DEPARTMENT OF HEALTH AND HUMAN SERVICES

NATIONAL INSTITUTES OF HEALTH

National Institute on Deafness and Other Communication Disorders

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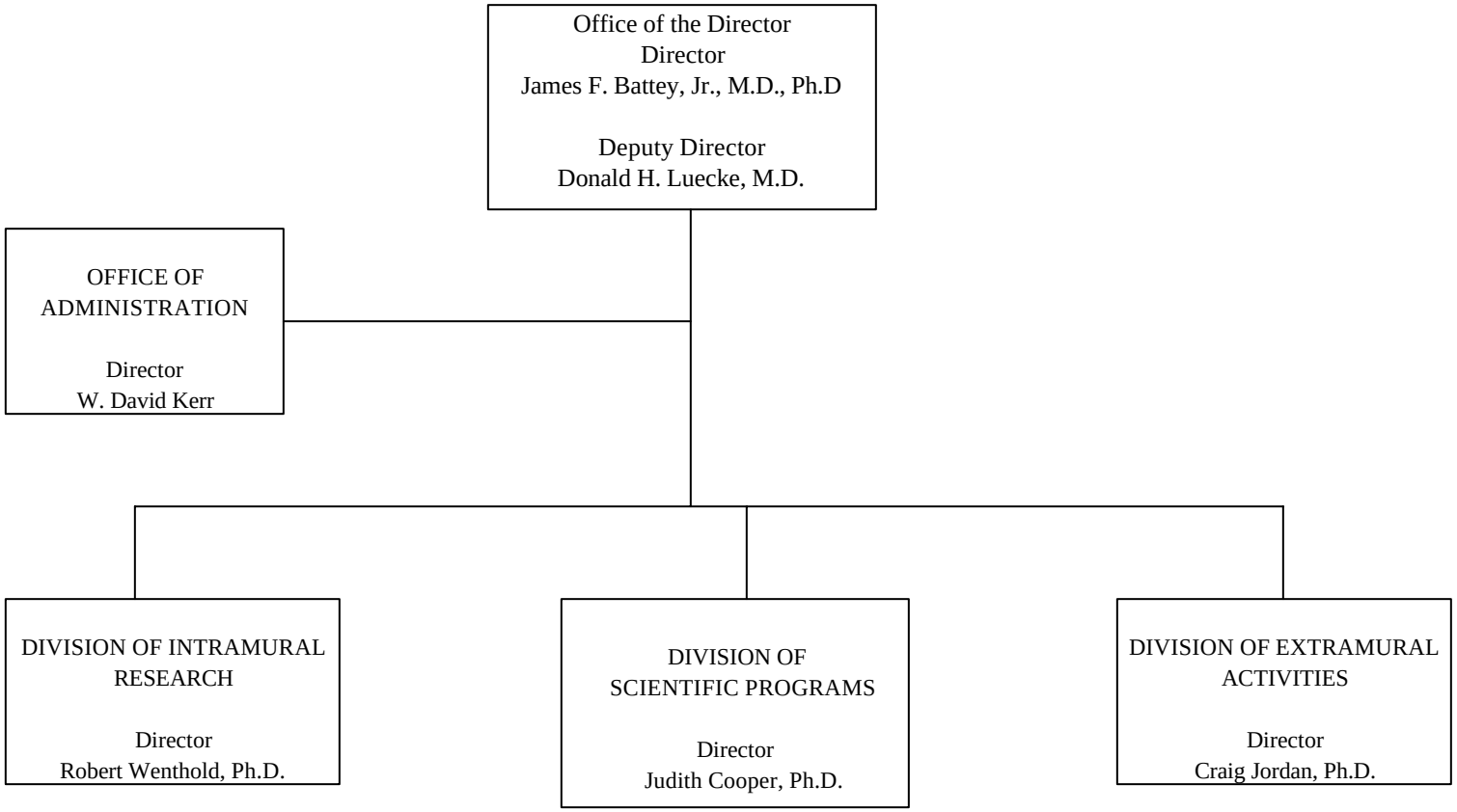

NATIONAL INSTITUTES OF HEALTH

National Institute on Deafness and Other Communication Disorders

For carrying out section 301 and title IV of the Public Health Service Act with respect to deafness and other communication disorders, [$ 384,477,000] *$393,507,000.*

[Department of Labor, Health and Human Services and Related Agencies Appropriations Act, as enacted by the Omnibus Consolidated Appropriations Act for Fiscal Year 2004]

National Institutes of Health
National Institute on Deafness and Other Communication Disorders

Amounts Available for Obligation 1/

Source of Funding	FY 2003 Actual	FY 2004 Final Conference	FY 2005 Estimate
Appropriation	$372,805,000	$384,477,000	$393,507,000
Enacted Rescissions	(2,423,000)	(2,424,000)	
Subtotal, Adjusted Appropriation	370,382,000	382,053,000	393,507,000
Comparative transfer from:			
Fogarty International Center for International Services Branch	14,000	0	0
Comparative transfer to NIBIB for Radiology Program	(22,000)	(21,000)	(0)
Comparative transfer to Buildings and Facilities	(90,000)	(86,000)	(0)
Comparative transfer to Office of the Director for program changes	(209,000)	(0)	(0)
Subtotal, adjusted budget authority	370,075,000	381,946,000	393,507,000
Unobligated Balance, start of year	0	0	0
Unobligated Balance, end of year	0	0	0
Subtotal, adjusted budget authority	370,075,000	381,946,000	393,507,000
Unobligated balance lapsing	(52,000)	---	---
Total obligations	370,023,000	381,946,000	393,507,000

1/ Excludes the following amounts for reimbursable activities carried out by this account:
FY 2003 - $2,337,000; FY 2004 - $2,400,000; FY 2005 - $2,500,000
Excludes $79,000 in FY 2003 and $116,000 in FY 2004 for royalties.

Justification

National Institute on Deafness and Other Communication Disorders

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Authorizing Legislation: Section 301 of the Public Health Service Act, as amended.
Reauthorizing legislation will be submitted.

Budget Authority:

FY 2003 Actual		FY 2004 Final Conference		FY 2005 Estimate		Increase or Decrease	
FTEs	BA	FTEs	BA	FTEs	BA	FTEs	BA
165	$370,075,000	153	$381,946,000	153	$393,507,000	0	$11,561,000

This document provides justification for the Fiscal Year 2005 research activities of the National Institute on Deafness and Other Communication Disorders (NIDCD), including HIV/AIDS activities. A more detailed description of NIH-wide Fiscal Year 2005 HIV/AIDS activities can be found in the NIH section entitled Office of AIDS Research (OAR).

INTRODUCTION

In April 2003, fifty years after the discovery of the double helix structure of DNA, an international consortium of scientists, supported in part by the National Institutes of Health, completed the Human Genome Project. Enabled by this landmark accomplishment, scientists supported by the National Institute on Deafness and Other Communication Disorders (NIDCD) have been studying the genes responsible for non-syndromic (not associated with any other problem) hereditary hearing impairment. In 1996, no genes were known to cause hereditary hearing impairment. At present, 54 genes have been identified, largely due to the contributions of NIDCD. Scientists are now focusing their efforts on identifying more genes, learning what role the genes have in deafness, and determining which genes affect certain populations of individuals. For example, recent studies have demonstrated that particular ethnic groups carry specific genetic mutations. Studying the genes that cause non-syndromic hereditary deafness will also permit early and more accurate genetic testing and foster the development of innovative intervention and prevention strategies, and more effective treatment methods for individuals with deafness and other communication disorders.

Disorders of hearing, balance, smell, taste, voice, speech, and language exact a significant economic, social, and personal cost for many individuals. NIDCD supports and conducts research and research training in the normal processes and the disorders of human communication that affect many millions of Americans. Human communication research now has more potential for productive exploration than at any time in history. With substantive investigations conducted over the past decades and the advent of exciting new research tools, the NIDCD is pursuing a more complete understanding of the scientific mechanisms underlying normal communication and the etiology of human communication disorders.

Story of Discovery: Vaccine for Middle Ear Infections
Imitation is the Highest Form of Flattery, Safer Too

Parents of infants and toddlers have become accustomed to recognizing the signs and symptoms of otitis media (OM) – irritability, tugging at ears, loss of appetite, loss of sleep, pain, or fever. In fact, OM, an infection or inflammation of the middle ear, is the most common reason for a sick infant to visit a doctor. OM is also one of the most significant health problems for children in the United States, costing approximately $5 billion annually[1]. OM begins when a viral or bacterial infection spreads from the throat to the middle ear. Viruses and bacteria can cause OM. The three main bacterial causes of otitis media, responsible for roughly equal numbers of cases, are *Streptococcus pneumoniae*, *Moraxella catarrhalis*, and Nontypeable *Haemophilus influenzae* (NTHi). Because of the substantial health burden associated with OM, the NIDCD initiated an intramural research program in the early 1990s to explore strategies in developing a vaccine against the microbes that cause otitis media.

Conventional vaccines are made by injecting an individual with either some or all of the bacterium or virus (called the antigen) to stimulate the production of antibodies against that specific bacterium or virus. The antibodies produced in response to the vaccine bind to the antigen, rendering it harmless. The specific proteins that make up the antibody-binding site are called epitopes. NIDCD intramural scientists developed a detoxified NTHi conjugate vaccine against NTHi. This particular vaccine proved to be both safe and effective in animal models and then in a 2002 Phase I clinical trial involving 40 normal human adult volunteers. In conjunction, NIDCD intramural scientists have also been working on a candidate vaccine for another cause of OM, *Moraxella catarrhalis*. Pre-clinical testing in animal models with vaccines for *Moraxella catarrhalis* demonstrated that the vaccines were safe and effective, eliciting a significant immune response that inhibited bacterial growth.

