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National Institute on Deafness and Other Communication Disorders

INTRODUCTION

The National Institute on Deafness and Other Communication Disorders (NIDCD) conducts and supports research on the normal and disordered processes of hearing, balance, smell, taste, voice, speech, and language. NIDCD uses a wide range of mechanisms to achieve its mission in biomedical and behavioral research and in research training. NIDCD scientists, research grant programs, individual and institutional research training awards, career development awards, center grants, and contracts to public and private research institutions are used to accomplish the Institute's research goals.

HIGHLIGHTS OF RECENT SCIENTIFIC ADVANCES RESULTING FROM INTERNATIONAL ACTIVITIES

The NIDCD Division of Intramural Research, in collaboration with scientists from Punjab University, Pakistan, discovered that mutations in a single gene lead to a particular form of deafness. This gene normally is responsible for the production of claudin 14, a protein in the inner ear. This discovery was made by studying genes in families with deaf members in Pakistan.

SUMMARY OF INTERNATIONAL PROGRAMS AND ACTIVITIES

Country-to-Country Activities and Bilateral Agreements

Canada

The Laboratory of Molecular Genetics, NIDCD, established a collaboration with the University of Toronto, Ontario, on a study of hereditary deafness in Ashkenazi Jews and is actively working on the genetic mapping and identification of a novel gene for deafness in a large family of Ashkenazi Jews. The research has already resulted in one publication about the hearing status associated with a particular allele (variant) of a known gene for deafness (GJB2), which codes for the protein connexin 26 *(American Journal of Human Genetics, March 2000)*.

India and Pakistan

The Laboratory of Molecular Genetics is working with the Genetics Unit of the All India Institute of Medical Sciences, New Delhi, and the Center of Excellence in Molecular Biology, University of the Punjab, Lahore, Pakistan. In India and Pakistan, high percentages of marriages are between first cousins or an uncle and a niece. Because these consanguineous families act as isolated subpopulations, they provide the opportunity for the investigators to localize and clone genes for hereditary deafness. During the past few years, this joint research has led to many publications on the loci of novel genes that cause deafness. In 2001, articles on this research will be published in *Cell* and the *American Journal of Human Genetics*.

Israel

The Section on Developmental Neuroscience, Laboratory of Cellular Biology, NIDCD, established a collaboration with the faculty at Sackler School of Medicine, Tel Aviv University, to determine the pattern of expression and biological effects of myosin VI during development of the auditory system. Myosin VI has been shown to be required for development of hair cells and for hearing, but the specific effects of this protein have not been determined.

Italy

The NIDCD Division of Intramural Research is working with the Institute of Molecular Genetics, National Research Council, Alghero, Sardinia, in a study of inherited deficits in the sense of bitter taste. This laboratory of the Institute of Molecular Genetics has developed a unique study population in a number of genetically isolated villages in the Ogliastra region of Sardinia. Such populations provide important experimental advantages for the study of common recessive genes, such as those that cause deficits in the sense of bitter taste in individuals of European origin. The goal of this research is to identify the genes that cause this deficit, and thus to increase understanding of the molecular mechanisms involved in this sense in humans.

Activities With International and Multinational Organizations

NIDCD continues to support and participate in two international research consortia to expedite the discovery of genes responsible for hereditary hearing impairment. (See the section on "Highlights of Recent Scientific Advances Resulting From International Activities.")

Extramural Programs

Norway

The NIDCD Epidemiology, Statistics, and Data System Branch has supported a research contract for the Genetic and Environmental Study of Hearing Loss in Nord-Tröndelag County, Norway. Using a population-based cohort of adults aged 20 years or older, the investigators are studying prevalence of genetic and environmental risk factors for age-related hearing loss and other hearing disorders, including tinnitus. Hearing is assessed directly with pure-tone audiometry, and for a subset of persons, otoacoustic emissions are used to measure cochlear function. The researchers developed a mathematical algorithm to identify audiometric notches in the higher-frequency ranges (3, 4, and 6 kHz), a characteristic of noise-induced hearing loss. The prevalence of notches increased with age in men, from 16% in those younger than age 25 years to 48% at 55–64 years of age. The increase is associated with such risk factors as loud noise at work and use of firearms. Questionnaires were used to ascertain environmental risk factors, including long-term

exposure to loud noise from occupational and recreational sources.

International Meetings

During fiscal year 2000, NIDCD staff participated at international meetings in various capacities, including the following:

- made a presentation on Large-Scale Modeling and Functional Brain Imaging of Human Working Memory, at the College de France, in Paris, in March 2000;
- attended a meeting on the Evolution of Language, in Paris, France, in April 2000;
- gave a presentation on Targeting of Receptors to Purkinje Cell Synapses, at the European Neuroscience Meeting, in Brighton, England, in June 2000;
- spoke on Targeting of Glutamate Receptors, at the 2000 Satellite Symposium: Synaptic Plasticity, of the Federation of European Neuroscience Societies, in Bristol, England, in June 2000;
- spoke on Synaptic Distribution and Surface Expression of Glutamate Receptors, at the Synapses 2000 meeting, in Munich, Germany, in June 2000; and
- made a presentation at the annual meeting of the Society for the Study of Ingestive Behavior, at Trinity College, in Dublin, Ireland, in July 2000.

Intramural Programs and Activities

The NIDCD Division of Intramural Research continues to support an international consortium with the purpose of expediting the discovery of genes responsible for hereditary hearing impairment. The consortium encompasses research on nonsyndromic and syndromic forms of hereditary hearing loss, such as Waardenburg syndrome and Usher syndrome. Scientists from countries including Belgium, Colombia, Finland, France, Germany, Israel, Japan, Norway, South Africa, and the United Kingdom, as well as scientists throughout the United States, continue their efforts to map the genes responsible for syndromic and nonsyndromic hereditary hearing impairment. Almost 60 genes have been identified for recessive and dominant nonsyndromic hereditary hearing impairment in families from Colombia, India, Indonesia, Israel, Lebanon, Newfoundland, Pakistan, Tunisia, and the United States, including Puerto Rico. The collaborative efforts fostered by the consortium have been instrumental in identifying a large number of the genes responsible for hereditary hearing impairment and in advancing the understanding of these disorders.

There is a regular exchange of training opportunities between NIDCD and foreign countries. Visiting Scientists, Visiting Associates, and Guest Researchers from a number of countries are making significant contributions to the research efforts of the Division of Intramural Research. Essentially all NIDCD laboratories are involved in this effort, which benefits both NIDCD and the scientists receiving the training.