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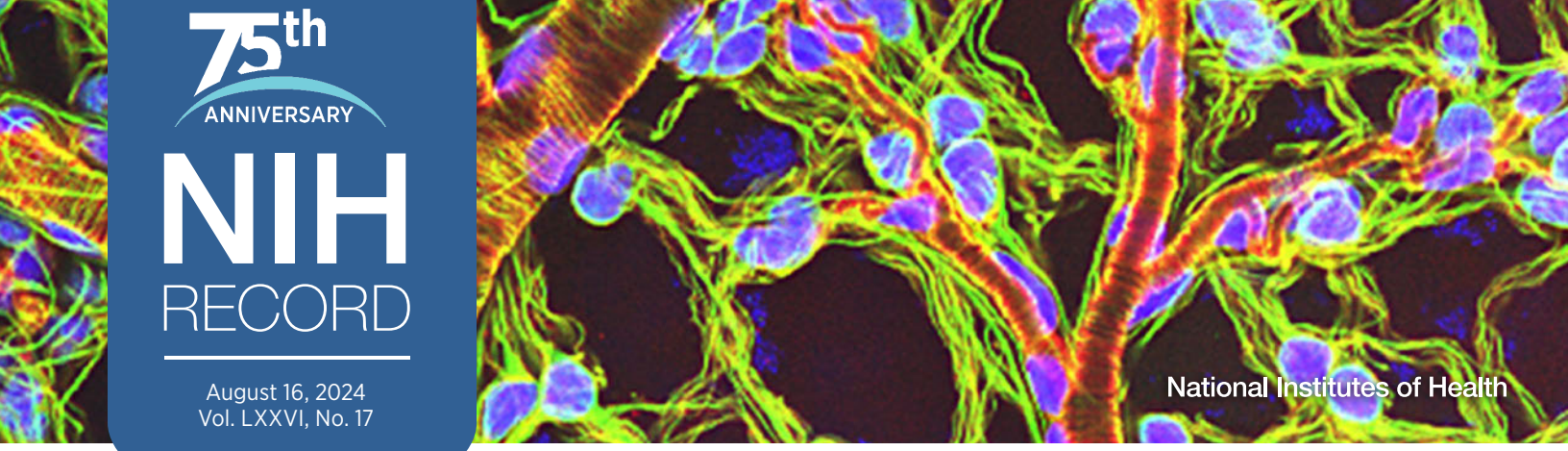


'A COMPLEX TAPESTRY'

Hanchard Explores Genomics of African Populations

BY DANA TALESNIK

The human genome can reveal all kinds of clues toward understanding, diagnosing and treating genetic diseases. Most genomic studies to date, though, have focused on European ancestry and therefore could be missing out on a goldmine of genetic variation found in other people.

"African populations on average are going to have much more genetic variation per genome than those of European ancestry," said Dr. Neil Hanchard, senior investigator at the National Human Genome Research Institute (NHGRI). Africa's populations are much older, he noted. Many groups migrated; lineages diverged.

"As people move, they're now interacting with different diets, different infectious agents and the different ecologies that have changed over time," Hanchard said. "We have this setup for a very complex genetic architecture."

Dr. Neil Hanchard (l) stands with NIH Deputy Director for Intramural Research Dr. Nina Schor.

PHOTO: DANA TALESNIK

In fact, there are more than 2,000 different ethnic groups across the African continent. "We need to be sequencing far more Africans to capture the full variation," he said.

Hanchard is studying several childhood disorders—sickle cell disease and pediatric HIV, malnutrition and hypertension—that are more common in populations of African ancestry. He spoke at a recent NIH Director's Seminar.

A geneticist and clinical researcher, Hanchard described his collaboration with Human Heredity and Health in Africa (H3Africa)—a consortium funded for 10 years by NIH, the Wellcome Trust and the African Academy of Sciences—working to identify and describe genetic variants in

SEE **HANCHARD**, PAGE 6

Christmas comes early for Inn. See page 12.

ALSO THIS ISSUE

BELONGING IMPORTANT FOR HEALTH

How Developing Community Connections Can Enhance Wellbeing

BY ERIC BOCK

Dr. Hahrie Han

Creating opportunities for people to build healthy relationships with each other can combat the epidemic of isolation and loneliness, said Dr. Hahrie Han, professor and inaugural director of the Stavros Niarchos Foundation Agora Institute at Johns Hopkins University.

"We live in a world where people tend to have lots of interactions but fewer

SEE **CONNECTION**, PAGE 8

THE SCIENCE THAT UNITES US

Celebrating 75 Years of NIDCR and NHLBI Research

BY VANESSA MCMAINS

This year, the National Institute of Dental and Craniofacial Research (NIDCR) and the National Heart, Lung and Blood Institute (NHLBI) each celebrated 75 years of research.

To commemorate the milestones, the two institutes recently paired up to host the NHLBI and NIDCR Joint 75th Anniversary Symposium: The Science that Unites Us, which covered their notable

SEE **ANNIVERSARY**, PAGE 4

Wong to Give NEI/FNIH Talk on Retinal Neural Circuits

Sept. 11

Dr. Rachel Wong, professor at the University of Washington, will deliver the 2024 Joram Piatigorsky Basic Science Lecture on Wednesday, Sept. 11, from 1 to 2:30 p.m. ET at the Porter Neuroscience Research Center. The lecture is co-sponsored by NEI and the Foundation for the NIH.

Dr. Rachel Wong

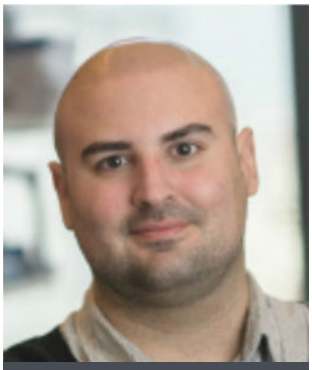
Wong's research focuses on development and regeneration of synaptic circuits in the vertebrate retina. Her current studies are based on the vertebrate retina of mice, human and non-human primates. Her lab applies a range of approaches to study neuronal structure, function and connectivity in normal and perturbed retinas.

Made possible by the generous philanthropic support of Lona and Joram Piatigorsky, this series brings attention to notable basic sciences contributions by eye and vision scientists to a diverse general scientific audience. For more information and to register, visit bit.ly/3LDXay1.