However, in the early 1980's, a scientist discovered a way to identify proteins that mimic the natural epitopes. The scientist coined these synthetic proteins "mimotopes." The mimotopes behave in a manner that is similar to epitopes to produce an immune response, but do not possess the harmful substances that can result in toxicity. In 2003, NIDCD intramural scientists turned to these state-of-the-art molecular biology techniques introduced decades ago, to create a candidate vaccine using mimotopes. The mimotopes were of a sugar-based component found on the surface of NTHi called lipooligosaccharide (LOS).

In hopes of making a more cost-effective, more stable, and safer NTHi vaccine, NIDCD intramural scientists replaced the natural epitopes of LOS with the synthetic mimotopes, reducing the likelihood that the vaccine might have toxic side-effects. The mimotopes not only immunologically mimic LOS from NTHi but will also bind to antibodies specific for NTHi LOS. Preliminary experiments showed that the mimic peptides attached to a carrier were as effective as the natural LOS-based vaccine in significantly decreasing the risk of disease in an animal model. Thus, the identified mimotope peptides are promising candidates for developing another novel vaccine for NTHi.

These studies are significant advances toward the long-term goal of developing a combined vaccine that reduces the incidence of OM caused by all major bacterial pathogens in children. Additional clinical research must be completed to ensure their effectiveness and safety. Vaccine-mediated prevention of OM is particularly important because repeated use of antibiotics to treat otitis media often produces drug-resistant bacterial strains.

Hou Y, Gu XX., Development of Peptide Mimotopes of Lipooligosaccharide from Nontypeable *Haemophilus Influenzae* as Vaccine Candidates. J Immun 170: 4373-4379, 2003.

SCIENCE ADVANCES

Age-Related Hearing Loss

[1]Gates GA. Cost-effectiveness considerations in otitis media treatment., Oto Head Neck Surg 114: 525-530, 1996.

Background: Age-related hearing loss (AHL) makes the everyday tasks of life difficult for millions of Americans. Unfortunately, determining exactly what causes susceptibility to AHL is not a simple matter of finding one faulty gene. Scientists are discovering that AHL susceptibility is due to defects in several genes. Studying AHL in humans is made even more complicated because it shows up later in life and it is difficult to determine how much hearing loss is due to non-genetic factors, such as noise, drugs that damage the ear, or disease. Scientists often study mice as models for these problems. The inner ears of mice and humans function similarly, and mice can be raised in an environment that is free of noise, disease, or damaging drugs. Moreover, disease-related mouse genes often have disease-related human equivalents.

Advances: Two groups of NIDCD-supported scientists have identified new genetic mutations in mice that play a role in susceptibility to AHL. Scientists at the Jackson Laboratory previously described mutations in a gene called *Ahl* that causes mice to develop AHL. However, they noted that different strains of mice with the same mutation developed hearing loss at different ages, and concluded that other genes must also play a role in AHL. Now they have described a second gene - called *Ahl2*- that seems to be responsible for the differences in when hearing loss begins in the different mouse strains.

At NIH, NIDCD intramural scientists have also described mutations in a mouse gene that help determine how much hearing a mouse with the mutation loses as it ages or is exposed to noise. Mice that have two copies of the mutated gene develop AHL, as do mice that inherit one mutated copy in combination with other genes that contribute to AHL.

Implications: The identification of genes that contribute to hearing loss in mice will help scientists identify similar genes in humans. Scientists may then use this information to design genetic diagnostic tests, preventive measures, and treatments for age-related hearing loss.

Johnson KR, Zheng QY., *AHL2*, a Second Locus Affecting Age-Related Hearing Loss in Mice. Genomics 80: 461-464, 2002.

Noben-Trauth K, Zheng QY, Johnson KR., Association of Cadherin 23 with Polygenic Inheritance and Genetic Modification of Sensorineural Hearing Loss. Nat Genet 35: 21-3, 2003.

New Way to Identify Usher Syndrome in Children

Background: Usher syndrome Type 1 is an inherited disorder. Children born with this disorder are deaf, suffer balance problems, and gradually lose their vision. Although Usher syndrome affects individuals of other racial and ethnic backgrounds, scientists have recently identified a clear pattern of its inheritance in Ashkenazi Jews. Ashkenazi Jews are descendants of Jews from Germany, Poland, Austria and Eastern Europe.

Advance: In 2003, a NIDCD-supported scientist identified a mutation within the gene known to be responsible for Usher syndrome. The particular mutation seems to be responsible for most of the Usher syndrome seen in Ashkenazi Jews.

Implications: Because scientists now know which gene is responsible for this type of Usher syndrome, they can develop genetic tests to detect the mutation in Ashkenazi Jewish children who are born deaf. By identifying children destined to lose their sight, parents and doctors can help them learn to communicate and prepare them for blindness. Some of these children will be appropriate candidates to receive a cochlear implant. Cochlear implants are small electronic devices that enable individuals who are deaf or have severe hearing loss to detect sound. This research will now enable doctors to provide important quality of life improvements for children with Usher syndrome.

Ben-Yosef T, Ness SL, Madeo AC, Bar-Lev A, Wolfman JH, Ahmed ZM, Desnick RJ, Willner JP, Avraham KB, Ostrer H, Oddoux C, Griffith AJ, Friedman TB., A Mutation of *PCDH15* among Ashkenazi Jews with the Type 1 Usher Syndrome. N Eng J Med 348: 1664-1670, 2003.

Newly-Discovered Genetic Mutation Responsible for Hearing Loss in Children

Background: Children with hearing loss face challenges learning to speak and interact with other people. Even though many cases of hearing loss in children are caused by inheritance of a faulty gene, doctors presently have few tests that help them distinguish one type of hereditary hearing loss from another. Establishing the cause of hearing loss is a critical first step toward identifying the best method to help a hearing-impaired child learn to communicate.

Advance: Scientists supported by NIDCD have identified a mutation in a gene called otoferlin that is believed to cause a form of hearing loss called non-syndromic recessive auditory neuropathy (NSRAN.) Children with NSRAN have hearing loss in both ears but do not have any other nerve problems or other symptoms. Importantly, children with NSRAN cannot benefit from hearing aids but report great benefit from cochlear implants.

Implications: Because doctors are now able to diagnose NSRAN, they can recommend that a child with it be evaluated as a candidate for a cochlear implant rather than a hearing aid. In addition, scientists can now investigate the otoferlin gene's function in the ear and how its mutation results in hearing loss.

Varga R, Kelley PM, Keats BJ, Starr A, Leal SM, Cohn E, Kimberling WJ., Non-Syndromic Recessive Auditory Neuropathy is the Result of Mutations in the *Otoferlin* (*OTOF*) Gene. J Med Genet 40: 45-50, 2003.

Gene Replacement Therapy Can Generate New Hair Cells

Background: The sensory hair cells of the inner ear play an important role in detecting sound, and people who lose hair cells due to diseases, infections, or accidents often lose some or all of their ability to hear. Scientists have determined that many forms of inherited deafness are also due to problems with hair cells. The hair cells of the inner ear act like miniature amplifiers. Sound waves that enter the inner ear are converted into a series of chemical and electrical signals within the cells. These signals are ultimately transmitted to the brain via the auditory nerve and interpreted as sound.

Advance: In the past, only birds or reptiles were thought to be capable of generating new hair cells. Now, NIDCD-supported scientists have discovered a way to use gene therapy to generate new hair cells in the ears of adult mammals. Scientists used a virus to transfer a gene called *Math1* into the ears of guinea pigs. *Math1* is expressed in developing hair cells, and its expression is thought to cause the cells to become hair cells, rather than becoming another cell type within the ear. The virus infects cells of the ear and causes them to produce the Math1 protein. Early experiments suggest that when the virus infects cells that do not normally express *Math1*, some of these cells become hair cells. In addition, the new hair cells also attract fibers of the auditory nerve, suggesting that the new cells may also be able to establish a link to the part of the brain that interprets sound – the auditory cortex.

Implications: If this work can be duplicated in human beings, it may one day enable scientists to use gene therapy to restore hearing to those who have lost it, or to enable deaf individuals to hear.

Kawamoto K, Ishimoto S, Minoda R, Brough DE, Raphael Y., *Math1* Gene Transfer Generates New Cochlear Hair Cells in Mature Guinea Pigs *in vivo*. J Neurosci 23: 4395-4400, 2003.

Discovery of a Major Cause of Genetic Deafness in East and South Asians

Background: Genetic abnormalities cause about 50% of severe childhood hearing loss, with 80 to 85% caused by autosomal recessive mutations. An autosomal recessive mutation causes hearing loss when each parent passes down an abnormal copy of the gene. The majority of autosomal recessive genetic, or hereditary, deafness is non-syndromic (not associated with any other problem). Further, approximately 10% of autosomal recessive hereditary deafness is caused by mutations in *SLC26A4* (formerly known as *PDS*), the Pendred Syndrome Gene. Pendred Syndrome is characterized by varying degrees of congenital deafness and thyroid goiter. Pendrin, the protein produced by *SLC26A4*, is found in the thyroid gland, kidney, and inner ear. Scientists have discovered more than 50 different deafness-causing *SLC26A4* mutations.

