

'RARE BIRD' SET TO SOAR Cancer Survivor Gives Back as Researcher, Future Physical Therapist

BY CARLA GARNETT

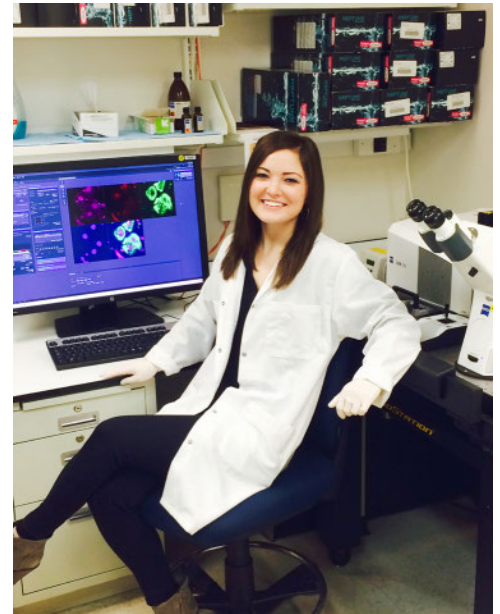
Lauren Stahl ignored the bump on her arm for a long time. After all, she was 18, a senior in high school, focused on important stuff like college applications. But the knot near her left elbow, sitting right on the funny bone, kept bothering her. It became painful. After a few months, she visited her doctor, who scheduled a procedure to remove what everyone thought was just a cyst. But Stahl had a bad feeling it was something more. She was right. She

was diagnosed with stage 1 spindle cell sarcoma, a very rare soft tissue cancer.

Despite the life-altering medical news, Stahl graduated from high school and enrolled in community college. One month into classes, she underwent two surgeries and radiation therapy and received a good prognosis. Life got back to normal...sort of.

"I had really changed," she explained. "Having cancer, at my age...the experience of being in the hospital, having radiation treatments made me realize how blessed I was. In my oncologist's office, I was always the youngest patient. And this cancer I had, nobody had ever seen before. I never met anyone else who had it. They were always calling me 'the rare bird.' I started to wonder how other people—those who had to have chemo or those with more serious cancers—managed to get through it all. I just felt that I had to help others have hope and see

SEE **SURVIVOR**, PAGE 4



Cancer survivor-turned researcher Lauren Stahl
PHOTO: ROSS LAKE



Music marks Black History Month; see p. 12.

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WINDOW INTO THE MIND

Linguistic Analysis Yields Reliable Diagnoses, Cecchi Shows

BY RICH MCMANUS

Anything that generates a pattern can be analyzed mathematically. Speech and language generate patterns, and the mathematical savvy of scientists such as Dr. Guillermo Cecchi of IBM's Thomas J. Watson Research Center holds the promise of enabling accurate diagnosis—from



Dr. Guillermo Cecchi

speech alone—of ailments ranging from psychosis, Parkinson's disease and post-traumatic stress disorder to chronic pain, Alzheimer's disease and depression.

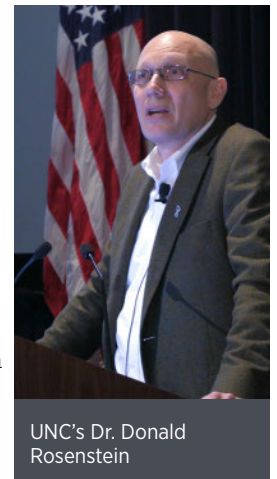
SEE **CECCHI**, PAGE 8

STUDYING SUICIDE

Is It Ethical to Enroll Suicidal Patients in Clinical Research?

BY DANA TALESNIK

Selecting volunteers for any clinical study requires great discretion. For patients with dire medical conditions, research trials offer hope for restored health and new treatments. But what happens when the volunteers are in active crisis? How do we help and protect patients with suicidal thoughts who are at risk for life-threatening behaviors? Is it



UNC's Dr. Donald
Rosenstein

SEE **SUICIDE**, PAGE 6



Kinzler To Give Next Lecture in NCI Series, Apr. 4

Dr. Kenneth Kinzler will be the next speaker in the 4th annual NCI Excellence in Molecular Diagnostics Lecture Series on Monday, Apr. 4 from 10 to 11 a.m. in Lipsett Amphitheater, Bldg. 10. He will discuss "The Cancer Genome as a Clinical Biomarker."

Kinzler is a professor of oncology at Johns Hopkins University School of Medicine, co-director of the Ludwig Center at JHU and associate director for basic research for the Sidney Kimmel Comprehensive Cancer Center. He has produced classic studies of the genes causing human cancer, including the discovery of APC, the gene that initiates virtually all colorectal tumors. He is also known for his development of genetic methods for analyzing gene expression and mutations in human cancer leading to his most recent work on defining the cancer genome for more than a dozen human tumor types.

Kinzler has coauthored more than 375 peer-reviewed articles on the molecular analyses of cancer and holds over 125 patents. He is a member of the National Academy of Medicine, the National Academy of Inventors and is a fellow of the American Association of Cancer Research Academy.

Kinzler will discuss the potential of tumor DNA as a clinical biomarker. In particular, the technical and clinical aspects of using cancer-specific somatic mutations to detect low levels of tumor DNA released into blood and other clinical samples will be described. Examples of clinical utility that will be highlighted include screening, liquid biopsies, resistance monitoring and prognosis.

The lecture series, sponsored by the NCI Division of Cancer Prevention, recognizes outstanding leaders who are making groundbreaking contributions in molecular diagnostics and who have demonstrated integrated approaches in the development of diagnostics.

For more information, contact Felicia Evans Long, (240) 276-5076 or evanslongf@mail.nih.gov.

LINDA BROWN

DESIGN RETROSPECTIVE

AN EXHIBIT OF WORK FROM HER 48-YEAR CAREER AT THE NIH MEDICAL ARTS AND PHOTOGRAPHY BRANCH

JOIN US FOR A GALLERY OPENING CELEBRATION

APRIL 14, 2016

4:00 —
6:00 PM

NIH CLINICAL CENTER—BUILDING 10—5SE CORRIDOR



Exhibit Honors Medical Arts' Brown

NIH Medical Arts is hosting an art exhibition featuring the work of Linda Brown, a designer and creative director with NIH Medical Arts for 48 years who died last fall. The retrospective show includes original silk screen posters created over a span of more than 4 decades, beginning with Brown's first work in 1966. All are welcome to celebrate Brown's life and work at the show opening on Thursday, Apr. 14 from 4 to 6 p.m. in the 5SE (southeast) corridor of the Clinical Research Center. Take the elevators from the parking information desk up to floor 5 and follow signs to 5SE. The show will be open from Apr. 1 to Sept. 30.