Lung Cancer Researcher to Deliver Wachtel Lecture/CCR Grand Rounds

Aug. 16

Dr. Alvaro Quintanal-Villalonga will receive this year's AAAS Martin and Rose Wachtel Cancer Research Award, which honors outstanding early-career investigators in cancer research.



Dr. Alvaro Quintanal-Villalonga

The award will be presented following his lecture, an NCI Center for Cancer Research (CCR) Grand Rounds titled, "Understanding Plasticity as a Mechanism of Resistance to Therapy in Cancer," on Friday, Aug. 16, from noon to 1:15 p.m. ET in Lipsett Amphitheater. For in-person attendees, there will be a lunch reception following the lecture in the FAES Terrace.

Quintanal-Villalonga, a lung cancer researcher, is assistant attending biologist and lab co-director, department of medicine at Memorial Sloan Kettering Cancer Center. He specializes in small cell lung carcinomas and resistance to targeted therapy.

This is the 10th lecture for the award, sponsored by the American Association for the Advancement of Science and Science Translational Medicine. The award winner's essay will be published in *Science Translational Medicine* the week of the award ceremony.

To register for the lecture and for additional information, see: https://go.cancer.gov/4YOcK4b

Speaking Up About Mental Health Essay Contest Winners Announced

Congratulations to the 18 winners and six honorable mentions for the 2024 Speaking Up About Mental Health Essay Contest.

The contest challenges high school students ages 16-18 to raise awareness of mental health. It gives students a platform to share ways to eliminate and/or reduce mental health stigma faced by young people, especially in diverse communities. More than 370 teens from 33 states submitted essays.

The National Institute of Mental Health, the National Institute on Minority Health and Health Disparities and the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development co-sponsored the contest. It's part of a Health and Human Services–wide initiative to tackle the nation's mental health crisis.

Read the award-winning essays at https://go.nih.gov/eQCZ1X5. NIH recognizes these talented essay winners for their thoughtfulness and creativity in addressing youth mental health.

The essays are written in the students' own words and are unedited.

NIH Seeks Input on Postdoc Experience

NIH is seeking insight from the research community on several recommendations to re-envision the postdoctoral experience. The request is open until Wednesday, Oct. 23.

Among the actions under consideration are:

•Limiting the amount of time a postdoctoral scholar can be supported by NIH funds to five years to speed transition into research careers

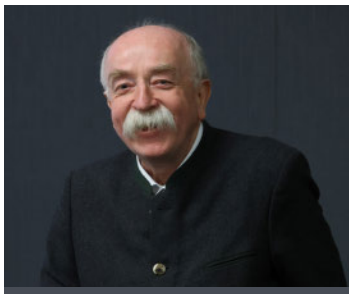
• Shortening the eligibility window and refocus review criteria for a key mentored career development award (K99/R00) to facilitate more rapid transition of postdoctoral scholars

• Enhancing training and professional development for postdoctoral scholars and their mentors

For more information and to submit feedback, see: https://go.nih.gov/amqQ7DD.

NIDCD Launches National Smell and Taste Center

The National Institute on Deafness and Other Communication Disorders (NIDCD) recently launched the National Smell and Taste Center (NSTC). The center is a collaborative effort among scientists, advocates and other experts who are dedicated to advancing understanding of the chemical senses (smell and taste) and related disorders through innovative research, comprehensive patient care, education and outreach.



Dr. Thomas Hummel, professor and director of the Smell and Taste Clinic at the University Hospital Carl Gustav Carus, Dresden, Germany, delivers the keynote speech.

An inaugural seminar in July included prerecorded congressional remarks, panel presentations, descriptions of cutting-edge research and discussions about innovations, challenges and opportunities for advancing smell and taste research.

"NIDCD has long recognized that smell and taste profoundly affect our daily lives," said NIDCD Director Dr. Debara Tucci, during opening remarks. "Chemosensory research also has implications and applications for other diseases, including Parkinson's disease, Alzheimer's and multiple sclerosis."

NSTC was formed through collaborations among several NIH research laboratories and clinics to address the need to strengthen and expand smell and taste research—a need that captured international attention during the Covid-19 pandemic. The center is co-led by Dr. Joshua Levy, NIDCD clinical director, and Dr. Paule Joseph, chief of the National Institute on Alcohol Abuse and Alcoholism's section of sensory science and metabolism. An advisory council of leading researchers, clinicians, patients and advocates will assist in defining NSTC's mission, prioritizing its activities and ensuring its efforts reflect community needs.

NSTC alliances within NIH and with international researchers will accelerate advances in smell and taste research that have applications across several diseases and conditions. Planned partnerships include projects with the National Institute on Aging's Baltimore Longitudinal Study of Aging, the National Institute of Neurological Disorders and Stroke's functional neurosurgery section and the NIH Intramural Center for Alzheimer's and Related Dementias. The collaboration will also include the Clinical Center.

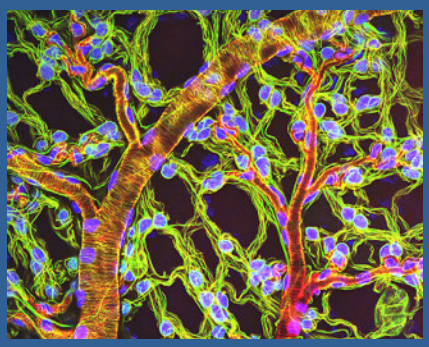
During the event, panelists discussed advancing smell and taste research in the post-Covid-19 era, challenges and solutions for smell and taste research and the personal experiences of patient advocates who have experienced smell loss.

View the recorded event at https://videocast.nih.gov/watch=54861.

For more information on the center, see: https://www.nidcd.nih.gov/research/labs/national-smell-taste-center.

Meeting speakers, panelists and participants gather in Bldg. 35, following the inaugural seminar of the National Smell and Taste Center.

PHOTOS: CHIA-CHI CHARLIE CHANG



ON THE COVER: *Insects have breathing tubes that carry air through their exoskeleton directly to where it's needed. This image shows the breathing tubes embedded in the weblike sheath cells that cover developing egg chambers in a lubber grasshopper.*

IMAGE: KEVIN EDWARDS, JOHNY SHAJAHAN, DOUG WHITMAN/ILLINOIS STATE UNIVERSITY

The NIH Record

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Anniversary

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accomplishments and areas of overlapping research.

Public Health Impact

Since its inception, NIDCR has driven research on topics such as the mouth's microbiome, pain, head and neck cancer, tissue regeneration, craniofacial development and the biology of saliva and the salivary glands.

