

FATHER OF CANCER IMMUNOTHERAPY Rosenberg’s Research Spans a Half-Century and Counting

BY DANA TALESNIK

About 55 years ago, Dr. Steven Rosenberg had a hunch that a patient’s own immune system could help fight cancer. Since arriving at NIH in 1974, he has painstakingly pursued



ARNON THONGKONGHAN/SHUTTERSTOCK

this line of inquiry with some ground-breaking results.

In the beginning, his hunch

diverged from all scientific literature. “It was hypothetical—no one had ever demonstrated an immune manipulation that could cause cancers to disappear,” said Rosenberg, chief of surgery at the National Cancer Institute (NCI), a position he has held for 49 years.

His research journey was inspired by two unusual cases early in his career.

In 1968, while a surgical resident at Brigham Hospital in Boston, Rosenberg was tasked with removing the gallbladder of a 63-year-old patient. The



Dr. Steven Rosenberg

patient’s chart revealed he was hospitalized 12 years earlier with stomach cancer that had spread to the liver. Nothing could be done; no treatment was given.

“When I operated on him, he had no cancer,” recounted Rosenberg. “He had undergone one of the rarest events in all of medicine, a spontaneous regression of his metastatic cancer.”

A few years earlier, a patient at Brigham had developed widespread kidney cancer following an organ transplant. It turned out, the kidney he’d received was cancerous. When the immunosuppressive drugs—given to prevent organ rejection—were stopped, his body rejected the kidney and, incredibly, his cancer disappeared.

“That told me if you could spark a strong enough immune reaction, you could get large, vascularized cancers to disappear,” Rosenberg said. “That then set me on the

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The NSO performs at NIH. See story, p. 12.

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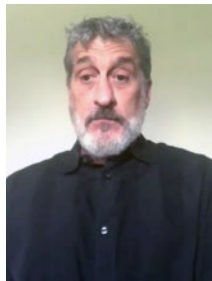
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Rizzi Appeals for Accessible, Usable, Functional Digital Environments

BY ERIC BOCK

Much of the digital world is inaccessible to people with disabilities, said Albert J. Rizzi, during the final DDM Seminar of 2023. That prevents them from living their life to the fullest.

“When we make things universally accessible and usable for people with disabilities, we wind up making it a better place for people of all abilities,” said Rizzi, founder and CEO of the My Blind Spot, a non-profit that ensures digital environments are accessible, usable and functional for people with disabilities.



Albert J. Rizzi

SEE ACCESSIBILITY, PAGE 4



PHOTO: COURTESY SOULSIITBOMBAY

SCHOLAR STUDIES SOCIAL FACTORS Is Women’s Empowerment a Key to Climate Adaptation?

BY AMBER SNYDER

Adapting to climate change involves effort from all parts of society, from large-scale down to the individual level. The NIH Climate Change and Health Initiative seeks to reduce health threats from climate change across the lifespan and build health resilience in individuals, communities and

SEE CLIMATE, PAGE 8



-  11:30 am NIH K-9 Demo
-  11:45 am warm-up
-  12:10 pm race starts

#NEI5K

NEI to Host Annual 5K Walk/Run/Roll

On Wednesday, Oct. 18, the National Eye Institute will host its fourth 5K “Walk/Run/Roll” on the NIH campus, starting at 11:30 a.m. The course will begin (rain or shine) on the lawn in front of Bldg. 1.

NIH Recreation and Welfare Association fitness instructors will lead a warm-up. Enjoy music, meet the NIH Police K-9 unit and view a demo. In addition, attendees can learn about the NIH Blood Bank and a family dinner program at the Children’s Inn at NIH. Keyworkers for the Combined Federal Campaign will also be available to chat about charities.

The walk/run/roll will start at 12:10. The course will exit campus, circumnavigate its perimeter and return through security (so remember to bring your ID badge). This event is sponsored by NEI in partnership with the Office of Research Services’ Division of Amenities and Transportation Services and the R&W.

Sign language interpretation will be available. If you need additional reasonable accommodation to participate, contact Lilly Sadler at sadlerla@mail.nih.gov or (301) 451-8007.

For more details, and to register as an individual or a team, visit nei.nih.gov/nei5k.

NIH Launches Community-Led Research Program to Advance Health Equity

NIH is funding a first-of-its-kind community-led research program to study ways to address the underlying structural factors within communities that affect health, such as access to safe spaces, healthy food, employment opportunities, transportation and quality health care.

Through its Common Fund Community Partnerships to Advance Science for Society (ComPASS) program, NIH made 26 awards to community organizations and a coordinating center, totaling approximately \$171 million over five years, pending the availability of funds.

Through these awards, ComPASS will enable research into sustainable solutions that promote health equity to create lasting change in communities across the nation.

Advancing Health Equity

NIH Designates People with Disabilities as a Population with Health Disparities

In September, Dr. Eliseo Pérez-Stable, director of the National Institute on Minority Health and Health Disparities (NIMHD), designated people with disabilities as a population with health disparities for research supported by NIH. The designation is one of several steps NIH is taking to ensure people with disabilities are represented in NIH research.

“Toward this effort, NIMHD and other NIH institutes launched a new research program to better understand the health disparities faced by people with disabilities who are also part of other populations designated as having health disparities,” said Pérez-Stable.

NIMHD is the lead NIH institute on monitoring minority health and health disparities research. Designated populations experience significant disparities in their rates of illness, morbidity, mortality and survival, driven by social disadvantage, compared to the health status of the general population.

A health disparity designation helps to encourage research specific to the health issues and unmet health needs of these populations.

Other NIH-designated populations with health disparities include racial and ethnic minority groups, people with lower socio-economic status, underserved rural communities and sexual and gender minority groups.

People with disabilities often experience a wide and varying range of health conditions leading to poorer health and



PHOTO: FIZKES / SHUTTERSTOCK

shorter lifespan. In addition, discrimination, inequality and exclusionary structural practices, programs and policies inhibit access to timely and comprehensive health care, which further results in poorer health outcomes.

NIH also issued a notice of funding opportunity calling for research applications focused on novel and innovative approaches and interventions that address the intersecting impact of disability, race and ethnicity, and socio-economic status on health care access and health outcomes.

