

# ADVANCES IN EAR, NOSE & THROAT

**January 2013**  
SPECIAL EDITION

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## Research Enriches Care for Patients Receiving Cochlear Implants

**R**esearch into the use of cochlear implants to treat hearing loss and/or deafness in children and adults is ongoing in the Departments of Otolaryngology at NewYork-Presbyterian/Columbia University Medical Center and NewYork-Presbyterian/Weill Cornell Medical Center. Physicians stress that valuable cochlear implant research is occurring within the broader context of their mission to provide excellent clinical care; their aim is to deliver positive outcomes while investigating the causes of and solutions for their patients' loss of hearing. Areas of study include determining the best surgical candidates for implantation and developing atraumatic implant techniques.

"We provide outstanding care preimplantation with audiology evaluation and support during surgery, and then postoperatively with both the surgical and audiology teams following up with patients," said Anil K. Lalwani, MD, Director of the Division of Otolary, Neurotology and Skull Base Surgery, and Director of the Columbia Cochlear Implant Center at Columbia University Medical Center. "Surgically, we have refined our implantation techniques in order to make sure we can perform this procedure with as little negative outcome as possible. We use facial nerve monitoring, which allows us to minimize risk when inserting the implant electrode." Dr. Lalwani is also Professor and Vice Chair for Research at Columbia University College of Physicians and Surgeons.

Three cochlear implant devices have been FDA-approved, and physicians use each one of them. Recently, physicians have studied the effects of anesthesia use during cochlear implantation in both pediatric patients and the elderly (>70 years of age). In both populations, results showed that anesthesia is well tolerated, and for the elderly, presence of comorbidities is a better predictor of postoperative complications. Other ongoing work is centered around using a piezoelectric cochlear implant introduced atraumatically into the inner ear to better preserve residual hearing, and analyzing the brain's activation to sound with

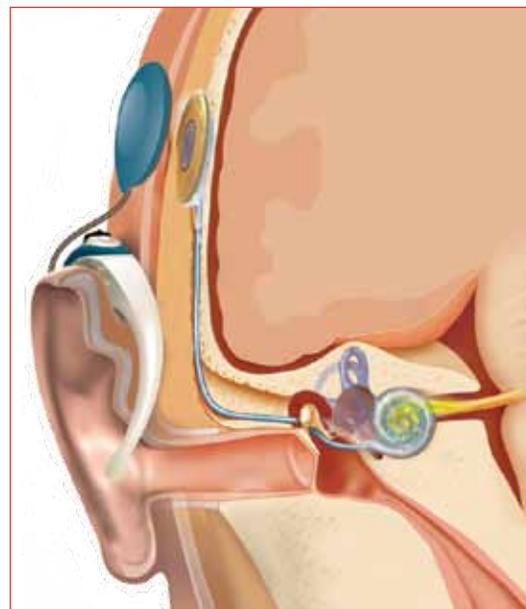


Illustration of cochlear implant.

positron-emission tomography before and after implantation to determine which patient factors influence success with the device. Dr. Lalwani, who has performed approximately 750 implantations in children and adults, stated that patients receiving implants are responding well overall to the intervention. "We are finding that the surgery isn't very risky and is well tolerated," he said.

### **Child-Friendly Environment**

Despite data showing minimal risk associated with implantation, the prospect of surgery in children can be complicated as young patients often present with a set of unique challenges related to evaluation and treatment. The ability to express auditory comprehension before and after surgery due to Down syndrome, autism, or developmental disorders; effects of pediatric anesthesia; and the presence of cranial/facial abnormalities or cardiac conditions are all potential factors to consider when attempting implantation in children.

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## Genetics Research Across Medical Specialties Now Yielding Secrets and Improving the Practice of Medicine

*The decoding of the human genome and subsequent concerted efforts by physician-scientists to decipher the relationships between specific genes and the diseases they influence have already yielded tremendous advancements in medicine. This work is fostering important strides in understanding and caring for people with diseases affecting all health systems, and much of the laboratory and translational studies, as well as clinical research, are being done at Columbia University College of Physicians and Surgeons, Weill Cornell Medical College, and NewYork-Presbyterian Hospital.*

**R**esearch abounds in every field. The field of geriatrics, for instance, was intrigued by a study led by Columbia University researcher Lawrence S. Honig, MD, PhD, Professor of Clinical Neurology in the Taub Institute, an Alzheimer's disease research center funded by the National Institute on Aging.<sup>1</sup> Dr. Honig's research found that telomere length relates both to the likelihood of the patient developing dementia and his or her overall remaining life span. This research could lead to the use of telomere length as an accurate biomarker of aging in people, as well as an early warning sign for future dementia.