NIH principal deputy director Dr. Lawrence Tabak, who also is a former NIDCR director, spoke of the institute's work toward improving quality of life. He referred to NIDCR's early research on fluoride and tooth decay as contributing to the most successful public health campaign in U.S. history: Many people keep their teeth nowadays in part because of fluorinated drinking water.

Beyond its significant influence on public oral health, NIDCR-funded research has resulted in more than 60,000 scientific publications and 176 drugs developed to treat a whole range of systemic conditions.

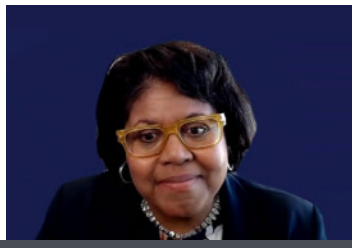
"An NIDCR legacy lies in public health impact driven by basic science that serves as a foundation for clinical research, which is then translated into clinical care and improved quality of life," said NIDCR Deputy Director Dr. Jennifer Webster-Cyriaque.

At NHLBI, numerous achievements in heart, blood, lung and sleep research have improved, lengthened and saved millions of lives. This includes public health recommendations and medications that have resulted in a 70% reduction in deaths from cardiovascular disease alone.

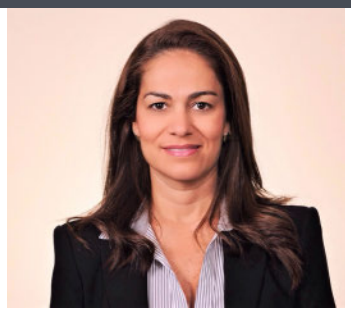
NHLBI's advances in blood diseases such as sickle cell anemia and lung diseases like cystic fibrosis—once fatal childhood diseases—now allow people to live well into middle age.

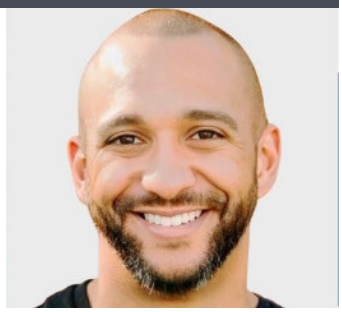
Dr. Gypsyamber D'Souza

"I look forward to the 100-year celebration to see how much more we can accomplish together," said Tabak.



Above (from l): NIDCR Director Dr. Rena D'Souza, NIH Principal Deputy Director Dr. Lawrence Tabak and NIDCR Deputy Director Dr. Jennifer Webster-Cyriaque speak at the virtual symposium. Below, other presenters included NHLBI Director Dr. Gary Gibbons; Dr. Apoena De Aguiar Ribeiro and Dr. Leith States.





The Oral-Systemic Connection

Much of the overlap between NIDCR's and NHLBI's research lies in the oral-systemic connection— the idea that the health of the mouth affects the health of the rest of the body, and vice versa.

During the symposium, a common thread pertained to viral infections. Some viral infections such as HIV are worsened by poor oral health and periodontal disease.

"Stomach flu" viruses like norovirus typically cause uncomfortable digestive symptoms in adults and older children. However, these viruses can be life-threatening to children under 5 years old, older adults and people with weakened immune systems. Until recently, these infections were thought to spread primarily through ingestion of fecal matter particles through improper handwashing.

NHLBI Senior Investigator Dr. Nihal Altan-Bonnet presented findings on her team's collaboration using mother-pup mice pairs to study viral spread. The team found these infections could spread through saliva and the virus in the saliva was much more infectious than the fecal matter. If the findings bear out in human studies, experts may need to modify public health recommendations to curb spread.

Multiple human papillomavirus (HPV) strains are known to increase the risk of cancer, with the HPV-16 strain most likely to cause cervical, vaginal, oral or head and neck cancers. People with weakened immune systems may be at higher risk of developing HPV-related cancers.

Dr. Gypsyamber D'Souza, professor of epidemiology at the Johns Hopkins University, and her team observed that people with HIV were more likely to have HPV infection than people without HIV. HPV infections typically take a year or two to resolve or go dormant in healthy adults. Yet among more than 1,800 people in the study, oral HPV infections took an average of four years to clear. People with HIV and persistent oral HPV infections, and particularly those infected with the HPV-16 strain, may be at highest risk for developing head and neck cancer, according to D'Souza.

Dr. Apoena De Aguiar Ribeiro, research associate professor at University of North Carolina, Chapel Hill, shared findings from an analysis of the mouth's microbiome in people with HIV. These research participants were three times more likely to have lost all their teeth compared to the national average and were more likely to have untreated tooth decay. When it came to the mouth microbiome, Ribeiro found that inflammation and HIV infection reduced microbial diversity as well. These findings suggest that an imbalance in the microbiome may serve as a biomarker of disease severity in people with HIV.

Whole Person Health

At the Department of Health and Human Services (HHS) and NIH, clinicians are committed to caring for the whole person, not just treating a disease or a symptom, said Dr. Leith States, chief medical officer, Office of the Assistant Secretary for Health and acting director, HHS Office of Science and Medicine. However, not everyone has reaped the benefits of NIH's medical advances discovered over the years. In a pre-recorded video, NIDCR Director Dr. Rena D'Souza said, "We must translate scientific discoveries into treatments and care that everyone can access, not just the privileged."

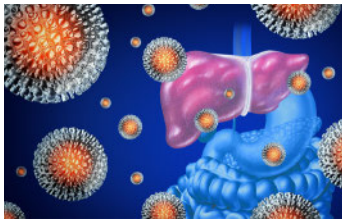
NHLBI Director Dr. Gary Gibbons addressed disparities in cardiovascular health and how NHLBI is working to tackle the problem.

One example is high blood pressure in pregnancy, or preeclampsia. Black and Latina women have a two-to-four-times higher risk of developing preeclampsia than White women. Gibbons said scientists are using continuous blood pressure monitoring, artificial intelligence and machine learning to measure slight variations in blood pressure or changes in the vasculature that could be predictive of preeclampsia.

Gibbons said, "As we enhance our ability to predict, we can use more precise precision medicine to identify those at greatest risk, anticipate and reduce that risk."

FDA Grants Authorization to First Hepatitis C Test

The FDA has granted marketing authorization for the first point-of-care hepatitis C RNA test, which was validated in part by NIH Rapid Acceleration of Diagnostics (RADx) Tech. This game-changing rapid test that can be used in patient care settings delivers results in about an hour.



