

New drug therapy promises great potential

A Le Bonheur Children's researcher has proven that a new concept in drug design can treat human disease.

John DeVincenzo, MD, a pediatric Infectious Disease specialist at Le Bonheur, has found a simple chain of sugars called RNA – Ribonucleic Acid – can be designed on computers and synthesized into powerful disease-fighting therapies.

The therapies work by shutting down disease-causing genes through a process known as RNA interference (RNAi). The discovery of natural RNAi won the Nobel Prize in 2006. RNAi drugs showed promise in animals but had never proven effective in humans.

Using the RNAi discovery, DeVincenzo and his co-investigators at Alnylam Pharmaceuticals in Cambridge, Mass., tackled respiratory syncytial virus, the most common cause of infant hospitalization and an infection with no therapy or vaccine. In healthy adults, RSV infections are mild and disappear without medical intervention.

DeVincenzo's team infected 88 healthy adults with RSV cultures collected and grown from Le Bonheur patients. He then administered RNAi drug therapy to half the study participants in the form of a nasal spray and a placebo to the other half. Findings from DeVincenzo's study proved that RNAi therapy shut down a

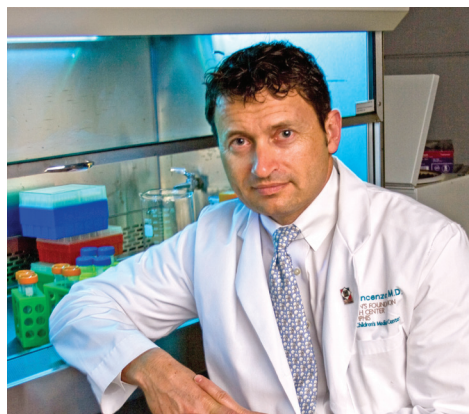
gene critical to RSV, thus preventing the virus from replicating. Patients who received the RNAi drug had significantly less infection than those receiving the placebo. The findings pave the way for this new type of drug therapy to treat a variety of human diseases including cancers, genetic diseases and viral infections.

"The next step in this discovery is already being undertaken," said DeVincenzo. "We are in the midst of a clinical trial to test the RNA interference drug in lung-transplant recipients who have become naturally infected with respiratory syncytial virus." The aerosol form of the RNAi drug, proven safe in the previous

phase of study, is being tested again in the clinical trial's current phase. DeVincenzo's goal is to test RNAi drug therapies to reduce RSV infections in infants.

DeVincenzo said the drug could receive approval as an orphan drug – a treatment for rare conditions – as early as 2013 if the current clinical trials prove very successful. Approval for using RNAi treatment on children who suffer from RSV will take longer.

DeVincenzo is a professor and researcher for the departments of Pediatrics and Molecular Sciences at the University of Tennessee Health Science Center. His studies were conducted at Le Bonheur's Children's Foundation Research Center.



John DeVincenzo, MD

LE BONHEUR HOSTS GRAND OPENING CELEBRATION

Le Bonheur Children's Hospital hosted a Grand Opening celebration this summer for its new \$340-million, 610,000 square-foot hospital. When it opens for patients in early December, the new Le Bonheur will be the largest children's hospital in Tennessee.

The 255-bed hospital nearly doubles Le Bonheur's current space for patient care, research and teaching. Featuring the

latest advancements in technology and comforts for patients and their families, the new Le Bonheur will allow the hospital to continue to be a resource to its families.

Once it's LEED certified, Le Bonheur will be the fifth sustainable children's hospital in the nation. Some of the green features include a modular energy plant, recycled



construction materials and motion sensors.

STUDY SHOWS ATV-RELATED SPINE INJURIES ON THE RISE



Jeffrey Sawyer, MD

A nearly 10-year review of all-terrain vehicle accidents involving children across the United States shows that ATV-related injuries, including those in the spine, continue to increase at an

alarming rate.

From 1997 to 2006, the number of children injured in an ATV-related accident increased 240 percent. The number of spinal injuries children suffered from those accidents increased 467 percent.