The researchers examined telomere lengths from DNA samples of white blood cells obtained from 1,983 individuals aged 66 to 101 years. These patients were followed for an average of 8 years. After adjusting for age and education, among other factors, researchers found that those individuals with shorter telomeres had higher rates of both dementia and mortality. The researchers must now examine whether shorter telomeres directly increase the risk for dementia and death, or if the telomeres are being influenced by some other factor that is both shortening telomere length while at the same time increasing dementia and mortality risk.

Within psychiatry, schizophrenia has long been known to be genetic in origin, but the networks of genes involved in this disability have not been well characterized. A recent paper published in *Nature Neuroscience* found a link between schizophrenia and autism.<sup>2</sup> Columbia researchers examined a collection of mutations associated with schizophrenia and found occult interrelations among genes that had

previously been thought to be unrelated. The researchers found that most of the mutated schizophrenia genes were related to 2 main gene networks, which together affect key processes, including axon guidance, synapse function, neuron mobility,

### Columbia researchers have found occult interrelations between genes in 2 main gene networks, which together affect key neural processes.

and chromosomal modification.

The research, which was led by Dennis Vitkup, PhD, Associate Professor in the Department of Biomedical Informatics at Columbia's Center for Computational Biology and Bioinformatics, also looked at genes mutated in patients with autism and found the similarities were surprisingly robust. Noting that the genetic networks for autism and schizophrenia are closely intertwined, the researchers postulated that many other psychiatric disorders also might share the same genetic networks and interrelated molecular processes.

Significant research on the genetics behind psychological illness is being undertaken at Weill Cornell Medical College. As just one example, Francis S.Y. Lee, MD, PhD, Professor and Vice Chair for Research in the Department of Psychiatry and Professor in the Department of Pharmacology, who is also an Attending Psychiatrist at the Hospital, directs efforts focused on using genetic models to define the role of growth factors, such

as brain-derived neurotrophic factor, and their affect on the pathophysiology and treatment of affective disorders.<sup>3</sup>

Pulmonology has begun to explore the use of gene-based vaccines targeted against pulmonary infectious organisms. At Weill Cornell Medical College, a team led by Stefan Worgall, MD, PhD, Division Chief of the Pediatrics Pulmonology, Allergy and Immunology Division, has developed capsid-modified adenovirus vectors<sup>4,5</sup> to heighten immune responses from genetic vaccines against both *Pseudomonas aeruginosa* and respiratory syncytial virus. In research on the pathogenesis of cystic fibrosis, Dr. Worgall is investigating the interaction of alveolar macrophages with *P. aeruginosa*.

Nephrologists and psychiatrists, meanwhile, were interested in the results of a large multinational study in which Columbia University played an important role.<sup>6</sup> The study, led by Ali Gharavi, MD, Associate Director of the Division of Nephrology at NewYork-Presbyterian/Columbia, is the first to link congenital kidney disease, which together with urinary tract defects accounts for about one-fourth of all birth defects in the United States, with neurodevelopmental disorders. The study found that 10% of children born with kidney defects have genomic alterations that have been linked with neurodevelopmental delay and mental illness. The finding is important because it paves the way for identifying subgroups of patients with kidney defects whose treatment will be guided by specific genetic information. The finding also alerts physicians who care for children with congenital kidney disorders that there may be a genetic basis for a neurodevelopmental delay or a mental illness that will occur later in life.

A co-author of this study was Wendy Chung, MD, PhD, Director of Clinical Genetics at NewYork-Presbyterian Morgan Stanley Children's Hospital. Her research interests span multiple areas, including the molecular genetics of

obesity and diabetes; congenital heart disease; the genetic foundations of cardiomyopathies, arrhythmias, long QT syndrome, and pulmonary hypertension; congenital diaphragmatic hernias; mental retardation; inherited metabolic conditions; and susceptibility to breast and pancreatic cancers. She is Director of the Pediatric Heart Network Genetic Core, the Pediatric Neuromuscular Network Molecular Core, the New York Obesity Center Molecular Genetics Core, and the Diabetes and Endocrine Research Center Molecular Genetics Core. She also serves as Director of the Clinical Cancer Genetics Program and the Fellowship Program in Cytogenetics and Molecular Genetics.

Perhaps no area of medicine has been as affected by research into the genetic foundations of disease as much as oncology. Examples of genetic discoveries in oncology are plentiful. An important recent discovery is the revelation that certain cases of glioblastoma are caused by the fusion of 2 genes.<sup>7</sup> Researchers, led by Antonio Iavarone, MD, Professor of Pathology and Neurology at Columbia's Institute for Cancer Genetics at the Herbert Irving Comprehensive Cancer Center at NewYork-Presbyterian/Columbia, conducted genetic analyses of patients with glioblastomas, searching for evidence of gene fusions. They found them, with the most common being fusions involving the fibroblast growth factor receptor (*FGFR1* or *FGFR3*) and transforming acidic coiled-coil (*TACCI* or *TACC3*) genes. The protein produced by the fusion of *FGFR-TACC* disrupts the

mitotic spindle, causing aneuploidy, and from there tumorigenesis. The finding is important because it provides researchers with a protein target for pharmaceutical research for a cancer that is especially difficult to treat.