This new technology could help patients who test positive for the disease get treated right away rather than the current approach, which requires lengthy laboratory processing.

The RADx Tech program aims to speed development, validation and commercialization of innovative virus testing.

For more information, see: go.nih.gov/TBWV4Ok.

Benign Nail Condition Linked to Rare Syndrome That Increases Cancer Risk

The presence of a benign nail abnormality may lead to the diagnosis of a rare inherited disorder that increases the risk of developing cancerous tumors of the skin, eyes, kidneys and the tissue that lines the chest and abdomen (e.g., the mesothelium). The condition, known as BAP1 tumor predisposition syndrome, is caused by mutations in the BAP1 gene, which normally acts as a tumor suppressor, among other functions. The findings are published in *JAMA Dermatology*.

Dr. Raffit Hassan

Scientists happened upon the discovery while studying participants who were enrolled in a screening for BAP 1 variants at the NIH Clinical Center. As part of the study, a dermatology screening was performed at enrollment and annually for participants aged 2 and older.

Patients were asked about nail health during a baseline genetic assessment, and one reported noticing subtle changes in his nails. His observation prompted investigators to evaluate other participants for nail changes and uncover this new finding.

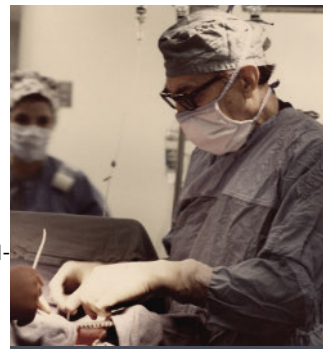
Biopsies of the nail and underlying nail bed in several participants confirmed the investigators' suspicion of a benign tumor abnormality known as an onychopapilloma. The condition causes a colored band (usually white or red) along the length of the nail, along with thickening of the nail underlying the color change and thickening at the end of the nail. It typically only affects one nail.

However, among study participants with known BAP1 tumor predisposition syndrome aged 30 and older, 88% had onychopapilloma tumors affecting multiple nails. Researchers suggest that nail screening may be particularly valuable in a patient with a personal or family history of melanoma or other potential BAP1-associated malignancy.

Dr. Raffit Hassan, principal investigator of the clinical protocol in which these patients were enrolled, said, "This discovery is an excellent example of how multidisciplinary teams and natural history studies can reveal insights about rare diseases."

NLM Welcomes Applications for 2025 DeBakey Fellowship

The National Library of Medicine (NLM) is accepting applications for its 2025 Michael E. DeBakey Fellowship in the History of Medicine. This fellowship provides up to $10,000 to support research using the historical collections of NLM, which span 11 centuries, encompass a variety of digital and physical formats and originate from nearly every part of the globe.



Dr. Michael DeBakey (1908-2008) in surgery

PHOTO: COURTESY OF NLM

Collections include the DeBakey papers—representing the diverse areas in which DeBakey made a lasting impact, such as surgery, medical education and health care policy—along with the papers of many other luminaries in science and medicine.

Anyone over age 18, of any academic discipline and status, who has not previously received this fellowship may apply. Non-U.S. citizens may apply. Group applications should be submitted under the name of a single principal researcher.

The application deadline is midnight on September 30, 2024. Details of the fellowship can be found here: https://www.nlm.nih.gov/news/DeBakey_Fellowship_2025.html.

Hanchard

CONTINUED FROM PAGE 1

diverse African populations.

After 10 years, H3Africa boasts more than 50 projects in 34 African countries with more than 100,000 study participants. All principal investigators must be from the African country where the grant originated, Hanchard explained, to root this initiative in Africa and better facilitate community engagement.

Hanchard described a "complex tapestry" of interwoven populations across the African continent. When H3Africa began, Nigeria was the sequencing hub, and Yoruba and Igbo people became proxies for West African genetic variation. Soon the program expanded to include 50 ethno-linguistic groups.

Hanchard describes his research during a recent NIH DIrector's lecture in Bldg. 1

Delving into this data, "we're starting to see the full breadth of diversity," Hanchard said, including some unusual outliers with respect to geography. The Berom people of Nigeria, for example, are genetically removed from other West African groups due to earlier migration patterns.

"People are using Yoruba or Igbo as proxies for Africa but they're probably not even great proxies for Nigeria," he said.

H3Africa researchers have uncovered more than three million novel single-nucleotide variants, most in newly sampled population groups. More specifically, they've found a substantial number of loss-of-function (LOF) variants—associated with disease—shared across all African populations.

"What's really interesting is we can see a number of genes that are known Mendelian genes [single-gene diseases]," he said. And they're occurring in much higher frequency in these populations than expected.

Some of Africa's genetic variation evolved to spur immunity, following predictable geographic patterns.

The variant responsible for sickle cell disease, for example, is most prevalent across equatorial parts of Africa where it evolved as protection against malaria. This allele (gene variant) is much less common in the southern, drier parts of Africa.

Also more common in equatorial parts of Africa, the *APOL1* allele predisposes people to end-stage kidney disease. But that same variant protects against the parasitic disease trypanosomiasis or, African sleeping sickness.

Researchers also have found variants in certain African countries that are distinct from all other African genomes they'd sequenced.

In these cases, Hanchard said, "We have this interplay of ancestry and genetic variation that's medically relevant."

Hanchard focused much of his talk on pediatric HIV. An H3Africa effort called CAfGEN (Collaborative African Genomic Network), in conjunction with Hanchard's prior affiliation Baylor University, is studying pediatric HIV disease progression. There's been a marked decline in new childhood HIV infections due to efforts to prevent mother-to-child transmission. But HIV remains pervasive, particularly in sub-Saharan Africa, where more than 1.3 million children are living with HIV.

• • •

"African populations have much more genetic variation than those of European ancestry... We need to be sequencing far more Africans to capture the full variation."

