who'd previously occupied a hospital bed, but was now being taken care of at home, and administer what medicine they needed and so forth.

That's a whole other story of the start of the home health program, forgotten what it was called, but Dr. <u>Martin Cherkasky</u>, who was hospital director, was very active in forming this new program based at Montefiore Hospital.

So, he then mobilized, as a consequence of rearranging the bedding situation at the hospital, for patients who were not getting active treatment, but could be treated at home.

He then was able to get patients in there that they were actively treating, and he started intensive research on calcium metabolism, started a program with radioactive iodine for thyroid cancer, quite a number of things that were started at Montefiore Hospital.

AC: And what was the language that your family spoke at home?

JL: Well, there were three of us, my father, my grandmother, and I.

My mother had died shortly after coming to the United States. She discovered that she had breast cancer while we were on board the <u>SS Île de France</u>, coming to the United States, and she succumbed about two years later.

There were three of us. My grandmother only spoke German, but my father really only wanted to speak English, and he spoke it quite well. My mother was the linguist in the family, and she was teaching my father how to speak English while we were on the ship coming to the United States, so she started him off.

AC: Amazing.

JL: She was a psychiatrist who trained with Anna Freud.

PG: So, it's just an amazing family.

JL: And she was studying for medical boards while we were on a ship to the United States, preparing to take a medical examination, which she needed to have, which she passed. Of course, she was never able to practice.

PG: When did she die?

JL: I think, 1940. Two years after we arrived.

AC: Do you remember what her treatment, if any, looked like at that time?

JL: I don't think she received anything other than palliative care. I don't know. I was sort of pushed out, I was sent to a boarding school to study out of town. My father was busy with his job, with taking care of my mother, and with trying to get his parents out of Hungary.

He was very busy, and I would've been in the way, so they got me off to a school out of town, which did not work well for me. I was then boarded with old friends of my father's from Vienna; one was a well-known pathologist, and another was a neurosurgeon who really did some pioneering work in the autonomic nervous system. Anyway, they each took me for some months while my mother was dying. PG: Meanwhile, your father is playing with hormones, trying to figure out what role they play in cancer. Was it breast cancer? Was he trying to cure breast cancer?

JL: He was doing studies on breast cancer.

PG: Wow.

JL: He did some of the early work on treatment of breast cancer with estrogens, <u>B.J. Kennedy</u>, and my father published some papers.

PG: Wow. I knew BJ Kennedy, too... Thinking back, a lot of kids, young doctors were being told not to go into oncology, but oncology was all around you, it looks like.

JL: Yes, that's true.

PG: It's, like, everywhere.

JL: That's true. And when I was at the National Cancer Institute, I was confronted by these naysayers very frequently, "You're wasting your time, Laszlo."

PG: At NIH, or was it at UChicago? Did they tell you to just go into cardiology, like all the other smart people?

JL: They were too busy doing their own things to bother about me, what I decided to do.

They were supportive of whatever I wanted. They really were largely surgi-

cally oriented, and they wanted me to stay and go into surgery, but I was not interested in that specialty of medicine, except to learn about what they can do for patients and how to prepare patients for surgery, and how to take care of them postoperatively.

And for that, they were superb as far as I was concerned. But I wasn't interested in learning how to tie knots and do surgical procedures.

AC: At the beginning of our call, you painted a pretty dismal picture of what childhood leukemia looked like at the time. Why is it, do you think, that you wanted to go into that?

JL: Well, I didn't particularly choose to go into that.

I chose to go to the National Cancer Institute because I didn't get into the Heart Institute, and I was assigned to the leukemia ward, and a very interesting thing happened while I was on the leukemia ward.

We had a lecture from <u>Dr. Dean Burk</u>, who was a PhD at the National Cancer Institute, and a kind of a contrarian—so, a superb scientist. He would go every summer to work with Farber in Germany, and they worked on both cancer metabolism and photosynthesis, which were their two interests.

And then he would come back for the rest of the year at the National Cancer Institute. He was a basic scientist.

He came to give a lecture one time to our group at the NCI at the invitation of Dr. Zubrod. He talked about how all cancer cells have this unique feature of aerobic metabolism, which distinguishes them from normal cells, which don't do that kind of thing to raise their ATP. So, I asked Dr. Burk afterwards if I could meet with him, and I said, "Can we test this out on human cells, leukemic cells?"

He said, "Well, I don't know how to do that."

I said, "Well, I can get the leukemic cells if you will help me with the technological aspect," and he said, "Yes, if you'll do the work, I'll help you."

So, what I would do is, when I had patients who had high blood counts with leukemic cells, I would take a large sample down to Building 6 over to Building 10, and I would go down the hill to his lab.

And then we would separate out the white cells from the red cells and concentrate the cells away from some of the plasma, and then we would incubate those cells the way he would incubate mouse cancer cells in Warburg flasks, on a shaking water bath, if you have ever seen those.

These would be little flasks, and they would be in a large vat of water, and then we would test how much oxygen the cells were consuming, how much CO2 they were producing, and we could calculate how much aerobic glycolysis they were consuming, and how much anaerobic glycolysis they were making.

You can either make glucose in the presence of oxygen, which is aerobic, or in absence of oxygen, which is anaerobic glycolysis.

And I began to get some things that were really quite interesting—some of which followed the Warburg Hypothesis, but some of which were contrary to Warburg's Hypothesis.

It turns out that myelocytes—they got lots of their ATP from anaerobic glycolysis, but lymphocytes did not—they breathe like normal cells. So, I was able to compare the metabolism of normal leukocytes to leukemic leukocytes, work that was partially done at the NCI, and partly done after I finished at NCI, and went on to Duke.

But we then turned to studying how drugs influence cell metabolism. While I was taking care of patients, I was also working in the laboratory with Dr. Burk.

And as my rotations through the National Cancer Institute continued, and I was assigned a different ward, I still maintained contact with the leukemic service and was able to get samples for our work in the laboratory.

AC: While you started all of this research, would you ever have conversations with your father about it? What was that like?

JL: I would have conversations with him about it. He was very interested in it. In fact, he had done a little bit of work in Vienna with a Warburg apparatus and cancer cells, so he was very interested in what I was doing.

But I was full-time to help the Cancer Institute. I didn't spend much time in New York to actually see him.

He was very busy in New York, taking care of his new division.

PG: Going back to, maybe going back to your arrival to NCI. The year is what, 1956?

JL: It would've been 1957.

PG: Events in Hungary had just taken place, so it's a pretty scary time, too.

JL: Yeah.

PG: A doctor's draft is still ongoing. You're the first of the Yellow Berets, right? You would be considered that?

JL: I didn't care for the terminology, but yes.

PG: Well, people said this very proudly. They did like it, calling themselves Yellow Berets.

JL: I thought it was a most wonderful opportunity to get started in my life's career and at the same time meet my service obligations. It was just a wonderful, wonderful thing.

PG: So, you wander in. I think, if I'm not wrong, Zubrod first joined NCI in 1956, as well. He was there for about a year trying to figure out how to spend some money.

JL: Yeah.

PG: Freireich had just come in and Zubrod gave him an order to cure childhood leukemia.

JL: That's right.

PG: So, what was your meeting with Zubrod like?

JL: Well, I really cared for the man. He was just a wonderful gentleman. A solid scientific background in clinical research and knew what he wanted and what he expected of people—how to conduct ethical research, taking care not to abuse patients in any way during the course of clinical studies on them. Tom Frei came before Freireich. That is a very interesting story, which I know you know, since you read the book, how they met. Freireich thinks he's going into his office, and sees the office where he's going—and saw the name Emil Frei III.

He thought they'd misspelled his name and got it all wrong. It was really Emil Freireich, no period. Emil J Freireich. Yeah, that was a very interesting story.

Zubrod was the master architect of this relatively small team of people. They weren't only working on leukemia. There were others who were working on other things, as well. The real characters were Frei and Freireich, with Freireich being really two standard deviations beyond the mean.

PG: But getting back still to Zubrod. Here's a guy who went to Columbia, who practiced, well, before anything he was a young doctor working in the malaria program.

JL: Yes.

PG: Did you talk about that? Because, I mean, obviously he's fascinated by ethics of research, and he had done stuff that predates any ethical construct and probably couldn't have been done again, and shouldn't have been done again.

JL: I don't recall discussing malaria with Zubrod. I know he discussed his work on pneumococcal pneumonia at Hopkins and some of the research trials that he set up there. He used that framework for doing some of the studies at NCI with double blind studies and insisting on careful controls.

He imbued Frei and Freireich, although Freireich didn't always get it, in quite the way in which Zubrod meant. They were a very interesting trio, those people. And Jim Holland had preceded Frei, and really started the leukemia program at the NCI. But he left after a year or so, going back to Columbia.

PG: But can we get back to Zubrod? Because when I think about that guy and his place in history, if he were not where he was, we would not be right now where we are, I think.

Because here's a guy who understood how to do clinical research. He understood the methodology of research. He understood how trials should be structured. He understood ethics of the thing because he had done things both ways, ethically and not ethically, or what would be considered ethical right now. What was it like to work with him?

Because when you had those patients you were taking care of, those kids who are dying, you had to get parents to say, "Yeah, try it."

JL: Yes.

PG: What was that like? How did he see all of this?

JL: It was very difficult, because you can't be involved in the care of a threeyear-old child who's bleeding from all orifices without being emotionally involved yourself. Doctors tell themselves that they can leave all this stuff behind them when they go home at night.

I never could do that. I always took those problems home with me, which wasn't necessarily healthy. But I got support from Tom Frei. I rarely had to go to Gordon Zubrod unless there was a problem with Frei or Freireich.

Freireich was the bigger problem, because he wasn't quite as imbued with some of the—maybe not fair to say this because it's a different time—but he wasn't quite as imbued with the ethics of what you should and shouldn't do to patients.

He took the point of view, "If they're going to die, we've got to do something now. We can't just sit around and pretend that everything's going to be alright."

So, he was all gung-ho to try drugs that—it was like my father, not wanting to treat Babe Ruth without having studied the drug in normal subjects to find out what the dosages should be.

I think at the time that I was on the leukemia service, Freireich was more of my boss than Frei. I would go back to Frei when I had problems with Freireich, and eventually I felt I could go to Zubrod, but he didn't want to overrule his young guys, Frei and Freireich, unless there was a real moral dilemma, which...

PG: It happened a lot with Freireich?

JL: We tried to keep that to a minimum, I would say. Tried to solve the problems ourselves before they got to that stage.

Oftentimes, Freireich would give ground on it.

He paid good attention to Tom Frei, who was a much more level-headed thinker about patient problems of this kind.

Freireich was a doer. When he saw the pathway, he wanted to go through that door, whether it was wide open or not. And he wanted to go through that door. AC: How would Frei sort of temper that in Freireich? How would they interact?

JL: They would interact every day. They would sit down and talk for hours at the end of the day and sort of plan what's the next step. Get a feel for how the patients were doing. There was a lot of give and take between those two people, and then we participated.

I was one of a number of young doctors like myself. In fact, quite a number of my Harvard medical classmates ended up at the National Cancer Institute at about the same time. <u>David Nathan</u> was with me. David Nathan eventually became head of the Farber Center. He was one.

Tom Waldmann, who you may not have known, was still at NCI until a few years ago when he died, doing brilliant basic science work there. There were a few others. There were a lot of good, young people to interact with Freireich and Frei. They were young themselves. They were only a year or so more advanced than we were in terms of clinical training. Everybody was pretty new at this stuff.

Compared to [William] Dameshek, or some of the other greats in American hematology, who had years of experience taking care of patients with leukemia, we were beginners. They were a bit contemptuous of us because they had never seen anybody do well taking care of patients with leukemia. They were some of our harshest critics, I would say.

They didn't think much of folks who were inclined to spend time taking care of patients with leukemia. The man who was head of hematology/oncology at the Army Institute in Washington—he was very opposed to what we were doing. PG: Freireich, did he ever tell you about his personal history? Where he's from, all of this? All of the things that are actually, largely, in this book? Did he tell you those stories in real time or much later?

JL: It wasn't until I decided to look back on this period and write about it that I really sat down with him to talk about his personal development in medicine. And a strange journey it was for him having come from nothing, really, absolutely nothing—no father, a mother who couldn't speak the language, didn't know anything about education. They were virtually penniless.

PG: Did you even know that Freireich was Jewish, or did that never even come up?

JL: It never even came up.

PG: So, you had no idea?

JL: No.

PG: That's really fascinating. Until you sat down with him and the tape recorder?

JL: Right. I didn't know their personal lives and I was very interested in Freireich's journey. I mean, when he writes, "I learned to be a mean person when I was an intern at Cook County Hospital."

He describes how the nurses had a special place in the back of the ward where they put patients who they thought weren't going to make it. They didn't even take the doctors to make rounds on them. They just let them die. I didn't know that story at all until afterwards.

Or Tom Frei's interesting story about his family being in the glass-making business.

PG: Church glass. They're still in business.

JL: Is that right?

PG: Yeah. I think the company still exists.

JL: Well, it was an interesting background. And Zubrod in public health being assigned to a general hospital with 1,000 patients—1,000 patients! And he was, like, the only doctor.

PG: It's just amazing.

JL: He ended up learning something along the way from every experience that he had. So did these other people, as well.

Some of the basic scientists and their background—<u>Howard Skipper</u> in Birmingham, Alabama. How he supported himself as a football player. He is a very modest guy. He said, "I got hit in the head too many times to remember certain things."

And <u>Gertrude Elion</u> coming up very poor without much encouragement to go into chemistry. She ended up working for a bakery for a period of time to support herself, and then being picked up by George Hitchings.

I worked very, very closely with Hitchings and Elion when I was at Duke and they were at Burroughs Wellcome. We encouraged them to move from the New York area. They actually brought

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or sign-up at: https://cancerletter. com/news-alerts/ Burroughs Wellcome down to the Research Triangle Park.

They were being crowded in New York and they needed to move somewhere. Dr. [Wayne] Rundles, who was my boss at Duke, and I, worked on Hitchings showing them the advantages of moving into the Research Triangle area and having any amount of space that they needed. It was a great opportunity, and they made the most of it.

PG: That's amazing.

JL: It was a great opportunity for us to work with them, too.

PG: How did you decide to write this book? Because it's the classic of this field. It's required reading.

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We did what we could by stopping the bleeding in the nose, packing the nose, giving antibiotics to children with high fevers, and so on, as best we could. But it was a time that these children were just not going to do well. You knew that walking in. JL: Well, I don't know. I got to a certain point. I had more time away from patients and was able to look back. I had the opportunity to start the book by interviewing some... I took the opportunity to meet Joe Burchenal and various others, Howard Skipper, and others in my travels when I joined the cancer society. I had the opportunity to become a temporary research fellow with the Rockefeller Association.

My wife and I had something like six or eight weeks at their place.

When it first came out, I would get calls from parents who had children with leukemia and they would write and tell me that this was very helpful to them.

PG: Well, this is a really great book. It was helpful to anybody who is interested in the history of cancer—it's the book.

JL: Well, it's a great subject. I think you can see where I was coming from. I wrote it in the hope that young people would see that this was a career that they could do because the background of the scientists was so ordinary.

It wasn't that their parents had been great scientists and, therefore, they were destined to become great scientists themselves.

They came from different aspects of the world, and they were driven by their own ambitions and talent. So, I think anybody could do it if they had the ambition and the talent. I was hoping to inspire young people and sorry that didn't sell more widely than it did.

But they did their best with it, I think.

Edna (Eti) Cukierman, PhD, and Igor Astsaturov, MD, PhD Marvin & Concetta Greenberg Pancreatic Cancer Institute

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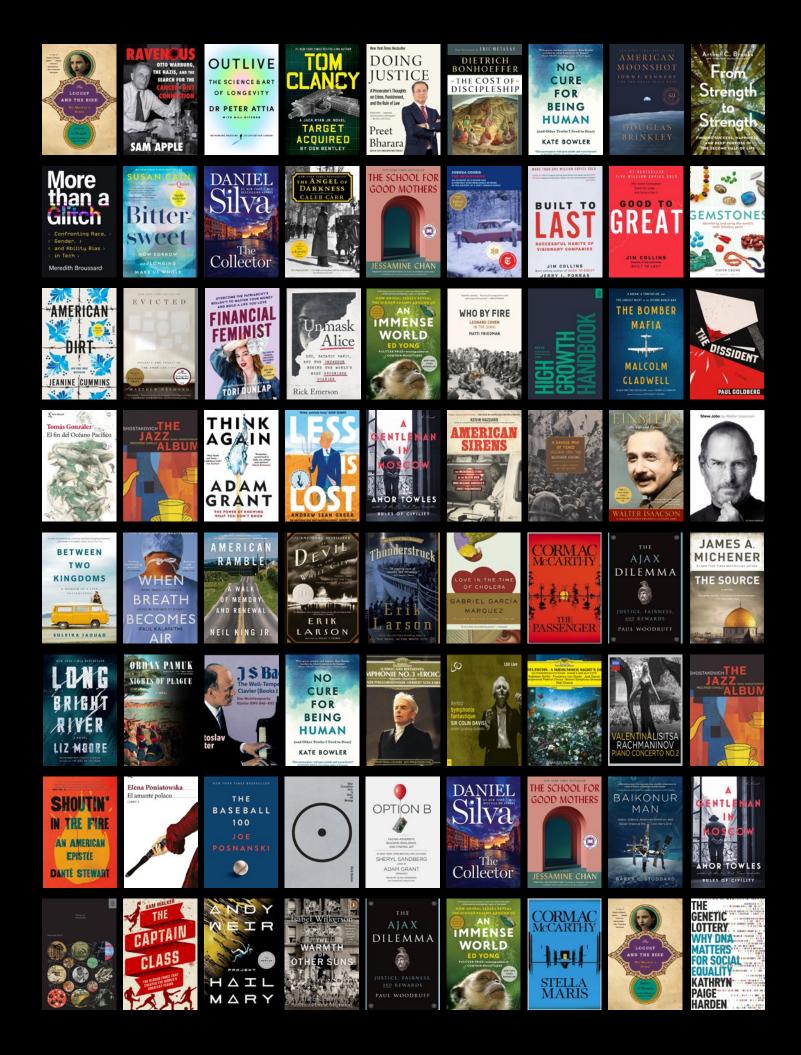
or more than 100 years, researchers at Fox Chase Cancer Center have been making groundbreaking discoveries that deliver better cancer care. With the expertise of scientists and clinicians like Dr. Edna Cukierman and Dr. Igor Astsaturov, we are driving the mission to improve human health.

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BOOK REVIEW

What are you reading in 2023?

By Katie Goldberg

Every August since 2020, *The Cancer Letter* has asked a diverse panel of clinicians, basic scientists, early-career faculty, patient advocates, government officials, and regulators to tell us what they are reading.

With over 30 contributors per year and now hundreds of book recommendations, some trends have emerged.

Take a look back at the summer reading lists of years past:

- **2020:** "What the hell is going on?"
- **2021:** "How can we be better?"
- **2022:** The year of the thriller

Will any trends emerge in 2023?

With 74 books recommended—33 works of nonfiction, 30 novels, 10 memoirs, and 1 play—analysis can get tricky.

Of the nonfiction books, 14 are scientific, 13 are about equity and social justice, 9 are historical, 9 are about leadership, 8 are about personal growth, and 2 are about sports. Karen Knudsen, chief executive officer of the American Cancer Society and the American Cancer Society Cancer Action Network, recommended "The Captain Class: A New Theory of Leadership" by Sam Walker—a book about both leadership and sports.

"Although, as a die-hard Eagles fan, I find it hard to look at the picture of Tom Brady on the front cover, 'The Captain Class' is an interesting primer on leadership," Knudsen said. "If you are a sports fan and find value in understanding different types of leadership strategy, this book is for you!"

Knudsen offers one possible future revision. "In my opinion, it needed a section on Super Bowl 52, covering the leadership styles of Eagles Nick Foles and Malcolm Jenkins… Just saying…"

Knudsen is also rereading "Othello:"

"I hadn't read 'Othello' in a long while, and enjoyed diving again into this powerful tragedy, which effectively demonstrates the devastating impact of racism, manipulation, and jealousy. No matter how many times I read it, I still find myself hoping for Othello to see through the trap laid for him, but alas he 'loved not wisely, but too well."

