

**DEPARTMENT OF HEALTH AND HUMAN SERVICES
NATIONAL INSTITUTES OF HEALTH**

Fiscal Year 2006 Budget Request

**Witness appearing before the
House Subcommittee on Labor-HHS-Education Appropriations**

**Dr. Paul Sieving, Director
National Eye Institute**

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**William Beldon
Deputy Assistant Secretary, Budget**

Mr. Chairman and Members of the Committee:

I am pleased to present the President's budget request for the National Eye Institute (NEI) for FY 2006. This budget includes \$673 million, an increase of \$4 million over the FY 2005 enacted level of \$669 million comparable for transfers proposed in the President's request. As the Director of the NEI it is my privilege to report on the progress laboratory and clinical scientists are making in combating blindness and visual impairment and about the unique opportunities that exist in the field of vision research.

GLAUCOMA AND OPTIC NEUROPATHIES

Glaucoma is a group of eye disorders that causes optic nerve damage that can lead to severe visual impairment or blindness. Elevated intraocular pressure (IOP) is frequently, but not always, associated with glaucoma. Glaucoma is a major public health problem and published studies find it is the most common cause of visual impairment and blindness in African Americans.

The prevalence of glaucoma is three times higher in African Americans than in non-Hispanic whites¹. Additionally, the risk of visual impairment is much higher and the age of onset is earlier than in Whites. An NEI-supported follow-up study to the *Ocular Hypertension Treatment Study* (OHTS) found that early treatment of elevated IOP reduces the risk of developing glaucoma in African Americans. Of the participants

¹ The Eye Diseases Prevalence Research Group: Prevalence of open-angle glaucoma among adults in the United States. *Arch Ophthalmol* 122:532-538, 2004.

in the treatment arm of the study, 8.4 percent developed glaucoma whereas 16.1 percent in the observation group developed the disease. Additionally, the OHTS follow-up study found that certain biological characteristics of the eye including corneal thickness are helpful in predicting who will likely develop glaucoma and who will benefit from therapy. This study provides important treatment and prognostic information for clinicians in caring for this at risk population.

RETINAL DISEASES

Retinal diseases are a diverse set of sight-threatening conditions that include age-related macular degeneration, diabetic retinopathy, retinopathy of prematurity, retinitis pigmentosa, Usher's syndrome, ocular albinism, retinal detachment, uveitis (inflammation) and cancer (choroidal melanoma and retinoblastoma). This year, NEI supported laboratory researchers made great strides in developing therapies for these diseases. For example, a recent NEI study found that eye injections of bone marrow stem cells from adult animals prevented vision loss in two rodent models of retinitis pigmentosa (RP). These findings raise the possibility of a therapy in which patients could receive an injection of their own bone marrow stem cells to preserve vitally important central vision.

Age-related macular degeneration (AMD) is a leading cause of blindness and visual disability in older age Americans. The inability to prevent the development of AMD and its complications is largely due to an imprecise understanding of the pathologic mechanisms of the disease. Genetic and environmental factors have

previously been implicated in the disease. A recent NEI supported study in animal models has found evidence that inflammation may also play a role. These animal models suggest that the immune system contributes to the disease and offer new insights into possible mechanisms of the disease. The availability of animal models of the disease will also allow for the testing of new intervention strategies.

CORNEAL DISEASES

The cornea is the transparent tissue at the front of the eye. Corneal disease and injuries are the leading cause of visits to eye care professionals, and are some of the most painful ocular disorders.

The epithelial cells of the cornea form a surface barrier that protects the underlying tissues from the external environment. When this layer is damaged, the epithelial cells normally respond quickly to close the wound and reform the barrier. In some cases, however, this response is defective, leading to the formation of persistent and painful corneal ulcers. Development of more effective treatments for this condition has been hampered by the limited information about the cellular and biochemical events that regulate corneal wound closure. This year, scientists at the NEI discovered that an enzyme called Cdk5 plays a central role in regulating the migration of epithelial cells to close corneal wounds. More importantly they discovered that drugs which inhibit Cdk5 promote cell migration and wound closure. These findings suggest a new therapeutic approach for treating persistent corneal ulcers and other conditions that impair wound healing. Animal studies are in progress to determine whether inhibitors of Cdk5 can

safely be used in the eye to enhance wound healing.