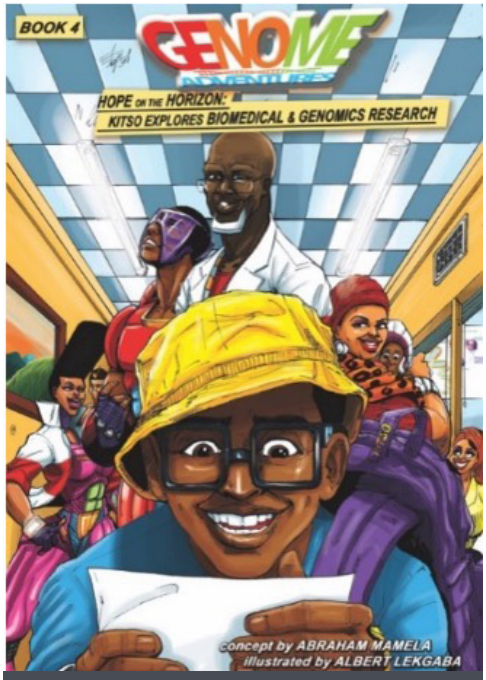
-DR. NEIL HANCHARD

• • •

From the CafGEN clinical cohort, researchers have observed that without antiretroviral therapy, HIV-positive children progress at different rates. At one end of the spectrum are the long-term non-progressors—adolescents with no symptoms—and at the other end are the rapid progressors who develop AIDS-like symptoms within a couple of years.

Hanchard (r) gathers with trainees and colleagues who attended his lecture. (from l): Dr. Edmond Wonkam Tingang, postdoctoral fellow; Aparna Haldipur, senior research technician; Dr. Jackie Piekos, postdoc; Marion Amujal, CAfGEN graduate student; Dr. Qing Li, staff scientist; and Jared Redmond, postbaccalaureate fellow.

PHOTOS: DANA TALESNIK



To help foster community engagement, the Wellcome Trust developed comic books, such as the one above, and translated them into African and other local population languages. *Genome Adventures* tells the story of a child enrolled in a genetics study.

Genomic sequencing shows alleles common in rapid progressors, including ones specific to certain African regions, and others associated with HIV protection. Deep dives into these genes at the individual and population level are revealing new clues.

Researchers found a correlation between LOF genes and country-specific HIV mortality. Certain variants are only seen among Africans such as a damaging, rare variant in a gene known to enable HIV replication.

"These variants are much more [common] in the GI tract and reproductive tract, which is interesting because that's the interface for vertical transmission between mother and child," Hanchard said.

Overall, Hanchard emphasized, in all of their testing, "We have to be mindful of the ancestries we're dealing with, and that Africa is not just a monolith." And so much of this work is enabled and buttressed by local clinicians and investigators.

"It's really important to do [genetic mapping] in an equitable framework where there's partnership, empowerment and community engagement," he said, "where we can start by building the research capacity and have it ripple out so it [benefits] everyone."

NCI Discovery on Liver Cell Diversity Could Help Scientists Understand Tumor Complexity

Dr. Natalie Porat-Shliom

Nearly a century ago, scientists made a peculiar observation that adjacent liver cells, called hepatocytes, organize into clustered zones that differ in their appearance under the microscope. Now, researchers from NCI's Center for Cancer Research (CCR) have found that this hepatocyte diversity is shaped in part by the nutrient-sensing ability of their mitochondria.

The discovery, published earlier this year in *Nature Communications*, has important implications for understanding how cells take on different characteristics in the same tissue — a hallmark of many tumors.

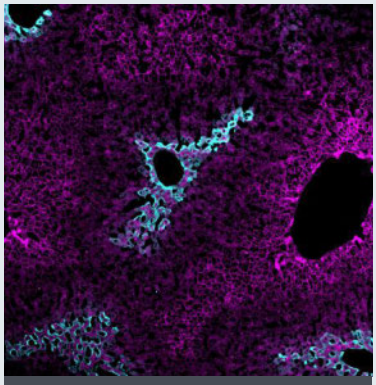
"Tumor heterogeneity is a big problem in cancer biology because different cells have different biological behaviors, and this can cause resistance to treatment," explained Dr. Natalie Porat-Shliom, a Stadtman investigator in the Thoracic and GI Malignancies Branch and lead researcher on the study. "Mechanistically, we don't really understand what gives rise to heterogeneity and how to treat it, but the reality is that normal tissues are also extremely heterogeneous."

This fact is often disregarded when scientists study liver tissue by putting samples in a tube and collecting data from all the cells combined. Porat-Shliom's team, however, took a different approach to understanding the liver's complexity. Using a cutting-edge technique called intravital microscopy, they examined the livers of living, anesthetized mice under the microscope.

Homing in on the mitochondria using a mitochondria-targeting fluorescent tag, they found two types of mitochondria in the liver: one type in hepatocytes near arteries and veins that carry blood into the liver for processing, and another type of mitochondria in hepatocytes near veins that carry blood away from the liver.

When they looked more closely at the proteins in the two types of mitochondria—by removing the livers and separating the cells—they found that not only did the mitochondria house different sets of proteins, but even the way the proteins were modified to affect their function differed. The team showed that these differences could be shifted with drugs that manipulate the mitochondria's nutrient-sensing activity.

"You can imagine the mitochondria as a communication hub," Porat-Shliom explained. They are constantly sensing nutrient signals from the environment and translating that into different mitochondrial activities and metabolic output. This, she continued, affects the behavior and appearance of the cells and their mitochondria based on their location in the organ.



Immunofluorescence staining of a liver section showing distribution of hepatocytes near veins and arteries that carry blood into the liver (magenta) and away from the liver (cyan).

IMAGE: LAURYN BROWN

Now, the team is collaborating with clinicians to determine if cancers that spread to the liver tend to invade one zone of hepatocytes more so than another.

Ultimately, Porat-Shliom's team hopes to relate their findings about mitochondrial zonation in the mouse model to what is happening in human disease. "The first step is to understand how things normally work. Then you can compare and contrast that with what goes wrong," she said.

Connection

CONTINUED FROM PAGE 1

relationships," said Han, during a fireside chat with U.S. Surgeon General Dr. Vivek Murthy. Moderated by National Institute on Minority Health and Health Disparities Deputy Director Dr. Monica Webb Hooper, the chat was part of the Murthy Distinguished Lecture Series on Public Health Leadership.

The civic institutions where people used to go to build relationships, such as faith communities or hobby and recreational organizations, have decayed over the past 50, 60 or 70 years, Han said.

Loneliness and isolation severely impacted the social development of many children during the Covid-19 pandemic. Most people spend their time online, which limits their ability to build relationships. However, people are having more interactions than ever before.

"During my day, I have interactions with lots of people, " Han said. "Online, I might read a post and like it. I might also talk to the checker at the grocery store."