Postbaccalaureate Poster Day Planned, Apr. 20

Postbac Poster Day is scheduled for Wednesday, Apr. 20 at the Natcher Conference Center from 10 a.m. to 3:30 p.m. The keynote address will begin at noon and will be followed by presentation of Postbac Distinguished Mentoring Award(s) to NIH investigators selected by the postbacs. Poster session I will take place from 10 a.m. to noon and poster session II is from 1:30 to 3:30 pm.

Poster Day provides an opportunity for postbacs to share the research they have been conducting at NIH and at the same time develop scientific communication and networking skills. Posters will be reviewed by teams composed of graduate students, postdocs and staff scientists/clinicians. The authors of the top 20 percent will receive a letter acknowledging their accomplishments.

Investigators, staff scientists and scientific administrators can make a particularly important contribution to the event by visiting posters and engaging their authors in discussion. For more information, visit https://www.training.nih.gov/postbac_poster_day.

Next Protocol Navigation Lecture, Apr. 4

The IRP Protocol Navigation Training Program Seminar Series continues with a lecture to be held Monday, Apr. 4 from 2 to 3 p.m. in Bldg. 50, Conf. Rm. 1227/1328. The program is a trans-NIH effort to develop resources and tools and to provide training for intramural staff and contractors involved in protocol development, writing, coordination and management. Dr. Sara Chandros Hull, chair of the NHGRI IRB and director of the NHGRI bioethics core, will present "On Becoming the Central IRB of Record for a Multi-Site Study: Opportunities, Challenges and Lessons Learned." For more information, contact Marcia Vital, (301) 451-9437, vitalm@mail.nih.gov.



NPR's Diane Rehm will give Rall Lecture.

NPR's Rehm to Deliver Rall Lecture, Apr. 7

Diane Rehm, host of National Public Radio's *The Diane Rehm Show*, will deliver a talk titled "On My Own" at the annual J. Edward Rall Cultural Lecture on Thursday, Apr. 7 at 3 p.m. in Masur Auditorium, Bldg. 10.

Rehm is a native Washingtonian who began her radio career in 1973 as a volunteer producer for WAMU 88.5, the NPR member station in Washington, D.C. She was hired as an assistant producer and later became the host and producer of two health-oriented programs. In 1979, she began hosting WAMU's local morning talk show *Kaleidoscope*, which was renamed *The Diane Rehm Show* in 1984. The lecture will be in interview format, with NIH director Dr. Francis Collins asking Rehm about her 35

The lecture will be in interview format, with NIH director Dr. Francis Collins asking Rehm about her 35 years as radio host.

years as radio host. The two will also discuss Rehm's new book *On My Own*, which speaks out about the long drawn-out death (from Parkinson's disease) of her husband of 54 years and her struggle to reconstruct her life without him.

The lecture honors the memory of Rall, founder of the Clinical Endocrinology Branch (now within the National Institute of Diabetes and Digestive and Kidney Diseases)

and scientific director of the National Institute of Arthritis and Metabolic Diseases, which is now represented by NIDDK and the National Institute of Arthritis and Musculoskeletal and Skin Diseases. It was Rall who recommended in 1984 that NIH add a cultural lecture to its long-standing Director's Lecture series, reflecting his broad interest in science and his desire to enrich the NIH scientific community.

Seating for the lecture is on a first-come, first-served basis. For more information or to request reasonable accommodation, contact Jacqueline Roberts at (301) 594-6747 or robertsjm@mail.nih.gov.

Straus Lecturer Will Discuss T-Cell Response to Herpesviruses

Dr. David Koelle will deliver the 2016 NIAID Stephen E. Straus Memorial Lecture on Infectious Diseases. Koelle's lecture, titled "The T-Cell Response to HSV and VZV: Discovery through Clinical Trials," will be



Dr. David Koelle

held on Friday, Apr. 8 at 2 p.m. in the Bldg. 50 1st floor conference room 1227/1233. The lecture series honors Straus, who served NIAID for 30 years as a senior investigator and lab chief and died in 2007.

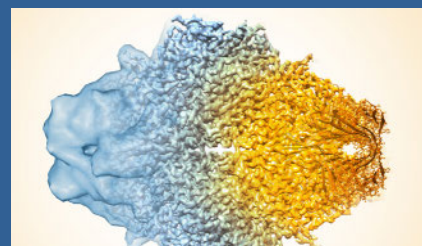
Koelle is a professor in the division of allergy and infectious diseases

at the University of Washington and has ancillary appointments in the departments of laboratory medicine and global health and affiliations with the Fred Hutchinson Cancer Research Institute and Benaroya Research Institute. Throughout his 25-year career, he has worked with alphaherpesviruses, a family of viruses that includes herpes simplex virus (HSV)-1, HSV-2 and varicella zoster virus (VZV).

His lecture will address his lab's research to discover and prioritize antigens important for inducing immune responses to viruses such as HSV and VZV. While effective vaccines exist for VZV, they have been elusive for HSV. Koelle's lab has undertaken detailed studies of the CD4 and CD8 T-cell

responses to HSV-1 and HSV-2, uncovering an unexpected level of cross-reactivity with VZV. This work has helped to identify possible target antigens for HSV vaccines and has contributed to the development of HSV vaccine candidates that have reached pre-clinical and clinical stages.

Koelle earned his B.S. in cellular and molecular biology from the University of Washington in 1980 and his M.D. from the same institution in 1985. He completed an internship and residency in internal medicine at Tufts-New England Medical Center and a fellowship in infectious diseases at UW. He is a fellow of the American College of Physicians and the Infectious Diseases Society of America and a member of the American Society for Clinical Investigation.



ON THE COVER: Composite image of a cryo-electron microscopy density map for the enzyme β -galactosidase, demonstrating the gradual increase in quality of cryo-EM structures from low to high-resolution.

IMAGE: VERONICA FALCONIERI, SRIRAM SUBRAMANIAM

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The *NIH Record* is recyclable as office white paper.

