Research into new methods to treat pain

The teamwork of a doctor and a scientist is helping expand the tools available for treating chronic pain.

Dr. Andrew Mannes, an anesthesiologist and the chief of the Clinical Center department of perioperative medicine, and Michael Iadarola, a senior research scientist within that department, are working together to increase the understanding of pain's molecular biology.

“We are a unique team. Mike brings the science; I bring the medicine,” Mannes said. “We bring our unique perspectives to solving this collaboratively.”

Both have long been interested in the treatment of severe and chronic pain. The pain management field is in need of new treatments, especially for chronic pain, Mannes said.

“The most commonly used medications to treat pain are opioids (e.g., morphine, oxycodone). The pain reliving properties of opioids have been known for about 5,000 years,” Mannes said. “We have been using the same family of drugs to treat severe pain for that long.”

But opioid drugs like morphine have unwanted side effects including nausea, impaired consciousness, vomiting and hallucinations. With long-term use, opioids frequently lose their effectiveness requiring patients take higher and higher doses to control pain.

Many new drugs have not progressed to clinical practice because there’s a lack of understanding of the drugs underlying molecular mechanisms and targets or the emergence of unexpected side effects.

Jump-starting genomic opportunities at the CC

To advance clinical researchers’ use of genomic data in the coming decade, the NIH recently announced a new, two-year initiative called the Clinical Center Genomics Opportunity.

The program will underwrite the DNA sequencing and analysis of a total of 1,000 exomes, which are the functionally important 1-2 percent of an individual's genome that codes for proteins. Until now, only a few clinical research projects in the NIH intramural program have included exome sequencing.

“We’re trying to jump-start genomic medicine,” said Dr. Michael M. Gottesman, deputy director for intramural research at NIH. “We first need to build an infrastructure for clinical genomic sequencing that can be used by researchers in their projects at the NIH Clinical Center.”

The program, set to launch this summer, will begin with a review committee’s selection of projects that take optimal advantage of CC phenotyping resources—imaging, detailed documentation of physiological changes in patients and annotations of medical consequences of diseases.

Experts find genetic cause of disease in Hatfield’s first patient

A research team has discovered the gene underlying the disease of the first patient enrolled in the Hatfield Clinical Research Center nearly 10 years ago.

On April 3, 2005, the patient was enrolled in a research protocol of Dr. Constantine Stratakis, director of the division of intramural research and head of the section on genetics and endocrinology at the Eunice Kennedy Shriver National Institute of Child Health and Human Development.

The patient has Carney complex, a rare genetic disorder that affects only 700 people. The condition is characterized by skin pigmented spots resembling freckles, over-active endocrine glands that produce too many hormones, and different types of benign and cancerous tumors.

Nursing staff were recognized for their continuous dedication to caring for others during National Nurses Week, May 6-12.

Events included: the U.S. Public Health Service’s annual nurse recognition day; an American Nurses Association educational webinar on transforming health care through nursing leadership; a Clinical Center Grand Rounds on understanding protective immunity by an attenuated malaria vaccine; a panel discussion on clinical research nurses leadership; and healthy lifestyle activities.

The week was hosted by the Clinical Center nursing department and their recognition and retention committee.

Reflections...
At the end of May, the Clinical Center nursing department said farewell and happy retirement to Nurse Recruiter Cynthia Herringa. For more than 14 years, Herringa managed programs and processes to plan, source, recruit and retain the highest quality employees for the nursing department. Since 2000, it’s estimated that she helped onboard approximately 1,400 nursing professionals. She served on the department’s internship-fellowship evaluation workgroup that focuses on incorporating new developments in the specialty practice of clinical research nursing. “Cynthia really understands the role of the clinical research nurse,” said Dr. Clare Hastings, chief nurse officer. During her career, Herringa also helped underserved communities by taking leave to provide health care to foreign countries.

Eric Cole, Clinical Center deputy chief of the office of administrative management, was elected chairperson of the Maryland Developmental Disabilities Council in early April. Cole is in his second term as a member of the council, which he was appointed to by the governor of Maryland. The council works to advance the inclusion of people with developmental disabilities in all facets of community life. “We are thrilled that Eric was elected to serve as the chair of the council for the next two years,” said Brian Cox, executive director of the council. “His experience, leadership skills and ability to work effectively with a wide range of people make him the perfect choice.”