Han's research focuses on the study of organizing, movements, collective action, civic engagement, and democracy.

Relationships differ from interactions. In a relationship, both parties have expectations of a shared future. There are two types of relationships: transactional and social, she said.

In a transactional relationship, both parties have a shared future, but each person protects their self-interest. Social relationships, on the other hand, can be more fulfilling because people invest into these relationships "without knowing what they're going to get back."

Because there are so many opportunities to have social interactions in digital communities, they encourage what social scientists call the "habit of exit."

If a person gets uncomfortable in an online situation or heated conversation, they can leave and find another community.

This virtual lecture was the third in a public health leadership series hosted by Dr. Vivek Murthy, the 19th and 21st U.S. surgeon general.

Once a person develops that habit, he or she doesn't learn a set of skills that are necessary for long-term connection. They don't learn how to work through conflict. People behave differently if they know they aren't leaving when things get too hard.

Young people struggle with loneliness and isolation, said Murthy. Although they stay in touch with each other through social media, they do not always have relationships with each other. Instead, they compare themselves to their peers, which leads to lower self-esteem. They also report being less comfortable in situations that require interacting with strangers.

"We have to build social muscles," agreed Han. "We've lost the proverbial gyms where people would go and learn how to engage in these kinds of activities."

People must have the opportunity to organize their lives around the things they hold sacred, she added. Young people aren't given opportunities to learn how to live together. They feel society encourages them to prioritize their careers over relationships.

Governments around the country are starting to fund programs that address loneliness and isolation, said Murthy. They are investing in research and supporting initiatives that help communities cultivate healthy relationships.

Schools, for instance, are teaching students how to recognize, understand and manage their emotions to they can build relationships with others. Building social connections is just as important as math and reading, he argued.

"These kinds of programs are really important," said Murthy. "We can't assume young people are going to grow up with a strong skillset when it comes to navigating, building and maintaining relationships and negotiating conflict."

Evangelical megachurches, or houses of worship with more than 2,000 congregants, are one of the few social institutions that have been growing. The average megachurch grew 34 percent between 2015-2020. Han said some of these churches have a motto, "belonging comes before belief." In other words, being part of a community doesn't depend on what a person believes.

"They create a community of belonging, which is how I think they draw people in," she said. "People are hungry for places like that."

People who don't feel like they belong anywhere are in a state of hypervigilance. Those who are alone respond differently to threats. Murthy believes the rise in mental health challenges is connected to loneliness and isolation.

"Rebuilding connection is not just a health issue," he concluded. "It's an economic, educational and national security issue. It's important for the health and wellbeing of society."

The full lecture can be viewed on demand at https://videocast.nih.gov/watch=54661.

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"Rebuilding connection is not just a health issue. It's an economic, educational and national security issue. It's important for the health and wellbeing of society."

-DR. VIVEK MURTHY-

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Protein Screening Does Not Improve Risk Prediction for Hypertension

Results from a large NIH-supported study show that protein analyses taken during the first trimester of pregnancy did not improve predictions for identifying people at risk for experiencing conditions related to having high blood pressure, hypertension, during pregnancy. Since there is an urgent need to better predict people at risk for hypertensive disorders of pregnancy, researchers have been studying if proteins taken from blood or urine samples could provide this insight.

For this study, researchers analyzed 6,481 proteins from 1,850 participants who had a first pregnancy between 2010 and 2013. Participants provided a blood sample during the study enrollment and had study check-ins during their second and third trimesters, after delivery and two to seven years after their pregnancy.

The protein analysis was used in different modeling equations to assess if proteins or their combinations with clinical data, such as maternal age and cardiovascular disease risks, during early pregnancy could provide clues for the 753 participants who experienced a hypertensive disorder of pregnancy. The conditions assessed included gestational hypertension, marked by high blood pressure that typically develops after 20 weeks of pregnancy, and preeclampsia, a significant rise in blood pressure after 20 weeks of pregnancy that can damage organs and is marked by elevated levels of protein in the urine.

The prediction models, which included three different types of assessments, did not significantly improve risk predictions for these events. These criteria currently include risk factors such as having obesity, diabetes, high blood pressure or a baby later in life.

Hypertensive disorders of pregnancy affect about 10-15% of people and are associated with increased risks for having a pregnancy complication, heart attack, stroke and in severe cases death.

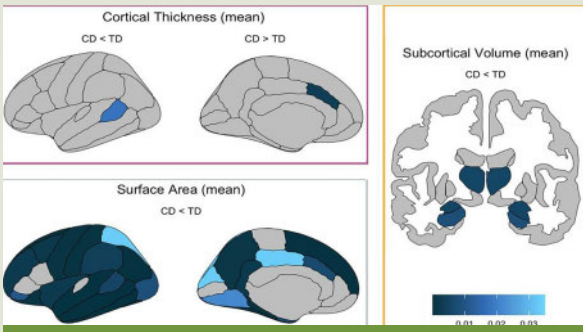
Youth with Conduct Disorder Show Differences in Brain Structure

A neuroimaging study of young people who exhibit a persistent pattern of disruptive, aggressive and antisocial behavior known as conduct disorder, has revealed extensive changes in brain structure. The most pronounced difference was a smaller area of the brain's outer layer, known as the cerebral cortex, which is critical for many aspects of behavior, cognition and emotion. The study, co-authored by NIH researchers, is published in *The Lancet Psychiatry*.

A collaborative group of researchers examined standardized MRI data from youth ages 7 to 21 who had participated in 15 studies from around the world. The group analyzed 1,185 youth diagnosed with conduct disorder and 1,253 youth without the disorder.

Youth with conduct disorder had lower total surface area across the cortex and in 26 of 34 individual regions, two of which showed significant changes in cortical thickness. Youth with conduct disorder also had lower volume in several subcortical brain regions, including the amygdala, hippocampus and thalamus, which play a central role in regulating behaviors that are often challenging for people with the disorder. Although some of these brain regions, like the prefrontal cortex and amygdala, had been linked to conduct disorder in previous studies, other regions were implicated in the disorder for the first time.

Youth who exhibited signs of a more severe form of the disorder, indicated by a low level of empathy, guilt, and remorse, showed the greatest number of brain changes. The study also provides novel evidence that brain changes are more widespread than previously shown, spanning all four lobes and both cortical and subcortical regions.