National Institutes of Health
Turning Discovery Into Health

Survivor

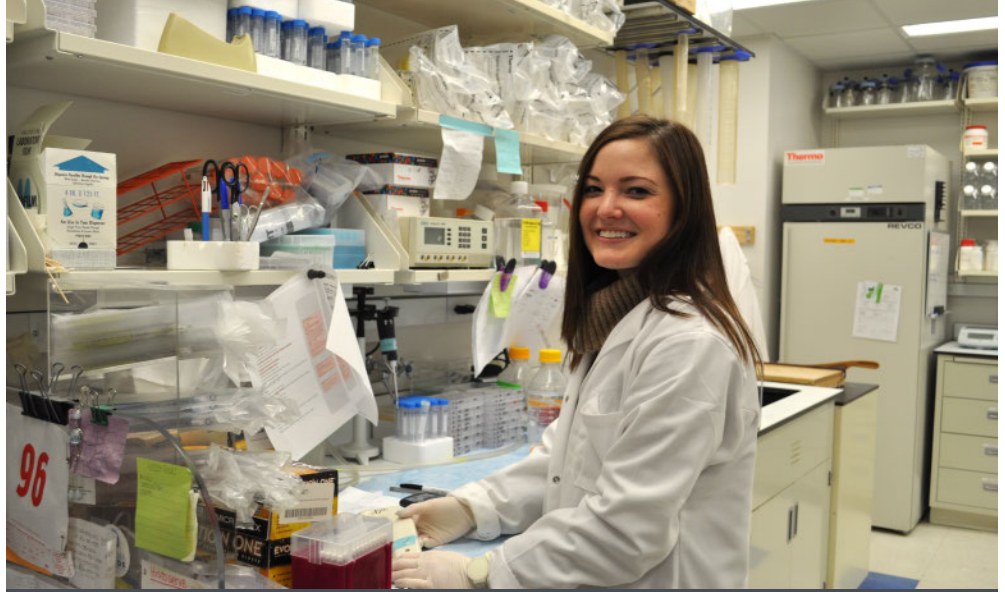
CONTINUED FROM PAGE 1

the light at the end of the tunnel. I had this tremendous need to give back in some way.”

A few months ago, Stahl, a post-baccalaureate researcher in the Laboratory of Genitourinary Cancer Pathogenesis at NCI’s Center for Cancer Research, began a blog, “Scars Create Stars,” to reach out to other cancer survivors.

“What I really wanted to convey,” she wrote in her first post, “was that whatever your scar(s) might be, it doesn’t have to defeat or define you. Scars are just a part of your story. And whatever those scars might be, you can use them to propel you forward and to make a difference in the lives of those around you.”

This was just Stahl’s latest move to translate her passion into practice. Before cancer, she’d planned on a career in psychology and counseling and was pursuing such courses in college. After her treatments, she decided she wanted to be a cancer researcher and eventually go into medicine. Always an above-average student, she switched her major to



Stahl is almost finished the first half of a potential 2-year NCI postbac stint studying prostate cancer.

PHOTO: CARLA GARNETT

principal investigator of an NIH-funded lab studying Ewing sarcoma and co-leader of the Molecular Oncology Program at the Lombardi Comprehensive Cancer Center. “Lauren was incredibly persistent, but in a kind way, in order to join our lab group. Once on the team, she was the kind of member that would take on any task that would benefit the mission of the lab, and do it well.”

After graduating from Georgetown, Stahl considered taking a gap year before going


marathon for St. Jude’s Children’s Research Hospital on Mar. 12. Her survivor story is featured on the American Association for Cancer Research Foundation’s web site.

February marked Stahl’s 5-year survivor anniversary. That meant the 23-year-old had to face a new battery of PET and CT scans to make sure she was cancer-free.

“I had flashbacks entering the hospital again,” she recalled. “Pieces of my past experience, the fears, all came back. I mean, I was 95 percent confident that the cancer was gone, but that other 5 percent can be crippling. The uncertainty can overwhelm you, until you get the all-clear.”

“N-E-D—no evidence of disease.” That’s actually the only term any survivor wants to hear after completing the periodic monitoring. Have studying tumors first hand, working at NIH and learning more about the disease than the typical person with cancer made Stahl’s experience as a patient more or less nerve-racking?

“Well, in many ways, it’s a lot more calming and reassuring having worked with a lot of dedicated researchers who are really devoted to finding new treatments and therapies,” she said. “The other side is realizing that there are more than 200 types of cancer, so there’s never going to be ‘a cure for cancer.’ The goal is to find therapies to reduce the harsh side effects of chemo and other treatments...When you’re going through cancer, it’s scary. I can say that from my own personal experience. If I can help someone else through it, if I can share my own positive outlook, then I’ll feel like that was the reason I got through it.”

You can find her blog at <https://scarscreatestars.wordpress.com/>. 

★ ★ ★
“I’m really passionate about helping people use their experience with cancer to motivate themselves, to drive themselves in ways they never thought they could.”

-LAUREN STAHL

★ ★ ★

biology and earned a generous scholarship to Georgetown University. She immediately looked into cancer labs there and attempted to join a prestigious program studying sarcomas. But she encountered a rather significant obstacle: Dr. Jeffrey Toretsky rarely accepted undergraduates into his research program.

“But I was really persistent,” Stahl said, smiling. “I read papers and studied everything the lab was doing for 2 years.” Toretsky, himself an ex-NCI fellow under former Pediatric Oncology Branch chief Dr. Lee Helman, consented and became Stahl’s mentor.

“I had accepted undergraduates before Lauren, but due to the time commitment and emotional maturity required for lab work, I have a very high bar to accept undergraduates into the lab,” said Toretsky,

into medical school. One year wasn’t enough research experience for her; she wanted to learn more. Stahl was offered a post at NIH. She’s now just about finished the first half of a potential 2-year NCI postbac stint studying drug targets for prostate cancer. Still, she’s raring to make more of a difference. Wanting to balance research with teaching and patient care, she decided to apply for study in a physical therapy program.

“I’ll still get to work with kids and cancer patients,” Stahl said. “I’m really passionate about helping people use their experience with cancer to motivate themselves, to drive themselves in ways they never thought they could.”

She’s also determined to lead by example. In addition to her blog, which is already affiliated with Stupid Cancer—the largest charity for young adult cancer—she ran her first

Future of Antibiotics Is Subject of LaMontagne Lecture

Hailed as one of the most important achievements in medicine, the discovery and subsequent introduction of antibiotics meant that people could be treated and cured of once-fatal bacterial infections. However, the overuse and abuse of antibiotics is a growing public health concern, both in the United States and around the globe.

Over time, bacteria have evolved to develop resistance to drugs that normally would kill them or limit their growth. As a consequence, many antibiotics have become less effective and are enabling untreatable strains of carbapenem-resistant *Enterobacteriaceae* (CRE) and other bacteria to survive and multiply. Dr. Ramanan Laxminarayan will discuss this problem and potential solutions during the 2016 John Ring LaMontagne Memorial Lecture titled “The State of the World’s Antibiotics” at 3 p.m. on Tuesday, Apr. 5 in Lipsett Amphitheater, Bldg. 10.

Laxminarayan is director and senior fellow at the Center for Disease Dynamics,



Dr. Ramanan Laxminarayan speaks here Apr. 5.

Economics & Policy in Washington, D.C., and a senior research scholar and lecturer at the Princeton Environmental Institute at Princeton University. He is also a distinguished professor of public health at the Public Health Foundation of India.