Advance: The prevalence of genetic deafness can also vary according to the ethnic background. For instance, recessive mutations of *SLC26A4* are a common cause of Pendred syndrome and non-syndromic deafness in western populations. However, since not much is known about the frequency of *SLC26A4* mutations in Eastern populations, NIDCD-supported scientists have begun to investigate the frequency of *SLC26A4* mutations in southern and eastern Asia, a region which comprises nearly one-half of the world's population. The scientists have discovered nine different *SLC26A4* mutations, including five new mutations never seen before in any population and four already identified but rarely observed outside of East Asia. In addition, each ethnic group within East and South Asia had its own unique *SLC26A4* mutations. In some groups, such as in Koreans, *SLC26A4* mutations are the most common known cause of deafness.

Implications: These results suggest that the frequency of deafness caused by *SLC26A4* mutations is relatively common and constant among all global populations. Thus, ethnic background is quite important and it should be noted when genetic testing is performed, since different mutations in a spectrum of genes are more likely to cause deafness in a given population.

Park HJ, Shaukat S, Liu XZ, Hahn SH, Naz S, Ghosh M, Kim HN, Moon SK, Abe S, Tukamoto

K, Riazuddin S, Kabra M, Erdenetungalag R, Radnaabazar J, Khan S, Pandya A, Usami SI, Nance WE, Wilcox ER, Riazuddin S, Griffith AJ., Origins and Frequencies of *SLC26A4* (*PDS*) Mutations in East and South Asians: Global Implications for the Epidemiology of Deafness. J Med Genet 40: 242-248, 2003.

Commonly Used Drug, Methotrexate, Shown Ineffective in Treating Autoimmunity in Inner Ear Disease

Background: Autoimmune inner ear disease (AIED) is a relatively rare disorder that causes potentially reversible bilateral, rapidly progressive, hearing loss and/or dizziness. Left untreated, this condition can lead to total deafness. Glucocorticoids, powerful anti-inflammatory steroids, have been the most common treatment of AIED, usually resulting in the restoration of some hearing. Unfortunately, long-term use of these drugs is associated with significant side effects. Encouraged by the success of methotrexate, an immunosuppressive drug used to treat rheumatoid arthritis and cancer, doctors have been using methotrexate as a substitute for long term treatment with glucocorticoids for approximately the past five years. Until now, there has been no controlled study to compare the benefits and hearing improvements of methotrexate with those of glucocorticoids.

Advance: NIDCD-supported scientists have undertaken a clinical study to determine whether methotrexate is effective in the treatment of AIED. The trial is a double-blind, randomized, placebo controlled, phase 3 clinical trial. Ten study sites spanning the continental United States participated in the trial. Using the largest prospectively enrolled cohort of individuals with AIED, the study showed that methotrexate was not effective in maintaining hearing recovery in individuals with AIED who had been previously treated with high-dose glucocorticoids.

Implications: More studies are needed to develop and rigorously evaluate effective (and ideally less toxic) therapies for AIED using randomized, controlled clinical trials.

Harris JP, Weisman MH, Derebery JM, Espeland MA, Gantz BJ, Gulya AJ, Hammerschlag PE, Hannley M, Hughes GB, Moscicki R, Nelson RA, Niparko JK, Rauch SD, Telian SA, Brookhouser PE., Treatment of Corticosteroid-Responsive Autoimmune Inner Ear Disease with Methotrexate. JAMA 290: 1875-1883, 2003.

New Short Electrode Will Allow Greater Benefit from Cochlear Implants

Background: Cochlear implants are commercially available miniature hearing prostheses capable of assisting those who are profoundly deaf or severely hearing impaired. Approximately 60,000 individuals all over the world have received cochlear implants[2]. The implant bypasses damaged or missing hair cells to send electrical signals through an array of electrodes within the cochlea (inner ear). Current cochlear implants send sound information that covers the entire frequency range. In order to send both high and low frequency information, the electrodes of the cochlear implant are inserted as far into the cochlea as possible. Unfortunately, inserting the electrodes

[2]National Institutes of Health/National Institute on Deafness and Other Communication Disorders. They Said It Couldn't Be Done. NIH Publication No. 03-5360. July 2003.

into the cochlea compromises any residual (remaining) hearing the individual may have had prior to implantation.

Advance: Consequently, scientists developed a new shorter electrode to help an additional population of individuals with hearing loss. These individuals have a considerable amount of residual hearing and their primary hearing loss is in sounds in the high frequency range. They are also experienced, yet unsuccessful, adult hearing aid users with severe-to-profound hearing impairment who would not have been conventional cochlear implant candidates. The short electrode is inserted into the base (or bottom) of the cochlea to restore hearing at high frequencies, while preserving low frequency hearing, or residual hearing, in the apex (or top) of the implanted ear.

Implications: The preliminary data demonstrates residual hearing can be preserved with this short electrode, and provides evidence that this is most beneficial for understanding speech in a noisy background. Furthermore, the innovative short electrode may be an ideal treatment for those with presbycusis, which is the loss of hearing that gradually occurs in most individuals as they grow older. Therefore, this new electrode design allows many more people with some degree of hearing loss to benefit from cochlear implant technology.

Gantz BJ, Turner CW., Combining Acoustic and Electric Hearing. Laryngoscope 113: 1726-1730, 2003.

Turner CW, Gantz BJ, Vidal C, Behrens A., Speech Recognition in Noise for Cochlear Implants Listeners: Benefits of Residual Acoustic Hearing. In Press.

Regenerating Auditory Hair Cells is Elementary Genetics

Background: As they assume their mature identities during development, mammalian auditory hair cells stop dividing. Cyclin dependent kinases (CDKs) are molecules that tell cells to divide. CDKs are actively regulated by CDK inhibitors (CKIs), which are molecules that tell cells to stop dividing. Together, CDKs and CKIs work together to maintain mature hair cells in a continuous non-dividing state. In practical terms, this means that the auditory hair cells of the inner ear cannot regenerate if they are damaged or lost because of trauma, injury or disease. Moreover, it is likely that CDKs and CKIs play a role in hearing loss, but the actual mechanism is largely unexplored.

Advance: The first scientific relationship between CKIs and the auditory system was determined by NIDCD-supported scientists. They examined the ears of mice that lack two forms of CKIs, *Kip1* and *Ink4d*. Without the CKIs, more than the normal number of sensory hair cells developed in both sets of mice. Despite the presence of extra hair cells, all the mice became hearing impaired soon after birth. Scientists determined that the animals' hearing loss was due to loss of hair cells.

Implications: These data emphasized the importance of CKI pathways in the active homeostasis of the auditory system. Although there are currently no mutations for hearing loss mapped to the

gene for *Ink4d* in humans (*CDKN2D*), these data suggest that a mutation, or disruption of a similar gene could potentially cause human hearing loss.

Chen P, Zindy F, Abdala C, Liu F, Li X, Roussel MF, Segil N., Progressive Hearing Loss in Mice Lacking the Cyclin Dependent Kinase Inhibitor *Ink4d*. Nat Cell Bio 5: 422-426, 2003.

Discovery of Gene Mutation That Specifically Affects Balance

Background: Balance disorders can interfere with walking, operating a moving vehicle, or just standing up and can lead to disorientation, falling and injury. By analyzing genetic mutations that specifically affect the sense of balance but do not affect hearing, scientists discovered a new gene in the ear, *otopetrin 1*. In the inner ear, small fluid-filled pouches containing dense calcified granules called otoconia, play a role in the sense of balance. The otoconia are imbedded in a gel-like substance overlying a sheet of sensory hair cells. When the head tilts, gravity pulls the otoconia downward, bending the tiny sensory hair cells, which sends a nerve signal to the brain, informing the body of its new position.

Advance: NIDCD-supported scientists have discovered that two mutations in *otopetrin 1* that affect balance: tilted and mergulhador. Mice possessing two copies of either of these mutations lack otoconia but still exhibit normal hearing, hair cells and nerves, which indicates that *otopetrin 1* is responsible for only otoconial development. The gene is responsible for a protein, otopetrin, which is expressed during otoconia development. This protein is believed to be incorporated in vesicles within the gel-like matrix, where it may form channels to regulate the ionic environment needed to make the calcium carbonate crystals of the otoconia. This is the first molecular characterization of gene mutations that cause a specific deficit in otoconial formation, and thus are unique for vestibular function, without affecting other structures or hearing functions of the ear that do not depend upon otoconial function.

Implications: While there are many possible causes for balance disorders, discovery of this new genetic link will help scientists determine how otoconia is produced and maintains the sense of balance. Because otoconia have been known to degrade with age, understanding how genes regulate otoconial development could lead to possible regenerative treatments for individuals with balance disorders.

Hurle B, Ignatova E, Massironi SM, Mashimo T, Rios X, Thalmann I, Thalmann R, Orntiz DM., Non-Syndromic Vestibular Disorder with Otoconial Agenesis in *tilted/mergulhador* Mice Caused by Mutations in *Otopetrin 1*. H Mol Genet 12: 777-789, 2003.