“To the disability community, we hear you and thank you for sharing your lived experiences with NIH,” said Acting NIH Director Dr. Lawrence Tabak. “This designation marks an important step in an agency-wide effort to advance health equity for people with disabilities which also includes updating the NIH mission statement to accurately reflect our goal of turning scientific discoveries into better health for all, including people with disabilities.”

NIH is directly funding research projects led by community organizations. Leaders from the organizations will work in collaboration with their research partners at academic institutions and other organizations in all phases of the research process. ComPASS projects study social determinants of health—the social, physical, and economic conditions where people are born, grow, live, work, age and play—that contribute to health inequities.

“The ComPASS research model harnesses diverse perspectives and expertise to examine systemic factors that impact the health of individuals, communities, and populations,” said NIH Acting Director Dr. Lawrence Tabak. “We are excited to see how results from these awards exemplify the transformative power of community-driven research.”



Dr. Nitin Verma presented NEI with *Twenty Minute Miracles*, a photo book by Hemma Kearney and Ellen Smith about the East Timor Eye Program. Shown are (from l) Dr. Kapil Bharti of NEI; Anu Verma; Dr. Jack Murphy of NCI, Dr. Nitin Verma, Michael Cheetham of NIH Office of the Director, Dr. Gyan “John” Prakash and Dr. Brian Brooks, both of NEI.

PHOTO: DUSTIN HAYS

Filling the Eye Care Gap Down Under

BY DUSTIN HAYS

When people think of Australia, they think of kangaroos and sandy beaches, said Dr. Nitin Verma, an ophthalmic surgeon and chair of the global eye health committee of the Royal Australian and New Zealand College of Ophthalmologists (RANZCO). “But today I’ll talk about ophthalmology—not just about ophthalmology in Australia but also the South Pacific, a region which I think the whole world has forgotten.”

This summer, Verma visited NIH and shared his lifetime perspective on the delivery of vision care to underserved populations in the Australia/South Pacific region—roughly 50-million people scattered across vast stretches of land and ocean. His talk was part of the Global Health Vision Lecture Series, sponsored by the National Eye Institute (NEI) and NIH’s Global Health Interest Group (GHIG).

As RANZCO president (2020–2022), Verma was central to Vision 2030 and Beyond—RANZCO’s plan to improve vision health across Australia with special emphasis on vulnerable populations such as indigenous people who have a three-fold greater risk of blindness from eye disease.

Underpinning the plan, a living document, are six “pillars”: workforce training, service delivery, closing the gap for indigenous people, preventive health, global health and sustainability. In coordination with their roadmap for vision, RANZCO published a reconciliation action plan to ensure that solutions are conceived and carried out in a culturally appropriate manner.

“You can’t just walk in and say, ‘I have a solution!’ We don’t have a solution. We have to do it together,” he said.

Community-building has been at the core of Verma’s long, distinguished career. He’s worked to improve accessibility and quality of care in Papua New Guinea and sparsely populated regions of Australia. He arrived in East Timor just after their independence from Indonesia in 1999.

“The whole country was destroyed in the wake of Indonesia’s departure,” Verma said.

The health care infrastructure had collapsed, along with everything else. Crime was so rampant that everyone carried a gun, even when jogging, he noted.

With assistance from the World Health Organization, in 2000 Verma set up makeshift eye clinics with teams of care providers who donated their time and expertise.

Some patients came to the clinics by canoe, he said. But no matter how they arrived, they nearly always entered the clinic with late-stage eye disease, including advanced cancer.

“We could do what we could do, and we did what we could, but it was always too late,” Verma said.

With help from partners in Australia, India, Switzerland, Cuba, Nepal and elsewhere, he helped establish the East Timor Eye Program to develop a long-term solution. Baked into the plan was the goal of eventually handing over the program to the Timorese.

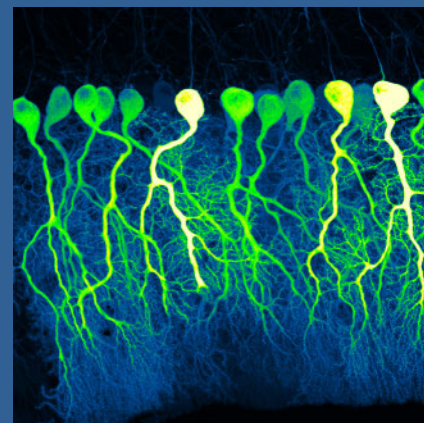
In partnership with Sydney University, the program trained local students in routine eye care, surgery, nursing, optometry, low vision, research and more.

Beyond medical training, the program provided advocacy training to teach skills in administrative tasks such as supplies procurement, grant writing, and how to collaborate with local and foreign politicians and bureaucrats.

“I’ve heard a lot of incredible stories, but these leave me speechless,” said NEI Director of International Programs Dr. Gyan “John” Prakash in closing remarks.

To learn more about the East Timor Eye Program, visit <https://shorturl.at/iWX69>.

The Global Health Vision Lecture Series is sponsored by NEI, Fogarty International Center and GHIG. The series was created by NEI’s Office of International Programs in 2012 to foster the global collaboration and exchange of information among international vision researchers and eye health clinical scientists. **R**



ON THE COVER: *First place winner, photo category, 2023 Show Us Your BRAINS! Photo & Video Contest. “Dark Commute at 4 a.m.” A confocal image of sparse GCaMP6f-expressing Purkinje cells in mouse cerebellum resembles the industrious contours of pre-dawn commuters.*

IMAGE: SILAS BUSCH/UNIVERSITY OF CHICAGO

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Accessibility

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Rizzi is one of the 62 million Americans living with a disability. In 2006, he contracted fungal meningitis, a rare, life-threatening infection that causes swelling of the areas around the brain and spinal cord. As a result of the infection, he lost his vision. It could've been worse.

"I could've been blind, deaf and paralyzed," he said. "Only being blind was a good thing."

Until then, he didn't know any other people with blindness. He only knew of celebrities with vision loss, such as Ray Charles, Stevie Wonder, Helen Keller and José Feliciano. He quickly realized he had to overcome digital barriers.

"I had to learn a whole new way of navigating the internet," he said. "I have a computer that talks to me called a screen reader. Unless the world is coded that way,

★ ★ ★

"Going to work cures so many ills. It improves our mental health, makes us feel like valued contributors and gives us a reason to wake up in the morning."

-ALBERT RIZZI

★ ★ ★

I can't access anything, ostensibly disabling the world to me."