CATARACT

Cataract, an opacity of the lens of the eye, interferes with vision and is the leading cause of blindness in developing countries. It is also a major public health problem in this country. Throughout life, the lens carries out a process of continued growth with epithelial cells dividing and differentiating into fiber cells. As epithelial cells differentiate into fiber cells they become denuded of certain cell components so they will not interfere with vision or cause cataracts. NEI supported scientists have recently discovered that the epithelial cells “borrow” enzymes involved in programmed cell death, or apoptosis, to mediate the destruction of these cell parts. Apoptosis is a normal biologic process that guides an orderly destruction of cells that are no longer functional or needed. This study defines a critical step in how fiber cells are formed and will spark further investigation into whether alterations in apoptotic enzymes play a role in cataract formation.

STRABISMUS, AMBLYOPIA AND VISUAL PROCESSING

Developmental disorders such as strabismus (misalignment of the eyes) and amblyopia (commonly known as "lazy eye") are among the most common eye conditions that affect the vision of children. In addition, published data estimates that more than three million Americans suffer from visual processing disorders not correctable by glasses or contact lenses.

It is estimated that 20 percent of preschool children ages 3-4 have a treatable

eye condition². While many states are developing guidelines for preschool screening programs, none of the commonly used vision tests have been evaluated in a research-based environment to establish their effectiveness. Initial results from the NEI-sponsored Vision in Preschoolers (VIP) Study found that 11 commonly used screening tests vary widely in identifying children with symptoms of common childhood eye conditions such as amblyopia, strabismus, and significant refractive error. When the best tests are used by highly skilled personnel in a controlled setting, approximately two-thirds of children with one or more of the targeted disorders were identified. These better tests were able to detect 90 percent of children with the most severe visual impairments. The ongoing VIP study will continue to provide state and local agencies with data to select the most effective vision screening exams that are currently available. The VIP study will also help ensure that more children are detected and treated at an early stage when therapy is most effective.

A fundamental issue in neuroscience has been the inability of nerve cells to regenerate. If researchers could develop therapies that overcome this limitation, the deleterious effects of many neurologic diseases and central nervous system (CNS) injuries might be reversed or greatly improved. NEI-supported researchers provoked nerve cell regeneration in rodents by activating a nerve cell's natural growth capacity and using gene therapy to suppress the effects of growth-inhibiting factors. Although vision was not restored, this combined approach stimulated nerve cell regeneration three times greater than prior attempts. Regeneration of the mature CNS would provide an

² Comparison of preschool vision screening tests as administered by licensed eye care professionals in the Vision in Preschoolers Study. *Ophthalmology* 111(4): 637-50, 2004.

opportunity to treat blindness and other neurologic diseases.

HEALTH DISPARITIES

Census 2000 data indicate that 12.5 percent of residents in the United States, or 35 million people, are Latino. Based on these data, it is estimated that by the year 2025, 61.4 million Latinos will live in this country, making this the fastest growing minority population. However, there is little available data to ascertain the prevalence and severity of major eye diseases in this population. Results from the NEI-sponsored *Los Angeles Latino Eye Study* (LALES) suggest that Latinos have some of the highest rates of visual impairment and blindness in the United States. The prevalence of visual impairment and blindness in Hispanics increased with age and women were more frequently affected than men. From a socio-economic perspective, Latinos who were unemployed, divorced or widowed, or less educated had increased rates of visual impairment and blindness. The prevalence statistics, coupled with the socio-economic data from LALES concerning the factors that negatively influence access to health care, will aid the NEI, through its public education programs, to devise strategies that better target these at-risk populations.

NIH ROADMAP

A major theme of the NIH Roadmap, *Re-engineering the Clinical Research Enterprise*, is aimed at accelerating and strengthening the clinical research process. This Roadmap theme is consonant with the NEI's own goal of supporting the highest quality clinical research. The NEI and vision research community have anticipated these opportunities by creating networks such as the Pediatric Eye Disease Investigator

Group (PEDIG) and the newly launched Diabetic Retinopathy Clinical Research Network. Continuation and expansion of these initiatives should facilitate and hasten the translation of research discoveries from the laboratory to the clinic for the benefit of those afflicted with a range of eye disorders and diseases.

NIH NEUROSCIENCE BLUEPRINT

The NIH Neuroscience Blueprint was launched in 2004 to further enhance cooperation among fifteen NIH Institutes and Centers that support research on the nervous system. Blueprint participants are developing an initial set of initiatives focused on tools, resources, and training that can have a quick and substantial impact because each builds on existing programs. Among the Blueprint initiatives for FY 2006, NEI will participate in the systematic development of genetically engineered mouse strains for research on the nervous system and training in neuroimaging and computational biology. NEI will also participate with other Institutes in an initiative to provide specialized neuroscience resources such as animal model, imaging, gene sequencing and screening facilities.

Mr. Chairman, this concludes my prepared statement. I would be pleased to respond to any questions you or other members of the committee may have.