Regulation and Regeneration of Nerves in the Olfactory System

Background: The olfactory system is unique among sensory systems because the sensory neurons in the nose can undergo replacement at regular intervals and especially in response to acute trauma. Olfactory sensory neurons are exposed to the environment, infection from bacteria and viruses, toxic airborne chemicals, head injury, and aging. Several mechanisms appear to exist that maintain a constant population of these neurons. The growth and differentiation of immature neurons into adult sensory neurons must be tightly regulated in order to maintain the correct

number of neurons in the adult.

Advance: NIDCD-supported scientists have shown that a protein, GDF11, provides an inhibitory signal to maintain the proper number of sensory neurons during development. The scientists observed that elevated GDF11 activity resulted in a decrease in neurogenesis, while the lack of GDF11 resulted in a high level of neuronal growth. The regulatory role of GDF11 is not limited to the olfactory epithelium. GDF11 and its naturally occurring antagonist, follistatin, are widely expressed throughout the central nervous system (e.g., hippocampus, cerebellum and retina), and may play a more global role in the regulation of the size of neuronal populations during early brain development. GDF11 is a member of the transforming growth factor-β protein family, a large group of proteins with multiple roles in controlling development, differentiation and cell numbers in a variety of tissues and cell types.

Implications: An understanding of the role of GDF11 in the development of the olfactory system will likely provide insights into the various control mechanisms that govern development and neurogenesis in other regions of the brain.

Wu HH, Ivkovic S, Murray RC, Jaramillo S, Lyons KM, Johnson JE, Calof AL., Autoregulation of Neurogenesis by GDF11. Neuron 37: 197-207, 2003.

Identifying Genes Important for the Sense of Taste

Background: The worldwide obesity epidemic is causing health professionals to focus their attention on how people choose which foods to eat. Because taste plays an important role in food choice, scientists are interested in figuring out how taste buds tell the brain that they have tasted something, and which taste genes are responsible for sensing different food flavors.

Advance: Vegetables such as broccoli, cauliflower, cabbage, and brussels sprouts contain compounds related to phenylthiocarbamide (PTC.) For more than 50 years, scientists thought that the ability to taste PTC and similar compounds was determined by a single gene. If an individual inherited the PTC-tasting version of the gene, then they detected its bitter taste. If the tasting version of the gene was not inherited, the compound had no taste to that individual. Now NIDCD scientists, in collaboration with scientists in California and Utah, have identified a gene that regulates a person's sensitivity to the bitter taste of PTC. This explains why people seem to demonstrate a range of sensitivity to PTC's taste and may even influence whether or not an individual likes to eat broccoli and other vegetables containing PTC-like compounds.

Another group of scientists supported by NIDCD has illuminated some of the finer details about how taste buds detect flavors and send this information to the brain. Mice that have been engineered to lack either of two different taste-related genes are unable to taste sweet, bitter, and amino acid flavors, but can still taste sour and salty flavors. This demonstrated that: (1) the missing genes are required for the detection of sweet, bitter, and amino acid tastes, (2) messages about the detection of those three flavors are sent to the brain through the same signaling pathways, and (3) detection of sour and salty flavors depends upon different genes than those involved with sweet, bitter, and amino acid detection. When the scientists restored one missing gene product exclusively to taste buds that express bitter taste receptors, the mice were able to

taste bitter flavors but not sweet or amino acid flavors. This suggests that individual taste buds detect only one flavor rather than multiple flavors.

Implications: Because they determine an individual's sensitivity to a particular taste, inherited genes probably influence food choices. Doctors may now be able to use this knowledge to prevent and treat obesity and to overcome poor nutrition due to poor food choices. Increased knowledge about how taste cells tell the brain that they have detected a particular flavor may also help doctors restore the sense of taste to those who have lost it due to injury, disease or aging.

Kim UK, Jorgenson E, Coon H, Leppert M, Risch N, Drayna D., Positional Cloning of the Human Quantitative Trait Locus Underlying Taste Sensitivity to Phenylthiocarbamide. Science 299: 1221-1225, 2003.

Zhang Y, Hoon MA, Chandrashekar J, Mueller KL, Cook B, Wu D, Zuker CS, Ryba NJP., Coding of Sweet, Bitter and Umami Tastes: Different Receptor Cells Sharing Similar Signaling Pathways. Cell 112: 293-301, 2003.

Vocal Fold Paralysis

Background: Vocal fold paralysis is a genetic disorder that can be inherited in families. The vocal folds are two bands of smooth muscle tissue that lie opposite each other and are located in the larynx or voice box. When at rest, the vocal folds are open to allow an individual to breathe. Voice is also produced by vibration of the vocal folds. To produce voice, air from the lungs passes through the folds, causing vibration and thus making sound. The sound from this vibration then travels through the throat, nose, and mouth (resonating cavities). The size and shape of these cavities, along with the size and shape of the vocal folds, help to determine voice quality. Paralysis of the vocal folds impacts voice quality and inhibits an individual's ability to communicate. This disorder can also cause life-threatening breathing difficulties in affected newborn infants.

Advance: Intramural scientists at the NIDCD and the National Institute of Neurological Disorders and Stroke are studying a family in which this disorder occurs and have found that vocal fold paralysis is due to degeneration of the nerves involved in movement. Weakness in the muscles of the arms and legs can also accompany this disorder. In the study, genetic analyses were used to locate the site of the causative gene to a section on chromosome 2. Further studies revealed that mutations in the dynactin gene, which resides at this location, are responsible for this disorder. Dynactin is a molecule that helps transport materials within nerve cells, and this research finding suggests that dynactin transport is essential for health and maintenance of motor nerve cells.

Implications: This finding allows for a genetic tool for diagnosing vocal fold paralysis, which can aid in the clinical and neonatal management of this disorder. In addition, these findings provide better understanding of motor nerve cells and the molecular mechanisms that cause motor nerve degeneration.

Puls I, Jonnakuty C, LaMonte BH, Holzbaur EL, Tokito M, Mann E, Floeter MK, Bidus K,

Drayna D, Oh SJ, Brown RH Jr, Ludlow CL, Fischbeck KH., Mutant Dynactin in Motor Neuron Disease. Nat Genet 33: 455-456, 2003.

Learning to Speak by Feeling

Background: Most people believe that individuals learn to speak from hearing spoken words. NIDCD-supported scientists have shown that somatosensory touch and movement are also used to help us know how to coordinate our mouth and breath to produce words. Furthermore, without auditory input, deaf individuals must learn how to speak using touch and motion patterns. Once the sounds, feelings, and movements involved in making a particular sound are learned, this information is stored in the brain so the sound can be repeated easily.

Advance: In a NIDCD-supported study, scientists used a robotic device, connected to the individual's bottom teeth, to push on the jaw during speaking to measure jaw movements in three separate tasks: vocalized speech saying the utterance "siat" (pronounced "see-at"), silent speech (speech without vocalization) mouthing "siat," and a non-speech jaw movement. The silent speech condition was used to remove auditory feedback. All individuals adapted their jaw movements to say words naturally while wearing the device during the vocalized and silent speech tasks. Adaptation was not seen in the non-speech jaw movement task.

Implications: The study demonstrated that somatosensory and auditory feedback are used independently during speech production. This finding also supports the idea that deaf individuals have the capacity to be competent oral speakers by using somatosensory inputs related to movement in speech production.

Tremblay S, Shiller DM, Ostry DJ., Somatosensory Basis of Speech Production. Nature 423: 866-869, 2003.

Diagnosing Speech and Language Disorders: Leveling the Testing Field

Background: Instruments or procedures which provide objective and reliable information about the nature and stability of childhood language impairments are of crucial importance in diagnosing a language disorder and defining the child's need for and type of treatment. Most currently available language measures were designed to identify the speech and language problems of Standard English speakers. Identifying language deficits is particularly problematic for children from culturally, racially and linguistically diverse backgrounds. Many children from multicultural populations are often incorrectly identified as language impaired because culturally appropriate language assessment instruments or procedures are unavailable. Similarly, children from multicultural populations who have genuine language disorders, which are in need of remediation, may go unrecognized.

Advance: The NIDCD identified the need to support the development of language assessment instruments or procedures appropriate for use with children from non-standard English speaking environments. In response, the NIDCD awarded a contract to produce a dialect-sensitive language test that was to be as accurate for African American English-speaking children as it was for speakers of the Standard American dialect. Before such a test could be devised however,

milestone data on typically-developing African American English-speaking children had to be established because no comprehensive baseline data were available. Language milestone information was gathered in four domains of language: Syntax, Semantics, Phonology, and Pragmatics. The data distinguished difference from disorder with a two-stage analysis, establishing the dialect status of the children, with other items to uncover disordered response patterns. The most effective items were carried forward into the final test, the Diagnostic Evaluation of Language Variation (DELV).

Implications: The test was recently published by The Psychological Corporation. Speech language pathologists are receiving it with great enthusiasm and it promises to play a major role in reducing the number of minority children placed in special education based on linguistic and cultural differences. It represents a significant advance in the accurate identification of speech and language disorders.

Seymour H., Diagnostic Evaluation of Language Variation (DELV). The Psychological Corporation. 2003.

Abnormal Functional Asymmetry in Language Association Cortex in Autism

Background: Many individuals with autism are impaired in their ability to interact appropriately with others individuals because of deficits in language, communication, and social skills. Over the years, scientists have attempted to understand the cause of these deficits, by using neuroimaging technologies to study the brain's structure and function in individuals with autism. However, structural imaging studies of autism, to date, have not focused on structural measures in the regions of the brain (left hemisphere) specifically related to language.

