National Eye Institute

Annual Report of Intramural Research

October 1, 1989
to
September 30, 1990

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 EY 00248-03 LI

PERIOD COVERED
October 1, 1989 to September 30, 1990

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Magainin Therapy of Infectious Keratitis

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation.)*

PI:	Rubens Belfort, Jr.	M.D., Ph.D.	Visiting Scientist	LI, NEI
Others:	Robert B. Nussenblatt	M.D.	Clinical Director	LI, NEI
	Rashid Mahdi		Biologist	LI, NEI
	Juan Lopez	M.D.	Visiting Associate	LI, NEI

COOPERATING UNITS *(if any)*

LAB/BRANCH
Laboratory of Immunology

SECTION
Section on Clinical Immunoregulation

INSTITUTE AND LOCATION
NEI, NIH, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
8.0	6.0	2.0

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Studies are being conducted in animals to determine the in vivo activity of a new class of antimicrobial peptides isolated from the skin of the African frog *Xenopus laevis* and called magainins. The family of peptides consists of two closely related peptides, each 23 amino acids, that inhibit growth of numerous species of bacteria and fungi in vitro. An animal model of experimental bacterial keratitis induced in adult New Zealand white rabbits were used to determine the in vivo relevance of the antimicrobial activity of magainins. *Pseudomonas aeruginosa* was primarily considered because it is the most destructive and the most difficult to treat corneal infection in humans. Topical treatment with magainin drops was started immediately after the infection. The control animals were treated with the vehicle or with gentamycin. These studies have shown potential activity of the magainin in the treatment of *Pseudomonas* corneal ulcers. Although the animals could tolerate the treatment well, magainin drops induced severe chemosis with conjunctival hyperhemia which can aggravate the inflammation related to the infection.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 EY 00265-01 LI

PERIOD COVERED
October 1, 1989 to September 30, 1990

TITLE OF PROJECT (*80 characters or less. Title must fit on one line between the borders.*)
T Cell Vaccination in Experimental Autoimmune Uveitis

PRINCIPAL INVESTIGATOR (*List other professional personnel below the Principal Investigator.*) (*Name, title, laboratory, and institute affiliation.*)

PI:	Evelyne Beraud	Ph.D.	Visiting Associate	LI, NEI
Others:	Satoshi Kotake	M.D.	Visiting Fellow	LI, NEI
	Chi-Chao Chan	Ph.D.	Medical Officer	LI, NEI
	Stephen M. Oddo	M.D.	Special Volunteer	LI, NEI
	Rachel R. Caspi	Ph.D.	Visiting Scientist	LI, NEI

COOPERATING UNITS (*if any*)

LAB/BRANCH
Laboratory of Immunology

SECTION
Section on Immunoregulation

INSTITUTE AND LOCATION
NEI, NIH, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
1.41	1.41	0.0

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK (*Use standard unreduced type. Do not exceed the space provided.*)

Autoimmune T lymphocytes can be used under appropriate conditions to induce resistance to the specific autoimmune disease that they usually produce. This practice, termed "T cell vaccination," has been successful in other experimental autoimmune diseases. Our investigations revealed that experimental autoimmune uveitis in rats can be down-regulated by this procedure.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 EY 00245-03 LMOD

PERIOD COVERED
October 1, 1989 to September 30, 1990

TITLE OF PROJECT (*80 characters or less. Title must fit on one line between the borders.*)
Molecular Biology of Cataracts

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation.)*

PI:	Teresa Borras	Ph.D.	Biologist	LMOD, NEI
Others:	Ignacio Rodriguez	Ph.D.	Staff Fellow	LMOD, NEI
	Pedro Gonzalez	Ph.D.	Visiting Fellow	LMOD, NEI
	Carlos Hernandez-Calzadilla	Ph.D.	Special Volunteer	LMOD, NEI

COOPERATING UNITS *(if any)*
Department of Chemistry, Karolinska Institute, Stockholm, Sweden (Dr. Hans Jörnvall, Ph.D.); Diabetes Programs Branch, National Institute of Diabetes and Digestive and Kidney Diseases, NIH (Flora de Pablo, M.D.)