In 2014, Laxminarayan served on the U.S. President’s Council of Advisors on Science and Technology’s antimicrobial resistance

working group. Currently, he is a voting member of the U.S. Presidential Advisory Council on Combating Antimicrobial Resistance. An economist and epidemiologist by training, his research integrates the use of epidemiological models of infectious disease and drug resistance into the economic analysis of public health problems.

Laxminarayan will review the current supply of antibiotics and highlight promising new products in the development pipeline. He will also describe global patterns and trends in antibiotic resistance and antibiotic use in humans and animals. Further, Laxminarayan will discuss interventions to help streamline antibiotic use that could be applied in many different countries.

The NIAID-sponsored lecture honors contributions to NIH and public health made by LaMontagne during his 30-year career with NIAID. He earned international recognition and widespread admiration for his distinguished leadership and accomplishments in fighting emerging and re-emerging infectious diseases. He served as NIAID deputy director from 1998 until his untimely death in 2004. [R](#)

NIEHS Science Informs Response to Flint Water Crisis

NIEHS and National Toxicology Program director Dr. Linda Birnbaum recently addressed NIH’s institute and center directors about the environmental emergency in Flint, Mich.

She presented background data on lead and current plans for addressing the problem of contaminated drinking water in Flint, a city with a declining population and a high rate of poverty that is now under federal and state emergency declarations because of its lead-contaminated water.

In January, President Obama issued an emergency declaration to help the 30,000 water subscribers in the affected area. The action includes immediate funding for distribution of bottled drinking water, filters for home faucets and water testing kits. HHS, under the stewardship of Dr. Nicole Lurie, assistant secretary for preparedness and response, is in charge of the federal response in Flint.

She called on NIEHS to provide scientific leadership and coordination of the research efforts focused on the Flint situation. The institute has a long history of research on the health effects of lead and of responses to disasters such as the Gulf oil spill, Superstorm Sandy and the Ebola outbreak.

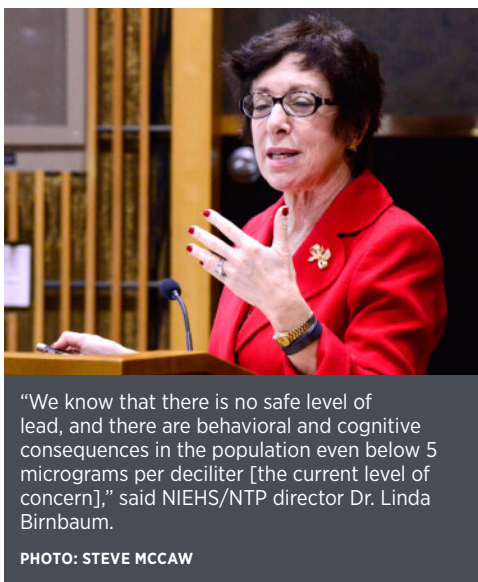


PHOTO: STEVE MCCAW

Once the humanitarian aid, immediate medical interventions and infrastructure improvements are completed, Birnbaum envisions an ongoing role in Flint for federal agencies, including NIEHS and its grantees. “Educational and nutritional enrichment may have a positive

impact on children with elevated blood lead,” she explained. “[There are] opportunities for longitudinal research on various issues.”

In addition, health and safety training for workers involved in removing and repairing damaged pipes, supported by the NIEHS Worker Training Program, will likely be important for the coming months, if not years.

Multiple federal agencies are involved and physicians and mental health professionals are already on the front lines. The Federal Emergency Management Agency and the State of Michigan are providing drinking water to residents.

The NIEHS response includes reviewing new proposals for time-sensitive and researcher-initiated grants and working with current NIEHS grantees at the University of Michigan, Michigan State University and Wayne State University, who are using their resources and community connections to address community concerns.

“We are committed to helping the people of Flint recover from this crisis, and already we are making substantial progress in supporting the state’s top priorities,” Lurie said.—**Eddy Ball**

Suicide

CONTINUED FROM PAGE 1

ethical to enroll such patients?

This dilemma was discussed at Bioethics Grand Rounds on Feb. 3 in Lipsett Amphitheater.

“I don’t think it’s responsible to talk about this kind of research without considering the possibility that by studying individuals who have recently been suicidal, there will be a suicide attempt or completed suicide here in the hospital [during the study],” said discussant Dr. Donald Rosenstein, director of the Comprehensive Cancer Support Program and vice chair, division of hospital psychiatry, at the University of North Carolina, Chapel Hill.

Suicide has become the leading cause of injury-related death in the U.S. More than 40,000 Americans kill themselves every year and, equally troubling, this rate has remained stable for more than 5 decades. But research is lacking in this field, especially on people actively considering or having recently attempted suicide. Instead, most studies have evaluated patients who have made at least one suicide attempt at some time in their lives, possibly many years ago.

“Suicidal patients often are excluded

• • •

“You need to take a giant step back and ask how is suicidal behavior different from so many other conditions that we study at the NIH, which are very serious conditions associated with substantial morbidity and mortality.”

-DR. DONALD ROSENSTEIN

• • •

from our psychiatric research,” said Dr. Elizabeth Ballard, a clinical psychologist and research fellow in NIMH’s Experimental Therapeutics and Pathophysiology Branch.

“In fact, depression clinical trials are getting more restrictive,” said Ballard. “Very few are working with people who are currently experiencing suicidal thoughts.”

That’s precisely the group Ballard and her team is recruiting in a current neurobiology of suicide protocol. The study evaluates four research groups, the most acute of which consists of people who have seriously considered or attempted suicide in the past 2 weeks. All groups will undergo neurological imaging and psychological evaluations; the acute group also will receive the drug ketamine, an anesthetic believed to have a fast antidepressant effect and the potential to rapidly reduce suicidal thoughts.

In this study, patients can continue taking their current medications but may have a delay in starting new antidepressants for 1-2 weeks. The investigators are careful not to call this a treatment trial, said Ballard, since ketamine is not yet FDA-approved for depression. Therefore, without the prospect of clinical benefit, she posited, is it ethical to enroll patients who are actively in crisis?

Before recruiting patients for this protocol, investigators consulted with the Clinical Center’s department of bioethics for more than a year to identify potential risks and safeguards and participated in an intensive institutional review board assessment. Getting the green light to study people currently thinking about suicide sets this study apart, said Ballard, from the many studies that don’t include actively suicidal patients.

Rosenstein, also a former NIMH clinical director and IRB chair, said it’s not only ethical, but also necessary, to study at-risk patients and better understand suicide. This protocol, he said, has social value, fair subject selection, independent medical monitors, proper scientific methodology and a favorable risk-benefit ratio. The NIMH study also builds in such safeguards as a secure inpatient setting, a clinical research advocate from the human subjects protection unit, specialized staff training and a detailed informed consent process.