Notably, this year, three oncology-affiliated authors are featured on the reading list.

Frederick Appelbaum, executive vice president of Fred Hutchinson Cancer Center, is the first reading list contributor to have previously appeared on the reading list as an author. His book, "Living Medicine: Don Thomas, Marrow Transplantation, and the Cell Therapy Revolution," was published this year. It was recommended last year by Thomas Lynch, president and director of Fred Hutch, while he was reading the final draft.

An excerpt of this book is <u>available in</u> the Cancer History Project, alongside a conversation with Appelbaum.

Appelbaum credits his book for inspiring his recommendations this year. "While working on the book, I spent a lot of time reading nonfiction science, and I haven't been able to break the habit," he said.

Appelbaum's reading recommendations this year include "An Immense World" by Ed Yong. "The book is filled with answers to questions you never thought to ask—why does a dog have slits on the side of its nose, what's the strange shaped head of a hammerhead shark all about? As Yong makes clear, the diversity of sensory systems among living things is astounding," Appelbaum said. "An immense amount of work must have gone into creating 'An Immense World.""

Charles Fuchs, senior vice president and global head of oncology and hematology drug development at Genentech and Roche, also appears as a recommender on this year's reading list. His book, "A New Deal for Cancer: Lessons from a 50 Year War," a collection of 19 essays co-edited with Abbe R. Gluck, was published in 2021.

An excerpt from this book, "Essential Underreimbursed Services," appears in the Cancer History Project, and a conversation with Gluck and Fuchs ran in The Cancer Letter.

Fuchs recommends five nonfiction books—two books about leadership, two biographies, and Malcolm Gladwell's "The Bomber Mafia: A Dream, a Temptation, and the Longest Night of the Second World War."

"Each of these books offers accounts of how innovative thinkers and organizations can change the world," Fuchs said.

Paul Goldberg, editor and publisher of *The Cancer Letter*, also appears as an author on this year's reading list.

Goldberg's latest novel, "The Dissident," is recommended by Wafik El-Deiry, director of Legorreta Cancer Center at Brown University, and Ruben Mesa, president of Atrium Health Levine Cancer Institute and executive director of Atrium Health Wake Forest Baptist Comprehensive Cancer Center.

El-Deiry's full list of book recommendations can be found in this issue (*page 46*).

"Although I am just at the beginning, this promises to be a witty and satirical cold war mystery about Viktor, a Jewish 'refusenik' in 1976 Moscow and forced to solve a murder mystery in 9 days—or be blamed for the event himself! Excited to see how Viktor and his ragtag band of fellow 'refuseniks' solve the mystery!" Mesa said.

Mesa, who previously contributed to the reading list in 2021, is a longtime fan of a good murder mystery—particularly by Daniel Silva. "Come mid-July I eagerly await the latest installation in the fun 'capers' of the master art restorer/ Israeli master spy Gabriel Allon! Quite the career combination! Indeed, we all thought working towards a cure for cancer was challenging as a career path."

Silva's books have been recommended every year since 2021, and this year, of the 30 recommended novels, 9 are mysteries or thrillers.

This might not be a coincidence. Electra Paskett, the Marion N. Rowley Professor of Cancer Research at the Ohio State University College of Medicine, said last year that her love for a good "whodunit" comes down to a professional interest:

"As an epidemiologist, I am trained to solve puzzles and look for connections," said Paskett, who is also the director of the Division of Cancer Prevention and Control in the Department of Internal Medicine at OSU College of Medicine. "As a cancer researcher, this applies to my passion, which is to figure out strategies and solutions to the thorny problem of who gets cancer and why and how to prevent cancer." Memoir also features prominently on the list this year, with 10 recommendations overall, including 5 recommendations for memoirs about cancer survivorship.

Suleika Jaouad's "Between Two Kingdoms: A Memoir of a Life Interrupted" is frequently recommended—twice this year and once in 2022. Mesa calls it "a story of survivorship, renewal, and what it means to become well."

"Between Two Kingdoms" was the inaugural book of the Atrium Health Wake Forest Baptist Comprehensive Cancer Center and Levine Cancer Institute #IntegratedCancerCenter Book Club.

"Even though I am an oncologist, or perhaps even more so because of my work, I felt my heart ache for her over and over again," said Samyukta Mullangi, a medical oncology and hematology fellow at Memorial Sloan Kettering Cancer Center, who also recommended Jaouad's memoir.

"The narrative is honest, heartfelt, and absolutely devastating. I truly think everyone in our field should read this one."

Last year, Clifford A. Hudis, chief executive officer of the American Society of Clinical Oncology, also recommended the book, calling it "truly informative and engaging from beginning to end."

Leonidas Platanias, director of the Robert H. Lurie Comprehensive Cancer Center of Northwestern University, offers another sort of recommendation—a soundtrack.

"As another composer once said, Bach is the beginning and the end of all music," Platanias said. "In my opinion, he is the biggest genius ever. The Well Tempered Clavier is perfection in classical music. An incredible work."

The Cancer Letter has created a playlist of Platanias's recommendations—available through Spotify.

Frederick Appelbaum, MD



Executive vice president, Professor, Clinical Research Division, Metcalfe Family/Frederick Appelbaum Endowed Chair in Cancer Research, Fred Hutchinson Cancer Center; Author, "Living Medicine: Don Thomas, Marrow Transplantation, and the Cell Therapy Revolution"

- An Immense World: How Animal Senses Reveal the Hidden Realms Around Us, by Ed Yong
- The Genetic Lottery: Why DNA Matters for Social Equality, by Kathryn Paige Harden
- Baikonur Man: Space, Science, American Ambition, and Rus- sian Chaos at the Cold War's <u>End</u>, by Barry L. Stoddard
- The Baseball 100, by Joe Posnanski

I love to read. Up until a few years ago, just about the only genre I didn't read was romance novels. Then I started writing my own book, which was published earlier this year, "Living Medicine: Don Thomas, Marrow Transplantation, and the Cell Therapy Revolution." While working on the book, I spent a lot of time reading nonfiction science, and I haven't been able to break the habit. Three of my four recent favorites fall into that category.

"An Immense World," by Ed Yong, is a magnificent book about the unexpected and sometimes bizarre ways creatures sense the world around them. The book is filled with answers to questions you never thought to ask—why does a dog have slits on the side of its nose, what's the strange shaped head of a hammerhead shark all about? As Yong makes clear, the diversity of sensory systems among living things is astounding. An immense amount of work must have gone into creating "An Immense World."

Harden's "The Genetic Lottery" is, I think, an important book that presents the evidence that genetic differences exist

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I read it in two gulps, and it would have been one if my wife hadn't made me turn out my bedside lamp. I raise a glass of Armenian cognac to the author, and you will too.

– Frederick Appelbaun

between different populations (populations, not races) and that these differences influence everything from athletic performance to financial success. She makes the important point that refusing to recognize the role of genetic luck limits our ability to create a fair society.

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"Baikonur Man," by Barry Stoddard, is a much lighter read. It's a wonderfully entertaining, amusing blend of coldwar nostalgia and attempts at protein crystallization. I read it in two gulps, and it would have been one if my wife hadn't made me turn out my bedside lamp. I raise a glass of Armenian cognac to the author, and you will too.

"The Baseball 100" is obviously not science, but rather a series of mini-biographies of the 100 greatest baseball players in history, at least according to Posanski. Each bio-sketch is filled with arcane facts and entertaining stories. I limit myself to one a night and will mourn day 101.

Gideon Blumenthal, MD



Vice president, Global oncology regulatory affairs, Merck

- Who by Fire: Leonard Cohen in the Sinai, by Matti Friedman
- Outlive: The Science and Art of Longevity, by Peter Attia
- From Strength to Strength: Finding Success, Happiness, and Deep Purpose in the Second Half of Life, by Arthur Brooks

"Who by Fire: Leonard Cohen in the Sinai:" Matti is one of my favorite authors, and this is a fascinating account of who the poet and singer Leonard Cohen wound up in the desert on the front lines of the Yom Kippur War. An interesting account of a country and a singer at a crossroads.

"Outlive: The Science and Art of Longevity," by Peter Attia: Dr. Attia, a veteran of Dr. Rosenberg's lab in the Surgical Branch at NCI, is so diligent and comprehensive as he tries to tackle the four horsemen of the health apocalypse cancer, cardiovascular disease, neurodegenerative disease, and metabolic disease. Dr. Attia has practical tips on how to live a better and longer life—which my take home is no shortcuts and lots of extensive cardiovascular exercise (mainly in Zone 2) as well as strength training.

"From Strength to Strength: Finding Success, Happiness, and Deep Purpose in the Second Half of Life," by Arthur Brooks: I am a huge fan of Arthur Brooks—he has an engaging/upbeat writing and speaking style and dives into the social science, theology, philosophy as we need to transition from fluid intelligence to crystallized intelligence as we age.

Kadija Ferryman, PhD



Core faculty member, Johns Hopkins Berman Institute of Bioethics; Assistant professor, Department of Health Policy and Management, Bloomberg School of Public Health, Johns Hopkins University

 More Than a Clitch: Confronting Race, Gender, and Ability Bias in Tech, by Meredith Broussard

This is a great book written in an accessible style that explains how AI and algorithms can be discriminatory.

Narjust Florez, MD

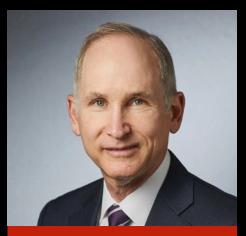


Associate director, Cancer Care Equity Program, Thoracic Oncologist, Lowe Center For Thoracic Oncology, Dana-Farber Cancer Institute

- Financial Feminist: Overcome the Patriarchy's Bullsh*t to Master Your Money and Build a Life You Love, by Tori Dunlap
- Emotional Intelligence, Harvard Review

"Financial Feminist" shows how financial independence is essential for women—and tricks about investing. "Emotional Intelligence" allows you to find purpose and learn how to keep your team motivated.

Charles S. Fuchs, MD, MPH



Senior vice president, Global head, oncology & hematology drug development, Genentech and Roche; Former director, Yale Cancer Center; Former physician-in-chief, Smilow Cancer Hospital; Author, <u>"A New Deal for</u> <u>Cancer: Lessons from a 50 Year War"</u>

- Good to Great: Why Some Companies Make the Leap...and Others Don't, by Jim Collins
- Built to Last: Successful Habits of Visionary Companies, by Jim Collins
- The Bomber Mafia: A Dream, a Temptation, and the Longest Night of the Second World War, by Malcolm Gladwell
- Einstein: His Life and Universe, by Walter Isaacson
- Steve Jobs, by Walter Isaacson

We have the great privilege and responsibility of changing the lives of patients with cancer—a challenge that constantly requires us to consider innovative new approaches. Each of these books offers accounts of how innovative thinkers and organizations can change the world.

Patricia A. Ganz, MD



Distinguished Professor of Health Policy & Management and Medicine, UCLA Fielding School of Public Health, David Geffen School of Medicine at UCLA; Director, Center for Cancer Prevention & Control Research, Jonsson Comprehensive Cancer Center

- Nights of Plague, by Orhan Pamuk
- <u>A Gentleman in Moscow</u>, by Amor Towles

"Nights of Plague," by Orhan Pamuk, written by him in Turkish and published just before the start of the COVID pandemic, translated into English and published in 2022. It recounts a story set in the last days of the Ottoman empire (early 1900s) with an outbreak of bubonic plague on a fictional island (Mingheria) in the Mediterranean, which is inhabited by both Turks and Greek orthodox residents.

A doctor and his wife (a princess, daughter of a deposed sultan) are sent there to investigate the rumors of plague, along with an eminent chemist. The 700+ page book is full of intrigue, murder and death from plague, as well as the political challenges faced by the failing empire and the need to obtain help from the west to provide a blockade of the island.

How the plague was handled—quarantine, topical treatment of buboes, rumor and romance—keeps one's interest going, but you do need to devote the time to get to the end of the book. I have read several other books from this Nobel laureate and enjoyed his writing with respect to exotic settings (neighborhoods in Istanbul), rich character development, and cultural context. This book mixes history and fiction, as well as the interpersonal aspects of human relationships, but was a longer read.

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Reading this novel in the current context of the Russian invasion of Ukraine and Putin's fanatical drive for a historic greater Russia makes one understand that there is nothing new in this world.

– Patricia A. Ganz

"A Gentleman in Moscow," by Amor Towles, was an engaging and quicker read, tracing the fate of Count Alexander Rostov who loses his privileged status as a result of the Bolshevik revolution. After being placed under house arrest at the Hotel Metropol, across from the Kremlin, he carves out a new life for himself in this new community.

9)

Over time we see the transformation of Russia into the Soviet Union mostly through the Count's trials and tribulations at the hotel, including becoming the guardian of a young girl whose parents are sent off to the countryside. Life at the Metropol reveals what life was like for the privileged and communist party members, as well as those who worked to serve them at the hotel, including the Count.

Reading this novel in the current context of the Russian invasion of Ukraine and Putin's fanatical drive for a historic greater Russia makes one understand that there is nothing new in this world. Although the novel may not be historically completely accurate, the human stories are very moving and capture what some people certainly must have experienced during those turbulent times.

Lucio N. Gordan, MD



President and managing physician, Florida Cancer Specialists & Research Institute

 American Sirens: The Incredible Story of the Black Men Who Became America's First Paramedics, by Kevin Hazzard • The Devil in the White City: Murder, Magic, and Madness at the Fair That Changed America, by Erik Larson

I recently read "American Sirens" as a recommendation from our pediatrician, friend, and patient of mine.

This is a top-20 book in my recent list and memory. The book is about the Freedom House EMS history and the setup of the first "real" paramedics in the US. They faced many challenges, including racism from the community, the police, and the government. However, the paramedics persevered and saved countless lives, and they helped to set the standard for paramedic care in the United States. Very powerful, must-read.

Since I have a daughter headed to college at University of Chicago in the fall this year, a urologist friend gave me the recommendation for "The Devil in the White City," which I just finished. This 2003 book is excellent, and full of incredible historical details about the city of Chicago and its history around the 1893 world's fair. The author also runs a parallel thriller story which is interesting, dark, and complex.

Bobby Green, MD



President and CMO, Thyme Care

American Ramble: A Walk of Memory and Renewal, by Neil King

I first learned about "American Ramble" while following the author, Neil King, on Twitter as he set out on—and tweeted about—his 330 mile walking journey from Washington, DC, to NYC. Rarely have I had such extended anticipation for a book. I was counting down the time until it became available.

The story is wonderful as it weaves together a trip of self discovery for Mr. King, with off-the-beaten-path stories of our nation's past, all while giving some insight, and maybe also some hope, into the internal strife that has been tearing us apart these last several years.

66

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– Bobby Green

In many ways, it's also a story about cancer. We learn of his brother who

has a glioma. And we learn of the author's own experience with diffuse large B-cell lymphoma. First, the lymphoma delayed his trip, then, successful treatment allowed him to proceed and we learn he is in remission—or what he beautifully refers to as a "clearing" from cancer.

Hagop M. Kantarjian, MD



Chair and professor, Department of Leukemia, Samsung Distinguished Leukemia Chair in Cancer Medicine, MD Anderson Cancer Center; Fellow of health policy, Baker Institute for Public Policy, Rice University

- A House for Mr. Biswas, by V.S. Naipaul
- Victory City, by Salman Rushdie
- The Cairo Trilogy, by the Egyptian novelist Naguib Mahfouz
- 'Tis: A Memoir, by Frank McCourt
- American Rust, by Philipp Meyer
- <u>The Son</u>, by Philipp Meyer
- A Strangeness in My Mind, by Orhan Pamuk

- The Locust and the Bird: My Mother's Story, by Hanan al-Shaykh
- <u>A Tale of Love and Dark-</u> ness, by Amos Oz
- Sabbath's Theater, by Philip Roth
- <u>Birds Without Wings</u>, by Louis De Bernieres
- Empire Falls, by Richard Russo
- Leo Africanus, by Amin Maalouf

Here is a list of the best novels (or novelists) I have read recently (or ever), which may or may not be to others' tastes:

"A House for Mr. Biswas," by V.S. Naipaul, is a semi-autobiography of the author's youth in Trinidad. Others are "A Bend in the River," "Miguel Street," and "A Flag on the Island," wonderful collections of short stories. His brother, Shiva Naipaul was also a novelist, and wrote several humorous novels ("Fireflies," "Love and Death in a Hot Country") but died young.

"Victory City," the most recent novel by Salman Rushdie, is a wonderful saga of the magical birth of a city and its course over the next 250 years. Rushdie is my all-time favorite author. Other outstanding novels are "Shame" (his best??), a historical novel set in a Pakistan-like country, "The Moor's Last Sigh," and "Midnight's Children." I hope he wins the Nobel Prize in Literature this year (or soon).

"The Cairo Trilogy," by the Egyptian novelist Naguib Mahfouz, is a family saga in Cairo during the reign of King Farouk and later president Gamal Abdel Nasser. It's very funny but some of Mahfooz's cachet humor may be lost in translation. I was addicted to his novels as an adolescent.

"Tis: A Memoir," by Frank McCourt. McCourt started writing quite late in his life and published an exceptionally entertaining trilogy of his life, starting in Ireland then moving as a teacher in the US. "'Tis," the second memoir of the trilogy, is, in my view, the most entertaining. "Angela's Ashes" and "Teacher Man" were also wonderful.

Two great novels, "American Rust" and "The Son," by Philipp Meyer. The latter is the story of a multi-generational family in the newly born Texas and later during the oil boom.

"A Strangeness in My Mind," by Orhan Pamuk, describes the expansion of life in Istanbul as told by different characters. Of all his novels, I found this one the most entertaining. He recently published "Nights of Plague" (very good but too long). Some other good novels are "My Name is Red" and "The Museum of Innocence," while some others I found more difficult to absorb.

"The Locust and the Bird: My Mother's Story," by Hanan al-Shaykh, is a moving telling of the author's mother's life. I consider her the best living Arab novelist today, and this is her best book in my opinion. If you like it, then try "Only in London" and "Beirut Blues". The translated work is good, but they read best in the original language.

"A Tale of Love and Darkness," by Amos Oz, depicts the author's youth and life in the newly born state of Israel—the best novel/biography by Oz (in my opinion). I also loved reading "Judas", a novel set in 1959 that depicts a student of religion and his views on Judas Iscariot.

"Sabbath's Theater," by Philip Roth—and if it resonates with you then try "American Pastoral" and "Goodbye Columbus."

"Birds Without Wings," by Louis De Bernieres, a novel set in the background of the collapsing Ottoman empire and subsequent struggles between different religious/ethnic communities.

"Empire Falls," by Richard Russo. The novel is set in a small town in Maine with many entertaining and memorable characters, in particular the owner of the "Empire Grill." If you like it, then read "Nobody's Fool" and others of Russo's many entertaining novels.

"Leo Africanus," by Amin Maalouf, a historical novel about a real-life character who lives in the 16th century and chronicles his travels and the rise in different cultures and empires. Maalouf published many entertaining novels like "The Rock of Tanios" and "Balthasar's Odyssey." Best read in the original French, but the translated works are excellent.

Here I will list several single novels or authors I find very entertaining, and you may wish to try some of the novels/ authors: Many of John LeCarre's recent novels ("The Tailor of Panama," "Our Kind of Traitor," "The Russia House"). "Shrine of Gaiety," by Kate Atkinson, and the Brodie's police series. "The Mambo Kings Play Songs of Love," by Oscar Hijuelos. "The Bastard of Istanbul," by Elif Shafak. "The Feast of the Ghost," by Mario Vargas Llosa. "This is Where I Leave You," by Jonathan Tropper. "One Hundred Years of Solitude," and "Love in the Time of Cholera," by Garbriel García Márquez. "Middlesex," by Jeffrey Eugenides. "A Case of Exploding Mangoes," by Mohammed Hani.