The review was conducted by Le Bonheur Children's Orthopedic Surgeon Jeffrey Sawyer, whose results were published in the July 2010 edition of *Orthopedics Today*. Results have also appeared in *Family Circle* and *Parents* magazines, and will be published in the *Journal of Pediatric Orthopaedics*.

In his research, Sawyer found 70 percent of children who incurred a spine injury in an ATV-related accident were younger than 16, the minimum age recommended by the American Academies of Pediatrics and Orthopaedics – and the median age for children who incurred this injury was 12.9 years old. Most patients were boys (76 percent), white (85 percent) and privately insured (63 percent).

Sawyer found that while boys tend to be injured more often, older-aged girls are at higher risk for spine injuries when they have an accident.

"ATV injuries have risen dramatically due to a variety of factors including increased power of the vehicles, some of which can reach speeds of 100 mph," Sawyer said. "The biggest misconception is that these are toys rather than motor vehicles. We hope to use this data to further educational and legislative efforts to prevent ATV-related injuries in children."

He gathered data using the Kids' Inpatient Database, pulling data from years 1997, 2000, 2003 and 2006.

Sawyer is an assistant professor of Orthopaedics at the University of Tennessee-Campbell Clinic in Memphis and the American Academy of Orthopaedics spokesperson on ATV safety.

Study Examines Effectiveness of Tent for H1N1 Triage

When the novel influenza virus pandemic hit Memphis in late 2009, a surge in

patient visits placed an enormous strain on Le Bonheur's Emergency Department. Le Bonheur was challenged to find innovative ways to care for children with flu-like symptoms.

The hospital was the first pediatric facility in the nation to implement a nurse-driven, triage-out protocol for children with H1N1 infection by using a climate-controlled tent in the ED parking lot. ED physician Jay Pershad, a professor of pediatrics at the University of Tennessee Health Science Center, examined the tent's impact on quality metrics and cost of emergency care from an institutional perspective.

"This process change was a great example of a successful partnership between the ED and hospital administration," Pershad said. "The tent was unique because it provided medical and social distancing for a highly contagious illness."

Pershad recently presented part of this data as an abstract at the American Academy of Pediatrics's Pediatric Emergency Medicine

leadership conference in San Antonio.

Pershad conducted a before-after interven-

tion study examining two distinct periods during the surge, which was defined by an average daily ED census of greater than 250 patients. "We found that our key performance metrics: ED length of stay, recidivism rates and percentage

of patients who left without care, were very favorably impacted, despite the strain on our resources," Pershad said. "The average cost of medical screening in the tent was about \$30.50 per patient. The incremental cost effectiveness ratio, which represented additional institutional costs to decrease elopement rate by 1 percent, was about \$625.50, with the tent being the dominant strategy."

Le Bonheur's transfer center called caregivers of all patients who were triaged out, following their visit. "Our anecdotal experience was they were uniformly satisfied with the care rendered. There were financial ramifications related to set up costs and augmented staffing but these were offset by the protocol's success and experience gained."



Le Bonheur patients with flu-like symptoms were screened in a climate-controlled tent in late 2009, as hospital ED visits soared during the peak of the H1N1 outbreak. Subsequent research measured the effectiveness of the tent in three key areas: ED length of stay, recidivism rates and percentage of patients who left without care.

| | Pre-tent (Aug. 23-Sept. 10) | Tent (Sept. 11-Oct. 1) |
|----------------------------|-----------------------------|------------------------------------|
| Total Patients Visit to ED | 5,809 | 5,864 (1,141 screened in the tent) |
| Left Without Care | 12.9% | 1.82% (p<0.0001) |
| Mean ED Turnaround Time | 282 minutes | 152 minutes (p<0.0001) |
| Overall ED Return Visits | 5.03% | 5.36% (1.7% for tent) |

Researcher tackles opioid tolerance in children

A Le Bonheur physician is leading research to improve the safety and effectiveness of opioids like morphine that are commonly used for pain relief in children. Many children develop tolerance to opioids, even after short-term use of these pain medications.

Kids who develop opioid tolerance need higher and higher doses of these drugs and have a hard time coming off therapy, because of “narcotic abstinence” or opioid withdrawal symptoms.