“After being [at NIH] for 18 years right out of training, I felt like when I landed back at an academic center, it was almost unrecognizable from how inpatient clinical care had been practiced when I was a resident,” said Rosenstein. “There was a time when someone who was severely depressed, with or without suicidality, would be hospitalized for a month with a genuine, in-depth effort to understand how they got there and really to do some intensive inpatient work. Now it’s very often a matter of people being



“I don’t think it’s responsible to talk about this kind of research without considering the possibility that by studying individuals who have recently been suicidal, there will be a suicide attempt or completed suicide here in the hospital [during the study],” said Rosenstein.

PHOTOS: BILL BRANSON



NIMH's Dr. Elizabeth Ballard

be transferred or committed; in that regard, it complicates the voluntary component of research like this, Rosenstein said. For those who complete the study, follow-up assessment and care may be needed. "We know discharge from hospitals is a critical time for acute suicide risk," said Ballard.

It's important to recognize that many suicidal patients, even in trials, might not admit the severity of their situation. "We have to have a lot of humility about what we can take from either a structured interview or a clinical review," said Rosenstein. In one study of 100 inpatient suicides, he said, 78 of the patients said they were not suicidal, then went on to kill themselves.

"If we could know more about this suicidal state," said Ballard, "maybe we could develop better, more effective treatments." **R**

hospitalized only when they're suicidal and only for as long as they're actively suicidal. The comparison between the care provided in this research protocol and standard care is not even close in many respects."

And, Rosenstein said, the conditions that carry increased risk of suicide make it all the more important to study. "You need to take a giant step back and ask how is suicidal behavior different from so many other conditions that we study at the NIH, which are very serious conditions associated with substantial morbidity and mortality."

While he finds great value in this research protocol, Rosenstein said he hopes it will pave the way for more studies that include patients with comorbid substance abuse problems and medical illnesses that can make them prone to highly lethal behaviors.

"I do not think that the research risks of this protocol are particularly high," said Rosenstein, "certainly compared to the risks associated with having a condition that renders you suicidal or some of the risks associated with usual care, which quite honestly often keep me up at night because of how many poor disposition options we have."

In the NIMH protocol, subjects must score at least 90 percent on a consent quiz, indicating they understand their decision to enroll. If a patient opts to leave the study and is deemed high risk, the patient may have to

'MEDIATION ANALYSIS'

MacKinnon To Give Next 'Mind the Gap' Seminar, Apr. 8

Dr. David P. MacKinnon, Foundation professor, department of psychology, Arizona State University, will present on the topic "Applying Mediation Analysis to Understand How



Interventions Work" at the next Medicine: Mind the Gap seminar. The event is scheduled for Friday, Apr. 8 from 11 a.m. to noon via NIH Videocast, <http://videocast.nih.gov/>.

MacKinnon will describe mediation analysis methods with attention to solutions for some

of the limitations of these methods. He has been developing, evaluating and applying methods to assess how interventions work for 30 years. He received the Merit Research in Time Award from the National Institute on Drug Abuse for his research on mediation analysis. He was a consulting editor of the journal *Prevention Science* and is on the editorial board of *Psychological Methods*. MacKinnon has been a principal investigator on several NIH grants.

He will accept questions before and during his presentation via email at prevention@mail.nih.gov and on Twitter with #NIHMtG.

Register for the event at <https://prevention.nih.gov/programs-events/medicine-mind-the-gap>.

Have a question about some aspect of working at NIH? You can post anonymous queries at <https://nihrecord.nih.gov/> (click on the Feedback tab) and we'll try to provide answers.

Feedback: There were numerous large trees removed to make room for the new day care facility. How many were removed and what is NIH doing to replace those that were taken down?

Response from the Office of Research Services and Office of Research Facilities: The trees removed from the Northwest Child Care Center site will be replaced one for one once the building is complete. Most of the trees were relatively young and will be replaced with only slightly younger trees, consistent with the proposed NIH Forest Conservation Plan being finalized



Artist's rendering of the south elevation of the new Northwest Child Care Center, due to debut on campus in spring 2017

for approval by the Maryland department of natural resources, forest service. Some of the trees removed were damaged or diseased. NIH was able to reuse some of the trees for play elements in the playground of the existing preschool on campus and some were converted to mulch for reuse onsite. The remainder were hauled offsite and sawn into boards for reuse.

Feedback: Southbound Convent Dr. gets very backed up in the morning at Lincoln Dr., sometimes past Center Dr. There used to be a straight and left turn lane on southbound Convent at Lincoln but now there is one lane for left and straight and one right turn lane (which is very infrequently used except for parking of contractors). Is it possible to separate the straight and left turns so that traffic moves faster?

Response from ORF: Thank you for bringing this issue to our attention. A change was made to the intersection during the expansion of the Porter Neuroscience Research Center. ORF will take corrective action to include re-striping the southbound lanes of Convent Dr. to improve the situation and/or restore it to the previous configuration.



Cecchi's work has been highlighted in the popular press, including the *New York Times* and *Forbes* magazine. "As they say, a picture in *Forbes* is worth a thousand citations," he quipped.

PHOTOS: RICH MCMANUS

Cecchi

CONTINUED FROM PAGE 1

In short, the way you talk, and write, can yield not only a medical diagnosis, but also the likelihood that you will convert, in time, to a condition.

Speaking at an NIMH lecture series in the Neuroscience Center, Cecchi, a native of Argentina whose first language is Spanish, demonstrated that the title of his talk—"A privileged window into the mind: language as a tool for diagnosis of mental disease"—applies not just in English, but also in other tongues.

Trained in both physics and psychiatry, Cecchi might most accurately be considered an opportunist. He realized that there was both an Everest of data—63.3 million patient visits for mental disorders, according to the CDC, where an interview is the main source of information—and a powerful new analytic arsenal buttressed by "an explosion of artificial intelligence/machine learning tools, computational power and algorithms."

It dawned on Cecchi that the kind of analysis done routinely on everyone's emails by vendors seeking to sate our consumer appetites "has not penetrated at all the mental health community." He and his colleagues knew that computer science provided the mathematical tools to study language as it applies to psychiatry. Their challenge was to quantify psychiatric dysfunction by some new measure.

For a series of pilot studies, they used tools that have been around since the 1950s,

including Noam Chomsky's technique for determining the "logical scaffold of language," graph theory and complex networks, and "semantic embedding," which measures the relative meaning of words by frequency of occurrence and appropriateness of related terms. Quipped Cecchi, "The big [IT] companies use it to scan your emails."