And finally, I do not think I read any non-medical books from 1972 to 1989. This is when I was first introduced to Elmore Leonard's books and the crime/ police genre. The first English novel I read was "Killshot" in 1989, which I enjoyed so much that I then read many of Leonard's novels before and since (best are "City Primeval," "Swag," "Get Shorty," etc). I diverted then to other noir fiction/ police genre writers like James Cain, Ross MacDonald, Raymond Chandler, and Joseph Wambaugh.

I hope you enjoy at least some of these recommendations.

Karen Knudsen, MBA, PhD



Chief executive officer, American Cancer Society, American Cancer Society Cancer Action Network

- The Captain Class: A New Theory of Leadership, by Sam Walker
- Less is Lost, by Andrew Sean Greer
- Othello, by William Shakespeare

Although, as a die-hard Eagles fan, I find it hard to look at the picture of Tom Brady on the front cover, "The Captain Class" is an interesting primer on leadership. If you are a sports fan and find value in understanding different types of leadership strategy, this book is for you! In my opinion, it needed a section on Super Bowl 52, covering the leadership styles of Eagles Nick Foles and Malcolm Jenkins... Just saying...

"Less is Lost" is the follow up to the Pulitzer winner "Less," which I found hilarious. Laughter is medicine, and this book does not disappoint. Our main character is as absurd as he is lovable, and I'm chuckling just thinking about it.

I hadn't read "Othello" in a long while, and enjoyed diving again into this powerful tragedy, which effectively demonstrates the devastating impact of racism, manipulation, and jealousy. No matter how many times I read it, I still find myself hoping for Othello to see through the trap laid for him, but alas he "loved not wisely, but too well."

Amy Leader, DrPH, MPH



Associate professor of population science and medical oncology, Associate director of community integration, Sidney Kimmel Cancer Center; Public health teaching faculty, College of Population Health, Thomas Jefferson University

- Long Bright River, by Liz Knight
- A School for Good Mothers, by Jessamine Chan
- Warmth of Other Suns: The Epic Story of America's Great Migra-tion, by Isabel Wilkerson
- Evicted: Poverty and Profit in the American City, by Matthew Desmond
- American Dirt, by Janine Cummins

Our Office of Community Outreach and Engagement launched a book club to learn more about our catchment area. Known as "COE Reads," we select a book that's set in our catchment area and then have a book chat with the author and a community partner that ties into the story. "Long Bright River" is a murder mystery that takes place in Kensington, a troubled yet resilient community in Philadelphia, and "A School for Good Mothers" is a story of conflict and what we hope isn't the future of motherhood.

As a population scientist, I love to learn about communities and people through well-told stories. Some of my most recent favorites are "Warmth of Other Suns," "Evicted," and "American Dirt."

Ruben Mesa, MD



President, Atrium Health Levine Cancer Institute, Executive director, Atrium Health Wake Forest Baptist Comprehensive Cancer Center, Enterprise senior vice president, Atrium Health; Vice dean of cancer programs, Professor of medicine, Wake Forest University School of Medicine

- Between Two Kingdoms: A Memoir of a Life Interrupted, by Suleika Jaouad
- The Collector, by Daniel Silva
- The Dissident, by Paul Goldberg

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Come mid-July I eagerly await the latest installation in the fun 'capers' of the master art restorer/Israeli master spy Gabriel Allon! Quite the career combination! Indeed, we all thought working towards a cure for cancer was challenging as a career path.

– Ruben Mesa

Sitting on my Yeti lawn chair, reading a book, looking out over the cool waters of Lake Michigan in Door County, WI—this is my favorite way to unwind on summer vacation. A chance to unwind, rest, and recharge.

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In my family, there is great discussion and controversy as to which platform is best to enjoy your summer reading! My daughter, an avid reader, loves nothing better than a traditional physical book (and keeps a pristine copy of all her favorites in her private library) while bringing the reliable Kindle to the beach for ease of use. For myself, although nothing beats a physical book, nothing beats the utility of the iOS "Books" app. I can read whenever the moment arises on my phone or iPad (whether waiting to board a plane, standing in a long Starbucks queue, or chilling on the beach).

Now, what am I reading this summer? I always like to have 2-3 books in the mix,

so depending on my mood I can enjoy something truly for fun, for enrichment, or for inspiration.

On the inspiration front, I am excited to be reading the inaugural offering of the new #IntegratedCancerCenter Book Club between our newly-integrated Atrium Health Wake Forest Baptist Comprehensive Cancer Center & Levine Cancer Institute, organized by TCL contributor and our amazing faculty member in Radiation Oncology & director of Survivorship—Stacy Wentworth, MD.

The first book is "Between Two Kingdoms: A Memoir of a Life Interrupted" by Suleika Jaouad. This is an amazing and really well written account of the author's process of recovery after acute leukemia completely disrupted her life as a young adult.

The book tells the story of her recovery "journey," literally and figuratively, in which she recounts a 15,000 mile journey (accompanied by her new dog Oscar) as she drives across the country and meets individuals who wrote to her while she was fighting her leukemia. A story of survivorship, renewal, and what it means to become well.

On the fun front, come mid-July I eagerly await the latest installation in the fun "capers" of the master art restorer/ Israeli master spy Gabriel Allon! Quite the career combination! Indeed, we all thought working towards a cure for cancer was challenging as a career path.

This year's installment from Daniel Silva is called "The Collector," and, as usual, finds our protagonist restoring a "masterwork" when he is put in motion to find a stolen priceless painting. Invariably, this leads to a complex mix of intrigue, where timely global politics, complex "operations," and an entertaining resolution occur. Always a fun read, especially in the summer sunshine.

Finally, as a fan of great escapist spy thrillers, I am excited to also read the new offering from our own TCL editor and novelist, Paul Goldberg—"The Dissident." Although I am just at the beginning, this promises to be a witty and satirical cold war mystery about Viktor, a Jewish "refusenik" in 1976 Moscow and forced to solve a murder mystery in 9 days—or be blamed for the event himself! Excited to see how Viktor and his ragtag band of fellow "refuseniks" solve the mystery!

Samyukta Mullangi, MD, MBA



Medical oncology/hematology fellow, Memorial Sloan Kettering Cancer Center

- The Netanyahus, by Joshua Cohen
- Between Two Kingdoms: A Memoir of a Life Interrupted, by Suleika Jaouad
- Doing Justice: A Prosecutor's Thoughts on Crime, Punishment, and the Rule of Law, by Preet Bharara

"The Netanyahus" is a fictionalized account of Bibi Netanyahu's father, who arrives at a small college campus in upstate NY seeking an academic position—and it is one of the most memorable, entertaining, maddening novels I've ever read. I confess that I listened to it on Audible, and I think that doing so actually led to me missing out on some of its brilliance (the novel invites you to read and re-read sections in order to fully grasp how it works on so many different levels of verbiage, context, history, and edifice), so my plan is to read it the old-fashioned way this summer.

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Even though I am an oncologist, or perhaps even more so because of my work, I felt my heart ache for her over and over again. The narrative is honest, heartfelt, and absolutely devastating. I truly think everyone in our field should read this one.

– Samyukta Mullangi

"Between Two Kingdoms"—I am a few years late to this deeply moving memoir of a young woman's experience with leukemia from journey to remission. I'd read all of Suleika's NYT columns back in the day, when she was actively undergoing treatment, and this had been on my list forever. Even though I am an oncologist, or perhaps even more so because of my work, I felt my heart ache for her over and over again. The narrative is honest, heartfelt, and absolutely devastating. I truly think everyone in our field should read this one.

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"Doing Justice"—For those who may not be familiar, Preet Bharara was a former US Attorney for the Southern District of New York. He came to my class once when I was a student at Harvard Business School to talk about a case of business ethics, and I remember thinking that this man was so thoughtful and eloquent.

When I heard that he'd written a book, it immediately was added to my reading list. The book does not disappoint. It works both as a memoir of his tenure at SDNY as well as a meditation on the nature and dispensation of justice. I highly recommend this one as an audiobook, not only because he narrates it himself, but also because the stories are gripping, and listening to this book is an excellent way to get through the motions of one's week.

Augusto Ochoa, MD



Deputy director, LSU-LCMC Cancer Center, Chair, Department of Interdisciplinary Oncology, Professor of pediatrics, Al Copeland Cancer Crusaders Endowed Chair, Louisiana State University Health

- Thunderstruck, by Eric Larson
- The End of the Pacific Ocean (El fin del Océano Pacífico), by Tomas Gonzalez
- Love in the Time of Cholera, by Gabriel García Márquez

During my summer I read two books and am re-reading a third.

"Thunderstruck," by Eric Larson, is an interesting novel that slowly brings together two apparently unrelated situations happening in London in the late 1800's. One was the disappearance and apparent murder of the wife of a physician/ pharmacist and the second was the arrival of Guglielmo Marconi, to develop the wireless telegraph. Fascinating piece of history that I was not very familiar with. The narrative slowly weaves both stories together into a very interesting finale.

"The End of the Pacific Ocean (*El fin del Océano Pacífico*)" is by a new Colombian writer, Tomas Gonzalez. He has a rich narrative about a Colombian family visiting a jungle area of the Pacific Coast of Colombia (Bahia Solano), which was one of my favorite summer vacation spots when I was growing up. The narrative is very reminiscent of my experiences with the place and the people who live there.

I have started re-reading (for the third time), slowly, my favorite book, "Love in the Time of Cholera," by Gabriel García Márquez.

Shubham Pant, MD, MBBS



Associate professor, Department of Gastrointestinal Medical Oncology, Department of Investigational Cancer Therapeutics, The University of Texas MD Anderson Cancer Center

- When Breath Becomes Air, by Paul Kalanithi
- The Ajax Dilemma: Justice, Fairness, and Rewards, by Paul Woodruff

The book I read recently which had an impact on me was Paul Kalanithi's "When Breath Becomes Air."

As an oncologist dealing with mortality on a daily basis, we can sometimes become immune. This book, I think, is a must for every oncologist as it is a very human and personal story of the challenges, triumphs, ups and downs of a brilliant physician dealing with cancer. It helped me understand my patient's perspective better and helped me be a better physician in turn.

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As an oncologist dealing with mortality on a daily basis, we can sometimes become immune. This book, I think, is a must for every oncologist as it is a very human and personal story of the challenges, triumphs, ups and downs of a brilliant physician dealing with cancer. "The Ajax Dilemma" uses an example from Greek mythology to highlight how flawed leadership can lead to disastrous consequences.

Leonidas Platanias, MD, PhD



Director, Robert H. Lurie Comprehensive Cancer Center, Jesse, Sara, Andrew, Abigail, Benjamin and Elizabeth Lurie Professor of Oncology, Departments of Medicine and Biochemistry and Molecular Genetics, Associate vice president of cancer programs, Office for Research, Northwestern University

- Beethoven: Symphony No. 3 "Eroica"
- Berlioz: Symphonie fantastique
- Bach: "Well Tempered Clavier"
 Preludes and Fugues
- Rachmaninov: Piano Concerto No. 2
- Shostakovich: Waltz No. 2

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• Mendelssohn: "A Midsummer Night's Dream" - Overture

Beethoven's Symphony No. 3, "Eroica:" One of the best symphonies ever written. It was a highly innovative symphony when Beethoven wrote it, and for me it is inspiring every time I hear it.

Bach's "Well Tempered Clavier" - Preludes and Fugues: As another composer once said, Bach is the beginning and the end of all music. In my opinion, he is the biggest genius ever. The Well Tempered Clavier is perfection in classical music. An incredible work.

Rachmaninov's Piano Concerto No. 2: A remarkably emotional piano concerto by a remarkable composer. Truly stunning. One of the best pieces in the history of classical music.



As another composer once said, Bach is the beginning and the end of all music. In my opinion, he is the biggest genius ever.

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– Leonidas Platanias

Shostakovich's Waltz No. 2: My favorite classical waltz. A brilliant composition by an incredible composer.

Mendelssohn's "A Midsummer Night's Dream" – Overture: A great "summer" overture, by one of the greatest composers.

[**Editor's note:** These selections are available as a <u>Spotify playlist.</u>]

– Shubham Pant

Pavan Reddy, MD



Director, Dan L Duncan Comprehensive Cancer Center, Senior associate dean of cancer programs, Baylor College of Medicine

- <u>The Cost of Discipleship</u>, by Dietrich Bonhoeffer
- A Savage War of Peace: Algeria 1954-1962, by Alastair Horne

B.J. Rimel, MD

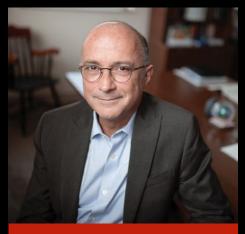


Medical director, Cancer Clinical Trials Office, Samuel Oschin Cancer Center, Associate professor of obstetrics and gynecology, Cedars-Sinai Medical Center

Think Again: The Power of Knowing What You Don't Know, by Adam Grant

This book is an interesting review from an organizational psychologist on how we get stuck on beliefs. Despite being a scientist, I found the insights into re-thinking very timely.

Carlos Rodriguez-Galindo, MD



Executive vice president, Chair, Department of Global Pediatric Medicine, Director, St. Jude Global, Co-associate director of outreach, Comprehensive Cancer Center, St. Jude Children's Research Hospital

- The Passenger, by Cormac McCarthy
- Stella Maris, by Cormac McCarthy
- El Amante Polaco, by Elena Poniatowska

I just read Cormac McCarthy's last two novels, "The Passenger," and "Stella Maris." What can I say about Cormac Mc-Carthy that has not been said already? His style, the depth of his thoughts, the complexity of his characters. I had been waiting (im)patiently for many years, and I must admit I was afraid that there would be no more coming from him after "The Road."

Like a reviewer put it, these two books, which immerse the reader in a complex intertwined story of love, loss, and despair, are "deliberately frustrating." Hard to read and at times difficult to understand—but as I finished them, I was ready to start reading them again, my Kindle full of highlighted passages that shine like pearls that never lose their splendor. A good farewell gift from this amazing writer.

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– Carlos Rodriguez-Galindo

Now I am reading 'El Amante Polaco' (The Polish Lover), by the French-Mexican author Elena Poniatowska. This is a fascinating novel about the last king of Poland, Stanislaw Poniatowski, ancestor of the author and a lover of Catherine the Great, and a travel in time between the Poland and Russia of the 18th Century, the Europe of the Wars, and the Mexico of today.

Somehow, it made me realize that while we all are the product of our times and our history, we also have the power to write them. Or, I should say, the gift? It is an extensive piece of work, comes in two volumes, but every page is worth it.

Ze'ev Ronai, PhD



- Director, Cancer Center at Sanford Burnham Prebys, Jeanne and Gary Herberger Leadership Chair in Cancer Research Professor, Cancer Metabolism and Microenvironment Program, Sanford Burnham Prebys Medical Discovery Institute
- No Cure for Being Human, by Kate Bowler

I find this book an inspirational memoir, which helps us realize how fragile we are, and at times, how to outperform our humanness.

Richard Silvera, MPH, MD



Assistant professor of infectious disease, Associate program director, Infectious Diseases fellowship, Icahn School of Medicine at Mount Sinai

 Unmask Alice: LSD, Satanic Panic, and the Imposter Behind the World's Most Notorious Diaries, by Rick Emerson

The way we think, talk about, and treat substance use and people who use drugs is fraught and burdened by so much stigma. The cultural conception of drug use as a moral failing runs deep, and we often don't consider what it's based on. Though many of us haven't read it, many of us have been influenced by "Go Ask Alice," by Beatrice Sparks, which tells a cautionary tale about a teenage runway's experience with drugs.

"Unmask Alice" is a fascinating investigation into how that influential book that has impacted our cultural conception of drug use is entirely fictional and the history and motivation behind why this book had such a cultural impact. It's a great step toward unpacking drug stigma to look at its rickety foundations.

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– Richard Silvera

NFN Scout, MA, PhD



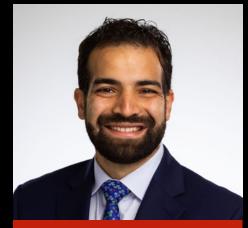
Executive director, National LGBT Cancer Network; Principal investigator, LGBTQ Tobacco-Related Cancer Disparity Network, Out: The National Cancer Survey

 <u>LGBT Populations and Cancer in the</u> <u>Global Context</u>, edited by Ulrike Boehmer and Gabriele Dennert

After formerly editing a book examining LGBTQI+ cancer in the U.S., Dr. Boehmer has now turned her attention to considering the same topic globally. I was impressed with how the editors found local authors to examine the issues in a wide variety of countries. I was also impressed with how much information the authors found about a subject I was worried would be quite narrow.

Ultimately, I found the book not only a great read for the topic itself, but also an amazing insight into health policy in different countries and the realities of living as a queer person in different contexts as well.

Ramy Sedhom, MD



Co-lead, Geriatric Oncology, Penn Cancer Service Line, Faculty member, Penn Center for Cancer Care Innovation, Clinical assistant professor of medicine, Clinical director of palliative care, Penn Medicine Princeton Health

 Option B: Facing Adversity, Building <u>Resilience, and Finding Joy</u>, by Sher-yl Sandberg and Adam Grant

As physicians, we are rarely taught how to address anticipatory grief or bereave-

ment. This book was a glimpse into what follows the death of a loved one. It left an indelible mark, and I hope makes me more compassionate to my patients.

Naoto T. Ueno, MD, PhD

Director, University of Hawai'i Cancer Center, Interim program co-leader, Cancer Biology and Therapeutic Program, Professor, Department of Medicine, John A. Burns School of Medicine, University of Hawai'i at Manoa

Bittersweet: How Sorrow and Longing Make Us Whole, by Susan Cain

Susan Cain's book, "Bittersweet," extends the insightful introspection and profound wisdom that marked her earlier work, "Quiet," a pioneering study of introversion. In "Bittersweet," Cain adopts this perspective to explore the human encounter with grief and desire, spinning an engaging tale highly pertinent to oncology.

For cancer healthcare providers, "Bittersweet" facilitates a more profound comprehension of the emotional components of cancer patients' experiences. This includes those grappling with grief, loss, and the weighty emotions often accompanying a cancer diagnosis. As "Quiet" illuminated the strengths and needs of introverted individuals, "Bittersweet" might guide healthcare professionals to enhance their empathy skills, a critical competency when dealing with patients confronting life-altering diseases such as cancer.

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For cancer healthcare providers, 'Bittersweet' facilitates a more profound comprehension of the emotional components of cancer patients' experiences. This includes those grappling with grief, loss, and the weighty emotions often accompanying a cancer diagnosis.

– Naoto T. Ueno

From a research vantage point, Cain's investigation of transmuting anguish into creativity and transcendence could spark fresh psychosocial research trajectories in oncology. Analogous to how "Quiet" broadened our comprehension of introversion, "Bittersweet" could contribute to a more thorough understanding of emotional resilience, personal evolution, and coping strategies among cancer patients and their loved ones.

While "Bittersweet" can offer further solace and comprehension, it is not a substitute for professional psychological assistance. Nevertheless, gaining insights from a layperson's viewpoint can be beneficial.

James L. Weese, MD



Vice president, Cancer Service Line, Advocate Aurora Health; Clinical adjunct professor of surgery, UW School of Medicine and Public Health

- Tom Clancy Target Acquired, by Don Bentley
- Gemstones: A Jewelry Maker's Guide to Identifying and Using Beautiful Rocks, by Judith Crowe

Generally, when I read outside of work, I like action stories and something to expand my knowledge of other areas. I've read a lot of Clive Cussler novels and Tom Clancy books—the most recent being "Target Acquired," by Don Bentley.

In addition, my wife has gotten me interested in making jewelry, so another recent book was "Gemstones: A Jewelry Maker's Guide to Identifying and Using Beautiful Rocks," by Judith Crowe.