KJS “Sunny” Anand, MBBS, D.Phil, has found opioid tolerance and withdrawal occur frequently in critically ill children and newborns. He proposes that “novel insights into opioid receptor physiology and cellular biochemical changes,” can help discover ways to prevent such tolerance and withdrawal. His work was published in

the May edition of *Pediatrics*, in a study entitled “Tolerance and Withdrawal from Prolonged Opioid Use in Critically Ill Children”.

In this review, Anand wrote that opioid tolerance tends to occur earlier in younger age groups, commonly develops during critical illness and results more frequently from prolonged intravenous infusions of short-acting opioids.

“Treatment options include slowly tapering opioid doses, switching to longer-acting opioids, or specifically treating the symptoms of opioid withdrawal,” Anand wrote in his study. “Novel therapies may also include blocking the mechanisms of opioid tolerance, which would enhance the safety and effectiveness of opioid analgesia.”



KJS “Sunny” Anand, MBBS, D.Phil

Short Scripts

Surgeons study casted patients

A Le Bonheur-led study on the most common reasons pediatric patients fitted for a cast return to the Emergency Room was featured in the April/May 2010 edition of the *Journal of Pediatric Orthopaedics*.

The study features the work of Le Bonheur and Campbell Clinic physicians Jeffrey R. Sawyer, MD, and Derek Kelly, MD. The study’s findings have led to the development of a Le Bonheur program that will educate and triage fracture clinic patients, eliminating the need to return to the ER, and ultimately reducing costs.

Study tackles tracheostomies

Le Bonheur intensivists recently published a study in *Intensive Care Medicine* entitled “Natural Course Regarding Pediatric Tracheostomy.”

The article was written to describe the hospital course of pediatric posttracheostomy patients, their underlying diagnosis and their demographic characteristics. The article can be found at <http://jic.sagepub.com/cgi/content/abstract/25/1/39>.

Heart Institute produces study

Le Bonheur cardiologists and cardiovascular surgeons authored an article in the May edition of the *Journal of Pediatrics* on the surgical management of intrapericardial teratoma in the fetus.

Intrapericardial teratomas are lesions that compress the heart and lungs and can result in tamponade if not treated expeditiously before the fetus is delivered. The study presents one of five successful cases in the world, and was managed by prenatal pericardiocentesis followed by surgical resection.

Le Bonheur Molecular Lab Named Center of Excellence

Le Bonheur Children's Hospital's Molecular Lab has been named a Molecular Center of Excellence (MCOE) by Roche Diagnostics.

Le Bonheur is just the second children's hospitals to earn MCOE status and joins a group of 35 MCOE laboratories across the country. Le Bonheur's molecular lab is led by Anami Patel, PhD, and John DeVincenzo, MD.

"With the combination of Roche's technologies, we will be able to offer the most advanced molecular testing to our physicians and patients," said Matthew Love, Le Bonheur's vice president for Strategy, Planning and Operations. "We anticipate that this will have a significant impact on providing great patient care and look forward to a strong partnership."

In molecular laboratories, genetic material is used to diagnose disease and illness – allowing for a more sensitive and quicker diagnosis for caregivers.

Le Bonheur's Molecular Lab currently conducts 15 tests, including RSV and Influenza A and B, leading causes of childhood illness. Last fall, the lab played a key role in diagnosing local cases of 2009 H1N1 influenza, ensuring Mid-South children received timely and appropriate care.

The Le Bonheur Molecular Lab also serves as a reference lab for several Mid-South hospitals and physicians – offering its cutting-edge molecular technology to the community.

Established in 2002, Roche's MCOE Program is designed to create an alliance network that enables regional laboratories across the United States to collaborate and capitalize on scientific knowledge in molecular testing and, in turn, help accelerate the advancement of new test methods and technology.



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Hospital, produced by Le Bonheur Marketing
 the medical staff for Le Bonheur Children's
Pediatric Notes is a quarterly publication for



50 N. Dunlap Street
 Memphis, Tennessee 38103

Non-Profit Org.
 US POSTAGE
 PAID
 Memphis, TN
 Permit No. 3093