LAB/BRANCH
Laboratory of Mechanisms of Ocular Diseases

SECTION
Section on Cataracts

INSTITUTE AND LOCATION
NEI, NIH, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
3.0	2.8	0.2

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Investigation of the molecular mechanisms of hereditary cataracts using as a model the nuclear hereditary cataract of strain 13/N guinea pigs continues. This year, the focus was on the further characterization of the ζ-crystallin-cDNA present in the lens of the cataractous animal. We developed a new method to construct cDNA libraries from small amounts of tissue and obtained a cDNA library from four heterozygous guinea pig lenses. Screening of this library produced normal and defective ζ-cDNAs. Sequencing of the cataractous ζ-cDNA revealed a 102 bp deletion corresponding exactly to 34 amino acids. The deletion, which does not interfere with the reading frame, is located toward the carboxy end of the protein. Analysis of the genomic DNA from normal and affected animals indicated that the deleted mRNA region is present in the genome of the cataractous animals. This result suggests that a mutation affecting the splicing mechanism is possibly the cause of the mRNA deletion.

In studies of the role of the zeta mRNA in the liver of guinea pigs, we isolated four clones from an adult liver cDNA library. Upon sequencing, two of the clones showed the poly A tail at different positions in the mRNA, confirming different processing of the ζ-crystallin gene in the liver versus the lens. Sequencing the coding region revealed that the amino acids of the liver protein are identical to those of the lens protein.

Having successfully cloned the complete ζ-crystallin gene, we are now analyzing it. Thus far, we have characterized six introns and a very long exon comprising the untranslated 3' end of the mRNA. Sequencing one of the clones has revealed the presence of one exon that corresponds exactly to the deleted region of the zeta mRNA of the cataractous animals.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 EY 00244-03 LSR

PERIOD COVERED
October 1, 1989 to September 30, 1990

TITLE OF PROJECT (*80 characters or less. Title must fit on one line between the borders.*)
Oculomotor and Visual Disorders in Humans

PRINCIPAL INVESTIGATOR (*List other professional personnel below the Principal Investigator.*) (*Name, title, laboratory, and institute affiliation.*)

PI:	James R. Carl	M.D.	Expert	LSR, NEI
Others:	Edmond J. FitzGibbon	M.D.	Senior Staff Fellow	LSR, NEI
	Michael E. Goldberg	M.D.	Chief NMS	LSR, NEI
	Michael J. Todd		Special Volunteer	LSR, NEI

COOPERATING UNITS (*if any*)

LAB/BRANCH
Laboratory of Sensorimotor Research

SECTION
Neuro-Ophthalmologic Mechanisms Section

INSTITUTE AND LOCATION
NEI, NIH, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
1.4	1.4	0.0

CHECK APPROPRIATE BOX(ES)

☒ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK (*Use standard unreduced type. Do not exceed the space provided.*)

Patients with a variety of oculomotor and visual problems were evaluated by clinical examination and high resolution eye movement recordings. Patients with cortical and cerebellar disease were evaluated for amount and type of clinical abnormality. Their eye movements in response to visual stimuli were tested using paradigms devised to test the various oculomotor sub-systems, which were correlated with the clinical findings. Patients with cerebellar deficits showed the expected saccadic dysmetria to visual targets and low gain pursuit. In addition, preliminary data suggest that some cerebellar patients cannot change the gain of their saccades.