Advance: NIDCD-supported scientists are examining the cerebral cortex, particularly the regions associated with language function, in a well-characterized group of children with autism. In the study, 16 boys with autism (ages 7-11 years), with nonverbal IQ greater than 80, were compared to 15 boys without autism as matched controls. Using neuroimaging techniques, brain imaging patterns in boys with autism were compared with the boys without the disorder. Scientists observed that the boys with autism had significant reversal in the size of region of the brain related to language; 27% larger on the right side in the boys with autism compared to 17% larger on the left in controls. In addition, one additional region was observed to have significant symmetry differences; the posterior temporal fusiform gyrus was larger on the left side in the boys with autism. This region of the brain is not involved in language but in visual face processing which is part of social function.

Implications: In boys with autism, language and social/face processing-related brain regions displayed abnormal asymmetry. These structural abnormalities may contribute to the debilitating language and social disturbances observed in autism.

Herbert MR, Harris GJ, Adrien KT, Ziegler DA, Makris N, Kennedy DN, Lange NT, Chabris CF, Bakardjiev A, Hodgson J, Takeoka M, Tager-Flusberg H, Caviness VS Jr., Abnormal Asymmetry in Language Association Cortex in Autism. Ann Neuro 52: 588-596, 2002.

Specific Language and Reading Impairments Linked in Families

Background: Children who do not develop language at the appropriate age in the absence of neurological disorders, hearing impairments, or lack of adequate opportunity have specific language impairment (SLI). SLI occurs in approximately 7% of school-age children. Research studies have consistently demonstrated that SLI clusters in families, suggesting that genetic factors may be an important cause of SLI. Approximately 20%-25% of family members of SLI children also show signs of SLI as compared to 3%-7% for family members of non-SLI children. In addition, more males have SLI than females. Moreover, previous research has suggested that reading problems, as well as oral language problems, occur in SLI children and aggregate within families.

Advance: NIDCD-supported scientists conducted extensive testing on each family member of a group of SLI children to examine whether language impairment (LI) and reading impairment (RI) also cluster in families. Results of this study showed that LI and RI were much more likely to co-occur in the same individual than to occur alone. In addition, results showed a high rate of oral LI and RI in both the SLI children and their family members. Further, as previous evidence has shown, within families, more males than females showed LI and RI (43% vs. 15% for language; 28% vs. 18% for reading).

Implications: This study supports the idea that language and reading impairments may be interrelated - caused by a combination of genetic and/or environmental factors. Examining the relations between language and reading in families may enhance our understanding of the extent to which each of these impairments may occur together in the same individual, how gender may affect the pattern of these impairments, and how family history may influence the potential risk of having either or both impairments.

Flax J, Realpe-Bonilla T, Hirsch LS, Brzustowicz LB, Bartlett CW, Tallal P., Specific Language Impairment in Families: Evidence for Co-Occurrence with Reading Impairments. J Speech Lang Hear Res 46: 530-543, 2003.

NIH Roadmap

NIDCD's mission includes the support of research to create assistive devices which substitute for lost and impaired sensory and communication function. The NIH Roadmap initiative, "Building Interdisciplinary Research Teams," will advance the NIDCD mission because it encourages collaboration of scientists from seemingly unrelated disciplines. Specifically, interdisciplinary collaborations between physicists, chemists, material scientists, psychologists, otolaryngologists, audiologists, speech-language pathologists, electrical engineers, biomedical engineers and others from a variety of scientific disciplines are necessary for developing assistive communications devices such as hearing aids and cochlear implants. This type of collaborative effort is already helping NIDCD-supported scientists develop an improved directional microphone for hearing aids.

NIDCD New Initiatives in Human Communication Research

Although NIDCD continues to encourage investigator-initiated research proposals, the Institute

also promotes research programs when new scientific opportunities arise or when research is needed to address a public health issue. The following programs were initiated by NIDCD to foster research in human communication:

- "The Role of Neuroimaging in Aphasia Rehabilitation" - to support studies examining the potential of neuroimaging to measure the effectiveness of treatments designed to restore speech to individuals who have lost their ability to speak (aphasia) following a stroke or traumatic brain injury.

- "Stem Cell Potential of the Mammalian Olfactory Epithelium" - to support studies using olfactory stem cells as a model system to understand both basic stem cell biology and how these stem cells participate in maintaining the olfactory system.

- "Identification and Classification of Childhood Speech-Sound Acquisition Disorders of Unknown Origin" - to support multidisciplinary teams of investigators working to determine why some children do not mimic speech sounds as accurately and early as other children and to develop treatments for this problem.

Innovation in Management and Administration

NIDCD program directors are using innovative ways to initiate research training and career development opportunities for individuals interested in research on human communication. There is a national need for additional minority scientists in fields of basic, clinical, and health services research. To address these needs, the NIDCD recently launched a program that will encourage graduate students, in particular minority individuals, to pursue careers in communication sciences and its disorders.

NIDCD Collaborates with Howard University Graduate Program

The Division of Intramural Research (DIR) of the NIDCD and the graduate program in the Departments of Microbiology, Physiology and Biophysics, Communication Sciences and Disorders, Genetics and Human Genetics, and Pharmacology at Howard University (HU), District of Columbia, have a shared interest in scientific progress as well as graduate education in the field of human communication. In providing mutual support of these interests, NIDCD research scientists will provide a program of research training and co-mentoring to pre-doctoral students at NIDCD's research facilities. NIDCD scientists will serve on thesis committees and attend

examination and committee meetings of the students they are mentoring; join in efforts to establish collaborative research with HU faculty; participate in graduate courses, seminars, and journal clubs at HU; provide up to three years of stipend support for full-time students doing dissertation research at NIDCD; continue communication with HU faculty who are involved with co-mentoring these students; and orient students wishing to rotate through NIDCD laboratories as well as to devise short-term training programs.

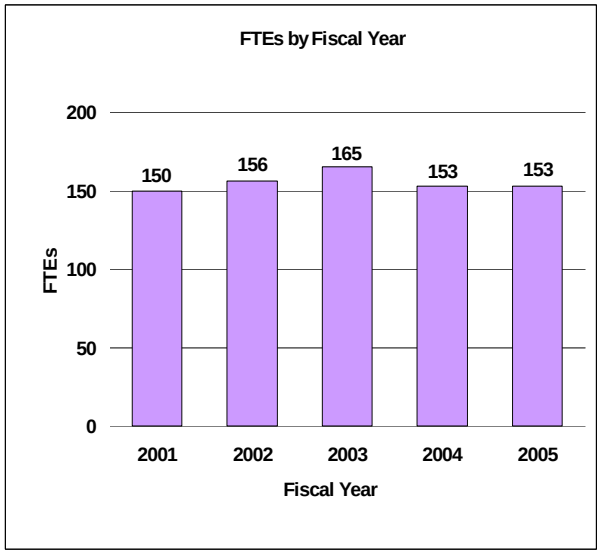
In turn, HU will provide the basic formal educational structure for students within its graduate program. All students will be required to complete course work and degree programs as set up by

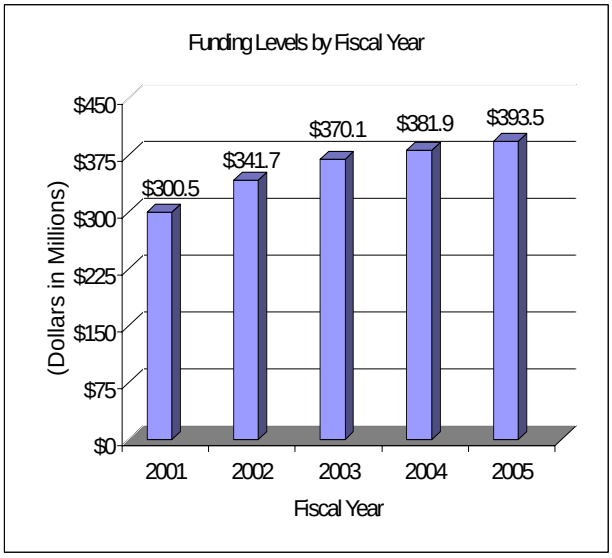
HU. In addition, HU will provide stipend support or tuition support; HU staff will provide long-term commitments to the students for continued education as long as the students remain in good standing in the program, encourage graduate students to rotate through, and/or have short-term research opportunities in NIDCD laboratories, and provide adjunct faculty appointments for those NIDCD staff members working with HU students who assist in teaching at HU.

Budget Policy

The Fiscal Year 2005 budget request for the NIDCD is $393,507,000, an increase of $11,561,000 and 3.0 percent over the FY 2004 Final Conference Level. Also included in the FY 2005 request, is NIDCD's support for the trans-NIH Roadmap initiatives, estimated at 0.63% of the FY 2005 budget request. This Roadmap funding is distributed through the mechanisms of support, consistent with the anticipated funding for the Roadmap initiatives. A full description of this trans-NIH program may be found in the NIH Overview.

A five year history of FTEs and Funding Levels for NIDCD are shown in the graphs below. Note that the Fiscal Year 2001 FTE figure is not comparable to the figures in the succeeding years due to NIH's consolidation of its Human Resources function in FY 2003.