One study assembled regular users of the recreational drug ecstasy. The challenge was to discover, by analysis of language alone, whether the study subject belonged to one of four groups: high-dose, low-dose, methamphetamine or placebo. The subjects were asked to talk for 20 minutes about someone close to them, with little intervention by the interviewer.

Scientists could determine, with almost 90 percent accuracy, the high-dose ecstasy population from placebo. Perhaps unsurprisingly, verbosity was "a strong signal" for those high on speed.

Interestingly, such common conversational flotsam as "like," "you know," and "just" seemed to vanish in those using ecstasy. "There was a very strong effect—they became more fluent," Cecchi said.

Another pilot study used graph theory to probe disorders of thought. This time, the study population included normal controls, schizophrenics and manic patients. They were to relate a recent dream, in 100 or fewer words. The short speech sample was then represented mathematically.

The resulting "graphical signatures" were unequivocal. "It jumps to the naked eye that there is a very clear difference," Cecchi said. Manic patients produced graphs full of loops—they were literally loopy—that wandered out and returned, topically. Schizophrenic patients had fewer loops, less even than normal controls.

A third study sought to predict the onset of psychosis, and followed a group of people for more than 2 years after they sat for a 40-minute session with a therapist, open-endedly discussing their problems. Graph theory and semantic embedding were of little use here, Cecchi said, but when scientists added a new feature—semantic coherence—accuracy improved dramatically.

"It turns out that 'flight of ideas' is very important for defining psychosis," he said. The math here simply computed the topical differences between consecutive sentences. "It yielded a very good signal."

Investigators learned that the logical complexity of speech is markedly greater in those who convert to psychosis.

As further proof of their deductive skills, the mathematicians submitted writing samples by *New York Post* reporter Susannah Cahalan, a diagnosed psychotic and author of the book *Brain on Fire*, to analysis. They were able to identify "very dramatic drops in coherence" that closely tracked Cahalan's journey through manic and schizophrenic phases, simply from her written texts (some of which, as you might have guessed, were not published).

Cecchi and his team are now applying their tools to Parkinson's disease, "where we don't expect purely linguistic components" to be predictive. Yet a 1-minute speech sample on the topic of what a typical day is like for a PD patient can spot the real patient with 76 percent accuracy, in both English and Spanish-speaking populations. Stuttering stands out as a marker in this group.

In a follow-up to the ecstasy study, using more subjects and fewer words, drug effect could be determined with 81 percent accuracy with the addition of new semantic features.

And a follow-up to the prodromal study of psychosis—a "story game" in which patients read a short story then attempt to retell it—showed 85 percent accuracy in predicting who would convert to psychosis. Again, faults in logical coherence were the giveaway. For reasons yet unclear, those who convert also employ markedly fewer personal pronouns, noted Cecchi.

Companies are now building cloud-based tools accessible by smartphones—you can speak and it will analyze the output, Cecchi said. Not only is verbal content a potential subject of study, but also one's tone and pitch—pure sound—may yield useful information.

"What we really need is much larger studies," concluded Cecchi. "There have only been a small number of small pilots so far, but I think that will change very soon."

During a brief but lively Q&A session, wherein participants wondered what insights the great American gusher of speech might really say about all of us, an audience member wondered whether one day, perhaps 10 years from now, our smartphones might beep and notify us that we're going nuts. Cecchi answered, "That will happen 3 years down the road, not 10." **B**



Dr. Elaine Mardis

Mardis Gives Director's Lecture, Mar. 30

Dr. Elaine Mardis, co-director of the McDonnell Genome Institute at Washington University School of Medicine (St. Louis), will deliver the annual NIH Director's Lecture (second of three) on "Translating the Cancer Genome: Transforming Cancer Care" on Wednesday, Mar. 30 at 3 p.m. in Masur Auditorium, Bldg. 10.

Mardis has research interests in the application of next-generation sequencing (NGS) to characterize cancer genomes and transcriptomes and using these data to support therapeutic decision-making. She co-led the teams that first used next-generation sequencing to characterize the whole genome of a patient with acute myeloid leukemia; first sequenced and compared a primary tumor to its metastasis and xenograft; and first reported whole-genome sequencing of samples from a breast cancer clinical trial. Beyond making discoveries in cancer genomics, she is leading efforts to facilitate the translation of basic-science discoveries about human genetic diseases into the clinical setting. She is devising NGS-based diagnostics, decision-support tools and databases and using genomics to design personalized cancer vaccines.

Mardis is also the Robert E. and Louise F. Dunn distinguished professor of medicine and professor of genetics and molecular microbiology at Washington University School of Medicine.

The lecture is part of the NIH Director's Wednesday Afternoon Lecture series. For information and reasonable accommodation, contact Jacqueline Roberts, (301) 594-6747.



ABOVE: A visiting congressional delegation includes members of the House subcommittee on appropriations that oversees NIH. Shown at the table are (from l) Rep. Mike Simpson (R-ID); subcommittee vice chair Rep. Steve Womack (R-AR); subcommittee chair Rep. Tom Cole (R-OK); and Rep. Nita Lowey (D-NY). **RIGHT:** NIH director Dr. Francis Collins greets Lowey at the CRC entryway.



Congressional Appropriations Delegation Gets NIH Briefing

PHOTOS: ERNIE BRANSON

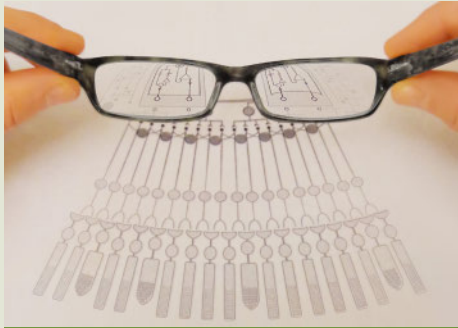
Congressman Tom Cole (R-OK), chair of the House subcommittee on appropriations that oversees NIH, and several fellow committee members and their staff visited NIH Feb. 29 for research briefings and tours of labs and patient care units in the Clinical Center. In addition to

hearing scientific updates on such current topics as the Zika virus, the group chatted with NCI chief of surgery Dr. Steven Rosenberg about immunotherapy and gene therapies for patients with advanced cancers, NINDS principal investigator Dr. Daniel Reich about imaging Alzheimer's disease and amyloid progression in the brain, and NIMH senior investigator Dr. Carlos Zarate about faster-working therapies for depression and suicide prevention.



ABOVE: Briefing members of Congress are NIH leaders (from l) NIA director Dr. Richard Hodes, NIAID director Dr. Anthony Fauci, Collins, NIH deputy director for science, outreach and policy Dr. Kathy Hudson and NCI acting director Dr. Doug Lowy. **BELOW:** At left, Lowy, Lowey and Hodes chat. At right, Simpson hears updates on several research topics in recent headlines, including the Zika virus and immunotherapy for advanced cancers.