Visual motion processing by normal subjects was evaluated using paradigms that tested the subjects' ability to predict future target motion in the generation of saccadic and smooth pursuit eye movements. Smooth pursuit in humans was found to be primarily based on prediction of future target motion and not on negative feedback to reduce retinal slip. A number of patients with unilateral cerebral hemispheric lesions showed pursuit deficits but had normal saccades to moving targets, suggesting that their lesions were not those of visual motion processing but actually of motor control.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 EY 00201-06 LMOD

PERIOD COVERED
October 1, 1989 to September 30, 1990

TITLE OF PROJECT (*80 characters or less. Title must fit on one line between the borders.*)
Structure, Expression and Gene Complexity of Aldose Reductase

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation.)*

PI:	Deborah Carper	Ph.D.	Biologist	LMOD, NEI
Others:	Susan Old	Ph.D.	Staff Fellow	LMOD, NEI
	Caroline Graham	B.A.	Chemist	LMOD, NEI

COOPERATING UNITS *(if any)*
National Children's Medical Research Center, Tokyo, Japan (Chihiro Nishimura, M.D.)

LAB/BRANCH
Laboratory of Mechanisms of Ocular Diseases

SECTION
Section on Cataracts

INSTITUTE AND LOCATION
NEI, NIH, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
3.0	2.0	1.0

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Aldose reductase (AR) is believed to play a major role in the secondary complications of diabetes. Studies in this laboratory have focused on the regulatory properties, potential inhibitor sites, and overall structure of aldose reductase. Better knowledge of these aspects of the protein should help in regulating the undesirable effects of this enzyme. For example, expression of large amounts of recombinant AR protein now set the stage for x-ray crystallography and site-directed mutagenesis studies with the goal of localizing the important functional sites of the molecule. Regulation of the gene for AR is also being studied. Controlling the expression of AR at the gene level may limit the effect this protein has on the accumulation of sorbitol in hyperglycemic conditions.

Rat lens and human placenta AR have been expressed in *Escherichia coli*. The recombinant proteins have been purified and have immunological and kinetic properties similar to their respective tissue AR, including the same substrate and inhibitor profiles.

Characterization of the promoter area of the AR gene shows one TATA and two CCAAT boxes and an approximately 14 kb gene. The nucleotide sequence is nearly complete.

We have found that AR is induced under hypertonic conditions in several cell types, including cultured dog lens epithelial cells and dog kidney endothelial cells. Recently, we have also found an 8- to 16-fold induction of αB-crystallin in these same cells grown in hypertonic media (550 mosM). It appears that AR and αB-crystallin are osmotic stress proteins.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
ZO1 EY 00123-10 OGCS

PERIOD COVERED
October 1, 1989 to September 30, 1990

TITLE OF PROJECT (*80 characters or less. Title must fit on one line between the borders.*)
Clinical Psychophysics of the Visual System

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation.)*

PI:	Rafael Caruso	M.D.	Visiting Scientist	OGCS, NEI
Others:	Muriel I. Kaiser-Kupfer	M.D.	Chief	OGCS, NEI
	Doris J. Collie	A.A.	Clinical Research Technician	OGCS, NEI
	Maria Bankiewicz	M.D.	Visiting Fellow	OGCS, NEI
	Patricia A. Mercer	M.P.A.	Clinical Research Technician	OGCS, NEI

COOPERATING UNITS *(if any)*
Georgetown University Center for Sight, Washington, DC (Despina Koutsandreas, B.S., Leanne Reuter, B.S.) and School of Optometry, University of California at Berkeley (Jay M. Enoch, Ph.D., Richard Knowles).

LAB/BRANCH
Ophthalmic Genetics and Clinical Services Branch

SECTION
Clinical Services Section

INSTITUTE AND LOCATION
NEI, NIH, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.55	0.55	0.0

CHECK APPROPRIATE BOX(ES)

☒ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The visual function of patients with ocular diseases or lesions in the visual pathways and of normal subjects is measured using psychophysical techniques. The data obtained are correlated with those obtained by electrophysiological testing of visual function. The results, which contribute to the diagnosis of ocular and neural disorders that affect vision, are needed to characterize the nature and evolution of the disorders. They are also valuable in the assessment of the effect of treatment regimens on the outcome of these diseases.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: ZO1 EY 00144-09 OGCS