NIH's highest priority is the funding of medical research through research project grants (RPGs). Support for RPGs allows NIH to sustain the scientific momentum of investigator-initiated research while providing new research opportunities. The FY 2005 NIH request provides for an aggregate 1.3 percent increase in average cost for Research Project Grants, consistent with the Gross Domestic Product Deflator. The NIDCD is providing an average cost increase of 1.9 percent for direct recurring costs in noncompeting continuation awards. Competing RPGs are

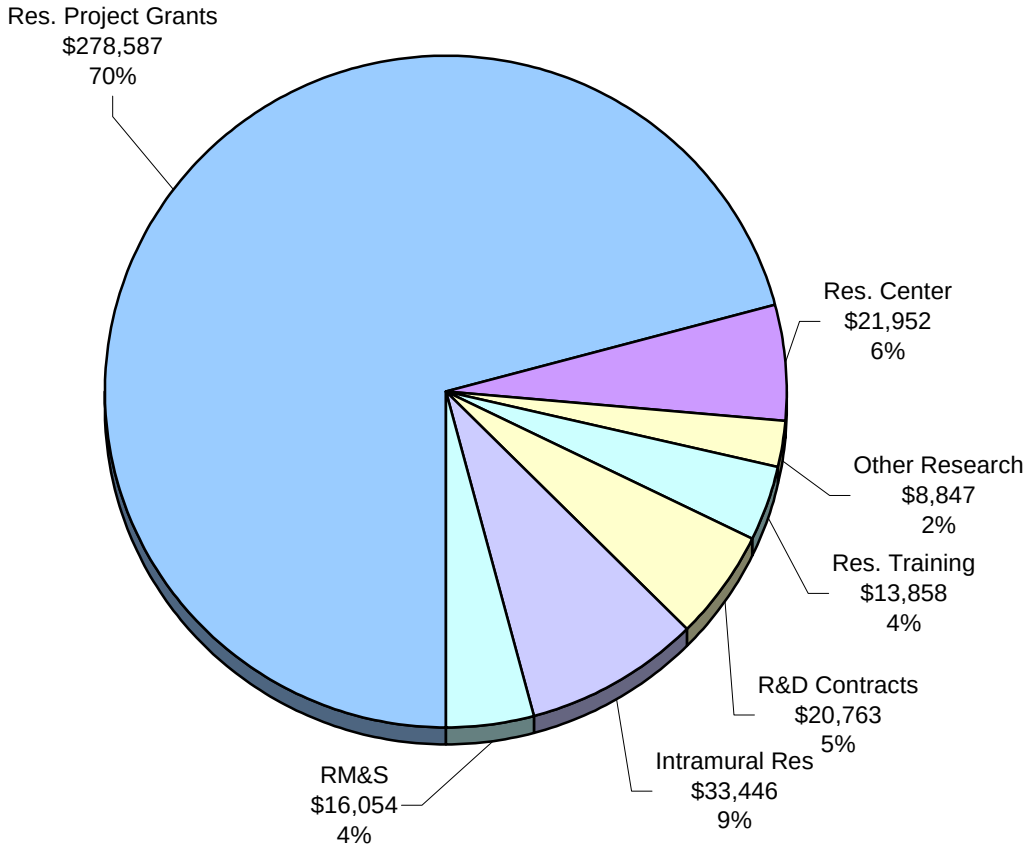
based on an average cost increase of 1 percent.

Advancement in medical research is dependent on maintaining the supply of new investigators with new ideas. In the Fiscal Year 2005 request, NIDCD will support 337 pre- and postdoctoral trainees in full-time training positions. Stipend levels for pre-doctoral and post-doctoral recipients supported through the Ruth L. Kirschstein National Research Service Awards will remain at FY 2004 levels.

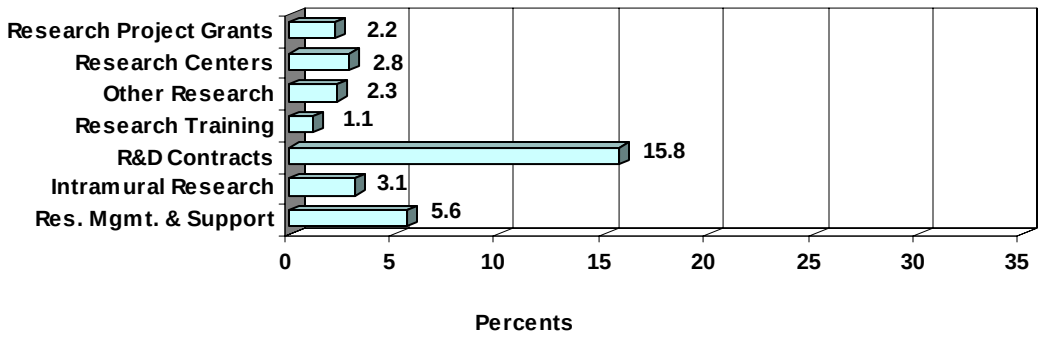
The Fiscal Year 2005 request includes funding for 25 research centers, 63 other research grants, including 42 clinical career awards, and 56 R&D contracts. Intramural Research and Research Management and Support receive increases to support increased pay and estimated inflationary increases in FY 2005.

The mechanism distribution by dollars and percent change are displayed on the following page:

FY 2005
Budget Mechanism
(Dollars in thousands)



FY 2005 Estimate
Percent Change from FY 2004 Mechanism



NATIONAL INSTITUTES OF HEALTH

National Institute on Deafness and Other Communication Disorders

Budget Mechanism - Total

MECHANISM	FY 2003 Actual		FY 2004 Final Conference		FY 2005 Estimate	
Research Grants:	No.	Amount	No.	Amount	No.	Amount
Research Projects:						
Noncompeting	640	$183,386,000	668	$196,091,000	683	$211,264,000
Administrative supplements	(98)	4,497,000	(27)	1,202,000	(27)	1,256,000
Full funded	8	902,000	9	1,000,000	9	1,010,000
Single year	236	66,478,000	224	65,275,000	189	55,757,000
Renewal	81	27,833,000	77	27,330,000	65	23,331,000
New	154	38,522,000	146	37,820,000	123	32,300,000
Supplements	1	123,000	1	125,000	1	126,000
Subtotal, competing	244	67,380,000	233	66,275,000	198	56,767,000
Subtotal, RPGs	884	255,263,000	901	263,568,000	881	269,287,000
SBIR/STTR	43	8,351,000	46	9,100,000	47	9,300,000
Subtotal, RPGs	927	263,614,000	947	272,668,000	928	278,587,000
Research Centers:						
Specialized/comprehensive	25	20,795,000	25	21,184,000	25	21,702,000
Clinical research	0	0	0	0	0	0
Biotechnology	0	0	0	164,000	0	250,000
Comparative medicine	0	100,000	0	0	0	0
Research Centers in Minority Institutions	0	0	0	0	0	0
Subtotal, Centers	25	20,895,000	25	21,348,000	25	21,952,000
Other Research:						
Research careers	38	6,164,000	41	6,674,000	42	6,801,000
Cancer education	0	0	0	0	0	0
Cooperative clinical research	0	0	0	0	0	0
Biomedical research support	0	448,000	0	7,000	0	9,000
Minority biomedical research support	0	0	0	0	0	0
Other	19	1,908,000	20	1,969,000	21	2,037,000
Subtotal, Other Research	57	8,520,000	61	8,650,000	63	8,847,000
Total Research Grants	1,009	293,029,000	1,033	302,666,000	1,016	309,386,000
Research Training:	FTTPs		FTTPs		FTTPs	
Individual awards	146	5,426,000	147	5,700,000	147	5,700,000
Institutional awards	196	8,140,000	187	8,006,000	190	8,158,000
Total, Training	342	13,566,000	334	13,706,000	337	13,858,000
Research & development contracts	54	17,259,000	55	17,937,000	56	20,763,000
(SBIR/STTR)	(0)	(0)	(0)	(0)	(0)	(0)
	FTEs		FTEs		FTEs	
Intramural research	82	31,520,000	79	32,435,000	79	33,446,000
Research management and support	83	14,701,000	74	15,202,000	74	16,054,000
Cancer prevention & control	0	0	0	0	0	0
Construction		0		0		0
Total, NIDCD	165	370,075,000	153	381,946,000	153	393,507,000
(RoadMap Support)		(0)		(1,312,000)		(2,478,000)
(Clinical Trials)		(2,805,000)		(3,450,000)		(3,550,000)

NATIONAL INSTITUTES OF HEALTH

National Institute on Deafness and Other Communication Disorders

Budget Authority by Activity

(dollars in thousands)

ACTIVITY	FY 2003 Actual FTEs	FY 2003 Actual Amount	FY 2004 Final Conference FTEs	FY 2004 Final Conference Amount	FY 2005 Estimate FTEs	FY 2005 Estimate Amount	Change FTEs	Change Amount
Extramural Research:								
Deafness and Other Communication Disorders		$323,854		$334,309		$344,007		$9,698
Subtotal, Extramural research		323,854		334,309		344,007		9,698
Intramural research	82	31,520	79	32,435	79	33,446	0	1,011
Res. management & support	83	14,701	74	15,202	74	16,054	0	852
Total	165	370,075	153	381,946	153	393,507	0	11,561

NATIONAL INSTITUTES OF HEALTH

National Institute on Deafness and Other Communication Disorders

Summary of Changes

FY 2004 Final Conference		$381,946,000
FY 2005 Estimated Budget Authority		393,507,000
Net change		11,561,000