Gastroenterologists have been interested in recent work performed by Manish Shah, MD, Director of Gastrointestinal Oncology at Weill Cornell Medical College, who with his colleagues elucidated the heterogeneity of gastric cancer, dividing it into 3 types.<sup>8</sup> The first type, noncardia gastric cancer, is linked to environmental factors such as high dietary salt, tobacco use, and increasing age; clinical factors such as *Helicobacter pylori* infection and use of nonsteroidal anti-inflammatory drugs; and genetic factors including immune regulatory single-nucleotide polymorphisms. A second type, diffuse gastric cancer, is associated with *CDH1* mutation and family history and has no known environmental or clinical factors. The third type, proximal gastric cancer, is caused by tobacco and alcohol use; has no known genetic link; and is associated with obesity, high body mass index, and gastroesophageal reflux disease. Dr. Shah's work has alerted those performing drug clinical trials that testing should be based on these subtypes and not on gastric cancer as a whole. Because of the genetic differences in subtypes, the effects of drug therapy may vary significantly between groups.

The field of clinical genetics is rapidly changing and improving the practice of medicine. As the field of genetics

continues to grow so too the physician-scientists at Columbia University College of Physicians and Surgeons, Weill Cornell Medical College, and NewYork-Presbyterian Hospital will continue to be at the forefront of integrating genetics into all specialties.

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"Caretakers of children with hearing loss at birth have to seek the input of other specialists because it is not too uncommon for clinicians to find other conditions affecting the child, such as developmental delays, visual problems, or heart issues," said Erik H. Waldman, MD, Clinical Director of Pediatric Cochlear Implants at NewYork-Presbyterian/Columbia and Assistant Professor of Pediatric Otolaryngology/Head and

Neck Surgery at Columbia University College of Physicians and Surgeons.

"At NewYork-Presbyterian Morgan Stanley Children's Hospital, we have pediatric geneticists, optometrists, and anesthesiologists, among others, all within a full-service pediatric health children's hospital."

The NewYork-Presbyterian Morgan Stanley Children's Hospital not only provides a child-friendly environment for

young patients undergoing potentially daunting procedures, but its physicians also work to provide services tailored to children for their comfort, such as sedated auditory brainstem response testing before surgery with a pediatric anesthesiologist on-hand. "What I think is unique about a place like NewYork-Presbyterian is that our doctors often uncover other, subtle issues that kids have that would

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Top Ranked Hospital in New York.  
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# ADVANCES IN EAR, NOSE & THROAT

## Important news from NewYork-Presbyterian Otolaryngology.

Current research projects, clinical trials, and advances in the diagnosis and treatment of patients with ear, nose and throat disorders

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perhaps be missed at other institutions because they may not incorporate the other pediatric specialists into the mix,” Dr. Waldman said. “Also, we’re not being discouraged by a patient’s comorbidities

patients of any age involves experts from multiple disciplines, including speech and educational specialists, and particularly, audiologists. The audiology team works with patients during much of their treatment course, evaluating the patient’s

with implants compared with the ability to comprehend speech and other sounds.

According to Dr. Lalwani, researchers want to better understand which areas of the ear control music appreciation and how it can be improved in patients with implants. “We are trying to define which characteristics of music are most important for patients’ music comprehension or music appreciation after receiving an implant,” he said. “That work is being conducted in collaboration with sound engineers who we have on staff and one of the implant companies.” Led by Jaclyn B. Spitzer, PhD, Director of Audiology and Speech-Language Pathology, audiology researchers previously have developed the Appreciation of Music in Cochlear Implantees test that “most audiology researchers are using with respect to music outcome in patients with cochlear implants,” Dr. Lalwani said.

In the future, other research topics include use of cochlear implants to treat tinnitus and single-sided deafness—“One in 10,000 people have hearing loss in one ear and cochlear implants may offer the potential of providing sound to the side that is without hearing capability,” Dr. Lalwani said.

**The best treatment approach for patients of any age involves experts from multiple disciplines, including speech and educational specialists, and particularly, audiologists. “What I think is unique about a place like NewYork-Presbyterian is that our doctors often uncover other, subtle issues that kids have that would perhaps be missed at other institutions because they may not incorporate the other pediatric specialists into the mix.”**

—Erik H. Waldman, MD

because often that is the type of child we take care of every single day, and not just for hearing loss, but for other medical conditions.” The physicians at the Hospital are continually trying to better understand how to treat pediatric hearing loss.

Both Drs. Waldman and Lalwani noted that the best treatment approach for

hearing before surgery as well as programming the cochlear implant and troubleshooting problems that may arise after surgery. This team has conducted a wealth of its own research into the use of implants, and now is focusing on music appreciation in implantees, which is an ability that often is deficient in patients