PERIOD COVERED

October 1, 1989 to September 30, 1990

TITLE OF PROJECT (*80 characters or less. Title must fit on one line between the borders.*)

Clinical Electrophysiology of the Visual System

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation.)*

PI:	Rafael Caruso	M.D.	Visiting Scientist	OGCS, NEI
Others:	Muriel I. Kaiser-Kupfer	M.D.	Chief	OGCS, NEI
	Maria A. Bankiewicz	M.D.	Visiting Fellow	OGCS, NEI
	Patricia A. Mercer	M.P.A.	Clinical Research Tech.	OGCS, NEI
	Doris J. Collie	A.A.	Clinical Research Tech.	OGCS, NEI

COOPERATING UNITS *(if any)*

Center for Sight, Georgetown University, Washington, DC (Despina Koustsandreas, B.S., Leanne M. Reuter, B.S.)

LAB/BRANCH

Ophthalmic Genetics and Clinical Services Branch

SECTION

Clinical Services Section

INSTITUTE AND LOCATION

NEI, NIH, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
1.10	0.55	0.55

CHECK APPROPRIATE BOX(ES)

☒ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither

☒ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The visual function of patients with ocular diseases or lesions in the visual pathways and of normal subjects is measured objectively with electrophysiological techniques. These data are correlated with those obtained with psychophysical tests of visual function. The results obtained contribute to the diagnosis of ocular and neural disorders that affect vision, and are needed to characterize their nature and evolution. They are also valuable in the assessment of the effects of different forms of treatment on the outcome of these diseases.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 EY 00257-02 OGCS

PERIOD COVERED

October 1, 1989 to September 30, 1990

TITLE OF PROJECT (*80 characters or less. Title must fit on one line between the borders.*)

Visual Function Diagnosis Service

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation.)*

PI:	Rafael Caruso	M.D.	Visiting Scientist	OGCS, NEI
Others:	Muriel I. Kaiser-Kupfer	M.D.	Chief	OGCS, NEI

COOPERATING UNITS *(if any)*

Center for Sight, Georgetown University, Washington, DC (Donna C. Optican, M.A.S., Despina Koutsandreas, B.S., Leanne M. Reuter, B.S.)

LAB/BRANCH

Ophthalmic Genetics and Clinical Services Branch

SECTION

Eye Services Section

INSTITUTE AND LOCATION

NEI, NIH, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.1	0.1	0.0

CHECK APPROPRIATE BOX(ES)

☒ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

This general service project provides diagnostic support for all research protocols conducted by the clinical sections of the National Eye Institute and other Institutes requiring assessment of visual function. Psychophysical and electrophysiological techniques are used to detect and quantify vision loss due to disorders of the ocular media, uvea, retina, optic nerve, and central visual pathways.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 EY 00184-08 LI

PERIOD COVERED
October 1, 1989 to September 30, 1990

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Cellular Mechanisms in Uveitis

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation.)*

PI:	Rachel R. Caspi	Ph.D.	Visiting Associate	LI, NEI
Others:	Stephen Oddo	M.D.	Special Volunteer	LI, NEI
	Horst Helbig	M.D.	Special Volunteer	LI, NEI
	Sina Bahmanyar	M.D.	Staff Fellow	LI, NEI
	Chi-Chao Chan	M.D.	Medical Officer	LI, NEI
	William Leake	M.S.	Biologist	LI, NEI
	Barry Grubbs	B.S.	Biologist	LI, NEI
	Yujiro Fujino	M.D.	Visiting Fellow	LI, NEI

COOPERATING UNITS *(if any)*

Immunology Research Unit, Klinikum Stegliz, Freie Universitat Berlin, Federal Republic of Germany (Tibor Diamantstein, Ph.D., Head); Arthritis and Rheumatism Branch, National Institute of Arthritis and Musculoskeletal and Skin Diseases (Ronald L. Wilder, Head)