Brain plots showing regions with significant group differences between youth with and without conduct disorder. **PHOTO: GAO, STAGINNUS, ET AL., THE LANCET PSYCHIATRY**

"Conduct disorder has among the highest burden of any mental disorder in youth. However, it remains understudied and undertreated," said Dr. Daniel Pine, chief, Section on Development and Affective Neuroscience, NIMH. "Understanding brain differences associated with the disorder takes us one step closer to developing more effective approaches to diagnosis and treatment, with the ultimate aim of improving long-term outcomes for children and their families."

Analysis Associates an HIV Drug with Elevated Cardiovascular Disease Risk

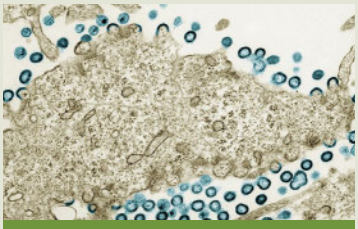


PHOTO: NIAID

Current or previous use of the antiretroviral drug (ARV) abacavir was associated with an elevated risk of major adverse cardiovascular events (MACE) in people with HIV, according to an exploratory analysis from a large international clinical trial primarily funded by NIH. There was no elevated MACE risk for the other antiretroviral drugs included in the analysis. The findings will be presented at the 2024 International AIDS Conference in Munich, Germany.

The Randomized Trial to Prevent Vascular Events in HIV (REPRIEVE) enrolled 7,769 study participants with HIV from 12 countries that found daily use of a cholesterol-fighting statin drug reduced the risk of major adverse cardiovascular events, such as heart attack and stroke, by more than one-third.

The REPRIEVE study team also performed statistical analyses to assess whether select ARVs were associated with MACE risk among study participants, all of whom had low-to-moderate cardiovascular disease risk. The ARVs selected for analysis had previously been linked to cardiovascular risk and included abacavir, tenofovir, zidovudine, stavudine, and drugs from a class called protease inhibitors (PIs). All were taken as part of multi-drug ART regimens.

In the investigators' analyses, participants with prior and current use of abacavir had a 50% and 42% elevated risk of MACE, respectively, compared to participants with no abacavir exposure. Former or current use of other ARVs was not associated with any change in MACE risk, and the co-administration of common ARV drug classes as part of an ART regimen did not impact the elevated MACE risk among participants with current or prior abacavir exposure.

According to the authors, these findings align with previous studies that also identified an elevated cardiovascular disease risk associated with abacavir. More research is needed to better understand these findings in the context of known cardiovascular disease risk factors, such as dyslipidemia, diabetes and hypertension, for people with HIV.

Dewey Receives NIDA's Lifetime Achievement Award

The National Institute on Drug Abuse (NIDA) recently presented a lifetime scientific achievement award to Dr. William Dewey, the Louis S. and Ruth S. Harris professor and chair of the department of pharmacology and toxicology at Virginia Commonwealth University.

Dr. William Dewey, founder of Friends of NIDA and professor at Virginia Commonwealth University Department of Pharmacology and Toxicology, addresses the National Advisory Council on Drug Abuse.

NIDA presented the award during the 147th meeting of the National Advisory Council on Drug Abuse to honor Dewey's unwavering commitment to addiction research and training.

Dewey's career is emblazoned with nearly 400 publications and seminal contributions that reflect his lifelong interest in understanding how addictive drugs in general, and opioids in particular, work. His work has focused on understanding the molecular mechanisms underlying opioid-mediated tolerance, dependence, and analgesia, using tools and approaches that include neurochemistry, pharmacology, whole-cell imaging and behavioral research.

In addition to his scientific contributions, Dewey has been among the staunchest supporters of NIDA's mission. He created the Friends of NIDA 20 years ago and, under his leadership, the Friends of NIDA coalition has leveraged the synergistic power of dozens of organizations including scientific and professional societies, patient groups, community organizations and others to educate policymakers and the public on the value of addiction research through education and advocacy.

Dr. Nora Volkow (r) presents the NIDA Lifetime Scientific Achievement Award to Dewey.

"Today we not only recognize his many contributions to science and training of future generations of scientists but also pay tribute to the enduring power of human curiosity, good citizenship and unwavering support of one's trainees and colleagues," said Dr. Nora Volkow, director of NIDA. "The work that will leave the greatest mark on our field is Bill's steadfast and lifelong commitment to research training."—**Molly Freimuth**

NIEHS Pathologist Receives Mid-Career Excellence Award

The Society of Toxicologic Pathology (STP) has selected National Institute of Environmental Health Sciences (NIEHS) Molecular Pathology Group lead Dr. Arun Pandiri as its inaugural Mid-Career Excellence Award recipient. The award was presented at a June 19 recognition ceremony during the STP annual symposium in Baltimore, Maryland.

STP Awards Committee Chair Dr. Kris Helke presented Pandiri with the Mid-Career Excellence Award Jun 19 in Baltimore.

PHOTO: ERIC STOCKLIN PHOTOGRAPHY

"Arun is the epitome of an outstanding scientist," said Dr. Robert Sills of the Division of Translational Toxicology (DTT), who nominated Pandiri for the award. "He is leading several noteworthy research activities and mentoring the next generation of scientists to address important public health problems using cutting-edge technologies."

Pandiri, whose career at NIEHS has spanned 15 years, was also the inaugural recipient of the STP Distinguished Early Career Award in 2014. His research group works to identify molecular signatures of exposures in rodent models of cancer, as well as in human tumor samples resulting from suspected exposures. They also have an active program investigating potential factors implicated in early-onset colorectal cancers.

"I'm grateful for the recognition by the top professional organization in my specialty," said Pandiri. "I feel it reflects the excellent team science at DTT, and I'm lucky to be working in such a collaborative and encouraging environment that provides so many opportunities for career advancement."

The STP Mid-Career Excellence Award is given to a member in good standing who has made outstanding contributions in toxicologic pathology in the middle phase of their career. Nominees are active members, within 11-20 years of last relevant training, who have distinguished themselves as leaders in industry, government, education and/or public service.—**Erica Hinton**

NIAAA VR Experience Wins Audio Description Award

The National Institute on Alcohol Abuse and Alcoholism (NIAAA) was honored in July for its Your Brain Virtual Reality (VR) experience. NIAAA received the 2024 Achievement in Audio Description public sector award from the American Council of the Blind's Audio Description Project.