Renee Wegrzyn, PhD



Director, Advanced Research Projects Agency for Health

- High Growth Handbook: Scaling Startups from 10 to 10,000 People, by Elad Gil
- Pieces of the Action, by Vannevar Bush
- Project Hail Mary, by Andy Weir
- American Moonshot: John F. Kennedy and the Great Space Race, by Douglas Brinkley

My go-to reading selections these days are usually a mix of science fiction (I read enough hard science all day at work) and building things like organization and culture.

"High Growth Handbook" is less of a read and more of a handy reference book. I use this text often to reflect on best practices when I'm hiring new executives and building a team. The personal user manual is such a handy tool to share with new team members, especially in a hybrid work environment when it can be harder to get to know someone. "Pieces of the Action," by Vannevar Bush, was just recently reissued. The reflections on building a new organization in government even decades ago are still insightful and relevant today (though thankfully with a bit less patriarchy...).

"Project Hail Mary," by Andy Weir, is easily my favorite book. The story of taking on the seemingly impossible, having an unexpected partnership be the key to the solution, and the "science" of the fiction was so creative and detailed. I laughed, I cried, I recommend this book to everyone!

The president officially announced my role as ARPA-H director last year on the anniversary of JFK's Moonshot speech. I picked up "American Moonshot: John F. Kennedy and the Great Space Race" to get smart on the original Moonshot, and like many, I was struck by his famous quote:

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My go-to reading selections these days are usually a mix of science fiction (I read enough hard science all day at work) and building things like organization and culture.

– Renee Wegrzyn

Certain aspects of the book, particular-

ly those related to ethnic and gender

interactions, have not aged perfectly,

but overall it is a remarkably creative,

thought-provoking, and enjoyable description of how we build on what

Robert A. Winn, MD

came before.

We choose to go to the moon in this decade and do the other things, not because they are easy, but because they are hard, because that goal will serve to organize and measure the best of our energies and skills, because that challenge is one that we are willing to accept, one we are unwilling to postpone, and one which we intend to win.

This really captures the Zeitgeist for the team at ARPA-H working hard to bring better health outcomes to all Americans. We've got this!

George J. Weiner, MD



Professor of internal medicinehematology, oncology, and blood & marrow transplantation, Professor of pharmaceutical sciences and experimental therapeutics, CE Block Chair of Cancer Research, Director emeritus, University of Iowa Holden Comprehensive Cancer Center

• The Source, by James A. Michener

I have gone retro and am re-reading "The Source," by James Michener, which was written in 1965. My takeaway is quite different than it was when I last read it 50 years ago.



Director and Lipman Chair in Oncology, VCU Massey Cancer Center, Senior associate dean of cancer innovation, Professor, Division of Pulmonary Disease and Critical Care Medicine, VCU School of Medicine, Virginia Commonwealth University

- The Creative ACT: A Way of Being, by Rick Rubin
- Shoutin' in the Fire: An American Epistle, by Danté Stewart

Rick Rubin's book has affected how I view creativity. It challenged me to go beyond my typical sources of creativity and to more deliberately commit to a creative practice of being.

Danté Stewart's semi-autobiography hit home, as it directly took on the challenges of the Black religious experience and living in America. He points out the difficulties at times of reconciling the two, and how both are often not neatly aligned. I will definitely read this book again.

Jedd D. Wolchok, MD, PhD



Meyer Director, Sandra and Edward Meyer Cancer Center, Professor of medicine, Weill Cornell Medicine

- Ravenous: Otto Warburg, The Nazis, and the Search for the Cancer-Diet Connection, by Sam Apple
- The Angel of Darkness, by Caleb Carr

Alexandria Carolan and Jacquelyn Cobb contributed to this story.

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BOOK REVIEW

Wafik El-Deiry took an extra suitcase on vacation—for the books on his 2023 reading list

His recommendations:



By Wafik S. El-Deiry, MD, PhD

Director, Legorreta Cancer Center at Brown University; Attending physician, hematology/oncology, Lifespan Cancer Institute; Associate dean, oncologic sciences, Warren Alpert Medical School, Brown University

had fun reading and sharing some book reviews with *The Cancer Letter* previously, and I thought I would try again with a new installment (*The Cancer Letter*, <u>Aug. 6</u>, 2021).

So, I took an extra suitcase on vacation with me. It's packed with 15 books that are at the top of my 2023 reading list. I hope to get through them all at some point.

I took a photo of each of these books in case the luggage gets lost. I share the image here, so you can pick and choose which ones you might want to read. The books are arranged collage-style, in no particular order. The picture itself is worth at least a thousand of my words.

The books reviewed here are:

- <u>Race Matters, 25th Anniversary: With</u> <u>a New Introduction</u>, by Cornel West
- <u>Rooted: Life at the Crossroads</u> of Science, Nature, and Spirit, by Lyanda Lynn Haupt
- Toxic Exposure: The True Story Behind the Monsanto Trials and the Search for Justice, by Chadi Nabhan, MD, MBA
- For Blood and Money: Billionaires, Biotech, and the Quest for a Blockbuster Drug, by Nathan Vardi



- The Measure, by Nikki Erlick
- <u>The Dissident</u>, by Paul Goldberg

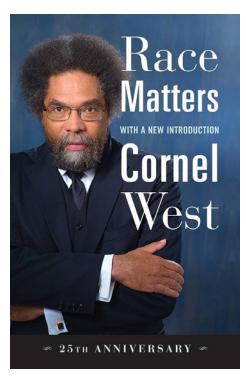
Other books in the suitcase:

- <u>The Hitchhiker's Guide to the</u> <u>Galaxy</u>, by Douglas Adams
- <u>The Daughter of Auschwitz:</u> <u>My Story of Resilience, Surviv-</u> <u>al and Hope</u>, by Tova Friedman and Malcolm Brabant
- Health Care Revolt: How to Organize, Build a Health Care System, and Resuscitate Democracy—All at the Same Time, by Michael Fine
- <u>Visions of America: Personal Narra-</u> <u>tives from the Promised Land</u>, edited by Wesley Brown and Amy Ling
- <u>Public Radio: Behind the Voic-</u> es, by Lisa A. Phillips
- <u>The Subtle Art of Not Giving a F*ck: A</u> <u>Counterintuitive Approach to Living</u> a Good Life, by Mark Manson
- <u>The Best American Short Sto-</u> <u>ries (2001)</u>, edited by Barbara Kingsolver
- <u>The Structure of Scientific Revo-</u> lutions, by Thomas S. Kuhn
- <u>The Nature of Prejudice</u>, by Gordon W. Allport

These books came from different sources for different reasons, and there are still others I'd like to read—such as Ben Stanger's recent release "From One Cell: A Journey Into Life's Origins and the Future of Medicine" that I'll get to eventually (hence, it's not in the images).

"A Spy Among Friends" by Ben Macintyre is another book I'd like to read. My son James, who just started law school, has been reading this one, and so I'll get to it eventually (it's not on the list—yet). "The Subtle Art...," a gift from a dear colleague in Baltimore, was one of the most practical presents I received this year. I will say no more, other than it is highly recommended for academics, and probably those in all walks of life.

Race Matters, 25th Anniversary: With a New Introduction



I had never heard of Cornel West or his books when I became aware that he's considering running for president for the 2024 election and that he is an academic intellectual and professor at Harvard. My curiosity was piqued.

The 25th anniversary version of his book, "Race Matters," would introduce me to his ideas that I was eager to learn about. Would I find out what he stands for so I can think more about his candidacy and also learn something from him?

Dr. West, back in the preface for the first edition, spoke of hatred for Black people in the U.S. as psychic violence

"reinforced by the powers of state and civic coercion," with physical violence "for the primary purpose of controlling their minds and exploiting their labor for nearly four hundred years."

He spoke of "American terrorism," "American barbarism," and slavery as a "distinctive assault on black humanity." The "white supremacy" and its impact extends to other races, he asserts. He states that the nearly 200 years after the American revolution were a failure of the American democracy as it relates to "arbitrary powers" of "government and economic institutions [...] against its citizens."

While he acknowledges progress, he informs us of what we know—that "white supremacy lingers."

Introducing the 25th Anniversary Edition, Dr. West writes:

"The nihilism in Black America has become a massive spiritual blackout in America. The undeniable collapse of integrity, honesty and decency in our public and private life has fueled even more racial hatred and contempt."

Dr. West speaks of "chauvinistic nationalism, plutocratic policies, and spectatorial cynicism run amok." The "only hope is prophetic fightback—a moral and spiritual awakening that puts a premium on courageous truth telling and exemplary action by individuals and communities."

He criticizes Wall Street, big banks, drone strikes, "Terror Tuesday at the White House." He complains about the "imperial meltdown," "ecological catastrophe," threats from nuclear, economic, political catastrophes, oligarchy, civic and cultural catastrophes.

As I read this it felt a bit like "the sky is falling," along with a depressing societal view. He gets into Sanders vs. Clinton among Black voters, and Trump after Obama as the "know-nothing white cruel face of the American Empire," after "the brilliant Black smiling face of the American Empire."

He is critical of both wars and killing. It is always annoying for me as a biomedical researcher to read "The Military... spends 53 cents for every taxpayer dollar in the US budget."

Dr. West speaks of the Black freedom struggle, the Black musical tradition, and "soulful kenosis," all of which "inspire and encourage others" by allowing "suffering to speak" the truth, along with the "neoliberal" threats that undermine these traditions.

He mentions "the Reverend William J. Barber II" as the "most Martin Luther King-like figure in our time."

He refers to himself as preferring to "be the hope" rather "than talk about hope," and that he's pulling from "the rich resources of the LGBTQ communities, the feminist movement, Indigenous people's struggles, the environmental justice and other abled communities, and immigrant rights and anti-imperialist organizations."

I really like "the implication is that only certain Americans can define what it means to be American — and the rest must simply 'Fit in'."

I like "we must admit that the most valuable sources for help, hope, and power consist of ourselves and our common history. As in the ages of Lincoln, Roosevelt, and King, we must look to new frameworks and languages to understand our multilayered crisis and overcome our deep malaise."

I love that quote from this book.

The intellectual and scholar in Dr. West comes through here with:

"We must invigorate the common good with a mixture of government, business, and labor that does not follow any existing blueprint. After a period in which the private sphere has been sacralized and the public square gutted, the temptation is to make a fetish of the public square. We need to resist such dogmatic swings."

He reiterates that we need "courageous leaders," and "democratic accountability."

Dr. West is an original thinker who analyzes the plight of Black Americans, challenges existing frameworks as he interjects what's missing in his view as the underlying structures:

"Culture is as much a structure as the economy or politics; it is rooted in institutions such as family, schools, churches, synagogues, mosques and communication industries (television, radio, video, music)."

He contrasts the "liberal structuralists" and the "conservative behaviorists" as flawed in their interpretations and conclusions. He surmises that the fight against nihilism was lost with integration and concludes this has led to increased suicides among African Americans.

He dwells on the Clarence Thomas SCO-TUS appointment, unwinding Blackness and racial reasoning to condemn Black leaders and advocate for moral reasoning.

Dr. West deals with Black leadership, Black intellectual conservatism, and warns of the downside of ignoring the misfortunes of the disadvantaged.

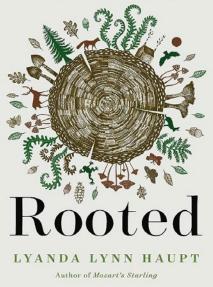
It is interesting to see—in light of the recent SCOTUS decision on affirmative action—that Dr. West views affirmative action negatively "as neither a major solution to poverty nor a sufficient means to equality." He sees that "affirmation of Black humanity, especially among Black people..., is a sufficient condition of such progress."

Other chapters that the readers will enjoy delving into focus on Black-Jewish relations, Black sexuality, Malcolm X, and Black rage.

I appreciate the book and recommend it to those who wish to understand more about who Dr. West is and what he stands for.

Rooted: Life at the Crossroads of Science, Nature, and Spirit

Life at the Crossroads of Science, Nature, and Spirit



I received this book, published in 2021, as a gift on Father's Day this year from my now adult, college-bound daughter, Julie, who said I would enjoy reading it.

I was determined to try and find out why my daughter thought I would enjoy reading this book. As the book has a one-word title, so do most chapters. For example: "Listen," "Shed," "Wander," "Immerse," "Alone," "Unsee," "Relate," "Speak," "Grow," and so on. The first, however, is "Frog Church" with an "invocation" and "tenets of rootedness."

These tenets of rootedness include "Ecology and Mysticism," "Everyday Animism," "Poetry and Science Intermingle," "Truth and Fact Are Not Synonyms," "Mystery," "Kindred, All," "Kith," "Reciprocity," "All Is Sacred," "Enchantment and Wonder," "Creativity and the Great Work," and Eccentricity."

The book quickly gets into ecological collapse and forestalled responses due to the COVID pandemic. There is reference to Rachel Carson's book "Silent Spring," DDT, and feminism. Rebecca Solnit's "Hope in the Dark" is mentioned.

I particularly liked that hope doesn't mean everything will be fine: "Mature hope involves a willingness to allow that brokenness and beauty sometimes intertwine."

I was reading about the concept of "earthing" as I sat at a serene shaded location at Turquoise Bay in Roatan, Honduras—a beautiful place that I'd highly recommend.



Turquoise Bay in Roatan, Honduras served as El-Deiry's vista as he read "Rooted."

There doesn't seem to be much science behind it, but there is the idea that walk-

ing barefoot on natural surfaces balances our body's positive ionic charge with the earth's negative charge, and that this may help prevent inflammation and other ailments, to paraphrase. Earthing can also help with pain, wound healing, and even "neuropsychological issues."

I don't disagree that connecting with nature can help calm anxiety and promote better sleep. However, I'm not sure that the magic here has anything to do with walking barefoot. The author does, however, tie walking barefoot with shedding, as when Moses in exodus was asked to shed his sandals, as he was walking on holy ground. The analogy is taken further with the concept of "beneathness:"

For the soil is alive and writhing beyond my sight with roots, mycelia, decomposers, bacteria, protozoa, worms, grubs, beetles—beyond counting, beyond knowing. The living and the dead brushing together to create the quietest symphony of sound and activity. Holy ground.

In a section about "Intelligent Feet," the reader is introduced to a biomechanist (I initially read this as biochemist) by the name of Katy Bowman, who has done research on the human body and has been critical of "modern walking for fitness mindset," where people count the number of steps in ultra-engineered shoes in less than stimulating environments. But Bowman has found that when her students walk on a forest floor, they walk more slowly—but this doesn't mean they perform less work.

The idea that the speed and steps are not the only measure of fitness seems like good advice, and besides, there's both physical and mental fitness. Certainly, she seems to be advocating for staying fit by being out and walking or running in nature. In a section titled "Wired to Wander," we learn that in 2014, John O'Keefe and colleagues were awarded the Nobel Prize in Physiology or Medicine for research on the location-grid neurons, residing in the hippocampus of humans and other animals ranging from birds to rats.

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I don't disagree that connecting with nature can help calm anxiety and promote better sleep. However, I'm not sure that the magic here has anything to do with walking barefoot.

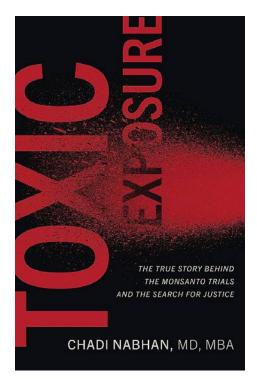
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I'm sure some of the readers will know that certain birds have an enlarged hippocampus as they need to find food, and sometimes that involves remembering locations they can return to. It was interesting to read as well about location-based memory and how sometimes we have a memory that may be confused with another memory at the same location. This is because apparently these grid neurons are intertwined with memory neurons.

As I read on into the book it felt like a wellness book about getting closer to nature and our "roots" in different ways, and along the way, if there is supporting science and other interesting information, then it was included. A good example is a section on solitude that reveals that, in today's world, we use about 95% of our brain as we are busier than ever with numerous distractions, including social media. An article from 2014 in *Science* tested subjects for their ability to endure 15 minutes of solitude with their thoughts but they could choose to give themselves an electric shock. It became clear most people couldn't last 15 minutes, but there was an outlier who gave himself 190 shocks. No comments. But time alone has benefits, as the book goes on.

Enjoy the read, and, for me, I can thank my daughter for sending it my way this summer.

Toxic Exposure: The True Story Behind the Monsanto Trials and the Search for Justice



I have known Chadi for several years, and most recently interacted with him in his role as chairman of the Caris Life Sciences Precision Oncology Alliance.

It is always a lot of fun to read a book when you know the author, and so once I was aware of the book that was released in 2023, I got my copy. The book is about Monsanto's herbicide Roundup that contains glyphosate that has been implicated as a carcinogen with occurrence of non-Hodgkin lymphoma in some individuals who used Roundup. Glyphosate has a Wikipedia page that weighs in on carcinogenicity and ends up with a statement that the evidence has been inconclusive and contradictory.

With that in mind, I delved into "Toxic Exposure" to learn more about the evidence.

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As a scientist who is also working to understand cancer causes in Rhode Island, I found the book eyeopening and, I would say, required reading for those interested in carcinogenesis and epidemiology.

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As I read the book, it became clear that it was a page-turner that I could not put down. Chadi gives the reader a glimpse into the legal process that unfolded between a multi-billion-dollar corporation (Monsanto, which was acquired by Bayer as trials were taking place) and patients who developed non-Hodgkin lymphoma after being exposed to weed killers containing glyphosate.

Chadi thoroughly researched the topic and provided brilliant testimony while being very self-conscious and analytical about how the various judges and juries might have perceived his comments.

He provides the reader with an understanding of the history of the EPA, an agency that started in the Nixon administration as the Environmental Quality Council. It is noteworthy that this occurred during the same administration that produced the <u>National Cancer Act</u>.

Chadi provides evidence on how the EPA might relate to a big corporation that sells a toxic product. He captures internal company communications that reveal a culture of risk mitigation and potential deception.

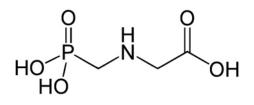
The courtroom drama and theatrics are fun to read, including the eloquent letter to a judge by a juror regarding Monsato's pursuit of retrial. The arguments in different cases are laid out. I found the one about choice particularly compelling, as the general public is owed that. Being informed of risks when they are known, and anything short of that amounts to cover-up and deception.

The book certainly recounts the pursuit of justice for the plaintiffs and the important role that Chadi played. He was very modest, yet he can be proud of what he has achieved as an immigrant from Syria who has had a positive impact on people's lives. Interwoven is his career path, including time he spent in Boston, and his fondness of American football and the Patriots—although soccer and Manchester United remain his favorite.

As a scientist who is also working to understand causes of cancer in Rhode Island, I found the book eye-opening, and I would say it is required reading for those interested in carcinogenesis and epidemiology.

It is hard to prove causality. I found it somewhat shocking that we don't know more about glyphosate. Also, I find it disappointing that corporate greed and lack of a direct search for truth, whatever it may be, is not how some big companies operate.

Instead, millions are spent on litigation and opinions.



The molecular structure of glyphosate.

It is compelling that glyphosate causes lymphoma and other tumors in rodents, and that there is a higher risk of lymphoma with extent of exposure and clinical cases. I thought, wouldn't it have been important to study mice deficient in p53 that develop lymphoma? Does glyphosate accelerate these tumors in p53-null mice? Does it increase the incidence in the p53 heterozygous mice that get fewer lymphomas?

The experiments are straightforward, and I would think painting glyphosate on the shaved skin of these mice would mimic what occurred to the soaked skin exposure of the first Roundup case (Mr. Johnson) litigated in California.

I also couldn't help but be reminded that "carcinogens leave fingerprints," and that it is also straightforward to detect and identify such signatures in genes such as p53 that might more directly get to causality. The genomes of the tumors from the exposed individuals are expected to hold some of the secrets of causality as well as response to therapy.

As far as the presence of the substance in the body long after exposure, current technologies allow for detection of infinitesimal amounts including in tumors by mass spectrometry. One would have thought that the industry and the EPA would embrace science more and even repeat studies that were limited by sample size in mice. In my own state, the <u>warning about glyphosate</u> is concerning.