LAB/BRANCH
Laboratory of Immunology

SECTION
Section on Immunoregulation

INSTITUTE AND LOCATION
NEI, NIH, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
1.45	1.43	0.02

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects
☐ (a1) Minors
☐ (a2) Interviews
☐ (b) Human tissues
☒ (c) Neither

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Cellular mechanisms of ocular immunologically mediated disease are being studied in animal models of experimental autoimmune uveoretinitis. In vivo functional long-term T cell lines and T cell clones are developed and maintained in vitro from lymphoid organs of experimental animals immunized with uveitogenic ocular proteins. The phenotype and functional properties of these cells, as well as their interaction with ocular resident cells are being studied. The goal of these studies is to identify the immunoreactive cells and mediators as well as the pathogenic mechanisms involved in the intraocular inflammatory process.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 EY 00258-02 LI

PERIOD COVERED
October 1, 1989 to September 30, 1990

TITLE OF PROJECT (*80 characters or less. Title must fit on one line between the borders.*)
Experimental Autoimmune Uveitis in the Mouse

PRINCIPAL INVESTIGATOR (*List other professional personnel below the Principal Investigator.*) (*Name, title, laboratory, and institute affiliation.*)

PI:	Rachel R. Caspi	Ph.D.	Visiting Associate	LI, NEI
Others:	Barry Grubbs	B.S.	Biologist	LI, NEI
	Chi-Chao Chan	M.D.	Medical Officer	LI, NEI
	William Leake	M.S.	Biologist	LI, NEI
	Benjamin Rubin	M.D.	Staff Fellow	LI, NEI

COOPERATING UNITS (*if any*)
Laboratory of Immunobiology, Rega Instituut, Katholieke Universiteit Leuwen, Belgium (A. Billiau, M.D., Head)

LAB/BRANCH
Laboratory of Immunology

SECTION
Section on Immunoregulation

INSTITUTE AND LOCATION
NEI, NIH, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.84	0.52	0.32

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK (*Use standard unreduced type. Do not exceed the space provided.*)

A new model of experimental autoimmune uveitis (EAU) is being developed in the mouse species, which has until now been considered refractory to induction of ocular autoimmunity. Different retinal antigens, as well as various immunization protocols, are being evaluated for efficacy of EAU induction. The pathological manifestations, disease course, and genetic background of susceptibility to disease in murine EAU are being studied in relationship to the induction protocol. The goal of these studies is to establish in the mouse species a rodent model of EAU that offers some important advantages over other rodent models of EAU. The extensive knowledge of the immunological parameters of the mouse and the availability of genetically defined strains will be of great value in the study of cellular mechanisms and immunogenetics of ocular autoimmune disease.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 EY 00124-10 LRCMB

PERIOD COVERED

October 1, 1989 to September 30, 1990

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Metabolism of the Retina and Pigment Epithelium

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation.)*

PI:	Gerald J. Chader	Ph.D.	Chief	LRCMB, NEI
Others:	Robert Waldbillig	Ph.D.	Expert	LRCMB, NEI
	R. Theodore Fletcher	M.S.	Chemist	LRCMB, NEI

COOPERATING UNITS *(if any)*

LAB/BRANCH

Laboratory of Retinal Cell and Molecular Biology

SECTION

Section on Gene Regulation

INSTITUTE AND LOCATION

NEI, NIH, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
1.7	1.2	0.5

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☒ (b) Human tissues ☐ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Insulin and insulin-like growth factor-1 (IGF-1) are abundant in ocular tissues. They may act as messengers, coding for differentiation in the eye, may be directly or indirectly involved in the visual process in the adult animal or control other important processes such as outer segment renewal. Equally important, receptors for these messengers are highly concentrated in developing retina, pigment epithelium, and sclera, and may play a role in differentiation of these tissues. All the components of an IGF-1 system are present in the retinal interphotoreceptor matrix (IPM). The photoreceptor region thus possesses an IGF-1 autocrine-paracrine system. Abnormal ocular growth during early retinal degeneration and experimental myopia, for example, could be associated with changes in insulin and IGF-1 concentrations, or possibly with binding to receptors and/or binding proteins.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 EY 00148-17 LRCMB