Additionally, he faced "low expectations about his ability."

Rizzi was an accomplished business owner and educator, but, once he lost his sight, he became "persona non grata." He was told he'd never work with children or be an executive again. "Nothing about that made me feel good about being blind," he recalled.

Rizzi's parents didn't raise him to give up. So, he started his non-profit to advocate to "make sure the digital platforms we're inextricably tied to in the 21st century work seamlessly" for people with disabilities.

People with disabilities need support, not sympathy. Everyone—whether disabled or not—has their own challenges and limitations. If people with disabilities are given reasonable adaptations and held



People with disabilities need support, not empathy, Rizzi noted.

accountable, Rizzi believes more of them will be visible at school and work.

"Going to work cures so many ills," he said. "It improves our mental health, makes us feel like valued contributors and gives us a reason to wake up in the morning."

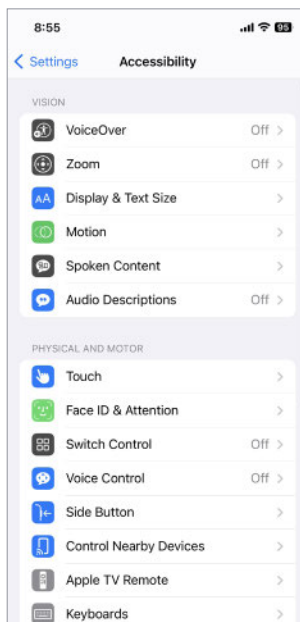
Telework during the Covid-19 pandemic has shown that working from

home is a way of life, not a reasonable accommodation for people with a disability. As much as 50% of work can be done remotely.

"That is opening up avenues to employment and academic enrichment for the disability community like never before," he said. "We need to challenge our design and development teams to make sure our platforms work."

Accidents and unexpected illness are the leading causes of disability, he said. Just about everyone will join the disability community at some point in their lives. Learning to live with a disability is traumatic, but it's not a life-ending event.

Some members of the public believe that people with disabilities "need assistance all the time." This view prevents them from becoming independent taxpayers. In many cases, however, they just need access to the right tools "to promote their



Turning on the accessibility settings on an iPhone, for instance, can help people with disabilities navigate the digital world.

ability and allow them to create and restore infinite possibilities."

Rizzi challenged companies and academic institutions to perform "disability-friendly audits" to identify ways to make technology and physical locations more accessible. For instance, could a person with a mobility impairment take their identification badge and hold it up to an access reader? Or are rooms clearly defined with Braille?

There are benefits to committing to making a workplace disability-friendly and ready. Including people with disabilities in the workforce improves morale and competition and increases brand and image awareness.

"We need to let people with disabilities rise to the heights of greatness," Rizzi concluded. "We need to support them as individuals and we need to demand it in our society." **R**



After emergency repairs, Bldg. 31's cafe recently reopened with limited services.

Limited Reopening for Bldg. 31 Café, Natcher Café Begins 'Pop-Up' Service

The Bldg. 31 cafeteria has reopened in a limited capacity, after emergency repairs were completed. Coffee service and continental breakfast foods are available in the morning, and grab & go pre-packaged food and beverages will be available for lunch. Full reopening is expected, once more extensive renovations are finished.

In addition, the Natcher cafeteria is coming back. The eatery in Bldg. 45 began "Pop-Up Service Days" in the first week of October. This is the first of a phased schedule focused on opening on days of large events scheduled at the Natcher conference center. A more regular operating schedule is the next phase, which will tentatively start later in fiscal year 2024.



Fellows of the Partnership for Public Service visit an NIDDK metabolic clinical research unit, led by Dr. Kong Chen (fourth from l).

PHOTO: JACQUELINE ROBERTS

Partnership for Public Service Explores DEIA Strategies, Visits NIH Labs

BY MYRANDA TARR

The Excellence in Government fellows from the Partnership for Public Service recently visited NIH's Bethesda campus. The group of 30 professionals received an overview of NIH and discussed various aspects of diversity, equity, inclusion and accessibility (DEIA) with NIH leadership. They also visited four labs and clinics in the Clinical Center (CC).

The partnership is a nonprofit, nonpartisan organization that aims to build a better government and stronger democracy.

The visit began with a presentation led by Dr. Alfred Johnson, NIH deputy director for management, and Julie Berko, Office of Human Resources director, about NIH and



Dr. Alfred Johnson, NIH deputy director for management, talks about a strategic systems approach to DEIA.

PHOTO: MYRANDA TARR

its strategic systems approach to DEIA. Johnson emphasized that NIH is working to “make sure we have the workforce of the future.”

He explained that while single organizations cannot accomplish everything at once, individual components are able to make a difference.

When asked for advice in making systemic changes and working with leadership, Berko

underscored how “relationships are your number one currency.” Johnson added that one must be “passionate, proactive and persevere.”

Participants broke into small groups and toured labs and clinics within four institutes—the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), National Cancer Institute (NCI), National Institute on Alcohol Abuse and Alcoholism (NIAAA) and National Eye Institute (NEI).

The group visiting the NIDDK metabolic clinical research unit was led by co-director Dr. Kong Chen who explained how the body generates heat at rest, during exercise and in cold environments.

Dr. James Gulley, co-director of the Center for Immuno-Oncology (CIO) and NCI clinical director, led another group to CIO laboratories where he explained his work in cancer immunotherapy.

A third group visited NIAAA's section of sensory science and metabolism clinical unit, led by family nurse practitioner Dr.

Carolyn Allen who provided a demonstration of some smell and taste tests the lab is conducting.

The last group joined Dr. Emily Chew, director of the Division of Epidemiology and Clinical Applications, where they discussed the use of eye images as a window into the health of the patient, including detecting the risk of heart disease and dementia. The visitors also viewed retinal images of an NEI patient.

An Inside Look at Smell, Taste and Obesity

On the NIAAA stop, Allen—along with two postbacs—explained the various tests their clinical unit administers to volunteer participants.

One protocol uses measures that test the sense of taste and smell in people with obesity versus people without obesity.

“We’re also trying to see whether people who have alcohol use disorder have lower



Postbacs from NIAAA's sensory science and metabolism clinical unit explain how they perform a taste test.

PHOTO: MYRANDA TARR

sense of smell or taste compared to people who are moderate drinkers or don't drink at all,” added Marinza Marzouk, a postbac in the clinical unit.