Eye cells multiply. NIH scientists uncovered how neurons in the eye may use math to distinguish moving objects.

PHOTO: DIAMOND LAB, NINDS

Eye Cells May Use Math to Detect Motion

Our eyes constantly send bits of information about the world around us to our brains where the information is assembled into objects we recognize. Along the way, a series of neurons in the eye uses electrical and chemical signals to relay the information.

In a study of mice, NIH scientists showed how one type of neuron may do this to distinguish moving objects. The study suggests that the NMDA receptor, a protein normally associated with learning and memory, may help neurons in the eye and the brain relay that information.

“The eye is a window onto the outside world and the inner workings of the brain,” said Dr. Jeffrey Diamond, NINDS senior scientist and senior author of the study published in *Neuron*. “Our results show how neurons in the eye and the brain may use NMDA receptors to help them detect motion in a complex visual world.”

Vision begins when light enters the eye and hits the retina, which lines the back of the eyeball. Neurons in the retina convert light into nerve signals that are then sent to the brain.

Using retinas isolated from mice, Dr. Alon Poleg-Polsky, a postdoctoral fellow in Diamond’s lab, studied neurons called directionally selective retinal ganglion cells (DSGCs), which are known to fire and send signals to the brain in response to objects moving in specific directions across the eye.

Electrical recordings showed that some of these cells fired when a bar of light passed across the retina from left to right, whereas others responded to light crossing in the opposite direction. Previous studies suggested these unique responses are controlled by incoming signals sent from neighboring cells at chemical communication points called synapses.

In this study, Poleg-Polsky discovered that the activity of NMDA receptors at one set of synapses

may regulate whether DSGCs sent direction-sensitive information to the brain.

“Cells in the eye can multiply,” said Poleg-Polsky. “The process may help these cells determine whether a tiger is sauntering by, or fast approaching as it’s looking for dinner.”

Marijuana Use Disorder Is Common, Often Untreated

Marijuana use disorder is common in the United States, is often associated with other substance use disorders, behavioral problems and disability and goes largely untreated, according to a new study conducted by NIAAA. The analysis found that 2.5 percent of adults—nearly 6 million people—experienced marijuana use disorder in the past year, while 6.3 percent had met the diagnostic criteria for the disorder at some point in their lives.

A report of the study, led by Dr. Bridget Grant of NIAAA’s Laboratory of Epidemiology and Biometry, appeared online Mar. 4 in the *American Journal of Psychiatry*.

Grant and her team found that the percentage of Americans who reported using marijuana in the past year more than doubled between 2001-2002 and 2012-2013, and the increase in marijuana use disorders during that time was nearly as large.

The researchers interviewed more than 36,000 U.S. adults about alcohol use, drug use and related psychiatric conditions. To be diagnosed with the disorder, individuals must meet at least two of 11 symptoms that assess craving, withdrawal, lack of control and negative effects on personal and professional responsibilities. Severity of the disorder is rated as mild, moderate or severe depending on the number of symptoms met.

Marijuana use disorder is about twice as common among men than women; younger age groups are much more likely to experience the disorder than people age 45 and over. The risk for onset of the disorder was found to peak during late adolescence and among people in their early 20s, with remission occurring within 3 to 4 years. The study also found that past-year and lifetime marijuana use disorders were strongly and consistently associated with other substance use and mental health disorders.

“These findings demonstrate that people with marijuana use disorder are vulnerable to other mental health disorders,” said Dr. Nora Volkow, director of NIDA, which contributed funding to the study. “The study emphasizes the need for such individuals to receive help through evidence-based treatments that address these co-occurring conditions.”



Findings suggest that children who have regularly consumed peanut-containing foods from infancy to age 5 as a peanut allergy prevention strategy can safely switch to consuming peanut as part of a normal diet.

Prevention Strategy Benefits Persist After 1-Year Peanut Avoidance

The benefits of regularly consuming peanut-containing foods early in life to prevent the development of peanut allergy persist even after stopping peanut consumption for 1 year, new clinical trial findings show. The results were published online Mar. 4 in the *New England Journal of Medicine*.

NIAID’s LEAP-On study is an extension of the Learning Early About Peanut Allergy (LEAP) study. LEAP showed that regular peanut consumption begun in infancy and continued until 5 years of age led to an 81 percent reduction in development of peanut allergy in infants deemed at high risk because they already had severe eczema, egg allergy or both.

At the end of LEAP, participants who enrolled in LEAP-On were instructed to avoid peanut consumption for 1 year to help investigators determine whether continuous peanut consumption is required to maintain protection against development of peanut allergy. After the avoidance period, peanut allergy prevalence was determined, as it was in LEAP, by an oral food challenge. Only 4.8 percent of the children who had regularly consumed peanut-containing foods during LEAP were allergic to peanut following the year of peanut avoidance. In comparison, the prevalence of peanut allergy was 18.6 percent among those who had avoided peanut throughout LEAP and LEAP-On.

“The findings suggest that children who have regularly consumed peanut-containing foods from infancy to age 5 as a peanut allergy prevention strategy can safely switch to consuming peanut as desired as part of a normal diet,” said Dr. Daniel Rotrosen, director of NIAID’s Division of Allergy, Immunology and Transplantation. “We expect that many will continue to enjoy peanut-containing foods consumed regularly and others will maintain their non-allergic status with moderate intervals of diminished or no peanut consumption.”



Dr. Amjad Shehadah

NINDS's Shehadah Receives ASA New Investigator Award

Dr. Amjad Shehadah, a vascular neurology fellow in the Stroke Branch of the NINDS Division of Intramural Research, has received the Mordecai Y. T. Globus New Investigator Award in Stroke from the American Stroke Association (ASA). Named for the late renowned cerebrovascular researcher, the award is given by ASA each year to a researcher-in-training.

Shehadah was honored for his research project, "Class IIa histone deacetylases are essential for neuronal remodeling and functional recovery after stroke," which he completed during his neurology residency at Henry Ford Hospital, Detroit. "In this study we identified a group of enzymes important for brain recovery after stroke. This discovery provides a novel target for stroke therapy," said Shehadah. He received the award at the International Stroke Conference in Los Angeles.

Shehadah earned his medical degree in 2005 from the Technion-Israel Institute of Technology in Haifa, Israel. In 2008, he came to the United States to pursue a postdoctoral fellowship in basic stroke research in Dr. Michael Chopp's lab at Henry Ford Hospital. Shehadah became a neurology resident at the department of neurology there in 2011, and served as a chief resident during his fourth year of residency. He joined NINDS in 2015.