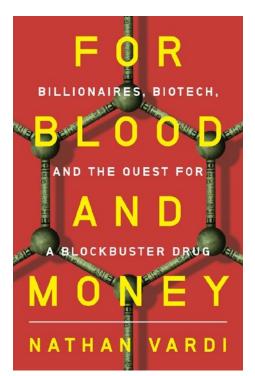
Glyphosate is an herbicide also known as "Roundup." In 2015, the UN World Health Organization's International Agency on Research on Cancer determined that it is a "probable carcinogen to humans." In 2019, the U.S. Agency for Toxic Substances and Disease Registry released its own draft Toxicological Profile for Glyphosate which affirmed the WHO's assessment. Recent studies have concluded that long-term exposure to the chemical increases the risk of developing certain cancers, in particular non-Hodgkin lymphoma. More research needs to be done on the effect of chemicals used in pesticides on human health, however, consumers can still reduce their risk of being exposed to toxic (or potentially-toxic) chemicals by choosing alternative products made with ingredients that are not harmful to human health.

It is a stronger concern about the carcinogenicity than the Wikipedia page. I was pleased to see that Rhode Island is among the <u>states with least glyphosate</u> <u>use</u>, although spraying of roads and in parks was being done a decade ago.

Even while judgements in court have already been made, academics like me want to know more about the science and lessons learned. I think, like how the tobacco industry settlement funded some research (much less than one would have expected), the chemical corporations should fund more research about environmental exposures that ultimately impact on human health.

We need more than <u>cleanup of super-</u><u>fund sites</u>. This problem is <u>global</u> and neither the knowledge base nor the policies are set.

For Blood and Money: Billionaires, Biotech, and the Quest for a Blockbuster Drug



The epilogue of this 2023 book begins on a day in May 2011, with a chief medical officer, Dr. Hamdy, who has just been fired from a small biotech company called Pharmacyclics.

The company was developing a BTK inhibitor for leukemia, an area he was excited about.

The book turns to Mr. Duggan, a successful businessman who lost his grown son to glioblastoma. He was a believer in Scientology and, by the age of 60, had amassed a net worth of \$65 million after various business ventures. He became interested in Pharmacyclics and started buying shares because the company had been testing a drug for brain cancer.

He met Pharmacyclics CEO, Dr. Miller, a Stanford clinical professor and spouse of Dr. Sandra Horning, past ASCO president and lymphoma expert. Miller had previously co-founded IDEC Pharmaceuticals with Stanford's Ron Levy to bring Rituxan to FDA approval for non-Hodgkin's lymphoma.

Duggan bought 10% of Pharmacyclics at a time when their drug Xcytrin was doing poorly in clinical trials and when their shares were \$1. Five years earlier, in 2000, the shares were \$80 and the company's market valuation was more than \$1 billion.

Interesting history is described about Celera, Craig Venter, and the \$6.6 million deal to get CRA-032675, a BTK inhibitor and analogues along with some HDAC inhibitors from Celera to Pharmacyclics. Celera didn't think BTK inhibitors would go anywhere and essentially gave them away.

Miller wrote an article in *The Wall Street Journal* that was critical of the FDA and Richard Pazdur, the agency's chief of oncology, for rigidity in the drug approval process. He wrote two other articles expressing views toward the FDA and their approval process—views others thought would not necessarily be helpful to his company or its drug Xcytrin.

Miller would pivot the company toward testing irreversible BTK inhibitors in lymphoma with colleagues at Stanford, and would, brilliantly, include patients with CLL so he could sample the cells in the blood.

But there was conflict with Duggan who came to own 15%, had a board seat at Pharmacyclics, and wasn't ready to give up on Xcytrin, which had gotten him interested in investing in the first place. He spent another \$2 million and ended up with 25% of the company to promote his agenda.

A fight ensued, and Duggan took over the company that was not doing well. How this happened is laid out, but what would happen next, including Hamdy's recruitment and his eventual ousting?

Hamdy would try to engage with luminaries such as Byrd, O'Brien, Staudt, and Wilson. Staudt would meet Pharmacyclics employees at the 2009 AACR meeting where he presented unpublished data implicating the B-cell receptor whose signaling involves BTK as a potential therapeutic target in lymphoma. But results at that point, including in dogs with PCI-32765, were less than spectacular, and the company was struggling. Duggan continued to invest and raise money.

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This is a must-read as a great modern drug developmentto-approval story: little pharma and big pharma deals, big money, fame, power, control, ego, ego, ego, and the intense human interactions throughout.

An aspect of this book I enjoyed reading as an academic entrepreneur is the insight into the mindset of investors. A good example is Rothbaum, who invests only his own money, so he controls everything and "owes no one anything."

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The tide would appear to turn in an unexpected way for Pharmacyclics, with an early signal in CLL. The dynamics of a Stanford fellow, Duggan, and Horning—by then at Genentech—standing by the poster made for fun reading, as did the fur coat Duggan wore to the ASH meeting in New Orleans.

Academia, at the meeting where the poster was presented, largely ignored the results, but the action started to take place on Wall Street, with interest in Pharmacyclics. Rothbaum took note. Staudt's published *Nature* paper would provide more validation, but there would be competition with other targets such as PI3Kdelta.

I appreciated insights from this book into clinical development strategy for a promising clinical-stage compound where the options are to go at it alone, partner, or sell. Other insights came from understanding asset dilution versus equity dilution, and how decisions about subsequent clinical trials in drug development can be so crucial to the future prospects of a promising drug.

It was good to read about how impartial academic investigators, such as Dr. Byrd at Ohio State's James Cancer Hospital or Dr. O'Brien at MD Anderson Cancer Center, were motivated to help patients and to learn the science and approaches from different companies. Hamdy was credited with being a good listener and allowing their ideas to move forward.

Biology trumps everything—and can make people nervous. What does it mean for the white cell count to go up while the lymph nodes shrink? And why would the count keep going up with continuous daily treatment, whereas with daily treatment for 4 weeks and a week of break resulted in decline? Was the disease worse? This is high stakes for investors and board members.

More would follow, including turmoil over development strategy. Certain

decisions were made by Hamdy with further conflict.

Another lesson is the small company versus big company approach to drug development, and early stage versus late stage. There is much to be learned by any biotech entrepreneur who is thinking about bringing new cancer drugs to market.

Another lesson that is generally obvious comes from a comment made by Duggan:

All I'm going to say is, when you're rowing a boat, everybody needs to row in the same direction.

How Pharmacyclics partnered with J&J in a \$1 billion co-development deal and how the drug became ibrutinib is explained for the students and the experts.

Another lesson is that things get better after a deep wound and when they appear to be at their lowest. This is true in science, biotech, and life. The path in the book involves new startups, licenses, and even some clear IACUC violations at Stanford and in a private home.

But injustices occur with people who are forced out not being credited in *NEJM* articles or losing tens to hundreds of millions by selling when they should have held on to stocks. Byrd and O'Brien would agonize over the ethics of the FDA prohibiting crossover design, and got Dr. Pazdur to clarify that crossover is not prohibited, as it allows access for patients to new drugs.

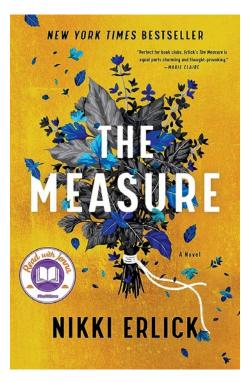
With a highly effective drug, clinicians get to a point of not wanting to use other drugs in the relapsed refractory CLL setting, and the ibrutinib data showed that it worked even with chromosome 17p loss which is associated with deletion of my favorite tumor suppressor, p53.

The book provides valuable insight into how the FDA views accelerated approval for less common versus more common cancers. The path of development for acalabrutinib through Acerta was another thrilling story of the investor/ chairman, his micro-managerial stronghold over decision making, and a good example of how the finances of FDA-approved drug availability in comparison trials—or pace of enrollment in new competing agent trials—impacts drug development and how competing patents stand in the way of progress.

This is a must-read as a great modern drug development-to-approval story: little pharma and big pharma deals, big money, fame, power, control, ego, ego, ego, and the intense human interactions throughout.

I don't think I gave too much away.

The Measure



This novel, published in 2022, starts with all adults in the world one day receiving a box with an inscription: "The measure of your life lies within," along with a string inside the box.

Nina, an anxious editor who has a roommate named Maura, saw the box on her doormat that has a Bob Dylan quote, "Be groovy or leave, man." Besides appreciating the quote, this got me interested in the blending of fiction and nonfiction, including familiar places on the Upper East Side.

Fear, curiosity, and caution were palpable as society worried about an unknown threat. Is it even real, beyond anecdotes that emerged of what happened to some adults with short or long strings? Would this affect the global economy? Politicians turned to scientists and as a few weeks went by, as more emerged about people who would come to be known as "short stringers" or "long stringers"—such as findings of incurable or curable diseases.

Government and even the pope weighed in—he called the small boxes a "gift from God." Some didn't feel that way, with their short string.

The chapters give the reader a glimpse into the lives of other characters intertwined in their relationships and experiences. Not everyone opened their boxes, and many threw them away. Support groups and online websites popped up.

The strings seemed to eclipse any other story because they seemed to be real in their ability to predict total life span within 2 years. There were conspiracy theorists and those who would tempt fate, only to survive due to their long string. Others would guess the length of someone's string by watching their behavior with life decisions. As I read the book, it occurred to me that we live in a world not too far from these strings. With technological advances in genomics and computational capabilities, it is conceivable that predicting lifespan is within reach. We know a lot of disease-causing genes, and we know many conditions with limited life expectancy. We know that all too well in oncology.

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As I read the book, it occurred to me that we live in a world not too far from these strings. With technological advances in genomics and computational capabilities, it is conceivable that predicting lifespan is within reach.

The difference, I think, is we can't anticipate accidents or random events that shorten people's lives. With the short and long strings they really predicted lifespan. The idea of support groups is also well-known in our field, as is genetic counseling. We have come to a point where people are informed of risks of knowing whether they carry a disease-causing gene mutation (for example, one that would cause early onset breast cancer or Alzheimer's disease). Another difference in real life is the hope that interventions and research discoveries could in the future impact on outcomes. But not in this novel with the strings.

One of the characters in a support group is a guy named Hank, a doctor at Memorial Hospital who was seeing patients come in with concerns about their short strings and were looking for screening tests. It was odd that a book published in 2022 would not mention COVID, though.

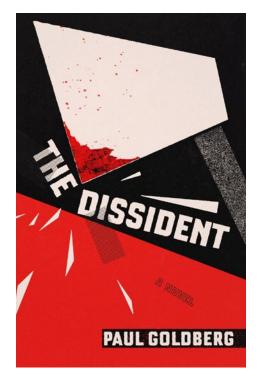
It was interesting to read about those who would show up to the hospital with a string where their time was basically up and demand help to stop it. And finances always creep into medicine, with hospitals deciding they wouldn't do anything to help those who were asymptomatic—after all, their early demise could involve an accident rather than a medical condition.

The book has a little bit of a feel of "The Twilight Zone," where short stringers meet their fate that is sealed in different ways right on time. The gun lobbyists started blaming the strings!

Issues of privacy, health care discrimination, and even political candidates' campaigns would be touched by string size. There is also a realization in planning a family that it is painful knowing with certainty that one would not be around at a certain age of their children.

As the mostly short chapters go on and on, the book also has a feel of brief entertaining episodes in a sitcom. Each chapter is focused on a different character and their continuing story. Some are sad with intense emotions. Betrayal, violence, romance, unexpected surprises, hope, and much wisdom for life and relationships await the readers.

The Dissident



I was honored to be asked by Paul in February, 2022, to look at a preprint of this novel, and these were some of my comments:

I read part I and it was great.

Interesting, articulate, primal, savage are words that come to mind.

A glimpse of the Jewish culture and a point in history during the cold war with global references, personal friendships, relationships and would be double agents.

Definitely a page-turner so far.

In the beginning I thought a map of the place where the wedding was in relation to where Schwartz and Foxman were found and maybe where Viktor's parents lived would be nice and where the river was and some of the streets.

There are many nice words with cultural meaning that would benefit from some sort of glossary.

Paul said:

Great idea re: map of Moscow, the boulevards, and tramway and trolleybus routes would be fun. Also, Bulgakov's house and Clear Ponds and Patriarch's Ponds. That's my Moscow! I will suggest it to the editor, who will say yes, I am sure. It's a compressed map.

The map showed up in the inside covers of the book that was published in 2023, and now I would have a chance to read the final product of Paul's years of work.

I'm reminded of sitting in a history class in 10th grade in New York, being taught about Russian history. The barbaric savagery came through loud and clear then, and I only wish I was a less distracted teenager at the time and learned more. Through this new fictional account, I would learn more from interesting events and experiences on the ground in Moscow. I am really looking to learn lessons about the culture and humanity as well as the politics that are all tied together.

Paul is a masterful storyteller and it's a delight to read his novel.

Part I of the novel starts with the wedding of Oksana Moksvina and Viktor Moroz, after a brief courtship in Moscow in the mid-1970's. There are vivid details of attire, fashion, menu at the wedding, and history—interwoven with references to the Bolsheviks, the Great October Socialist Revolution, along with a need to follow Jewish tradition for the wedding.

Viktor couldn't find his copy of "The Laws of Jewish Life," but there would be some old men, *alterkakers* (aka "old shitters"), who knew about Jewish weddings (*khasene in shtetl*).

There is a backdrop of life in Moscow at the time, with those who fear or don't fear the KGB. We read about jellied meat (*kholodetz*), Provencale cabbage, *salat Olivier*, Soviet mayonnaise, eggplant caviar, vodka, and so on. Vivid in his descriptions: "No finer *zakuska* than Hungarian fatback reclining upon a bed of sour rye has ever existed or can exist. Ukrainian fatback, which owes its whiteness to a coat of coarse salt, should not be neglected, and is not."

The description makes you salivate and want to taste these delicacies.

The *alterkakers* don't show up to confer some traditional Jewish blessings and no one volunteers to find them, so this falls upon Viktor the groom.

Viktor gets to the apartment of Albert Schwartz, aka "king of the refuseniks," who knew the *alterkakers*, only to stumble upon a horrific, fresh crime scene: Schwartz and Alan Foxman, an American diplomat and possible CIA operative, are badly butchered and left on top of one another in a sexual act.

Viktor knew Foxman, and they had previously spoken about anti-Semitism in America, with mention of 10% quotas in admissions at Harvard and Yale, but apparently not at the University of Chicago, where Foxman went.

The murders were just days before Henry Kissinger was to visit Moscow. We learn that Foxman had mentioned to Viktor that Kissinger was a "narcissistic prick," and that German Jews are referred to as Yekkes. Yekkes come up later in the book, and are explained through a joke in which someone who doesn't want to be thought of as a Yekke does something remarkably stupid in response to orders he is given.

Viktor didn't really understand the meanings and, after the murders, he felt he was in a nightmare that he must wake up from on his way back to his own wedding—and that he must also replace his blood-stained clothes on the way. Stolichnaya (vodka) is apparently superior to the Jack Daniels that Viktor had and is needed by then.

The wedding continues with vodka shots and a prayer.

The second part begins with the reader being introduced to Madison Dymshitz (aka Mad Dog), an American newspaper correspondent in Moscow, earlier in his life when he was a freshman at Harvard in the 60's. All I could think of was what a curious last name Paul came up with for a correspondent. Must be tough for the family members to live their lives with that last name.

During my vacation, I spent some time with my family on a short visit to a nice beach in Cozumel, Mexico. I entered Mexico with the book, "The Dissident," not really sure if it might be confiscated, but I wanted to keep reading. Well, nothing happened, and I was able to keep reading and leave Mexico to resume the vacation and my readings for the summer.

[Editor's note: Spoilers ahead!]

At Harvard, Mad Dog learned about the teachings of Marx: "Money is the jealous God of Israel, in the face of which no other God may exist." Viktor and Mad Dog get into a conversation about the Helsinki agreement, and, eventually, about the difference between "dissident" and "refusenik." Mad Dog thought they should be kept separate because of the dissidents' ideas of separating certain states from the USSR, which apparently did not come from the Jews or refuseniks.

It is clear that Mad Dog is looking for front page juicy news and not boring stuff that ends up in the back pages with travel ads. Page 19 is where such stories usually end up, and, as Mad Dog was showing Viktor, a story on that page showed a photograph that would be very significant. You'll have to read the novel to understand the significance.

Refuseniks are often seen singing Hatikvah, Israel's national anthem sometimes in Hebrew, in Russian, or in English. By the way, Mad Dog did make the front page after writing about how he was bitten by a Russian dog—there's stuff about dogs, including the most vicious ones.

We learn more about Oksana, her father, Rabbi Fishman, and the Moscow Choral Synagogue—where there is an inscription on the wall of a prayer to bless the state, as a kind of tax or rent. We also see the term "walrus prick," but you'll have to read the book.

The military state is ever-present with crushing violence to overpower the people. This includes, in some cases, the journalists. We learn early on in the novel that those who are known or who are foreign may not be roughed up as badly—or disappear as easily—because someone will notice.

It's also the case that when someone like Henry Kissinger (also known as HAK; he did make the cut at Harvard) visits, unsolved crimes can be brought up. It's also a small world where the foreigners in Moscow are connected to other famous individuals or academics in the U.S. and elsewhere.

I enjoyed reading a passage about fear and freedom. If we don't have fear, do we have freedom? "Does dispensing with fear beget freedom?" Both may be "illusory."

We get a glimpse into the life of a double agent with the fear and temptation to join either side. This is good stuff for those interested in the Cold War and global politics. The KGB admitted as much, and Viktor agreed that they could do that with the refuseniks, especially the ones whom they had a lot of information on.

At a certain point in reading the novel, I thought it would make a great movie, and the book should win a Pulitzer Prize. In any event, congrats to Paul on a masterpiece of literature of the highest quality.

The reader spends time with Viktor and Oksana throughout their relationship. We learn about Oksana's favorite food, meat pie that might be made of cat meat and deep fried in used motor oil, which gives them a deep smoky taste. We see them waltz and have a comedic exchange with an official about marriage rules to be "recognized by the Soviet state."

And here is a lovely quote about Comrade Mayakovsky, aka "The Poet," (Mayakovsky Square, Moscow): "They said it was love or lack thereof. Is a bullet through the heart from your own revolver in 1930 preferable to a bullet through the back of the head from someone else's in 1937?"

And another revelation in the context of Mad Dog, whose wife Melissa left to go back to Connecticut: "The Committee for State Security has entire departments that care passionately about sexual satisfaction of foreigners."

We learn about Yezhov, "Stalin's executioner, head of NKVD," and his diary that came Mad Dog's way, with a drawing of an "execution chamber" where "there is drain in middle. You can wash blood and brain with rubber hose or bucket of water."

Viktor was kidnapped by the KGB and given a choice: get fingerprinted and arrested for the murders or help them find the killer(s) in less than seven days when HAK visits. Neither choice was appealing as we entered part IV of the novel.

He sought advice that included that he shouldn't negotiate with Satan, and also that his chance for survival is actually greater if he chose the first option and went to a trial. But the KGB wanted his cooperation and assured him that HAK won't help the refuseniks.

Solving the murders along with the web of secrets and double agents, the involvement of the CIA and KGB, and some more surprises lie ahead for the readers.

You'll enjoy reading about the meeting between Brezhnev and Kissinger. HAK is still alive and recently in the news, so you'll have to decide what you think of him. I've always thought of him as a polished, wise diplomat, but I think after reading this novel I have new insights.

You'll enjoy reading the rest of Viktor's story. The novel captures the plight of the refuseniks in Moscow during the Cold War, before the Berlin Wall came down and the USSR was no more.