One partnership fellow asked if the lab is looking at whether obesity affects a person's sense of smell and taste or whether a person's sense of smell and taste impacts their propensity for obesity.

“It's the chicken and the egg,” answered Marzouk. “That's what we're trying to identify.”

Several individuals in the partnership group remarked on enjoying the inside look into the four ICs and mentioned finding the NIH visit informative and interesting. **R**

Rosenberg

CONTINUED FROM PAGE 1

path these past 50 years to try to figure out how that happened, and how to make it happen more often.”

An Aspiring Cowboy

Born and raised in the Bronx, New York, as a kid, Rosenberg wanted to be a cowboy. But that aspiration quickly turned to medicine.

Stories from his parents, Jewish immigrants who fled Poland, moved him deeply. Many of his relatives perished in



Rosenberg (l) at a weekly lab meeting (this one in 1998), where scientists, clinical fellows, technicians, students and nurses from his group convened to discuss the latest clinical and lab efforts

the Holocaust. His family’s history instilled in him a lifelong desire to end needless suffering.

After medical school, Rosenberg paused his surgical residency to pursue a Ph.D. in biophysics at Harvard. He then conducted lab research, including a stint as an NCI immunology fellow, before finishing his residency and coming to work permanently at NCI as a clinician-scientist.

Along the way, there were false leads and failed experiments. In many cases, the cancer won.

“Most things don’t work,” as is often the plight of any clinical research, noted Rosenberg. “The overwhelming majority of experiments do not work in ways, and give the kinds of results, that we seek.”

But he persevered. “Cancer is a devastating disease. It’s a holocaust,” he said. “Patients who are innocent develop problems they cannot control, while their families sit by impotently and watch them suffer and ultimately die of the disease. It’s

horrible. When you see that happening, as a doctor, you feel you have to do something about this. And that’s something that has kept me going for a very long time.”

Rosenberg ultimately became a cowboy, in a sense, exploring uncharted territory, pushing boundaries, all the while seeking to rein in cancer.

Studying Immune Warriors

Rosenberg began his quest to find an immune response to cancer by studying T lymphocytes—the body’s immune warriors. But these white blood cells don’t live long outside the body. Other researchers were

publishing studies with interleukin-2 (IL-2)—proteins made by white blood cells (leukocytes) that facilitate growing T cells [a type of immune cell] outside the body.

“I realized perhaps we could get anti-tumor lymphocytes to grow inside the body,” he said. “So I started administering IL-2 to treat patients.”

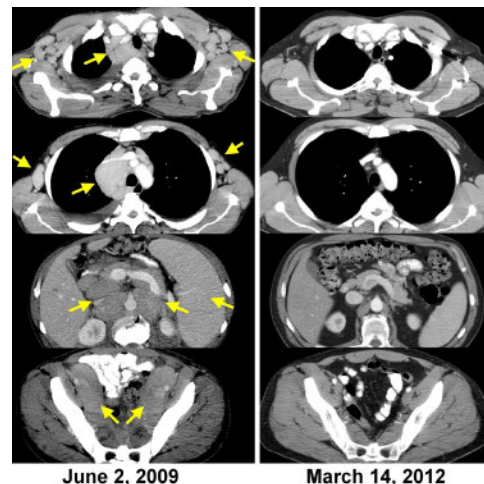
It was a discouraging time, recalled Rosenberg. His team

treated 66 patients in a row without success. Ongoing research showed IL-2 had a short half-life in the body of only about eight minutes. It needed to be given repeatedly in higher doses.

Then, a breakthrough. His 67th patient, Linda Taylor, received the right combination



Rosenberg in his office with patient Linda Taylor in 1984 (l) and 2014 (r). Taylor, the first patient to respond to IL-2 administration, remains cancer-free 39 years later.



CAT scans of the first patient to respond to treatment with adoptive transfer of autologous lymphocytes genetically engineered to express a chimeric antigen receptor (CAR) targeting CD19. The left side shows the lymphoma burden; at right, complete cancer regression ongoing more than 10 years later.

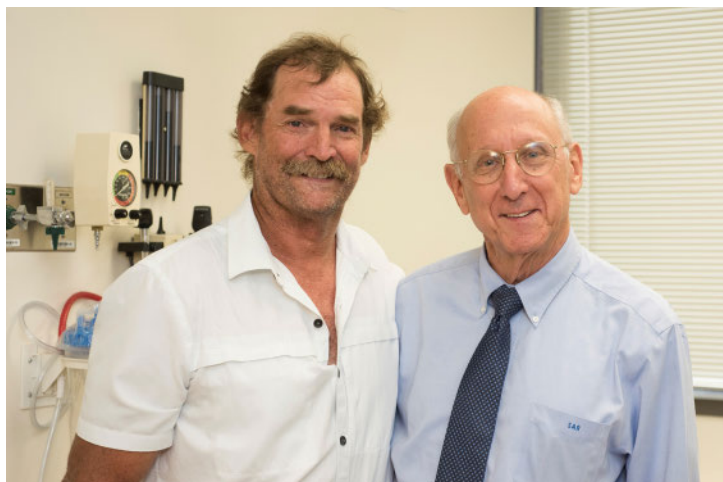
and her metastatic melanoma disappeared.

“Melanoma was previously a universally lethal disease once it had spread,” Rosenberg said. “Linda was treated in 1984 and is still alive and disease-free today.”

Subsequent large studies by Rosenberg’s group showed that IL-2 could induce cancer regression in 15-20% of patients with metastatic melanoma and kidney cancer. IL-2 became the first Food and Drug Administration (FDA)-approved immunotherapy for cancer in the 1990s.

Rosenberg’s team then discovered that lymphocytes that exist inside a tumor can recognize the cancer. The tumor is a sink for these immune cells, which they named “tumor-infiltrating lymphocytes” (TILs) and began administering TILs to patients.





Rosenberg (r) in the clinic with the first patient to respond to anti-CD19 CAR T-cell therapy, 10 years after treatment

“That was the first direct demonstration that lymphocyte transfer could cause tumor regression,” Rosenberg said. “That was developed to the point where, in our latest trials of almost 200 patients, 56% underwent a cancer regression and a quarter of patients with metastatic melanoma would undergo complete—what appeared to be durable—regressions. Now, we’re talking about

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“That’s what NIH does. We practice the best of today’s medicine, but we’re here to create tomorrow’s medicine.”