PERIOD COVERED

October 1, 1989 to September 30, 1990

TITLE OF PROJECT (*80 characters or less. Title must fit on one line between the borders.*)

Visual Control Mechanisms

PRINCIPAL INVESTIGATOR (*List other professional personnel below the Principal Investigator.*) (*Name, title, laboratory, and institute affiliation.*)

PI:	Gerald J. Chader	Ph.D.	Chief	LRCMB, NEI
Others:	R. Theodore Fletcher	M.S.	Chemist	LRCMB, NEI
	Lila Inouye	M.D.	Staff Fellow	LRCMB, NEI
	Betty J. Hayden	Ph.D.	Staff Fellow	LRCMB, NEI

COOPERATING UNITS (*if any*)

School of Veterinary Medicine, University of Pennsylvania (G. Aguirre, D.V.M., Ph.D.); Department of Anatomy, Erasmus University, Rotterdam, The Netherlands (S. Sanyal, Ph.D.); Department of Zoology, University of Lund, Lund, Sweden (T. van Veen, Ph.D.)

LAB/BRANCH

Laboratory of Retinal Cell and Molecular Biology

SECTION

Section on Gene Regulation

INSTITUTE AND LOCATION

NEI, NIH, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
2.7	2.2	0.5

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☒ (b) Human tissues ☐ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK (*Use standard unreduced type. Do not exceed the space provided.*)

Retinitis pigmentosa and retinoblastoma are important hereditary diseases that usually cause retinal dysfunction in the first decade or two of life. Thus, it is important to study genes and their protein products specific to the retina that may be abnormal either in function or concentration in these retinal diseases. As a model system for photoreceptor-specific proteins, we are studying the regulation of expression of interphotoreceptor retinoid-binding protein (IRBP), a retinoid-transport protein synthesized by the photoreceptor neuron and secreted into the interphotoreceptor matrix. In a second study, we have found that a specific cAMP-dependent protein kinase exhibits a defect in synthesis in human retinoblastoma tumor cells that is similar in osteosarcoma. Such a defect could cause the uncontrolled growth of retinoblastoma cells. In a third study, we have excellent new evidence for the general hypothesis of "transdifferentiation" because we have found that retinoblastoma cells highly express specific lens crystallins in vivo and in vitro.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 EY 00222-05 LI

PERIOD COVERED
October 1, 1989 to September 30, 1990

TITLE OF PROJECT (*80 characters or less. Title must fit on one line between the borders.*)
Immunopathology in the Eyes with Experimental Autoimmune Uveitis (EAU)

PRINCIPAL INVESTIGATOR (*List other professional personnel below the Principal Investigator.*) (*Name, title, laboratory, and institute affiliation.*)

PI:	Chi-Chao Chan	M.D.	Medical Officer	LI, NEI
Others:	Robert B. Nussenblatt	M.D.	Clinical Director	NEI
	Igal Gery	Ph.D.	Head, Section on Experimental Immunology	LI, NEI
	Rachel R. Caspi	Ph.D.	Visiting Associate	LI, NEI
	Ming Ni	M.D.	Visiting Fellow	LI, NEI

COOPERATING UNITS (*if any*)
University of Tokyo, School of Medicine (Manabu Mochizuki, M.D.); University of Montreal, School of Medicine (Francois G. Roberge, M.D.)