The winning video shows a rollercoaster traveling through different areas of the brain—the body's command center—and how alcohol affects these areas. The ride travels from the decision-making region, the prefrontal cortex, through the nucleus accumbens, to the emotion-regulating and threat-assessing amygdala, to the memory-making hippocampus and finally to the movement and balance-controlling area of the brain, the cerebellum.

This award celebrates outstanding contributions to the quality, availability and understanding of audio description. The video version of NIAAA's Virtual Brain that provides audio descriptions for users with low or no vision and captions for viewers who are deaf or hard of hearing is available at bit.ly/3zHv4PE.

'THE WAY SCIENCE THRIVES'

Former NIH Molecular Biologist Singer Remembered

BY CARLA GARNETT

Dr. Maxine Singer, president emerita of Carnegie Science and scientist emerita at NIH, died July 9 at age 93. In her more than 40-year formal association with NIH, Singer made a lasting impact in nearly every area of the agency's conduct of fundamental research as well as its administration and scientific workforce recruitment.

"Maxine Singer was the consummate scientist's scientist," noted NIH Director Dr. Monica Bertagnolli. "In addition to making research advances as a principal investigator in her own NIH lab and in the lab of other renowned NIH investigators over several decades, she made significant contributions to crucial areas of science policy that continue to guide the ethical conduct of vital research today."

Dr. Maxine Singer, in Masur Auditorium during NIH Research Festival 2010 for a memorial tribute to Nobelist Dr. Marshall Nirenberg

Singer joined NIH in 1956 as a new postdoctoral fellow. She'd been recruited from Yale by legendary NIH investigator Dr. Leon Heppel, a lab chief in what was then the National Institute of Arthritis, Metabolism and Digestive Diseases (NIAMDD) who was one of the few people in the United States at the time working in chemistry and biochemistry of nucleic acids.

Within a year and a half, Singer had her own independent NIAMD lab, where she conducted studies with a small group in the emerging field of nucleic acid research until 1975. That's when the National Cancer Institute's Laboratory of Biochemistry (LB) lured her to the other end of the same ninth floor corridor of the Clinical Center to lead the nucleic acid enzymology section. She rose to LB chief in 1980.

"As chief of the Laboratory of Biochemistry in NCI, she built a world class program through her own research and her ability to recognize and recruit outstanding scientists," said Dr. Michael Gottesman, chief of NCI's Laboratory of Cell Biology and former NIH deputy director for intramural research. "Her role in enabling Marshall Nirenberg's synthesis of nucleotides for his Nobel Prize-winning work elucidating the genetic code was absolutely critical."

One of Singer's recruits, NIH Scientist Emeritus Dr. Michael Lichten, retired chief of NCI's Laboratory of Biochemistry and Molecular Biology, recalled, "By the time I arrived, the Laboratory of Biochemistry was a model for a diverse program of investigator-initiated research programs. Maxine's broad scientific interests, and her belief that good science was best done when investigators had the freedom to follow their imagination, were responsible."

Singer brought Dr. Carl Wu to LB as an independent investigator in 1982 and he remained there for 30 years.

"A key attraction of the laboratory was Maxine's academic philosophy of encouraging young investigators to pursue problems of fundamental significance with complete freedom and long-term funding for a small group," said Wu, Bloomberg distinguished professor at Johns Hopkins School of Medicine. "That philosophy, initially held by very few department heads at NIH, later became formalized as the Tenure-Track Investigator Program by NIH Director Harold Varmus, resulting in the continuing infusion of the best young scientists into the intramural community. As our lab chief and authority on nucleic acids, Maxine always provided guidance, insightful scientific critique, and wise managerial advice and support."

In 1973, Singer co-led the Gordon Conference, where announcement of the first recombinant DNA experiment began a public debate about the safety of such experiments. As co–chair, she was one of the people who made the matter public and asked the National Academy of Sciences to undertake investigation of people's concerns about those experiments.

Singer was a lead organizer, with former Stanford professor and Nobel Laureate Dr. Paul Berg, of the 1975 Asilomar Conference on Recombinant DNA to discuss the potential biohazards and regulation of biotechnology. The meeting of more than 140 biologists, physicians and lawyers resulted in development of voluntary guidelines to ensure the safety of recombinant DNA technology.

The conference also brought more public attention to medical research and its conduct and is credited as an example of scientists joining together, acting preemptively to protect societal interests while simultaneously advancing knowledge in an important field.

In 1988, Singer left NIH to become president of what was then-the Carnegie Institution, where she served until 2002. She maintained her lab at NCI until 1997.

Another aspect of Singer's influence that has been underemphasized, Lichten continued, "is Maxine's breadth as an author. In addition to authoring three texts on genes and genomes with Paul Berg, she also coauthored with Paul an outstanding—and in my opinion, greatly unappreciated—biography, *George Beadle: An Uncommon Farmer* [2005] and a book on flower formation, *Blossoms, and the Genes that Make Them* [2018]."

Former colleagues suggest it was her ability to approach issues from multiple perspectives that sealed her legacy as a research collaborator and thought leader.

"Science thrives under conditions where individuals of talent and skill have real independence," Singer observed in a 1998 interview for an oral history of NCI.

At left, Singer, at a meeting called by NIH Director Dr. Donald Fredrickson on Feb. 19, 1977, to inform the scientific community and the media of legislation pending in Congress that was designed to regulate recombinant DNA research; at right, early days of the molecular biologist in an NIH lab

Christmas Comes Early at the Children's Inn at NIH

PHOTOS: CHILDREN'S INN AT NIH

The Children's Inn at NIH brought holiday cheer to its young residents during its annual Christmas in July event. On July 17, the Montgomery County Police Department and the NIH Police Department escorted Santa Claus to the Inn.

From there, good Saint Nick, police, residents and their families rode to the Rio Lakefront shopping center in Gaithersburg, Md. to Shop with a Cop. Each family paired up with a Montgomery County police officer and shopped for toy cars, dolls, decorative plants and more. After the store run, residents had dinner at the Silver Diner.**—Kristine Duru**

Santa visited with Children's Inn at NIH residents and their families during their summertime shopping spree.

Above, Santa and his motorcycle elves—members of the NIH and Montgomery County Police Departments—came to the Children's Inn at NIH and accompanied shuttles filled with families to Rio Lakefront in Gaithersburg.

Above, FOX 5's Gwen Tolbart interviews Santa about the Christmas in July event.

Each family was paired with an officer from the Montgomery County Police Department to shop for toys and other gifts.

After shopping, Inn residents and their families ate dinner at the Silver Diner.