—DR. STEVEN ROSENBERG

• • •

response rates in the 50% range, not the 15% range of IL-2.”

Going Down Two Research Paths

Building on many years of study and clinical trials, Rosenberg’s research went in two directions. One is continuing to use a patient’s own natural lymphocytes that can recognize cancer as a living drug. The second is to genetically modify immune cells to target cancer. Rosenberg was, in fact, the first person ever to insert foreign genes into a human, paving the way for the field of gene therapy.

Both types of cancer immunotherapy “are what we’re trying to improve now to fight the common solid cancers [that begin in major organs] for which there are no curable treatments, short of surgery, once they have

spread.” Solid cancers account for 90% of all cancer deaths.

“It turns out, lymphocytes were recognizing the DNA mutations that cause the cancer,” distinguishing malignant cells from normal ones, Rosenberg said. “That’s probably the final common pathway of all immunotherapies... It’s somewhat ironic that the very gene mutations that cause the cancer will turn out

to be its Achilles heel, to target it.

“We developed techniques to specifically study the mutation products that T cells recognized and have now developed that into a whole field of study,” he said. Initially, he focused on naturally occurring T cells.

When Rosenberg first proposed inserting genetically modified immune cells into patients, he not surprisingly faced major opposition—“it’s too risky” and “it’s immoral” were among the main arguments. When review board approval came, in 1984, the first patient received his own lymphocytes modified by a bacterial gene not

as treatment, but to see where they went in the body.

That led his team to identify the actual lymphocyte receptors that recognize the cancer and—years later, working with Dr. James Kochenderfer, a fellow in Rosenberg’s lab—gave rise to CAR [chimeric antigen receptor] T-cell therapy—a way to modify lymphocytes to attack B-cell malignancies such as lymphoma and leukemia.

“We treated the first patient ever to receive these CAR-T cells in 2009. He underwent a complete regression and is disease-free more than 12 years later,” Rosenberg said.

Scaling Up

One of Rosenberg’s former fellows started a company to commercialize these

new lab creations known as CAR-T cells, signing a cooperative research agreement with NCI. Five years later, it was sold in a multi-billion-dollar deal to Gilead Sciences.

“It’s a proud example of how findings made in government institutions can find their way out into the world,” Rosenberg said.

This process involves making retroviruses that insert and integrate appropriate genes into the patient’s normal T cells, growing them to large numbers and infusing them back into the patient. Now, NCI works with several pharmaceutical companies, with FDA approval, to develop cell transfer immunotherapies for patients with common solid cancers.

Creating Tomorrow’s Medicine

Rosenberg said one of the biggest challenges throughout his career has been understanding the underlying, complicated biology of cancer—the complexity of tumor recognition; identifying cells that cause cancer progression; understanding and overcoming treatment resistance.

“We study basic science and then try to translate it to patients,” he said. “That’s what NIH does. We practice the best of today’s medicine, but we’re here to create tomorrow’s medicine.”

There still is a desperate need to supplement the three existing forms of cancer treatments: surgery, radiation and chemotherapy.

“We now have this three-legged stool a lot more stable with the addition of this fourth leg,” Rosenberg concluded. “Immunotherapy has a lot of promise for developing more effective cancer treatments.” **R**

Next CCDI Webinar Set, Oct. 24

The Childhood Cancer Data Initiative (CCDI) will host its next webinar on Tuesday, Oct. 24 from 2 to 3 p.m. Attendees will hear from Dr. Angela Mariotto, chief of the Data Analytics Branch in NCI’s Division of Cancer Control and Population Sciences, on the combined potential of NCCR*Explorer and SEER*Stat, two tools available through the CCDI National Childhood Cancer Registry (NCCR). Through a live demonstration and real-world examples, attendees will learn how to harness these resources for cancer research and surveillance.

CCDI webinars are free and open to the public. Registration is required to receive the event link. For more information, visit <https://go.nih.gov/lr6XhTv>. For reasonable accommodation to participate, email CCDIevents@mail.nih.gov by Oct. 17.

Climate

CONTINUED FROM PAGE 1

nations around the world, especially among those at highest risk. The initiative includes eight climate and health scholars, who work with NIH to share knowledge and help build capacity for conducting climate-related health research.

Dr. Praveen Kumar, an NIH climate and health scholar at Boston College, recently gave a virtual lecture titled “Environmental Justice and Well-Being: Centering Women’s Empowerment to Improve Energy Access Among Poor Communities of Rural India.”

The NIH Climate Action plan acknowledges age and gender as key social and behavioral factors that influence susceptibility to climate-led impacts. Research shows climate change affects women and girls disproportionately in comparison to men and boys. Kumar has devised a method of individual-level climate adaptation strategies that also empower women.

“Women’s empowerment is key to changing behavior and building capacity for climate adaptation,” he said. He studies implementation science by evaluating methods and strategies that enable the uptake of evidence-based practice and research.

Kumar’s case study focused on rural India, where many people do not have

consistent access to electricity. He partnered with the Indian Institute of Technology Bombay on the SoULS program, also known as the Solar Urja (energy) through Localization for Sustainability Program.

SoULS teaches women to build, repair and sell solar-powered lamps, imparting marketable skills and providing a sustainable solution to inconsistent electricity access.

So far, SoULS has taught 7,436 women to assemble solar lamps. Of that number, 1,896 also received entrepreneurship training and there are more than 800 solar shops in practice today.

Aside from the women learning technical and business skills,

Kumar also saw a “transformational change” in the women’s assertiveness. He measured assertiveness, decision-making and satisfaction to gauge the participants’ sense of empowerment.

Decision-making also increased as the women learned new skills, Kumar observed. Decision-making and assertiveness are also translatable to home life and can enable women to have more say regarding factors like childcare and finances, he noted.

Interestingly, satisfaction seemed to decrease as the study went on.

In interviews with participants, Kumar learned that women often became less content as they learned more skills and started businesses. From the women’s answers, he posited “they now understand



Dr. Praveen Kumar



Under the SoULS Initiative, workshops are organized for school-going students to learn about clean energy (solar) tech and assemble their own solar study lamps.

PHOTO: COURTESY SOULSIITBOMBAY

what they can achieve and they have more anxiety over it, because the social structure around them has not really been helping them succeed.”