So far he’s identified three genetic defects resulting in Carney complex and at least two others that may contribute to the disease’s development, at least with regards to adrenal tumors. Stratakis’ lab has identified several other genetic defects that cause pituitary or adrenal tumors in patients with other conditions, such as multiple endocrine neoplasias, adrenal cancer or gastric stromal tumors.

“I’m confident that understanding the genetic basis of all patients with Carney complex will lead to a treatment that targets the cause of the disease,” Stratakis said. “Just because we don’t have a treatment yet, doesn’t mean we won’t find it in the days, months and years ahead.”

An article on the defect was published January 2014 in The Journal of Clinical Endocrinology and Metabolism: http://go.usa.gov/kSVm
Bedside medication barcoding, a new system to help avoid medication administration errors and keep patients safe, began as a pilot on select units January 2014 and was fully implemented in March.

When patients are admitted, they receive a wristband which includes a personalized barcode. To begin the medication administration process, the barcode is scanned to pull up the patient’s medication profile on a computer. Then, staff scan the medication to be administered. The scan prompts a computer to match the medication scanned with a medication order entered by the prescriber and against the medication dispensing information.

If the data match the order and the dispensing details, staff can move forward with medication administration. If data do not match at any of the steps, then the computer alerts the healthcare professional that medication and the order should be reviewed.

Barcodes have been used since 2007 for Clinical Center admissions. Their use has expanded to medications stocked in automated dispensing cabinets in 2009, tracking patients’ lab specimens in 2010 and dispensing of take home medications from the outpatient pharmacy in 2011.

The Clinical Center department of clinical research informatics (DCRI), pharmacy department, respiratory therapy, nursing department and the office of the director worked together on the program.

To implement bedside barcode technology to support the application had to be put in place. Dr. Jon McKeeby, chief information officer of DCRI, outlined challenges they faced in building the program specifically for the Clinical Center.

The hospital has used mobile computers called “Workstations on Wheels” (WOWs) for many years. Use of bedside barcoding would increase the volume of traffic on the wireless network.

“Creating a clinically reliable environment required assistance from the NIH center for information technology in providing a robust wireless network and DCRI in providing a Workstation on Wheels,” stated McKeeby.

To address this challenge, the center for information technology provided a wireless network that can reach all areas where patients are treated. Then DCRI updated the technology on over 300 WOWs to include new computers, an updated operating system and wireless scanners and printers for lab specimens. DCRI provides continuous maintenance and care for the WOWs.

In an effort to configure the application, the inpatient pharmacy department reviewed 4,400 medications to ensure each contained a barcode and those barcodes were included in the database. The pharmacy department’s bulk compounding section manually labeled over 60 items that were either difficult to scan or did not contain a barcode using a specialty packager and labeling equipment required for this project.

Scanning the barcodes took over four months to complete. A re-scan of each medication was conducted prior to the pilot and full implementation.

The pharmacy department’s procurement section continues to scan each medication brought into the hospital on a daily basis. The barcodes of new investigational medications released for use by the pharmacy department’s pharmaceutical development section are also tracked. The pharmacy department has scanned over 35,000 barcodes, and over 1,600 new barcodes have been added to the database.

The focus of the pharmacy department is to provide “an extra layer of checks to ensure that patients get the right medications,” said Dr. Jharana Tina Patel, quality assurance officer. “We want to get the right dose of the right medication by the right route to the right patient at the right time.”

Finally, nurses who provide the medication to patients needed to be trained on how to work with the system. The pharmacy department worked with DCRI to produce a training environment and with nursing and respiratory therapy to create training scenarios for hands-on learning.

Kathy Feigenbaum, clinical nurse specialist, outlined the efforts to get over 700 nurses instructed on the barcoding technology in eight weeks.

“We had lots of training sessions that we offered at different times. It was a two-hour block of time that everyone had to come to,” Feigenbaum said. “That was a challenge making sure everybody was scheduled for training and that you’re not compromising patient care. We wanted to create an environment where they could get their hands on the equipment to practice and really see how the system works.”