His research includes *in vivo* and *in vitro* studies on brain plasticity—the brain's

ability to adapt and change—and functional recovery after stroke. He used experimental stroke models to test different types of stem cells and pharmacological agents to induce brain regeneration and remodeling after ischemia (restricted blood flow to the brain). Shehadah's current research focuses on stroke recovery and post-stroke cognitive impairments in humans.



Dr. Regina James

James Joins NIMHD

Dr. Regina Smith James has joined NIMHD as a medical officer. She will serve as director of clinical and health services research in the Division of Scientific Programs. Her appointment will strengthen this direction of NIMHD's funding research, which will emphasize projects on minority health and health disparities in clinical settings, health services research and patient-clinician communication. James has also been the lead NIMHD representative in planning meetings for the Precision Medicine Initiative.

She has previously served as director of the Office of Health Equity at the National Institute of Child Health and Human Development, a program director at the National Institute of Mental Health and a clinical fellow in the Division of Intramural Research Programs at NIMH, where she conducted clinical trials on safety and efficacy of stimulant medications in children and adolescents. Her research interests include understanding and addressing how individual and population-level determinants affect health status, access and quality of health care across the lifespan.

Patients with Fatty Liver Needed

Researchers at NIDDK seek people with fatty liver disease to participate in a study. Scientists want to learn more about food metabolism in people with fatty liver disease. If you have been diagnosed with non-alcoholic fatty liver disease or steatohepatitis you may be interested in participating. Participants will stay 2 nights at the Clinical Center. Compensation is provided. For more information, call 1-866-444-2214 (TTY 1-866-411-1010) and refer to study 15-DK-0174.

Asthma Research Volunteers

Individuals 18 years or older with asthma are sought to participate in a 1- to 2-day research study in the Cardiovascular and Pulmonary Branch at the National Institutes of Health. A thorough medical evaluation and monetary compensation will be provided. If interested, call (301) 402-1553.

Study Seeks Healthy Older Adults

Healthy older adults ages 55-75 are invited to participate in an outpatient research study investigating the benefits of omega-3 oil and blackcurrant supplements on vascular health. The goal of the study is to determine whether the supplements improve blood flow and blood vessel function that can affect your heart. Eligible participants must be medication-free and in good general health. The study will be carried out in an outpatient clinic and includes 4 visits over 6 months. Compensation is provided. For more information, call 1-800-411-1222 (TTY 1-866-411-1010) and refer to study 14-NR-0034.

Volunteers Needed for Energy Study

NIDDK seeks healthy Caucasian men, 55-75 years old, and women 18-35 to participate in a research study. Doctors want to learn how the body burns energy at different temperatures. You will have an 8-day inpatient stay at the Clinical Center. Compensation is provided. For more information, contact the Office of Patient Recruitment, 1-866-444-2214 (TTY 1-866-411-1010). Refer to study 12-DK-0097.

NHGRI Seeks Volunteers

NHGRI researchers seek people with chromosome abnormalities involving the sex chromosomes for a research study. Compensation is provided. For more information, call 1-866-444-2214 (TTY 1-866-411-1010) and refer to study 12-HG-0181.



The Nasar Abadey Quartet entertains an audience in the Porter Bldg. atrium. At right, a woman who danced earns a reward from the bandleader.

'Spiritual Music' Celebrates Black History Month

BY RICH MCMANUS

If the highly successful "afternoon of jazz" held Feb. 25 in the Porter Bldg. atrium in celebration of Black History Month is to honor its inaugural guest artist, it will have to go by another name in future years.

Drummer Nasar Abadey led a quartet through half a dozen standards—leaning on the work of D.C. native Duke Ellington—in a 90-minute concert punctuated by Abadey's congenial dialogues about the music.

"This music represents good times," he began, stepping out from behind his drum kit to discuss the first tune, Ellington's *Take the Coltrane*.

"The blues is the foundation of jazz," he explained, adding that the music merges two traditions, one European, the other African.

"I don't like to call it jazz," Abadey said. That term has its origins in houses of ill repute, he noted. "This is a spiritual music. We consider it sacred."

Abadey, 69, who began playing drums at age 5 and who has accompanied such giants as Dizzy Gillespie, Ella Fitzgerald, Sun Ra and Pharoah Sanders, said there are two kinds of standard tunes. "There are the Tin Pan Alley songs, mostly from Broadway musicals, but with a jazz treatment, like *Body and Soul*. And then there are jazz standards, written by jazz musicians."

The second tune was Ellington's ballad *In a Sentimental Mood*.

The third offering, Sonny Rollins' *St. Thomas*, is really just a variation on Ellington's *I've Got Rhythm*, said Abadey. He invited the audience to "step outside yourselves. We're playing a song that's danceable...Do you all know each other? Now is the time to let each other know what you're all about!"

The Rollins song is known as a calypso, "pronounced kye-yip-so," said Abadey. "It's based on a west African rhythm called *fanga*. So fasten up! Got life insurance?"

Once the tune ended, he presented a free copy of his band's latest CD to a woman in the audience who had the courage to dance.

"These musicians—they are so professional, they play so well—we are not rehearsed at all," said Abadey, who turned out to be a charismatic music educator. "We're not reading music. We are playing this music from our hearts...Jazz musicians get to the point where you know the songs so well, you *play* them. We're improvising. We're just feeling it from within."

His bandmates included pianist Allyn Johnson, who directs the jazz studies program at the University of the District of Columbia, bassist James King, Jr., a touring musician just back from a West Coast swing, and tenor saxophonist Paul Carr, executive director and artistic director of the recently concluded Mid-Atlantic Jazz Festival, held each year just up the Pike in Rockville.

Defining rock 'n roll as another element of the blues, Abadey and his band launched into Herbie Hancock's *Cantaloupe Island*, which shares rock's

more percussive elements. "Any more dancers in the house?" Abadey shouted.

There was a bit of confusion about whether the show was supposed to last an hour, or 90 minutes. Abadey solved the problem by announcing *I Don't Know*, an improvisational workout.

"We're gonna see what happens," he said. "We're gonna stack it. We're going to totally improvise until someone in the band states a melody, then we'll all dive in. It'll be free for awhile, then it will go into something and you'll recognize the song." As with his other scholarly questions, the correct answer earned respondents a free CD.

It turned out that no one recognized the standard *All the Things You Are*.

The band finished with an uptempo blues, bassist Buster Williams' *Tokudo*.

Abadey and his band, impressed that the NIH audience offered serious attention, declared the gig a success. "We would really like to be back to see you again."

The performance was sponsored by the Porter Neuroscience Research Center arts committee and Dr. Larry Samelson, chair of the FAES music committee.



The audience enjoyed Abadey's comments about the music almost as much as the music itself.

PHOTOS: BILL BRANSON