

## NATIONAL INSTITUTE OF ENVIRONMENTAL HEALTH SCIENCES

### Address:

National Institute of Environmental Health Sciences  
National Institutes of Health  
Building 101, B242, P.O. Box 12233  
Research Triangle Park, NC 27709  
Web site: [www.niehs.nih.gov](http://www.niehs.nih.gov)

### Director:

Kenneth Olden, Ph.D.  
(919) 541-3201 (phone)  
(919) 541-2260 (fax)

### Legislative Contact:

Mary Gant  
(301) 496-2919 (phone)  
(301) 496-0563 (fax)  
Email: [gant@niehs.nih.gov](mailto:gant@niehs.nih.gov)

### Mission:

The mission of the National Institute of Environmental Health Sciences (NIEHS) is to reduce the burden of environmentally associated disease and dysfunctions by understanding (1) how environmental exposures affect our health, (2) how individuals differ in their susceptibility to these exposures, and (3) how these susceptibilities change as a function of time and age. NIEHS achieves its mission through multi-disciplinary biomedical research programs, prevention and intervention efforts and communication strategies that encompass training, education, technology transfer and community outreach.

### Selected Achievements and Initiatives:

#### *Protein Identified that Halts Progression of Alzheimer's Disease:*

Researchers have identified a protein in the brain that halts the progression of Alzheimer's disease in human brain tissue. The protein, known as transthyretin, protects brain cells from deterioration by blocking another toxic protein that contributes to the disease process. This discovery provides a new avenue for exploration, where drugs could be developed that boost the brain's level of transthyretin or methods could be developed for depositing it directly in the brain. It holds the promise of early pretreatment of people at high risk for Alzheimer's disease so they can prevent its development, as well as a possible means to treat people in early stages of the disease so that it doesn't progress and they preserve a higher level of cognitive function.

*Sister Study of Breast Cancer:* A unique study exploring gene-environment interactions in breast cancer development has begun nationwide recruitment. It will look at how genes, activities of daily life, and environmental exposures affect breast cancer risk. In order to get the information quickly, this study recruits 50,000 symptom-free women who have a sister that had breast cancer. These women are at increased risk of breast cancer, share many genes with their affected sibling, and would have experienced many of the same exposures. For these reasons, it is expected that a sufficient number of women will develop breast cancer within 10 years and their genes and exposures can be compared with those women in the study who did not develop the cancer. A broad range of exposures will be examined, including personal care and household products, workplace exposures, and dietary factors. A number of advocacy groups are working with the NIEHS on this project, including the American Cancer Society, Sisters Network, Inc., the Susan G. Komen Breast Cancer Foundation, and the Y-ME Breast Cancer Organization.

*Autism:* Autism is a devastating behavioral disorder that appears in childhood and lasts a lifetime. Its prevalence might be increasing, although changing diagnostic standards and greater awareness make it difficult to interpret time trends. Genetic factors are suspected of playing a role in autism because it often runs in families. Genetic factors alone, though, are unlikely to provide a full account of autism etiologies. Past studies have shown that "in

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utero” exposure to an environmental agent, thalidomide, dramatically increases autism risk. As with most disease, autism most likely arises from underlying genetic susceptibilities interacting with specific environmental triggers at particular times of life (in this case, early periods of pre or postnatal development) that confer enhanced vulnerability. A number of people have suspected that the mercury-containing compound thimerosal, used to preserve childhood vaccines, could be an environmental trigger for autism development, based on the established neurotoxicity of higher doses of mercury. Extensive epidemiological studies, however, have failed to provide any association between vaccines and autism and make clear that the very large increase in autism prevalence over the past ten years cannot be attributed to vaccination.

It is possible, however, that only a subset of children are susceptible to mercury effects, perhaps when coupled with an immunological challenge. Because the genetic susceptibilities of autism and most other neurodevelopmental disorders are not yet known, current epidemiological studies are unable to identify small susceptible cohorts that might be particularly vulnerable to the effects of thimerosal. Preliminary animal studies have provided an intriguing clue that NIEHS is now pursuing. In these studies, different mouse strains were exposed to thimerosal at ages and doses that corresponded to the standard protocol for childhood vaccinations. Only the immunologically deficient strain of mouse exhibited a response. In these mice, behavioral effects were seen and morphological changes were observed in the brain. This study did not have sufficient power to be definitive, but it did provide clues that are worth exploring.

NIEHS, through its Centers, is supporting other research relevant to autism. It is recruiting a cohort of 700 autistic children, in addition to control subjects, in California. This study will be examining possible environmental triggers for this disease, with results available after 2006. Animal models are also being developed that will enable researchers to assess social behavior in developing and mature animals. Such models could then be used to examine the effects of various toxicants, including thimerosal, on the development and performance of these behaviors. Another study is examining molecular and cellular mechanisms that might underlie some of the idiosyncratic responses within autistic children to chemicals they might have been exposed to during early stages of brain development. This project will use a variety of cellular and animal models to address immunotoxic and neurotoxic actions of environmental agents of interest.

### Appropriations History

*(\$ in thousands)*

FY 2001	\$564,810 (+27.7%)
FY 2002	\$645,422 (+14.3%)
FY 2003	\$697,767 (+8.1%)
FY 2004	\$710,701 (+1.9%)
FY 2005	\$727,347 (+2.3%)

### Extramural Research Project Grants

*(Includes SBIR/STTRs)*

FY 2001	612
FY 2002	640
FY 2003	629
FY 2004	571
FY 2005	562

### Success Rate — Research Project Grants

FY 2001	29%
FY 2002	29%
FY 2003	25%
FY 2004	19%
FY 2005	25%

### Research Training Positions Supported

FY 2001	528
FY 2002	521
FY 2003	520
FY 2004	518
FY 2005	525

### Research Centers

FY 2001	36
FY 2002	31
FY 2003	34
FY 2004	37
FY 2005	37