The collaborative effort paid off. “A lot of the nurses were saying that this was the smoothest implementation that they’ve had so far,” added Feigenbaum. “I think working together helped make the project launch successful.”

Information security, privacy awareness training courses combined

To reduce the burden of NIH staff having to complete two mandatory trainings, the Information Security and Privacy Awareness Refresher courses have been combined into one course. Using a HHS ID, staff can log into the training site (http://irtsectraining.nih.gov) and select the first course on the menu. NIH staff who do not complete the course by June 15 will have their accounts disabled.

The new format includes information security and privacy modules and provides a bookmarking feature that allows staff to return to the location they left in the course. This is different from the NIH HIPAA General Awareness course which, if staff have been instructed to take, must be completed in addition to the refresher.

Completion of the refresher will provide valuable information about staff responsibilities to secure NIH resources and protect health information. As staff complete both modules, they will also hear about what to do if NIH equipment is lost or sensitive data is transmitted unencrypted, to mitigate the risk of harm to the agency and individuals whose information has been compromised.

Staff may receive reminders to complete this training from their information systems security officer or privacy coordinator. If staff have been identified as having significant IT security responsibilities, they will be notified and asked to take a role-based security training. If you have questions please contact: Karen Plá, 301-402-6201, plak@mail.nih.gov or Cheryl Ann Seaman, 301-402-4461, cheryl.seaman@nih.gov.
Reducing patient risks with a huddle

Two hours into their busy shifts, the nurses in the general medicine unit on 5 NW excuse themselves from their patients’ bedsides, gather in a quiet space and focus for 10 minutes on how to make certain their patients are safe. During this critical time, each nurse shares safety and care issues that may have emerged since the beginning of their shift. Deliberately coming together as a team to discuss their concerns reduces the likelihood that adverse events will occur. Huddles and similar strategies to reduce patient risk are rapidly becoming a part of the culture of patient safety.

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“We set out to learn everything we could about every molecule pain-sensing neurons make,” Iadarola said.

Mannes and Iadarola use a next-generation DNA sequencing technique called RNA-Seq to better understand the molecular composition and signaling pathways of pain-sensing neurons.

“There is one particular population of nociceptive (pain-sensing) neurons that is responsible for transmitting many types of pain from the body to the central nervous system,” Mannes said. “We have isolated these neurons and used RNA-Seq to find out every molecule, and how much of each, these neurons make. A new level of understanding has been achieved that provides a more complete roadmap to the molecules in sensory neurons that underlie acute, inflammatory and chronic pain.”

The isolation of the neurons was done with Dr. Mark Hoon, chief of the molecular genetics unit in the National Institute of Dental and Craniofacial Research. With a better understating of pain’s molecular biology, Mannes and Iadarola look for agents that can be used to target specific pain pathways.

Through collaborations with the National Institute on Drug Abuse and the National Institute of Neurological Disorders and Stroke, their effort resulted in a drug called resiniferatoxin, also known as RTX, which is undergoing clinical trials to alleviate severe pain in patients with advanced cancer.

RTX is a non-opioid, non-addictive substance. It targets a protein produced by pain-sensing neurons and used for sensing heat and inflammation called transient receptor potential cation channel subfamily V member 1 (TRPV1). RTX selectively takes out the TRPV1 pain neurons while sparing other sensory neurons. But, this is a permanent solution, the pain neurons do not grow back.

Mannes and Iadarola are now researching new substances that will temporarily alleviate pain without permanently impairing pain neurons. Through their research on the RNA-Seq datasets, they have identified several new targets that have the potential for analgesic (pain relief) drug development. They are currently in the preclinical research phase.

“This is the early stage of discovery research. We are exploring the analgesic potential of several target molecules for use as new pain control agents,” Mannes said.

“The approach is firmly based on pain neurobiology and the underlying molecular repertoire of pain-related molecules that we now have determined,” said Iadarola.

A future implication of their research will be better treatment of acute and chronic pain.

“This includes not only post-operative pain but also pain from cancer and other conditions that Clinical Center patients present with,” Mannes said. “We have the capacity to connect our research to patient care and the capability to obtain patient samples for research use. The potential here is to create a whole new family of drugs to treat pain; our goal is to give doctors more tools to treat pain.”