CHANGES	FY 2004 Budget Base FTEs	FY 2004 Budget Base Budget Authority	Change from Base FTEs	Change from Base Budget Authority
A. Built-in:				
1. Intramural research:				
a. Within grade increase		$9,411,000		$130,000
b. Annualization of January 2004 pay increase		9,411,000		96,000
c. January 2005 pay increase		9,411,000		106,000
d. One less day of pay		9,411,000		(28,000)
e. Payment for centrally furnished services		5,145,000		154,000
f. Increased cost of laboratory supplies, materials, and other expenses		17,879,000		529,000
Subtotal				987,000
2. Research Management and Support:				
a. Within grade increase		7,660,000		134,000
b. Annualization of January 2004 pay increase		7,660,000		80,000
c. January 2005 pay increase		7,660,000		88,000
d. One less day of pay		7,660,000		(30,000)
e. Payment for centrally furnished services		1,608,000		48,000
f. Increased cost of laboratory supplies, materials, and other expenses		5,934,000		179,000
Subtotal				499,000
Subtotal, Built-in				1,486,000

NATIONAL INSTITUTES OF HEALTH
National Institute on Deafness and Other Communication Disorders

Summary of Changes--continued

CHANGES	FY 2004 Budget Base No.	FY 2004 Budget Base Amount	Change from Base No.	Change from Base Amount
B. Program:				
1. Research project grants:				
a. Noncompeting	668	$197,293,000	15	$15,227,000
b. Competing	233	66,275,000	(35)	(9,508,000)
c. SBIR/STTR	46	9,100,000	1	200,000
Total	947	272,668,000	(19)	5,919,000
2. Research centers	25	21,348,000	0	604,000
3. Other research	61	8,650,000	2	197,000
4. Research training	334	13,706,000	3	152,000
5. Research and development contracts	55	17,937,000	1	2,826,000
Subtotal, extramural				9,698,000
	FTEs		FTEs	
6. Intramural research	79	32,435,000	0	24,000
7. Research management and support	74	15,202,000	0	353,000
Subtotal, program		381,946,000		10,075,000
Total changes	153		0	11,561,000

NATIONAL INSTITUTES OF HEALTH
National Institute on Deafness and Other Communication Disorders

Budget Authority by Object

	FY 2004 Final Conference	FY 2005 Estimate	Increase or Decrease
Total compensable workyears:			
Full-time employment	153	153	0
Full-time equivalent of overtime & holiday hours	0	0	0
Average ES salary	$148,342	$150,567	$2,225
Average GM/GS grade	11.2	11.2	0.0
Average GM/GS salary	$73,625	$74,729	$1,104
Average salary, grade established by act of July 1, 1944 (42 U.S.C. 207)	$108,612	$110,241	$1,629
Average salary of ungraded positions	69,451	70,493	1,042
OBJECT CLASSES	FY 2004 Final Conference	FY 2005 Estimate	Increase or Decrease
Personnel Compensation:			
11.1 Full-Time Permanent	$7,980,000	$8,243,000	$263,000
11.3 Other than Full-Time Permanent	3,773,000	3,930,000	157,000
11.5 Other Personnel Compensation	426,000	434,000	8,000
11.7 Military Personnel	0	0	0
11.8 Special Personnel Services Payments	1,955,000	2,042,000	87,000
Total, Personnel Compensation	14,134,000	14,649,000	515,000
12.1 Civilian Personnel Benefits	2,882,000	2,983,000	101,000
12.2 Military Personnel Benefits	55,000	57,000	2,000
13.0 Benefits for Former Personnel	0	0	0
Subtotal, Pay Costs	**17,071,000**	**17,689,000**	**618,000**
21.0 Travel & Transportation of Persons	571,000	614,000	43,000
22.0 Transportation of Things	45,000	45,000	0
23.1 Rental Payments to GSA	0	0	0
23.2 Rental Payments to Others	662,000	682,000	20,000
23.3 Communications, Utilities & Miscellaneous Charges	491,000	503,000	12,000
24.0 Printing & Reproduction	124,000	125,000	1,000
25.1 Consulting Services	170,000	174,000	4,000
25.2 Other Services	2,535,000	2,818,000	283,000
25.3 Purchase of Goods & Services from Government Accounts	25,659,000	26,481,000	822,000
25.4 Operation & Maintenance of Facilities	1,742,000	1,786,000	44,000
25.5 Research & Development Contracts	8,542,000	11,118,000	2,576,000
25.6 Medical Care	223,000	232,000	9,000
25.7 Operation & Maintenance of Equipment	1,355,000	1,376,000	21,000
25.8 Subsistence & Support of Persons	0	0	0
25.0 Subtotal, Other Contractual Services	**40,226,000**	**43,985,000**	**3,759,000**
26.0 Supplies & Materials	4,211,000	4,401,000	190,000
31.0 Equipment	2,173,000	2,219,000	46,000
32.0 Land and Structures	0	0	0
33.0 Investments & Loans	0	0	0
41.0 Grants, Subsidies & Contributions	316,372,000	323,244,000	6,872,000
42.0 Insurance Claims & Indemnities	0	0	0
43.0 Interest & Dividends	0	0	0
44.0 Refunds	0	0	0
Subtotal, Non-Pay Costs	**364,875,000**	**375,818,000**	**10,943,000**
Total Budget Authority by Object	**381,946,000**	**393,507,000**	**11,561,000**

National Institute on Deafness and Other Communication Disorders

Salaries and Expenses

OBJECT CLASSES	FY 2004 Final Conference	FY 2005 Estimate	Increase or Decrease
Personnel Compensation:			
Full-Time Permanent (11.1)	$7,980,000	$8,243,000	$263,000
Other Than Full-Time Permanent (11.3)	3,773,000	3,930,000	157,000
Other Personnel Compensation (11.5)	426,000	434,000	8,000
Military Personnel (11.7)	0	0	0
Special Personnel Services Payments (11.8)	1,955,000	2,042,000	87,000
Total Personnel Compensation (11.9)	**14,134,000**	**14,649,000**	**515,000**
Civilian Personnel Benefits (12.1)	2,882,000	2,983,000	101,000
Military Personnel Benefits (12.2)	55,000	57,000	2,000
Benefits to Former Personnel (13.0)	0	0	0
Subtotal, Pay Costs	**17,071,000**	**17,689,000**	**618,000**
Travel (21.0)	571,000	614,000	43,000
Transportation of Things (22.0)	45,000	45,000	0
Rental Payments to Others (23.2)	662,000	682,000	20,000
Communications, Utilities and Miscellaneous Charges (23.3)	491,000	503,000	12,000
Printing and Reproduction (24.0)	124,000	125,000	1,000
Other Contractual Services:			
Advisory and Assistance Services (25.1)	170,000	174,000	4,000
Other Services (25.2)	2,535,000	2,818,000	283,000
Purchases from Govt. Accounts (25.3)	10,311,000	10,326,000	15,000
Operation & Maintenance of Facilities (25.4)	1,742,000	1,786,000	44,000
Operation & Maintenance of Equipment (25.7)	1,355,000	1,376,000	21,000
Subsistence & Support of Persons (25.8)	0	0	0
Subtotal Other Contractual Services	**16,113,000**	**16,480,000**	**367,000**
Supplies and Materials (26.0)	4,056,000	4,239,000	183,000
Subtotal, Non-Pay Costs	22,062,000	22,688,000	626,000
Total, Administrative Costs	**39,133,000**	**40,377,000**	**1,244,000**

NATIONAL INSTITUTES OF HEALTH

National Institute on Deafness and Other Communication Disorders

SIGNIFICANT ITEMS IN THE HOUSE AND SENATE APPROPRIATIONS COMMITTEE REPORTS

FY 2004 House Appropriations Committee Report Language (H.Rpt. 108-188)

Item

Neurofibromatosis (NF) – . . . . Research is now being conducted to cure deafness in NF mice through gene therapy, which could prove enormously beneficial for gene therapy in general and for patients suffering from meningiomas and other tumors. The Committee therefore encourages NIDCD to expand its NF research portfolio through all suitable mechanisms, including clinical trials and RFAs. (p. 81)

Action taken or to be taken

The NIDCD continues to support technologies to enhance the successful treatment of individuals with Neurofibromatosis type 2 (NF2). Individuals with NF2 may be required to undergo surgery to remove the acoustic neuroma. This procedure may result in damage to the auditory nerve and lead to deafness. Through the R&D Contracts mechanism, NIDCD continues to support the development of a cochlear nucleus auditory prosthesis for individuals who have lost their hearing from NF2. This implantable device would be of great benefit to deaf individuals that are unable to gain benefit from a conventional cochlear implant. If successful, physicians will have a viable means to restore hearing function to individuals with NF2. Additionally, in conjunction with NINDS, the lead institute at the NIH for NF research, NIDCD is participating in a trans-NIH Program Announcement soliciting applications for the establishment of National Centers for Neurofibromatosis Research. Recent discoveries have created important opportunities for basic, translational, and clinical research on the neurofibromatoses. The purpose of this recently published Program Announcement is to encourage the formation and development of research centers that can capitalize on these opportunities, and ultimately develop therapeutic intervention for individuals with neurofibromatosis. These new centers are intended to provide focused expertise and resources, and establish a multi-disciplinary environment that will accelerate research progress.

FY 2004 Senate Appropriations Committee Report Language (S.Rpt. 108-10)

Item

Aphasia – It has come to the Committee's attention that the state of the science for aphasia, a common and devastating acquired speech and language disorder, has gone virtually unchanged for decades. Based upon previous direction, the NIH recently hosted a symposium to discuss some of the current issues surrounding aphasia. The Committee applauds these initial efforts.