Low- and middle-income countries (LMICs) contribute the least to climate change, but they often suffer disproportionately from climate-related weather events compared to countries with the highest carbon emissions.

Kumar noted that the climate crisis affects women and girls disproportionately and exacerbates existing gender inequalities. Gender-based violence often increases directly after climate-led disasters, for example, and Kumar cited a study that showed how empowering women helps decrease gender-based violence and intimate-partner violence after such events.

As an NIH climate and health scholar, Kumar is now conducting research with his host institute/center, Fogarty International Center (FIC). He and the FIC Center for Global Health Strategies are inviting researchers to participate in his new case study, “Lessons from the field: Case studies to advance research on climate adaptations and their impact on public health.”

In this study, Kumar seeks to identify and understand current and historical adaptation responses in LMICs that address deteriorating health outcomes due to climate-led stressors. He hopes the knowledge collected by the case study will strengthen the evidence base around climate change adaptation and help identify research priorities and future research needs.

To learn more about the NIH Climate Change and Health Initiative, visit <https://www.nih.gov/climateandhealth>.



Kumar (third from r) with collaborators from IIT Bombay and solar lamp assemblers and distributors.

EMBRACING OPPORTUNITIES

Summer Interns Share Their Experiences

BY LIYA TADESSE

A place of learning and camaraderie—that's how NIH's intern programs are often described by their participants. After two years of virtual programs due to the pandemic, more and more interns got the chance this summer to explore the NIH campus and engage in hands-on research.

While some remote opportunities still existed, the majority of students relished the opportunity to conduct experiments and build connections on site. This article features two interns who enjoyed the in-person NIH experience.

Aspiring Doctor Makes the Most of NIH Internship

Amit Puthan, a driven and ambitious student, had his sights set on NIH due to its stellar reputation and ample funding for biomedical research. A student at CUNY Hunter College in New York City, Puthan initially aimed to conduct research locally, but his plans took a different turn and he found himself applying for the College Summer Opportunities to Advance Research (C-SOAR) cohort in the Intramural Research Training Award Summer Internship Program. Puthan first participated in C-SOAR virtually in 2022, and returned this summer in-person.

His interdisciplinary background as a biochemistry and special honors double major (along with a mathematics minor) provided a strong foundation for his research work. Now a recent graduate, Puthan set an ultimate goal to become a pediatric oncologist.

Under the mentorship of Dr. Kiyohito Taimatsu in the section on vertebrate organogenesis of the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD), Puthan delved into deep tissue staining and imaging techniques to understand pharyngeal development and cell migration in zebrafish. A typical day on campus involved running experiments, conducting literature searches and collaborating with colleagues during lunch breaks at Bldg. 31.

Puthan expressed enthusiasm for his future as a physician, acknowledging that the NIH internship



Puthan, a CSOAR intern since 2022, took advantage of in-person NIH training this year.



Amit Puthan (c) with his mentor Dr. Kiyohito Taimatsu (l) and postbac mentor John Prevedel (r)

offered him invaluable experiences that will strengthen his medical school applications.

"I did this program last year, but it was virtual, so I definitely expected a shift from virtual to in-person," Puthan said. "Now that I'm on campus, I've been able to expand my social network [and interact with mentors and fellow lab members more easily]...I'm able to ask questions anytime I want, and interact with the lab so much more."

Puthan emphasized the abundant opportunities and resources NIH provides its trainees and interns, including seminars from the Office of Intramural Training & Education (OITE) that offer guidance for pre-Ph.D. or pre-med students.

As he reflected on the various opportunities NIH offers, Puthan highlighted the CSOAR, Community College Summer Enrichment Program and the Undergraduate Scholarship Program as opportunities for students to gain experience in research and receive financial support. He also praised NIH's Summer Internship Program for providing hands-on experience with research.

"The postbac program that I'm doing could be useful for either medical or graduate school," Puthan stated. "Nowadays, medical schools are starting to emphasize biomedical research, like translational and clinical research, so having that additional experience in research...is really good for your application."

He also expressed his desire to continue conducting research in addition to practicing medicine, possibly by engaging in laboratory work or clinical trials.

"I also realized throughout this internship that I want to continue down this path of research... [not

as] the main focus of my practice, but it's definitely something I'm interested in and I feel like I'm getting good experience in it now as an intern."

Marketing Major Ventures into Biotech

Zene Howard, a marketing major at Ohio State University, found her way to NIH through a family friend working at the National Institute of Allergy and Infectious Diseases. She embarked on a summer internship in the Pathways program at the National Cancer Institute (NCI) as a technology analysis and marketing student intern.

Howard provides crucial support for marketing tech transfer projects led by different principal investigators. While she wasn't assigned a single dedicated project, she engaged in a range of marketing initiatives, gaining exposure to diverse areas within the realm of biotech marketing. The absence of strict project boundaries allowed her to fluidly contribute to various endeavors.

Howard said she didn't have many expectations coming in, but what made her summer exceptional was the on-site connection.

"What has really made my experience is the in-person factor because in our building, the majority of people are remote, but for my team to go in person every single week has just been very helpful," Howard shared.

"You can only get so much collaboration virtually, so being able to get acclimated in person was huge for me," she added. "I really appreciated that."

Being in-person allowed Howard to learn from everyone, gain new mentors in this new-to-her field and foster a deep appreciation for NIH.

As her internship concluded, Howard planned to chart a course within the realm of biotechnology: She's considering enrolling in a master's program focused on biotech business. The NIH experience not only provided her with a solid foundation but has also ignited a passion for continued exploration in this dynamic field.

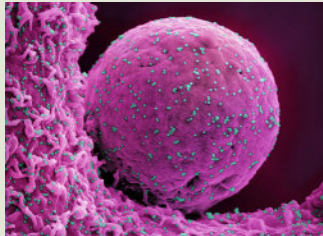
Puthan and Howard exemplify the adaptability and fervor of many interns at NIH, making the most of their experiences despite the challenges posed by the pandemic. As their internships end, students leave with newfound knowledge, networks and aspirations. **B**



Zene Howard, an NCI technology analysis and marketing student intern, used her on-site NIH experience to cultivate new mentors.

Clinical Trial To Test Immune Modulation for Hospitalized Covid-19 Patients

NIH launched a clinical trial to test whether early intensive immune modulation for hospitalized Covid-19 patients with relatively mild illness is beneficial. The placebo-controlled study, part of the global clinical trials consortium known as Strategies and Treatments for Respiratory Infections and Viral Emergencies (STRIVE), will enroll approximately 1,500 volunteers at research sites around the world. The trial is supported by NIAID in partnership with NCATS.