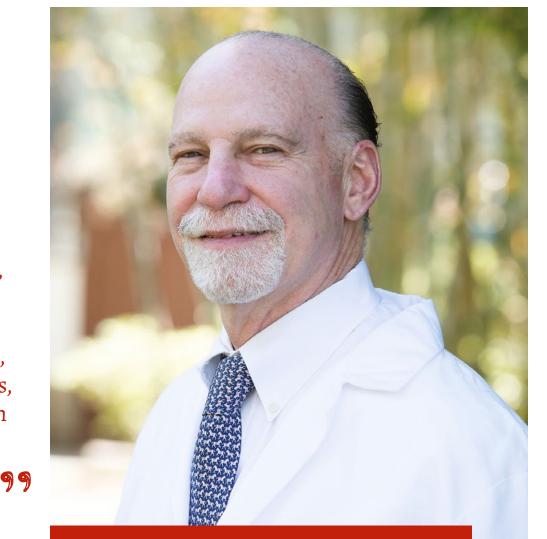
For those who care about truth and justice, you'll have to decide how you feel about what transpired. Life does go on, and I think the stories of history are things we must learn from.



Steve Rosen reads his poems—and tells us why he writes

66

I wrote the poem, 'Uncle Lenny.' She liked it, and she said, 'Dad, keep writing.' And so, every time I would get on a plane, for a number of years, I would write a poem if I had the time.



Steven T. Rosen, MD Executive vice president and director emeritus, Comprehensive Cancer Center and Beckman Research Institute of City of Hope; Professor, Division of Lymphoma, Department of Hematology & Hematopoietic Cell Transplantation Fifteen years ago, after the death of his favorite uncle, Steven Rosen committed his grief to paper.

Grief took the shape of a poem— "Uncle Lenny."

It was Rosen's first.

Over ensuing years, Rosen, an expert in hematologic malignancies who has served as director of the cancer centers at City of Hope and Northwestern University, has been writing poetry whenever he manages to steal a few moments.

His most recent collection, titled "<u>Heartfelt Reflections</u>," includes 200 poems. All have been translated into Spanish by Sol Gaitán, a Colombia-born poet, whose sister, Luz H. Gaitán-Dyer, is Rosen's patient of more than 40 years.



Rosen spoke with Paul Goldberg, editor and publisher of *The Cancer Letter*. Their conversation is also available as a <u>video</u>.

Paul Goldberg: Most people know you as the kind of guy who could write a CCSG grant application. Fewer people know about you as a poet. So, this is our opportunity to tell them.

Steven Rosen: Thank you, Paul. I appreciate it. It's not something that I think about in terms of a professional skill. It's been just a release, and it's been fun.

How did it begin? I see a poem that I suspect is important to you—"Uncle Lenny."

SR: My daughter is a businesswoman, but she went to USC for creative writing and is a published poet.

And when an uncle, Uncle Lenny, died he was like a second father—she said, "Put your thoughts on paper," because it was very emotional for me.

And I wrote the poem, "Uncle Lenny." She liked it, and she said, "Dad, keep writing."

And so, every time I would get on a plane, for a number of years, I would write a poem if I had the time. And so, she surprised me and took 25 of, say, the first 35 poems, and published it as a little piece called "Stolen Moments."

And a number of people saw it online when they would Google, and they said, "Keep writing."

And so, that motivated me to write again, in most instances when I was on a plane, going to a meeting or coming back. And over the years, periodically, after a glass of wine, I'd feel creative and write a poem or two; or when something meaningful happened in the world that I felt that I wanted to respond to in some philosophical way.

Well, you, you gave me a copy of "Stolen Moments" years ago, when you started. But can we talk about Uncle Lenny?

What's his last name?

SR: Chernick.

Chernick...

SR: My mother's brother. He didn't go to college. He served in the Korean War, and then became a rag man on the Lower East Side, with my father. And they worked together. they were the odd couple, for about 30 years, whereas my father was more the businessperson.

My uncle liked to drive the truck and deliver material, pick up material, always chitchat with people. Very passionate, loving individual.

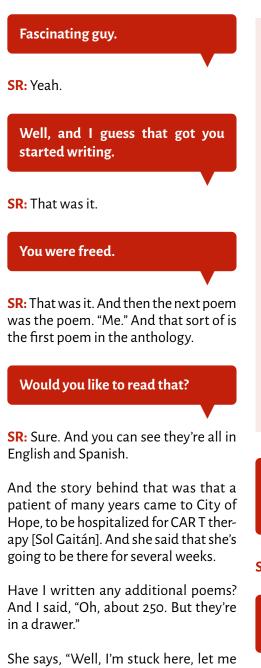
I wonder if you could read it.

SR: Sure:

He taught me to spit, wipe drip from my nose, swallow scotch with one gulp. Drove that truck like a limousine, owned the road. greeted the bums like they were generals. Couldn't tell if here, in fantasy, reflection or a tomorrow's moment. Potbelly, soulful, laugh, sway baby, sway, hug, all those girls. My uncle, my man, yes, my man, Took no shit, dignified sweatshirts, save your opinion. All got respect, color no issue, wealth, no issue. He's gone, tender words, real tears, real love. With his death some direction, with his death some comfort, with his death I am freed.

Everyone's asking, what did that mean? And what it meant to me at the time was my uncle didn't care what people thought about him.

And at his death, I realized that he was right. Be yourself and don't worry about what people think about you.



So, she read them. She liked them. She's from Colombia originally, and her sister

read them."

is a professor of Latin studies in New York. She [the sister] liked them, and she translated all the poems into Spanish.

And that's what appears in the anthology, which I'm very proud of.

So, I'll read to you:

ME

This for my children, few others could care, my voice my own. Libertarian, humanitarian, pragmatist not principles, but my essence, my philosophy. Pray to your god, choose your mate, govern your body, battle your addictions. No one's slave, no privileged births, equal without disclaims. Essentials for all, protection for all, justice, for all. Prison, for those who harm, praise for those that sacrifice, honor for those that heal. Respect, nature, treasure diversity, bless creativity. Let decency be your path, values, your guide, empathy your anthem.

The last book I have read that was poetry in Spanish and English was Pablo Neruda.

SR: There's nobody better.

What kind of poetry influences you?

SR: Pablo Neruda. If I could write like Pablo Neruda, that's all I would do.

You'd stop medicine. I think a lot of people, including your patients, would be very upset. I wonder if I could ask you to read "Leukemia Rounds."

SR:

Fifteen patients each with a separate story; private anguish, shared sorrow Fate or genetics brought you together; snuck up on you; no warning the victim Too cruel to comprehend; too complex to Unravel; too painful to discuss You lie in bed exhausted; afraid to ask the critical question: will I survive My challenge: find the answers: structure the cure Hope our mantra; prayer and research both okay; I will never abandon you

Hope. Our mantra of prayer and research both okay...

What would be another one that you'd like to read?

SR: You just pick a page. You said you wanted something from COVID?

I think COVID would be great. You have several COVIDs.

SR: Let me look and see. Which I don't know if any of them are particularly good, but we'll take a look.

Well, maybe I'll read the first two COVID ones, because they're short and quick.

An insidious fog blankets the planet Siphoning life from every shrub Aligned with the wind sans boundaries Lurking as a shadow filling each sinister crevice Cryptic origin absent lucid culmination We patiently wait knowing the only certainty is that our love will endure.

And then the next:

Time has lost its cadence Days blend without an apparent tomorrow Oppressive gloom hovers suffocating joy Finite or eternal torment Speculation more concrete than fact Future now an obscure journey

That was written at the beginning of COVID when... God knows what was gonna happen.

What was it like for you?

SR: It was very lonely. I was here in the executive area of our medical pavilion, and only the medical director and myself were coming to work.

And I came to work in part because I felt the obligation in part because I have patients. And we were all trying to sort out what would happen. I remember living in a hotel for two months, and because my son had COVID very early on, so, yeah. Sorry. I think it would be amazing to read "Metastatic Cancer."

SR:

I have witnessed the anguish of terminal cancer Emptiness that suffocates Helpless grappling with the inevitable No silver lining Only yesterdays remain Wishing there was reprieve

Now, one that's a little lighter—"Love."

Love is life's reward; a feeling without calculation; speaks to man's most fundamental need No labor; no plotting; no pretense The essence of happiness; the fabric of human Connection; the glory of each day Requires no promises; no rituals, no demands For love, has a silent voice; words symbolic; intimacy its core Grow old with me; cherish each memory; whisper our names

What about marriage? Since we're on that subject. Page 296.

SR:

Do you measure time by the seasons through the shape of the moon in the passage of a single day Is it the memory of Paris; the subway journey, the onion bagel Laughter in the tub; a cold winter's night; walking dogs up the hill Remember holiday meals, endless sporting events, a horseback ride in Ireland Children's toes; Chitchat and wine; ocean water mixed with sand Our first kiss; passion and ecstasy; a life together

Ironically, sadly, that marriage ended, not because of me, but it ended. And I've regrouped.

Let's see. I'll give you the one— "Five Decades."

This one has been published. Others chose it. So, it's been taken into another anthology. And it reveals a lot about my life, but...

She left me the morning of our forty sixth anniversary A poignant affirmation of seething anger Four children, an exquisite granddaughter, hundreds of devoted friends, a dozen dogs of varied breeds, a quarter horse and Palomino, 18 homes, three RVs of assorted lengths, cross country and global travel, scores of social events, classic movies, shows, and countless sporting contests, beach and mountain hikes, ten thousand blissful memories and three decades of supporting her father—all now meaningless commodities My punishment for all her disappointments in life Unconditional love an empty anchor, no longer valued Hopefully she would at least remember that I held her in my arms every night

So, now, you know my whole life.

It's amazing—that's Uncle Lenny's gift; right? The way that you were able to do that...

SR: So tell me about you. What are you up to?

Well... I write prose.

SR: I know you write very good prose. Yeah. Very wonderful.

Is there any other poem you would like to read?

SR: I haven't read this in a long time. I just happened to open the page. I have no idea if it'll come out good or bad, but I saw a poem that says "Meaning." So, let's see what meaning's all about.

It says:

We all struggle to find the uniform theme that brings meaning to the chaos of life That poignant concept that resonates with our mind, heart and surges through our marrow The great tragedy is the absence of a universal perception that can even for a brief moment provide comfort Age, magnifies the folly of sorting out a concrete motive for humanity So I just relish in the joy of love and intimacy For if you genuinely connect with another you are joined in the journey

What are you writing now?

SR: The last one I'm a few sentences into is about wine, because I go to a wine tasting and it seemed like something appropriate to write about since I hadn't written about it. And I enjoy it so much. But besides that, I'm just writing medical things, all the usual things that I'm engaged in.

Do you have any other thoughts? Anything I forgot to ask?

SR: Well, we can do one that's sort of more pithy about death.

If lucky one to two decades remain Leaves one numb, more philosophical and reflective of life's perplexity Impossible not to struggle with the finite terms of existence Can we measure one's impact when time is ephemeral Grasp the unifying concept that provides comfort or perhaps value Sustained by love I would prefer to live another day

So...

Thank you so much.

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Over the years, periodically, after a glass of wine, I'd feel creative and write a poem or two; or when something meaningful happened in the world that I felt that I wanted to respond to in some philosophical way.

99

OBITUARY

Pioneering oncologist Irwin H. Krakoff dies at 100



Irwin H. Krakoff, former director of the University of Vermont Cancer Center who has also served in key jobs at Memorial Sloan-Kettering Cancer Center and MD Anderson Cancer Center, died on Aug. 9 in Savannah, GA.

rakoff had turned 100 on July 20 (The Cancer Letter, July 28, 2023).

Born in Columbus, OH, to Morris and Freda Krakoff, he earned his undergraduate and medical degrees at The Ohio State University. After a residency at Boston City Hospital and service as a medical officer at the US Naval Base in Yokosuka, Japan, he began a long and distinguished career in cancer research, treatment and education at Memorial Sloan-Kettering Cancer Center.

One of the early pioneers, Krakoff served as chief of the chemotherapy service and vice chairman of medicine at MSKCC. His work focused on chemotherapy and pharmacology, and his scientific studies focused on reducing the side-effects of cancer treatments while maintaining their effectiveness.

While at MSKCC, he received the Alfred P. Sloan Award in recognition of his substantial contribution to the care of patients and the understanding of cancer.

In 1976, Krakoff was recruited by the University of Vermont Medical College to be the founding director of its cancer center. He held that post for 7 years during which the center was awarded major funding from the NCI (*The Cancer Letter*, July 29, 2022; June 4, 1976).

In 1983, Krakoff was recruited to become the head of the Division of Med-



Rosemary Mackey and Irwin Krakoff with Waun Ki Hong outside the couple's home in Savannah, GA. Source: Krakoff, from Hong's 2019 obituary.

icine at M.D. Anderson Cancer Center, where in ten years he built one of the world's most outstanding and respected new drug development programs, while insisting on quality clinical research and unbiased reporting (*The Cancer Letter*, July 22, 1983).

He counted among his greatest accomplishments the achievements of members of his faculty and the hundreds of fellows that he trained throughout his career. Krakoff's trainees included Waun Ki Hong (*The Cancer Letter*, Jan. 11, 2021) and Gianni Bonadonna (*The Cancer Letter*, <u>Sept. 11</u>, 2015).

Richard Pazdur, director of the FDA Oncology Center of Excellence, was one of the young physicians Krakoff mentored at MD Anderson.

In 1993, Krakoff was awarded the American Society of Clinical Oncology's highest honor when he gave the David A. Karnofsky lecture at its annual meeting.

After his retirement from M.D. Anderson, he and his wife Rosemary W. Mackey, a cancer center administrator, collaborated on consultations with major medical centers in the United States, Mexico, and Scotland in the restructuring of multidisciplinary clinical and administrative cancer programs; the last of which was the rebuilding of the Cancer Program at NYU Medical Center in New York.

"I last saw Irv Krakoff a few weeks ago when we celebrated his 100th birthday," said Jerome Yates, a friend who in 1976 recruited Krakoff to the top job at UVM.

"Over the past 50 years, our conversations were often punctuated by humorous observations that kept us both humble in our respective research pursuits," Yates said. "I was heavily involved in cooperative group clinical studies and he was actively contributing to cancer drug development. "He would get my attention by saying, 'You guys reach statistically significant answers to insignificant questions."

"Irv was always collaborative in his approach to colleagues, trainees and others involved in cancer research," Yates said. "He knew the right questions to ask and how best to pursue the right answers.

"I have lost a good friend, and oncology has lost a major contributor to research."

In a birthday greeting to Krakoff three weeks ago, FDA's Pazdur wrote:

The traditional Polish birthday wish/ greeting is '<u>sto lat</u>,' translating to 'one hundred years'—how fitting! I often think of Irv, <u>Marty Raber</u>, and my time with both at MD Anderson. Those years were the best of my career. Irv taught me many principles of leadership... Perhaps the best was allowing people space to develop, but always being there if needed. I often relate this principle to those MDs that I lead and attribute it to Irv.

So—sto lat, Irv!

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He would get my attention by saying, 'You guys reach statistically significant answers to insignificant questions.

Krakoff at this 100th birthday celebration, with Jerry Yates.



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Over the past 50 years, our conversations were often punctuated by humorous observations that kept us both humble in our respective research pursuits.



– Jerome Yates

Krakoff is survived by Mackey, his wife of 39 years, his two sons, Peter and Charles Krakoff, his daughter, Ellen (Nellie) Walcoff, two stepdaughters, Catharine Lentz and Claire Thompson, eleven grandchildren and two great granddaughters, all of whom he was immensely proud.

Funeral services will be private.



Members of MD Anderson Cancer Center's "Class of '83:" Isaiah J. (Josh) Fidler, Margaret Kripke, Mackey, and Krakoff. Source: Krakoff and Mackey, from Fidler's 2020 obituary.



Stay connected to our podcasts and conversations that matter.

During our 50th anniversary, we look back at the many scientific breakthroughs discovered at the Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins. Join conversations with Dr. Bill Nelson, Dr. Otis Brawley, Dr. Elizabeth Jaffee, and Dr. Stephen Baylin, among others. Join the conversation <u>here</u>.



1973-2023 TURNING RESEARCH INTO RESULTS



THE SIDNEY KIMMEL COMPREHENSIVE CANCER CENTER **IN BRIEF**



Boris C. Pasche named president & CEO of Karmanos, chair of Wayne State Department of Oncology



Boris C. Pasche was named president and CEO of the Barbara Ann Karmanos Cancer Institute and chair of the Wayne State University School of Medicine's Department of Oncology.

In these leadership roles and pending formal NCI approval, he will serve as the principal investigator of the Comprehensive Cancer Center Core Grant.

Pasche assumes the role Joseph Uberti served in an interim basis, following the retirement of Gerold Bepler.

Pasche arrives at Karmanos and WSU from Wake Forest Baptist Health in Winston-Salem, NC, where, in addition to his duties as an attending physician specializing in gastrointestinal malignancies, he held additional leadership and academic positions, including the Charles L. Spurr Endowed Chair of Cancer Research, chairman of the Department of Cancer Biology, and director of the Comprehensive Cancer Center, during which he oversaw an expansion that resulted in a doubling of the program's NCI funding, a hallmark of the strength of an organization's research programs (The Cancer Letter, Feb. 25, 2022).

Additionally, he directed the reorganization of its scientific programs and recruited 72 new faculty members. These efforts led to the successful renewal of the NCI core grant in 2016 and again in 2021.

Over a career that stretches more than 30 years, Pasche has served in various clinical and academic positions.

He was chief of the Division of Hematology/Oncology at the University of Alabama at Birmingham, where he expanded the clinical and research programs, recruited 19 new faculty members, and tripled its funding. He was also deputy director of the University of Alabama Comprehensive Cancer Center. Prior to that, he was the founder of the Cancer Genetics Program at Northwestern University in Chicago.

At Karmanos, Pasche will set the strategic vision for the future growth and development of the Karmanos, the largest cancer provider and researcher in Michigan and northern Ohio, and implement that vision, which includes planning and evaluation, scientific direction, community outreach and engagement, coordinated delivery of multidisciplinary clinical cancer care, advancement and development activities through the Karmanos Cancer Foundation and organizational administration.

As chair of the WSU Department of Oncology, Pasche will provide the strategic vision, leadership and planning to advance the department's cancer research and clinical care, including the recruitment of additional faculty to achieve this mission.

Thomas J. Herzog named president of GOG Foundation



Larry J. Copeland passes The GOG Foundation Inc. presidential gavel to Thomas J. Herzog.

Thomas J. Herzog was elected the president of The GOG Foundation Inc at the NRG Oncology summer meeting on July 20.

Herzog succeeds Larry J. Copeland.

A practicing gynecologic oncologist and member of the board of directors of GOG-F, he was the treasurer of GOG-F from 2014-2023. Prior to taking presidential office, Herzog was associate director of the GOG Partners program. He is currently deputy director of the University of Cincinnati Cancer Center and Paul & Carolyn Flory Professor in the Department of Obstetrics and Gynecology at the University of Cincinnati.

Herzog has also served on the board of directors or leadership council of the Society of Gynecologic Oncology, the Foundation for Women's Cancer, board of governors for the American College of Surgeons, American Board of Obstetrics and Gynecology-Gynecologic Oncology Division, and the International Gynecologic Cancer Society.

Herzog will be responsible for GOG-F, which includes the GOG Foundation corporate membership in the NRG Oncology Foundation Inc., and GOG-P program. The GOG-F, formerly known as the Gynecologic Oncology Group, in collaboration with the NSABP Foundation Inc. and the RTOG Foundation Inc., formed a new 501(C)(3), in 2012—NRG Oncology Foundation Inc..

In addition to the NRG responsibilities, Herzog will also oversee the GOG Partners program founded in 2013 and work alongside Robert Mannel, senior vice president of GOG-F. Mannel is also one of the group chairs that is responsible for the research conducted by the NRG Oncology clinical cooperative group that is a member of the NCI National Clinical Trials Network.

"Following a true legend like Dr. Copeland is not easy, but I pledge to honor the principles that he and Dr. DiSaia so effectively instilled in our group as tremendous leaders in our field," Herzog said in a statement. "I am cognizant of the need to ever improve our organization to face the challenges of maintaining our role as the premier clinical trials network in gynecologic malignancies in North America and beyond. Initiatives in diversity, operational transparency, translational research, site expansion, and improved trial efficiencies are ongoing, and will be further developed moving forward."