However, the Committee also recognizes that decades of insufficient research have resulted in numerous shortcomings in the areas of aphasia research, standards of care, rehabilitation and treatments. The Committee, therefore, urges a coordinated cross-functional effort involving the NIH, specifically NINCD, NIDCD, and NINDS, as well as other appropriate Federal healthcare agencies, specifically AHRQ, HRSA, and CMS, to address these concerns regarding aphasia.
(p. 142)

Action taken or to be taken

Research on aphasia is currently supported by the NIDCD, NICHD, NINDS, NIMH and NIA with NIDCD serving as the lead institute. As the primary institute conducting aphasia research, the NIDCD has cosponsored over the past year a symposium series, "New Perspectives in Language Research," with the NICHD, NINDS, NIMH and NIA. The September 2000 symposium, "Neural and Computational Bases of Language," highlighted leading contemporary approaches to the study of human language. The speakers, which included several scientists involved in aphasia research, presented and discussed new research exploring techniques of brain imaging, computational modeling, and linguistic analysis. The development of language across the lifespan and the effects of brain injury on language performance were major themes of this symposium. The March 2001 symposium on "Developmental Disorders of Language" also included scientists studying aphasia, language development, spatial cognition and the underlying neural systems. In addition, the NIDCD sponsored a planning workshop to formulate research recommendations on aphasia intervention and use of neuroimaging techniques. The workshop was entitled, "The Role of Neuroimaging in the Study of Aphasia Recovery and Rehabilitation: Research Needs and Opportunities." Other NIH institutes conducting aphasia research were invited to participate in the workshop. As a result of the workshop, NIDCD issued a Request for Applications (RFA) entitled "Role of Neuroimaging in Aphasia Rehabilitation." Approximately $1.5 million has been set-aside for meritorious applications in response to this RFA. NIDCD continues to participate in trans-NIH activities related to aphasia, as well as collaborate with other institutes to foster and advance research in this area.

Item

Environmentally-induced Hearing Loss – The Committee continues to be concerned by the number of Americans who suffer from chemical- and noise-induced hearing loss. The NIDCD's Wise Ears! Campaign is making significant inroads towards educating Americans of all ages, and the Committee strongly supports its expansion amongst school-age children. The Committee also supports expanded research on prosthetic and pharmacological therapies for hearing loss from noise stress, ototoxic drugs and other environmental traumas.
(p. 143)

Actions taken or to be taken

NIDCD is pleased to report that 94 organizations with nationwide impact have joined the WISE EARS!® Coalition to prevent noise-induced hearing loss in the public and the worker. Several initiatives have and will have direct impact upon school-aged children--among our most vulnerable to hearing loss--and those who can learn to be good "ear defenders" for life. One

major initiative is NIDCD's curriculum supplement, "How Your Brain Understands What Your Ear Hears," that is written for middle schoolers and has been classroom tested in all types of school environments. The lessons culminate in a powerful noise-induced hearing loss prevention message with required student learning activities. It will debut at national meetings of science and biology teachers in early 2004. Secondly, in a focused initiative to address a key cause of noise-induced hearing loss in young people, NIDCD developed a lesson in shooter safety that was inserted in the A*nnual 2003 Hunter Handbook*, the annual publication that is distributed to hunting and shooting instructors for classroom use. The message is also available from NIDCD and its Web site. WISE EARS!® is also being used at the local and regional levels as well. Programs have been held in classrooms across the country. For example, three thousand 4th and 5th graders in Houston learned about prevention, and materials were shared by teachers in 22 other states nationwide. Finally, the NIDCD "Kids and Teachers" Web site has become a major resource for information about how we hear through "I Love What I Hear!" activities in English and Spanish, with interactive quizzes and learning tools and new materials on understanding the damaging effects of noise and how to prevent them. The material is also available in hard copy for teachers without Web resources.

NIDCD supports applied research to develop improved hearing aids and other prosthetic devices, as well as basic research directed towards developing pharmacological therapies for hearing loss. Research is underway to study the possible use of gene therapy to regenerate damaged auditory hair cells, the effectiveness of drugs to treat autoimmune inner ear disease, and mechanisms to mitigate the ototoxic effects of certain antibiotics. The institute's research portfolio in these areas has expanded in recent years, and is expected to increase steadily in the future.

Item

Neurofibromatosis – . . . . The Committee urges the Institute to expand its research portfolio in collaboration with the NF community to address issues that are relevant to deafness and other communication problems associated with NF2. Research is now being conducted to cure deafness in NF2 mice through gene therapy, with enormous implications for gene therapy in general and for patients suffering from meningiomas and other tumors in particular. The Committee therefore encourages NIDCD to expand its NF2 research portfolio through all suitable mechanisms including RFAs and clinical trials. (p. 144)

Action taken or to be taken

Please refer to page 28 of this document for IC's response to this Significant Item regarding Neurofibromatosis.

NATIONAL INSTITUTES OF HEALTH
National Institute on Deafness and Other Communication Disorders

Authorizing Legislation

	PHS Act/ Other Citation	U.S. Code Citation	2004 Amount Authorized	2004 Final Conference	2005 Amount Authorized	2005 Budget Estimate
Research and Investigation	Section 301	42§241	Indefinite		Indefinite	
National Institute on Deafness and Other Communication Disorders	Section 464	42§285b	Indefinite	$368,240,000	Indefinite	$379,649,000
National Research Service Awards	Section 487(d)	42§288	a/	13,706,000	b/	13,858,000
Total, Budget Authority				381,946,000		393,507,000

a/ Amounts authorized by Section 301 and Title IV of the Public Health Act.

b/ Reauthorizing legislation will be submitted.

NATIONAL INSTITUTES OF HEALTH
National Institute on Deafness and Other Communication Disorders
Appropriations History

Fiscal Year	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation 1/
1996	$172,399,000 2/	$174,852,000	$170,540,000 2/	$174,852,000
Rescission				(119,000)
1997	179,090,000 2/	189,243,000	182,693,000	188,422,000 3/
1998	192,477,000 2/	198,373,000	198,583,000	198,857,000
1999	213,184,000 2/ 4/	216,995,000	229,887,000	229,887,000
Rescission	0	0	0	(152,000)
2000	235,297,000 2/	251,218,000	261,962,000	265,185,000
Rescission				(1,414,000)
2001	276,418,000	301,787,000	303,541,000	300,581,000
Rescission				(100,000)
2002	336,757,000	334,161,000	349,983,000	342,072,000
Rescission				(397,000)
2003	365,929,000	351,376,000	372,805,000	372,805,000
Rescission				(2,423,000)
2004	380,377,000	380,377,000	384,577,000	384,477,000
Rescission				(2,424,000)
2005	393,507,000			

1/ Reflects enacted supplementals, rescissions, and reappropriations.
2/ Excludes funds for HIV/AIDS research activities consolidated in the NIH Office of AIDS Research.
3/ Excludes enacted administrative reductions of $77,000.
4/ Reflects a decrease of $650,000 for the budget amendment for bioterrorism. Excludes enacted administrative

NATIONAL INSTITUTES OF HEALTH

National Institute on Deafness and Other Communication Disorders

Detail of Full-Time Equivalent Employment (FTEs)

OFFICE/DIVISION	FY 2003 Actual	FY 2004 Final Conference	FY 2005 Estimate
Office of the Director	7	6	6
Office of Administration	38	34	34
Division of Extramural Activities	22	19	19
Division of Scientific Programs	16	15	15
Division of Intramural Research	82	79	79
Total	165	153	153
FTEs supported by funds from Cooperative Research and Development Agreements	(0)	(0)	(0)

FISCAL YEAR	Average GM/GS Grade
2001	10.5
2002	10.8
2003	11.2
2004	11.2
2005	11.2

NATIONAL INSTITUTES OF HEALTH

National Institute on Deafness and Other Communication Disorders

Detail of Positions

GRADE	FY 2003 Actual	FY 2004 Final Conference	FY 2005 Estimate
ES-6	0	0	0
ES-5	0	0	0
ES-4	1	1	1
ES-3	0	0	0
ES-2	0	0	0
ES-1	0	0	0
Subtotal	1	1	1
Total - ES Salary	$142,500	$148,342	$150,567
GM/GS-15	22	20	20
GM/GS-14	10	9	9
GM/GS-13	16	15	15
GS-12	17	15	15
GS-11	13	12	12
GS-10	1	0	0
GS-9	17	15	15
GS-8	8	7	7
GS-7	4	3	3
GS-6	0	0	0
GS-5	2	2	2
GS-4	2	1	1
GS-3	2	2	2
GS-2	1	0	0
GS-1	0	0	0
Subtotal	115	101	101
Grades established by Act of July 1, 1944 (42 U.S.C. 207):			
Assistant Surgeon General Director Grade	1	1	1
Senior Grade Full Grade			
Senior Assistant Grade Assistant Grade			
Subtotal	1	1	1
Ungraded	65	65	65
Total permanent positions	117	103	103
Total positions, end of year	182	168	168
Total full-time equivalent (FTE) employment,end of year	165	153	153
Average ES level	ES-4	ES-4	ES-4
Average ES salary	$142,500	$148,342	$150,567
Average GM/GS grade	11.2	11.2	11.2
Average GM/GS salary	$70,455	$73,625	$74,729