Colorized scanning electron micrograph of a cell (pink) infected with the Omicron strain of SARS-CoV-2 virus particles (teal), isolated from a patient sample.

IMAGE: NIAID

Symptoms from an unregulated immune response to Covid-19 can include severe respiratory distress, which can be fatal. Immune modulators—treatments for modifying the immune system to better respond to disease or illness—are life-saving for certain hospitalized Covid-19 patients. However, the optimal timing for administering the medicines to achieve the best outcomes has not been defined.

“Patients with milder cases of Covid-19 are often administered one immune modulator and a second treatment is added only if the patient becomes severely ill,” said NIAID Acting Director Dr. Hugh Auchincloss. “It is possible that

adding a second therapeutic earlier in the patient’s treatment could prevent progression to severe illness and improve recovery. This clinical study aims to answer that question.”

The drug—abatacept (or Orencia)—used to test the strategy of early intensification of immune modulation is manufactured by Bristol Myers Squibb. It was first approved by the FDA as a treatment for arthritis. Researchers think it may also be useful as an immune modulator for Covid-19 by tamping down overactive immune responses.

Participants may enroll in the current trial if they are receiving supplemental low-flow oxygen upon being hospitalized for Covid-19 infection at one of the participating study sites. In addition to receiving the local standard of care, participants will be randomized to immediately receive either a single intravenous infusion of abatacept with dosage dependent on the patient’s weight, or a placebo infusion. Study investigators will closely track participants’ progress over the course of 60 days.

More than 270 international sites plan to participate in this program, which has continuous enrollment as Covid-19 surges in different parts of the world.

Researchers Discover Biomarker for Tracking Depression Recovery

Using a novel deep brain stimulation (DBS) device capable of recording brain signals, researchers have identified a pattern of brain activity or “biomarker” related to clinical signs of recovery from treatment-resistant depression. Findings from this small study are an important step toward using brain data to understand a patient’s response to DBS treatment.

The study was published in *Nature* and supported by NIH’s Brain Research Through Advancing Innovative Neurotechnologies, or the BRAIN Initiative.

Although the approach is still experimental, clinical research shows that DBS can safely and effectively treat cases of treatment-resistant depression, in which symptoms have not improved with antidepressant medications. People receiving DBS undergo surgery to have a thin metal electrode implanted into specific brain areas to deliver electrical impulses that modulate brain activity.

The small study enrolled 10 adults with treatment-resistant depression, all of

whom underwent DBS therapy for six months. Each participant received the same stimulation dose to begin and then stimulation levels were increased once or twice.

Later, researchers used artificial intelligence (AI) tools to analyze collected brain data from six patients and observed a common brain activity signature or biomarker that correlated with patients self-reporting feeling symptoms of depression or stable as they recovered. In one patient, researchers identified the biomarker and were retrospectively able to predict that a patient would fall back into a major depressive episode four weeks before clinical interviews showed they were at risk of a relapse occurring.

The patients in the study responded well to DBS therapy; after six months, 90% showed a significant improvement in depression symptoms and 70% were in remission or no longer depressed.

“This study demonstrates how new technology and a data-driven approach can refine DBS therapy for severe depression, which can be debilitating,” said Dr. John Ngai, director of the BRAIN Initiative. “It’s this type of collaborative work that moves promising therapies closer to clinical use.”

New Method Developed to Identify Potential Stroke Therapies

Researchers identified uric acid as a potential therapy to enhance recovery from acute ischemic stroke. The study was published in *Science Translational Medicine*.

In the study, researchers from NIH’s Stroke Preclinical Assessment Network (SPAN) rigorously tested the effectiveness of six novel therapies in reducing ischemic brain injury in rodents, including four FDA-approved drugs to treat other conditions. Uric acid was the only candidate that passed the efficacy boundary through all phases of analysis.

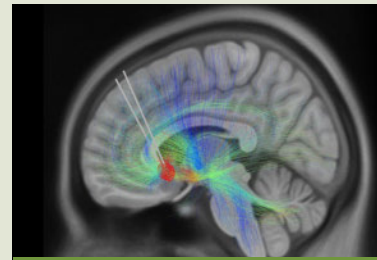
Ischemic stroke, a leading cause of disability and death in the U.S., occurs when a blood clot or other blockage in an artery cuts off blood supply to the brain. Current treatments are aimed at removing the clot by dissolving it with blood-thinners, surgically removing it from the blood vessel or a combination of both.

Although these treatments help patients recover, scientists are seeking a therapy that could protect the brain from damage, known as a cerebroprotectant, that occurs before or during the restoration of blood flow.

“We were faced with a critical need to redesign the entire preclinical approach,” said Dr. Francesca Bosetti, NINDS program director. “SPAN successfully applied well-known clinical research practices to a preclinical trial—randomization, pre-determined sample sizes, treatment masking, blinded analysis, and efforts to make results reproducible in other laboratories.”

In the current study, the efficacy of each of six treatments was assessed by giving animals a series of behavioral tests. After collecting the data, researchers used a new statistical method to evaluate the therapies at four points in the testing process. They also measured MRI brain scans of lesion volumes.

Uric acid has previously been tested in stroke patients, but not in combination with the clot-removal treatment modeled by the study, suggesting that the drug could do well in future trials. However, investigators recommend further testing in animal models before clinical trials in humans.



Two implanted DBS leads, with nerve fibers extending into different brain regions. Biomarkers can help scientists track depression symptoms and optimize DBS techniques.

IMAGE: KI SEUNG CHOI/MAYBERG LAB, ICAHN SCHOOL OF MEDICINE AT MOUNT SINAI

WORLD-CLASS SCIENTIST, MENTOR, FRIEND

NHLBI Mourns Former Director Lenfant

BY ANA CHOBAN

Former National Heart, Lung and Blood Institute (NHLBI) Director Dr. Claude Lenfant passed away on June 26 at age 94. He was the longest-serving NHLBI director, with a tenure from 1982 to 2003.

Lenfant brought the institute into the modern era of science with landmark initiatives such as the Programs of Excellence in Molecular Biology, the Proteomics Initiative and NIH's first gene therapy protocol.