Copeland, who now serves as immediate past president, presided over unprecedented growth in the clinical trials program, particularly in GOG-Partners, including a greatly expanded clinical trials portfolio, further expansion and engagement of its investigator base, development of a clinical trial mentorship program, and multiple educational initiatives focused on novel agents, clinical trial design and clinical trial execution.

Alexander Price named assistant professor at Wistar



Alexander Price was named assistant professor in the Gene Expression and Regulation Program of the Ellen and Ronald Caplan Cancer Center at The Wistar Institute.

Price's research focuses on how viral genomes are controlled during infection—specifically, how viruses regulate and exploit RNA transcription and processing. His work aims to identify and exploit therapeutic targets underlying how viruses hijack cellular transcriptional machinery to combat disease.

"We are immensely pleased to welcome Alex Price to Wistar. The Institute is committed to expanding our understanding of viruses' role in cancer as well as other disease, and the establishment of the Price Lab at Wistar represents a significant investment in the Institute's research capacity," Dario Altieri, Wistar president and CEO, director of the Ellen and Ronald Caplan Cancer Center, and the Robert and Penny Fox Distinguished Professor, said in a statement. "Alex's experience in viral RNA and DNA research makes it clear that he will make compelling, fresh contributions to Wistar's research program."

Yu "Sunny" Liu named assistant professor at Fox Chase



Yu "Sunny" Liu was named assistant professor in the nuclear dynamics and cancer research program and the Cancer Epigenetics Institute at Fox Chase Cancer Center.

Liu's research will center around the folding and regulation of the genome in three-dimensional spaces and how misfolding of the genome can lead to cancer. His team's long-term objective is to combine epigenetics, 3D genomics, and artificial intelligence algorithms to enhance cancer diagnostics and develop more effective therapies for the benefit of patients.

Previously, Liu worked as a postdoctoral researcher at the University of Massachusetts Chan Medical School, where he investigated the molecular mechanisms of genome folding and developed innovative methods for capturing chromatin.

From 2014-2015, Liu pursued a postdoctoral research position at the Lunenfeld-Tanenbaum Research Institute in Toronto. During this time, he developed an innovative approach for analyzing the whole transcriptome of archival tumor samples, which can improve the diagnosis of bladder cancer. He also investigated the role of cancer-associated enhancer RNAs.

Michael G. Tecce named assistant professor at Fox Chase



Michael G. Tecce was named assistant professor in the Division of Plastic and Reconstructive Surgery in the Department of Surgical Oncology at Fox Chase Cancer Center.

Tecce will focus on complex cancer reconstruction using microsurgery in

bone, soft tissue, and the lymphatic system. A Philadelphia native, he completed his residency in plastic and reconstructive surgery at the University of Pennsylvania, followed by a microsurgical fellowship at Memorial Sloan Kettering Cancer Center.

His research interests include utilizing technology-based platforms to improve delivery of patient care, microsurgical reconstruction, and management of lymphedema.

Tecce is a member of several professional organizations, including the American Society of Plastic Surgeons, the American College of Physicians, and the Pennsylvania Medical Society.

Tecce will be seeing patients at Fox Chase as well as Chestnut Hill Hospital. At these sites, in addition to providing high-level reconstructive services, he will be leading the development of a regional center of excellence in the management and treatment of lymphedema.

City of Hope receives \$32.3M from CIRM

Researchers at City of Hope were awarded \$32.3 million from the California Institute for Regenerative Medicine to support three novel phase I clinical trials evaluating innovative cell and gene therapy treatments for patients with acute myeloid leukemia and other diseases.

"These CIRM awards are a testament to City of Hope's commitment to the advancement of gene therapies for the treatment of human diseases," said John D. Carpten, City of Hope's chief scientific officer, Irell & Manella Cancer Center Director's Distinguished Chair, and Morgan & Helen Chu Director's Chair of the Beckman Research Institute, said in a statement. "Through our tireless pursuit of best-in-class research and innovation, we believe our work at City of Hope will benefit patients living with HIV or impacted by cancer, and we thank CIRM for its support to help make this a reality."

CIRM awarded a City of Hope team led by Elizabeth Budde, nearly \$12 million to develop and conduct a first-in-human phase I immunotherapy trial for acute myeloid leukemia, which has the highest mortality rate of all blood cancers.

"It is critical to find more effective therapies for patients whose AML has relapsed," Budde, a City of Hope associate professor in the Department of Hematology & Hematopoietic Cell Transplantation, said in a statement. "We are hopeful that this novel therapy will eventually enable City of Hope and other institutions to offer a new treatment for patients whose AML has returned. We are very grateful for the recognition and support from CIRM."

Most AML patients who go into remission after one treatment will develop the disease again and will then need a blood stem cell transplant from a donor. Even after a transplant, patients can still relapse, leaving them with few treatment options.

The CIRM-funded trial will be the first to use T cells from a healthy donor who has donated stem cells for the AML patient to undergo a transplant. These cells will be reengineered in a laboratory to express CD33CARs, or special receptors on a cell's surface.

These CARs will target the CD33 protein, which is found in more than 80% of AML cases. T cells harboring the CD33CARs will also be multiplied to millions and then infused back into the patient. The CARs are living cells and expected to multiply inside a patient's body and recognize and kill the cancer cells. Before receiving the CAR T-cell therapy, patients will receive chemotherapy to prepare their bodies to accept the CAR T cells.

The trial, which will enroll up to 18 AML patients who have relapsed after receiving a transplant, will evaluate the CAR T therapy's safety and its effectiveness in eliminating leukemia cells.

City of Hope's David Horne, Marissa Del Real, Karam Sandhu, and Anthony Stein, are co-investigators on this project.

Another City of Hope research team received \$9.05 million from CIRM to start a clinical trial using a novel blood stem cell transplantation procedure for severe aplastic anemia, a rare bone marrow disease that can turn into blood cancer and is currently difficult to treat. If successful, the treatment could also be used for other autoimmune diseases, such as treatment-resistant type 1 diabetes.

Currently, a blood stem cell transplant from a related or unrelated donor whose human leukocyte antigen genes match a patient's HLA is the most effective treatment for severe aplastic anemia. However, it is difficult to find unrelated donor matches for people of color due to a limited number of donors from various racial and ethnic groups. Transplants can also cause severe side effects, particularly in older patients.

Defu Zeng, a City of Hope professor with the Department of Immunology & Theranostics within the Arthur Riggs Diabetes & Metabolism Research Institute, has led research on the potential therapy, which involves induction of mixed chimerism in adult patients. Mixed chimerism refers to transplanting blood-forming stem cells from a healthy, half-matched family member donor into a patient who has received a milder, less toxic chemotherapy treatment free of radiation that removes some, but not all, of the patient's diseased bone marrow stem cells.

The phase I trial is expected to start later this year and will enroll up to six patients. City of Hope has treated patients with sickle cell diseases using this novel therapy in a clinical trial also funded by CIRM.

Catriona Jamieson from Aspera Biomedicines Inc. was also awarded \$3.2 million for a proposal titled, "Cancer Stem Cell Interception with Rebecsinib: A First-in-Class ADAR1 Inhibitor."

Baylor, Texas Children's awarded \$7.6M to study disparities for Latino survivors of childhood cancer

Researchers at Baylor College of Medicine and Texas Children's Cancer Center were awarded more than \$7.6 million over four years from NCI to comprehensively study late effects of childhood cancer in a diverse population of childhood cancer survivors, including their medical, neurocognitive, and psychosocial outcomes. In addition, they will evaluate potential educational and sociodemographic barriers to obtaining survivorship care.

In 2021, these researchers received a \$2 million award from the NCI to fund the "Survivorship and Access to care for Latinos to Understand and Address Disparities" study.

Pediatric cancer centers across Texas, including Texas Children's Cancer Center, Vannie Cook Children's Cancer Clinic, University of Texas Southwestern/ Children's Medical Center of Dallas, Cook Children's Medical Center, and El Paso Children's Hospital, enrolled children with cancer in this trial.

The recent award from the NCI will fund ongoing recruitment of childhood cancer survivors and collection of data about their long-term outcomes. In addition, data collection will be expanded to also include results of genotyping and metabolomic profiling studies, as well as clinical, demographic and social determinants of health data.

"We will study how individual children metabolize the chemotherapeutic agents that they receive, since differences in metabolism may impact the incidence of toxic side effects and, in turn, may limit the amount of chemotherapy delivered, ultimately impacting treatment effectiveness and outcomes," Michael Scheurer, co-principal investigator of the study, professor of pediatrics-hematology and oncology at Baylor, and associate director for excellence in cancer equity at the Dan L Duncan Comprehensive Cancer Center and Sidney L. and Donald F. Faust Chair of Pediatric Cancer Epidemiology at Texas Children's Hospital, said in a statement. "The information we gather in this study should provide insights into why we sometimes observe worse outcomes in Latino survivors of childhood cancer."

Lisa Kahalley, co-principal investigator of the study, will lead research on patient-reported experiences, including cognitive, behavioral, and psychosocial outcomes, as well as symptoms related to toxicities and late effects of cancer treatment.

"Because this is a longitudinal study, we will learn when certain issues become apparent or problematic for survivors. That will inform our timing as well as our focus on screening and interventions for childhood cancer survivors," Kahalley, professor of pediatrics-psychology, associate chief of pediatric psychology research at Baylor, and director of neurobehavioral oncology at Texas Children's Cancer Center, said in a statement. Kahalley also is a member of the Dan L Duncan Comprehensive Cancer Center at Baylor.

Another aim of the study is to better understand the barriers to survivorship care that Latino patients face, including their preferences for survivor education. Monica Gramatges, co-principal investigator of the study, is leading this component of the research.

As part of the SALUD study, her team conducted a survey of survivors and their caregivers to understand their preferences for content and education modalities. Using feedback from that survey, her team is developing two-minute animated videos that succinctly explain, in both English and Spanish, specific late effects and topics prioritized by survivors and their caregivers. Her team also is collecting patient-reported data on the facilitators and barriers to survivorship care, including focus group discussions to further examine the qualitative factors underscoring these barriers.

"Non-white people are underrepresented in survivorship research," Gramatges, associate professor of pediatrics-oncology at Baylor and co-director of the Long-Term Survivor Program at Texas Children's Cancer Center, said in a statement. Gramatges also is a member of the Dan L Duncan Comprehensive Cancer Center at Baylor.

"This NCI grant will allow us to fill a major gap in understanding the experience of Latino survivors of childhood cancer," Gramatges said. "Our hope is that these results will inform clinical practice guidelines that assess risk and inform screening for late effects of childhood cancer treatment. With input from survivors and their families, our goal is to transform the delivery of education for survivors in a way that will help engage them in long-term follow-up care."

Gracell Bio enters into \$150M private financing deal to expand on CAR T therapies

Gracell Biotechnologies Inc. has entered into a purchase agreement with a group of institutional and accredited healthcare specialist investors. Gracell will receive \$100 million in proceeds from the private placement of ordinary shares, with up to an additional \$50 million.

The transaction includes participation from new and existing institutional investors and is being led by Vivo Capital, with participation from investors including Adage Capital Partners LP, Exome Asset Management, Janus Henderson Investors, Logos Capital, OrbiMed, Pivotal Life Sciences, RA Capital Management and TCGX, among others.

Gracell intends to use the net proceeds from the proposed financing to fund research and development of its clinical-stage product candidates and research programs and for working capital and other general corporate purposes. The aggregate proceeds from this proposed financing, combined with current cash, cash equivalents, is expected to be sufficient to fund the current operating plan into the second half of 2026.

DeGregorio Family Foundation awards \$87,500 to Howard University researcher to study immunotherapy in gastric cancer The DeGregorio Family Foundation with the support of the Price Family Foundation and the Esophageal Cancer Awareness Association has awarded \$87,500 to Dawit Kidane-Mulat, associate professor at Howard University College of Medicine, to complete his grant focused on improving the effectiveness of immunotherapy in gastric cancers.

The overarching goal of this study is to harness XRCC1-deficient gastroesophageal cancer cells that will likely enhance the efficacy of immunotherapy response. Kidane-Mulat is examining how defective XRCC1 and DNA damage response targeting contributes to aberrant innate immune cells' inflammatory response.

This work lays the foundation for additional in-depth preclinical studies, and for the development of novel therapeutic strategies for stomach cancer.

"As a result of this award, I am generating a long line of research into understanding the basis of DNA repair/ response and immunotherapy treatment in stomach cancer," Kidane-Mulat said in a statement. "This grant award is opening a new opportunity to propel the field forward and build a solid foundation for future immunotherapy therapeutic strategies in gastric cancer."

The DeGregorio Family Foundation has raised more than \$8 million to fund innovative research focused on curing gastric and esophageal cancers.

Mount Sinai oncologist Krystal Cascetta, 40, and her infant daughter die in Somers, NY, home



Krystal P. Cascetta, a 40-year-old New York City oncologist, and her 4-monthold infant daughter were found dead at a home in Somers, NY, Aug. 5 in what police <u>describe</u> as a possible murder-suicide.

"The New York State Police Bureau of Criminal Investigation (BCI) Somers are investigating a murder/suicide in the town of Somers, NY. A preliminary investigation revealed that at approximately 7am, Krystal Cascetta entered her child's room and shot her baby and then turned the gun on herself. The scene is consistent with a murder/suicide."

According to her Mount Sinai profile, Cascetta was an assistant professor of medicine within the Division of Hematology and Medical Oncology at the Icahn School of Medicine at Mount Sinai, and site chief of the Mount Sinai Queens Infusion Center.

"We extend our deepest sympathies at this sad moment to Dr. Cascetta's family, friends, colleagues and patients," Mount Sinai officials said in a statement.

FUNDING OPPORTUNITIES



DKMS 2024 John Hansen Research Grant accepting applications

The application period for the DKMS John Hansen Research Grant 2024 began Aug. 1.

DKMS supports up to four outstanding research projects in the field of stem cell transplantation or cell therapy each year. The grant is aimed at young scientists who have obtained a doctoral degree no more than 10 years ago.

The grant amounts to €240,000 each and will be paid out over a period of three years. The application deadline is Nov. 30.

DKMS is the world's largest stem cell donor center, with more than 11.5 million registered potential stem cell donors. The non-profit organization is also deeply involved in the medical and scientific field.

"Every year, more than 1.2 million people around the world are diagnosed with blood cancer and, though a stem cell transplant can save the lives of many of them, not all patients are permanently cured afterwards," Marcel van den Brink, chairman of the DKMS Medical Council, said in a statement. "Still, relapses and severe complications, most notably graft-versus-host disease, pose major challenges to medicine and science. We want to contribute to the continuous improvement of stem cell transplantation and other cellular therapies."

To this end, DKMS runs its own research projects and is committed to ensuring excellent research for the future.

"It is a matter close to our heart and the DKMS John Hansen Research Grant enables talented young scientists to work on their promising projects for the benefit of patients worldwide," van den Brink said.

All information on the application modalities, as well as further details on the John Hansen Research Grant, are available on the DKMS Professionals' Platform. If you have any questions, interested parties are also welcome to contact DKMS by email at grant@dkms.org.



The Cancer Letter is taking a publication break. We will return on Sept. 8.



Associate Director for Research Administration UPMC Hillman Cancer Center, Pittsburgh, PA

UPMC Hillman Cancer Center (Hillman) seeks a talented and experienced individual to step into a highly supportive environment as Associate Director (AD) for Research Administration. This is a very exciting time for a new AD for Administration to join Hillman, a National Cancer Institute (NCI)-designated comprehensive matrix cancer center strongly supported by UPMC and the University of Pittsburgh School of Medicine. The Hillman Foundation has committed a large amount of continued support for our Center over the next 10 years, including nearly 100K ft² of new research building space in the adjacent "Assembly" building dedicated for Hillman members. The new AD will collaborate with over 330 Hillman Cancer Center members to promote and invest in strategic new projects, recruits, shared resources, and pilot programs. With our new expansion of space for Hillman researchers and extensive clinical network (over network 70 sites), Hillman is unified and supportive of cancer research, prevention, and therapy.

In 2020, Hillman celebrated its 34th anniversary and the renewal of its 5-year National Cancer Institute (NCI) Cancer Center Support Grant (CCSG) that resulted in Hillman Research Administration scoring in the 'Exceptional' range and qualifying Hillman for a 2-year merit extension. Hillman has over 330 members, 7 scientific programs, 12 CCSG-supported shared resources, \$110 million of peer-reviewed cancer-relevant funding with nearly \$50 million from NCI, and an institutional funding base greater than \$150 million.

The AD for Research Administration reports directly to the Hillman Cancer Center Director and is a member of Hillman's Senior Leadership Team. Primary duties and responsibilities include: primary coordination and assembly of the cancer center support grant (CCSG) P30 and annual reports, planning and management of NCI site visits and the external advisory board (EAB), oversight of Hillman facilities, scientific shared resources, development, facilitation and support of multi-component team science cancer research programs, as well as spearheading internal and external collaborative research endeavors. To meet the position requirements, the AD for Research Administration will collaborate with a team of administrators, fiscal leaders, and PhD/MD-level scientists, coordinate vision setting and strategic planning; support and participate in CCSG Research Program and Shared Resource activates; develop operational and administrative policies and procedures; work with the Hillman Fiscal Office to develop budgets and monitor spending; develop staff and space utilization plans; oversee facility operations; and communicate research outcomes to Hillman investigators, the NCI, and the public. To facilitate and advance Hillman science, the AD will also: coordinate CCSG preparation and submission; grow the funded research base, with emphasis on multi-disciplinary collaboration with internal and external investigators; work with the Hillman Development Office to promote and increase philanthropic donations; and assist in recruitment of faculty.

Pittsburgh is routinely ranked as one of the top-most livable and affordable U.S. cities. Located in the city of Pittsburgh's Shadyside neighborhood, Hillman is an NCI-designated comprehensive matrix cancer center focused on state-of-the-art cancer research, training the next generation of cancer researchers, and community outreach. Hillman serves 29 western PA counties serving nearly 5 million individuals and provides unique opportunities to collaborate with clinical and translational research programs involved in cancer patient care, including the University of Pittsburgh, Magee-Women's Research Institute, and UPMC Children's Hospital of Pittsburgh.

Candidates for the position must have a PhD, MD, or master's degree in business administration, policy, or other research administration-relevant field. Candidates also must have 5+ years in research administration, which includes an understanding of the regulatory requirements and complexities pertaining to animal and clinical research; detailed knowledge of NCI CCSG requirements; experience with NCI-funded cancer centers and site visits; and excellent written and oral communication, computer, people management, and interpersonal skills. Candidate may be eligible for an Associate Professor faculty position commiserate with experience.

To apply for requisition # 23005131, please complete an application on our Talent Center website – <u>https://join.pitt.edu</u>. Please also feel free to send a 1-page personal statement highlighting your qualifications and experience, along with your CV or resume, to Hillman Director, Robert L. Ferris, MD, PhD (care of <u>hollidaysm3@upmc.edu</u>).

The University of Pittsburgh is an Affirmative Action/ Equal Opportunity Employer and values equality of opportunity, human dignity, and diversity, EOE, including disability/veterans.

THE CLINICAL CANCER LETTER

CLINICAL ROUNDUP



City of Hope researchers develop a CAR T-cell therapy for advanced ovarian cancer, now in phase I

City of Hope researchers published preclinical research in *Nature Communications* demonstrating that a CAR-engineered T-cell therapy worked against ovarian cancer in the laboratory and in preclinical models.

"City of Hope's research helped develop CAR T-cell therapies for blood cancers, and these patients are now seeing long-term benefits from the therapy, but we can't stop there," Saul Priceman, associate professor in the Department of Hematology & Hematopoietic Cell Transplantation and associate director of Translational Sciences & Technologies in the T Cell Therapeutics Research Laboratory at City of Hope, said in a statement. "The next frontier is solid tumors, and City of Hope is taking on that challenge."

The therapy is currently in a first-in-human phase I trial at City of Hope for patients with advanced epithelial ovarian cancer who have already received platinum-based chemotherapy.