NHLBI's focus expanded with establishment of the National Center on Sleep Disorders Research (1993) and oversight of the Women's Health Initiative (1997), while continuing the commitment to heart, lung and blood disorders and blood safety.

Numerous clinical trials were conducted during Lenfant's tenure, including the Lung Health Study, the Multi-Center Study of Hydroxyurea and the Antihypertensive and Lipid Lowering Treatment to Prevent Heart Attack Trial.

Lenfant was particularly interested in promoting the institute's education programs. Throughout his time as NHLBI director, he was dedicated to balancing basic science research, implementation science, as well as patient and professional education and awareness.



Dr. Claude Lenfant

• • •

“...We have lost one of the giants in pulmonary medicine and science.”

—DR. JAMES KILEY

• • •

Born in Paris, France, in 1928, Lenfant spent much of his childhood moving around the country. He struck out on his own at age 18 and began working in a laboratory in Hôpital Marie-Lannelongue, located in Paris. Under the mentorship of renowned cardiologists Drs. Charles Dubost and Gabriel Nahas, Lenfant worked his way up from dishwasher to head of the laboratory in less than six years.


He established himself as a promising young researcher in the United States at the University of Washington, Seattle, where he was a professor of medicine and physiology and biophysics. He joined NIH as associate director for lung programs at NHLBI in 1972. Shortly after, he was named the first director of the Division of Lung Diseases (DLD) and became institute director in 1982.

Lenfant authored or co-authored more than 350 publications. He served on the editorial boards of numerous scientific publications, including the *American Journal of Physiology*, *American Review of Respiratory Disease*, *Proceedings of the Society for Experimental Biology and Medicine* and *Continuing Education for Family Physicians*.

Upon leaving NIH, he was granted the title of distinguished scientist emeritus. He continued his dedication to chronic disease control by serving as president of the World Hypertension League (2001-2006), executive director of the Global Initiatives for Asthma and the Global Initiative for Chronic Obstructive Lung Disease and the planning committee of the World Health Organization's Global Alliance Against Chronic Respiratory Diseases.

Dr. James Kiley, current director of DLD, remembers Lenfant fondly.

“I worked closely with Claude for much of my career at NIH,” Kiley said. “He was truly an inspirational leader and mentor to many. I know I can speak for the entire pulmonary community that we have lost one of the giants in pulmonary medicine and science.”

Lenfant is survived by his wife Dr. Suzanne Hurd, five children, 15 grandchildren and 19 great grandchildren. 

Healthy Volunteers Needed

Researchers at NIH's Laboratory of Malaria Immunology and Vaccinology are seeking healthy volunteers to be part of a malaria vaccine research study. Malaria is spread to humans after they are bitten by an infected mosquito. Likewise, a mosquito picks up malaria when they bite an infected person. For this study, researchers are developing a new, investigational vaccine with the goal of breaking this cycle. Compensation will be provided. Contact (866) 444-2214 (TTY users dial 711) or ccopr@nih.gov. Refer to study #001501. Online <https://go.nih.gov/qHyOvAW>.

Study Recruits People with DBA

Diamond-Blackfan anemia (DBA) is an inherited disorder that occurs when the bone marrow fails to make red blood cells, leading to anemia and bone marrow failure, with increased cancer risks. Researchers want to know whether the investigational drug Bitopertin is safe and effective in helping restore blood formation by targeting one of the defects in bone marrow found in people with DBA. If you or someone you know has been diagnosed with DBA and have not responded to therapy, has relapsed or is not able to tolerate current treatment, you may be eligible to participate in this study. There is no cost for tests, treatments or procedures. Travel, food and lodging may be provided. To learn more, contact the Office of Patient Recruitment at (866) 444-2214 (TTY users dial 711) or email ccopr@nih.gov for study #001528-H. Online: <https://go.nih.gov/LB196jG>.

EBV Vaccine Trial Needs Volunteers

NIAID researchers are enrolling healthy volunteers ages 18-29 living in D.C., Maryland or Virginia in an investigational Epstein-Barr virus (EBV) vaccine clinical trial. If you are eligible, consider joining research to stop the spread of EBV—the most common cause of infectious mononucleosis (mono) and associated with some cancers. Compensation will be provided up to \$2220 over the course of the trial. For more information, contact the Office of Patient Recruitment at (866) 444-2214 (TTY users dial 711) or ccopr@nih.gov. Refer to study #21-I-0005. Online: <https://go.nih.gov/GqYvJSI>.

Study Seeks Pregnant People

An NHLBI research study seeks pregnant people between ages 18 and 45 with sickle cell disease (SCD) who are at risk of having an infant with SCD to donate their baby's cord blood. Procedures provided at no cost. Contact the Office of Patient Recruitment at (866) 444-2214 (TTY users dial 711) or ccopr@nih.gov. Refer to study #01-H-0122. Online: <https://go.nih.gov/OeDgvaS>.

Full NSO Performs in CC Atrium, Celebrating Sound Health

Hundreds gathered in the Clinical Center atrium on Sept. 13 for a classical performance by the National Symphony Orchestra. Last year, a smaller NSO ensemble returned to perform in-person. This performance marked both the return of the full 60-person ensemble and the 11th anniversary of Sound Health.

“The NSO-Sound Health initiative is driven by the belief that music has a positive impact on mind, body and spirit,” said NSO Executive Director Jean Davidson in opening remarks. Sound Health is an ongoing partnership between NIH and the Kennedy Center for the

Performing Arts that explores how listening, performing or creating music affects mood, brain function and overall health.

Led by Conductor Steven Reineke, the NSO played classical works by Mozart, Dvořák and Coleridge-Taylor, among others. Some lively and upbeat, others slow and somber, the selections likely elicited a range of emotions as the music wafted throughout the atrium and up into the corridors and patient rooms above.

The performance was co-presented by the CC and the Foundation for Advanced Education in the Sciences.

PHOTOS: CHIA-CHI CHARLIE CHANG AND DANA TALESNIK



Above, Clinical Center CEO Dr. James Gilman (l) greets NSO Conductor Steven Reineke. Below, Jean Davidson, NSO executive director, opens the event.



Above (from l) at the Sound Health event, soloists Jing Qiao on violin and Harrison Linsey on oboe perform; a young patient enjoys the concert; and a view of the brass section. Below, the full orchestra as seen from the CC's third floor.