The trial, led by Lorna Rodriguez-Rodriguez, professor in its Division of Gynecologic Oncology in the Department of Surgery at City of Hope, is testing the therapy's safety, side effects, and activity in patients. The trial is currently enrolling patients for treatment.

The team's most recent research found that a CAR T-cell therapy targeting TAG72, a target found on the surface of ovarian cancer cells, eradicates cancer cells in mouse models.

"What's exciting about this is that TAG72 is also found on other cancer cells, including pancreatic, colorectal, breast, and brain tumors, so if the clinical trial in ovarian does well, we can investigate expanding this to other patients," Priceman said.

Priceman and his team also found that by adding the cytokine Interleukin-12, a protein that sends signals to the immune system, to the CAR T-cell therapy, the treatment worked more effectively against cancer cells in the lab. The cofirst authors Eric Hee Jun Lee and John P. Murad, along with the rest of the team, showed that IL-12 also enabled the T cells to fight the cancer, leave the tumor area, enter the bloodstream, and target other cancer cells around the body. IL-12 is not currently part of the current phase I clinical trial. The preclinical research also found that delivering the CAR T-cell therapy via an injection where the cancer is located, regionally, is also effective in enabling CAR T cells to target cancer elsewhere. This technology allows for both safety and improved anti-tumor activity in several cancer types tested to date.

Analysis challenges hypothesis that depression and anxiety increase cancer risk

Depression and anxiety are thought to increase a person's risk of developing cancer, but research results have been inconclusive. In an analysis of multiple studies from the Netherlands, the United Kingdom, Norway, and Canada, investigators found that depression and anxiety are not linked to higher risks for most types of cancer among this population. The analysis is published in *Cancer*.

Experts have suspected that depression and anxiety may increase cancer risk by affecting a person's health-related behaviors or by having biological effects on the body that support cancer development. Some research has supported an association between depression, anxiety, and cancer incidence, while other investigations have found no or negligible associations.

To provide additional insights, Lonneke A. van Tuijl of the University Medical Center Groningen and her colleagues examined data from the international Psychosocial Factors and Cancer Incidence consortium, which includes information from 18 prospective study groups with more than 300,000 adults from the Netherlands, the United Kingdom, Norway, and Canada.

The team found no associations between depression or anxiety and overall, breast, prostate, colorectal, and alcohol-related cancers during a follow-up of up to 26 years. The presence of depression or anxiety was linked with a 6% higher risk of developing lung cancer and smoking-related cancers, but this risk was substantially reduced after adjusting for other cancer-related risk factors including smoking, alcohol use, and body mass index.

Therefore, this analysis supports the importance of addressing tobacco smoking and other unhealthy behaviors including those that may develop as a result of anxiety or depression.

"Our results may come as a relief to many patients with cancer who believe their diagnosis is attributed to previous anxiety or depression," Van Tuijl said in a statement. "However, further research is needed to understand exactly how depression, anxiety, health behaviors, and lung cancer are related."

Researchers identify biological signature that may identify refractory ovarian cancer patients

Using a novel proteogenomic strategy and a variety of machine learning tools, investigators from the Icahn School of Medicine at Mount Sinai, Fred Hutchinson Cancer Center, and University of Arkansas for Medical Sciences Winthrop P. Rockefeller Cancer Institute have identified a 64-protein signature that may predict a subset of ovarian cancer patients who are unlikely to respond to chemotherapy.

The multicenter study, published in <u>Cell</u>, reports on a pioneering analysis of chemo-refractoriness in high-grade serous ovarian cancer. The work also implicates possible therapeutic targets for these patients.

Epithelial ovarian cancer causes more than 185,000 global deaths annually. HGSOC accounts for 60% of these deaths. Despite advances in treatment, mortality has remained the same for these patients in the past 40 years. Currently, there's no way to distinguish refractory cases, leading some patients to unnecessarily experience the adverse effects of platinum-based chemotherapy without the benefits.

"To address this critical unmet need, we performed a proteogenomic analysis to identify molecular signatures of refractory HGSOC and potential treatment targets. Predictors of chemo-refractoriness could enable precision oncology, sparing patients the toxicity and helping to identify the most effective therapy through targeted clinical trials," Pei Wang, professor of genetics and genomic sciences at Icahn Mount Sinai and co-corresponding author on the paper, said in a statement.

The investigators studied 242 tumor samples collected from HGSOC patients comprising both chemo-refractory and chemo-responsive individuals before they received chemotherapy. Using advanced computer models to analyze protein and gene expression profiles of the tumors, they found a specific group of 64 proteins that can predict which tumors won't respond well to the first-line platinum-based therapy. This prediction was confirmed in two independent cohorts of patients.

In addition, based on pathway activity measurements derived from the pro-

teomics data, the team also identified five new HGSOC subtypes, validated in two independent patient groups and in lab-grown tumor mouse models, suggesting that different treatment strategies may be needed.

Next, the researchers plan to confirm their findings in additional retrospective and prospective studies. Once validated, these tools can be used by clinicians to design customized alternative treatments other than the current standard chemotherapy to help patients with refractory tumors, the investigators said.

As a part of the research, the lab of Amanda Paulovich, a lead author of the study, is working on a test that uses a multiplex assay panel to measure the proteins in the prediction model faster and more efficiently. Paulovich is a professor at Fred Hutchinson Cancer Center in Seattle, where she holds the Aven Foundation Endowed Chair.

The test will combine information from multiple proteins to create a single score that indicates the likelihood of chemo-refractory disease. If successful, it could be a significant development for about 35% of patients with ovarian cancer who could avoid treatments that won't work for their specific type of cancer, the investigators said.

Loss of gene releases mutation-generating protein, rendering cancers resistant to treatment, UTSW researchers find

Loss of a gene known as SYNCRIP in prostate cancer tumors unleashes cellular machinery that creates random mutations throughout the genome that drive resistance to targeted treatments, a team led by UT Southwestern Medical Center researchers discovered. The findings, published in *Cancer Cell*, could lead to interventions that thwart this process in prostate and other cancer types, making them far easier to treat.

"This study paves the way for innovative strategies to fix the broken 'brake' for mutagenesis in cancer and curb resistance to treatments," study leader Ping Mu, assistant professor of molecular biology at UT Southwestern, is a Deborah and W.A. "Tex" Moncrief, Jr. Scholar in Medical Research, said in a statement.

Many cancers are typically initiated by mutations that develop in DNA and that additional mutations frequently form, driving tumors to grow and spread. Although drugs exist to target tumors bearing specific mutations, they don't cover the gamut of mutations that arise in cancer cells, Mu said. Thus, the more mutations present in a tumor, the more resistant it becomes to treatment. But how and why these additional mutations come about so quickly have been unknown.

Mu and his colleagues looked for genetic differences in the cells of prostate cancer tumors—the focus of the Mu lab—from samples taken from xenografted human tumors before and after the administration of antiandrogen therapy, a common treatment that starves prostate cancers of sex hormones that can fuel their growth. Although this treatment is often initially effective, prostate tumors nearly always become resistant to antiandrogen therapy over time.

In about half of the post-treatment samples, the SYNCRIP gene had disappeared. The researchers also found a variety of mutations that bore the signature of APOBEC proteins, cellular machinery that produces a specific type of mutation used for immune defense in healthy cells.

Further experiments suggested that SYNCRIP serves as a brake for a major member of the APOBEC protein family, known as APOBEC3B, keeping its activity in check. When SYNCRIP is lost, Mu said, APOBEC3B's function becomes uncontrolled, causing it to create random mutations throughout the genome. When the researchers genetically altered cells to remove APOBEC3B, they didn't accumulate mutations, even in the absence of SYNCRIP, confirming that their roles are linked.

Searching for genetic drivers of treatment resistance that arise from this process, the researchers scanned the genomes of post-treatment cells for APOBEC-caused mutations that prompted genes to become overactive. They identified eight genes that appear to be hot spots for APOBEC-driven mutations, all of which made antiandrogen therapy ineffective. When the researchers deleted these genes from the cells, they became responsive to therapy again.

Because mutations with APOBEC signatures are found in about 70% of human cancers, Mu said, the findings shed light on several mysteries in oncology. Those include why cancerous tumors tend to develop so many mutations quickly and why the mutation pattern is heterogeneous for different patients with the same cancer type and often among different cells in the same tumor.

Currently, cancers are treated by addressing these mutations individually, he added, which is effective only if a targeted treatment exists for a specific mutation. In the future, researchers may be able to develop treatments aimed at restoring SYNCRIP or inhibiting APOBEC proteins in order to prevent resistance-driving mutations before they develop.

Study shows how Epstein-Barr transforms B cells

Epstein-Barr virus infection is known to convert resting B lymphocytes into immortal cells that continuously multiply, which leads to posttransplant lymphoproliferative disorder and can evolve to lymphoma and other lymphoproliferative disorders. In a recent study, Japanese researchers discovered the molecular mechanisms of this growth transformation, demonstrating the Epstein-Barr virus induces nucleolar enlargement and increased proliferation in B cells by activating the cancer-related gene IMPDH2.

The research also revealed strong evidence supporting the efficacy of mycophenolate mofetil, an approved immunosuppressant, in inhibiting PTLD, highlighting its therapeutic significance.

The study, published in <u>Microbiology</u> <u>Spectrum</u>, used primary B cells from healthy donors instead of cell lines.

"Insights from EBV research that uses cell lines has been limited, because cell lines are already in an immortalized state," Takayuki Murata, the study's lead author, said in a statement. "To overcome this roadblock, we used primary B cells from healthy donors and then infected them with EBV. This allowed us to monitor the step-by-step growth transformation of B cells and analyze the mechanisms involved."

The researchers observed the primary B cells infected with wild-type EBV using electron microscopy and immunostaining. As early as two days after infection, the morphology of B cells showed significant alterations. An enlargement of the nucleolus—a region within the nucleus that produces ribosomes, the

cell's protein-producing machinery was observed, along with an increase in the number of nucleoli. Interestingly, nucleolar enlargement was followed by an enlargement of both—the nuclei and the cells.

The researchers then performed RNA sequencing on the infected B cells to understand the transcriptional changes.

"Among the genes showing significantly altered expression levels, one named IMPDH2 stood out, as it had previously been linked to similar morphological changes in glioblastoma," Atsuko Sugimoto from Fujita Health University School of Medicine, who was also a part of the research team, said in a statement. "Careful analysis showed that the levels of the IMPDH2 peaked two days after infection—coinciding with the timing of nucleolar enlargement. This suggested that we were on the right path."

The inhibition of IMPDH2 using silencer RNAs and the drug mycophenolic acid prevented the growth transformation of primary B cells after EBV infection, producing smaller nucleoli, nuclei, and cells. This confirmed that IMPDH2 induction played a key role in the growth transformation of EBV-infected B cells.

The next step involved understanding how EBV activates IMPDH2 expression. Three key viral genes—EBNA2 and LMP1—were tested because of their known role in EBV-induced B cell transformation. Interestingly, when EBV lacking EBNA2 was used for infection, IMPDH2 induction following primary EBV infection was blocked. This effect was not observed with LMP1 knockout.

"This very clearly demonstrated that EBV induces IMPDH2 expression EB-NA2-dependent mechanisms. In addition, cellular transcription factor MYC was also involved in the IMPDH2 induction," Sugimoto said. With several key pieces of evidence on their plate, the researchers finally set out to find the final piece of the puzzle. To highlight the clinical significance of their findings, they examined whether the drug mycophenolate mofetil could prevent B cell transformation and PTLD.

"Like MPA, which we tested in the earlier part of our study, MMF is an IMPDH2 inhibitor. More importantly, MMF is already a clinically approved immunosuppressant. That is why it was useful to test if it could be applied for the clinical prevention of PTLD," Murata said.

As expected, the administration of MMF in a pre-clinical mouse xenograft model led to improved survival and reduced splenomegaly. These observations confirmed that the use of MMF can inhibit PTLD development.

This study is the first to demonstrate that IMPDH2 activation and nucleolar hypertrophy are essential for EBV-induced B cell transformation and that IMPDH2 inhibition can suppress PTLD. It could lead to the adoption of MMF as an agent for the prevention of EBV-positive PTLD, providing significant relief to transplant patients.

DRUGS & TARGETS



FDA grants accelerated approval to Talvey for R/R multiple myeloma

FDA granted accelerated approval to Talvey (talquetamab-tgvs) for adults with relapsed or refractory multiple myeloma who have received at least four prior lines of therapy, including a proteasome inhibitor, an immunomodulatory agent, and an anti-CD38 monoclonal antibody.

Talvey is sponsored by Janssen Biotech Inc. The full prescribing information can be found on the <u>FDA's website</u>.

Efficacy was evaluated in MMY1001 (MonumenTAL-1), a single-arm, open-label, multicenter study that included 187 patients who had previously received at least four prior systemic therapies. Patients received Talvey 0.4 mg/kg subcutaneously weekly, following two stepup doses in the first week of therapy, or Talvey 0.8 mg/kg subcutaneously every 2 weeks, following three step-up doses, until disease progression or unacceptable toxicity.

The main efficacy outcome measures were overall response rate and duration of response as assessed by an Independent Review Committee using IMWG criteria. The primary efficacy population consisted of patients who had previously received at least four prior lines of therapies, including a proteasome inhibitor, an immunomodulatory agent, and an anti-CD38 monoclonal antibody. ORR in the 100 patients receiving 0.4 mg/kg weekly was 73% and median DOR was 9.5 months. ORR in the 87 patients receiving 0.8 mg/kg biweekly was 73.6% and median DOR was not estimable. An estimated 85% of responders maintained response for at least 9 months.

The prescribing information for Talvey has a Boxed Warning for life threatening or fatal cytokine release syndrome and neurologic toxicity, including immune effector cell-associated neurotoxicity. Because of the risks of CRS and neurologic toxicity, including ICANS, Talvey is available only through a restricted program under a Risk Evaluation and Mitigation Strategy.

The most common adverse reactions reported in the 339 patients in the safety population were CRS, dysgeusia, nail disorder, musculoskeletal pain, skin disorder, rash, fatigue, decreased weight, dry mouth, pyrexia, xerosis, dysphagia, upper respiratory tract infection, and diarrhea.

FDA approves Gavreto for NSCLC with RET gene fusions

FDA granted regular approval to Gavreto (pralsetinib) for adult patients with metastatic rearranged during transfection fusion-positive non-small cell lung cancer as detected by an FDA-approved test.

Gavreto is sponsored by Genentech Inc.

Gavreto was previously granted accelerated approval for the NSCLC indication on Sept. 4, 2020, based on initial overall response rate and duration of response in 114 patients enrolled in the ARROW trial—, a multicenter, open-label, multi-cohort trial. The conversion to regular approval was based on data from an additional 123 patients and 25 months of additional follow-up to assess durability of response.

Full prescribing information for Gavreto can be found on <u>FDA's website</u>.

Efficacy was demonstrated in a total of 237 patients with locally advanced or

metastatic RET fusion-positive NSCLC. Patients received Gavreto until disease progression or unacceptable toxicity.

The primary efficacy measures were ORR and DOR as determined by a Blinded Independent Review Committee. Among 107 treatment-naïve patients, ORR was 78% with a median DOR of 13.4 months. Among 130 patients previously treated with platinum-based chemotherapy, ORR was 63% with a median DOR of 38.8 months.

The most common adverse reactions were musculoskeletal pain, constipation, hypertension, diarrhea, fatigue, edema, pyrexia, and cough.

FDA approves companion diagnostic to Ayvakit in gastrointestinal stromal tumors

FDA approved the therascreen PDGFRA RGQ PCR kit, a companion diagnostic intended for use to aid clinicians in identifying patients with gastrointestinal stromal tumors who may be eligible for treatment with Ayvakit (avapritinib).

Ayvakit is approved in the U.S. for the treatment of adults with unresectable or metastatic GIST harboring a platelet-derived growth factor receptor alpha exon 18 mutation, including PDG-FRA D842V mutations.

The kit is the first platelet-derived growth factor receptor alpha assay to receive FDA approval as a companion diagnostic.

Qiagen and Blueprint Medicines collaboratively developed the PDGFRA companion diagnostic assay. The real-time qualitative PCR in vitro diagnostic assay detects the D842V somatic mutation in the PDGFRA gene to determine which patients may be a candidate for treatment with Ayvakit.

The tyrosine kinase inhibitor is designed to target the PDGFRA exon 18 D842V mutation and was approved by the FDA in 2020. GIST patients harboring the D842V mutation in PDGFRA exon 18 show primary resistance to previously approved TKIs.

The therascreen PDGFRA kit uses genomic DNA extracted from a patient's formalin-fixed paraffin-embedded tumor tissue. FFPE tumor specimens are processed using the QIAamp DSP DNA FFPE Tissue Kit for sample preparation and the Rotor-Gene Q MDx instrument for DNA amplification and mutation detection.

"The therascreen PDGFRA kit is an FDA approved and validated test, delivering results in a fast turnaround time. This ensures that physicians receive results promptly, enabling them to make informed treatment decisions for their GIST patients in a timely and effective manner," Jonathan Arnold, vice president and head of translational science and precision diagnostics at Qiagen, said in a statement.

GIST is a rare, genomically driven sarcoma of the gastrointestinal tract. Approximately six% of patients with newly diagnosed GIST have PDGFRA exon 18 mutations, the most common of which is the D842V mutation. Since the introduction of TKIs, including Ayvakit, the treatment of GIST patients with locally advanced and metastatic disease has dramatically improved.

FDA accepts Astellas's sNDA for Cresemba in children

FDA accepted the supplemental New Drug Application for Cresemba (isavuconazonium sulfate), a prodrug of isavuconazole, an azole antifungal drug, seeking approval for the treatment of invasive aspergillosis or invasive mucormycosis in pediatric patients aged one to 17 years old.

Cresemba is sponsored by Astellas Pharma US Inc.

Under the Prescription Drug User Fee Act, the FDA has set a target action date of Dec. 9.

Cresemba is already approved by the FDA for the treatment of IA and IM in adults. If approved for pediatric use, it may offer children significant advances in treatment or may provide a treatment where no adequate therapy exists. IA and IM are a major cause of morbidity and death among immunocompromised and hospitalized pediatric patients.

"While rare in the general population, invasive aspergillosis or invasive mucormycosis can be incredibly dangerous for immunocompromised children, including those faced with blood and other cancers, and there are very limited treatment options," Tadaaki Taniguchi, chief medical officer of Astellas, said in a statement. "The collective efforts by our research and development teams, which have led to the successful sNDA acceptance for Cresemba by the FDA, reflect our ongoing commitment to addressing vulnerable populations with high unmet medical needs."

The sNDA is based on results from a phase II open-label, non-comparative, multicenter study, evaluating the safety, efficacy, and pharmacokinetics of Cresemba for the treatment of IA or IM in pediatric patients aged one to 17 years old. Detailed results will be presented at a future medical meeting.

C2i Genomics and Ichilov bring cancer detection and monitoring platform to Israel

C2i Genomics and the Tel Aviv Sourasky Medical Center (Ichilov) entered into a strategic collaboration to provide precision oncology clinical testing using C2inform, C2i Genomics's whole genome minimal residual disease test to improve cancer detection and monitoring nationwide.

C2inform uses whole genome sequencing to identify cancer-related mutations by employing AI-driven pattern recognition to detect traces of cancer in patient blood samples at earlier stages compared to currently available technologies.

Through the partnership, C2i Genomics's and its whole-genome-based assay will be integrated into a nationwide healthcare system for the first time. With Ichilov Hospital Labs serving as the reference lab for cancer hospitals across Israel, C2inform tests will become accessible to the entire population of Israel, accounting for nearly 10 million people.

Through this collaboration, sequencing with WGS of circulating tumor DNA and matched tumors of cancer patients will be performed by Ichilov's Pathology Institute.

Afterward, sequencing raw data will be uploaded to C2 Genomics's cloud platform for processing and clinical interpretation. Ichilov Hospital will commercialize and offer the service to its patients while simultaneously enabling other hospitals and pharma companies in Israel to have access to the service.

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