LAB/BRANCH
Laboratory of Immunology

SECTION
Section on Immunoregulation

INSTITUTE AND LOCATION
NEI, NIH, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
1.15	1.15	0.0

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK (*Use standard unreduced type. Do not exceed the space provided.*)

Identity and topographic localization of immunocompetent cells and alteration of surface markers on ocular resident cells in rodents with experimental autoimmune uveoretinitis (EAU) were analyzed by immunohistochemical studies. In the early stage of EAU, T helper/inducers were the predominant cells in the eye; in the late stage, a relative increase of T suppressor/cytotoxic cells was observed. T lymphocyte specificity is directed to small fragments of antigen bound to cell surface major histocompability complex (MHC) molecules which are presented on the surface of specialized antigen-presenting cells. Expression of MHC class II antigens was observed on ocular resident cells such as RPE, retinal endothelium, keratocytes, fibroblasts, and ciliary epithelium. Both the infiltrating cell subpopulation and the expression of class II antigens on ocular resident cells can be altered by various immunomodulating agents, some of which—Qingaining, FK506, 15-deoxyspergualine, interleukin 2-PE40, and S-antigen—were evaluated for their immunopathological effects on EAU.

Clinical and immunopathologic examinations of the eyes of mice with EAU demostrated a chronic relapsing focal granulomatous inflammation and vasculitis in the retina and choroid. Development of subretinal neovascularization may also occur. The infiltrating cells were mainly macrophages and T helpers/inducers (CD4). The expression of MHC class II antigens is confined to ocular resident cells immediately at the inflammatory sites. Due to the chronicity and recurrence of EAU, the mouse may serve as a better model for human ocular inflammation.

Experimental endotoxin-induced uveitis (EIU) is a model for anterior uveitis in humans. The mechanism of this inflammation is still unclear. Because recently it has been suggested that activation of phospholipase A2 may play a role in the initiation and propagation of this disease, we studied the effect of a novel synthetic peptide and a PLA2 inhibitor, antiflammin, on EIU in rats.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 EY 00224-04 LI

PERIOD COVERED

October 1, 1989 to September 30, 1990

TITLE OF PROJECT (*80 characters or less. Title must fit on one line between the borders.*)

Sympathetic Ophthalmia: Immunopathological Findings

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation.)*

PI:	Chi-Chao Chan	M.D.	Medical Officer	LI, NEI
Others:	Robert B. Nussenblatt	M.D.	Clinical Director	NEI
	Alan G. Palestine	M.D.	Head, Section on Clinical Immunology	LI, NEI
	Toichiro Kuwabara	M.D.	Chief, Laboratory of Ophthalmic Pathology	LI, NEI

COOPERATING UNITS *(if any)*

LAB/BRANCH

Laboratory of Immunology

SECTION

Section on Immunoregulation

INSTITUTE AND LOCATION

NEI, NIH, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.12	0.12	0.0

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☒ (b) Human tissues ☐ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

This project has been terminated.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 EY 00225-05 LI

PERIOD COVERED
October 1, 1989 to September 30, 1990

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Post-Inflammatory Complications in Uveitis

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation.)*

PI:	Chi-Chao Chan	M.D.	Medical Officer	LI, NEI
Others:	Robert B. Nussenblatt	M.D.	Clinical Director	NEI
	Rachel R Caspi	Ph.D.	Visiting Associate	LI, NEI

COOPERATING UNITS *(if any)*
Bascom Palmer Eye Institute (Donald G. Puro, M.D.); University of Montreal, School of Medicine (Francois G. Roberge, M.D.)

LAB/BRANCH
Laboratory of Immunology

SECTION
Section on Immunoregulation

INSTITUTE AND LOCATION
NEI, NIH, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.26	0.26	0.0

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☒ (b) Human tissues ☐ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Postinflammatory complications in uveitis patients include destruction of photoreceptors, gliosis, choroidal scar, and formations of cyclitic and pupillary membranes, snowbanking and epiretinal membrane. Postinflammatory membrane composition may play an important role in the cause of these complications associated with uveitis. In this study, eyes enucleated from patients with end stages of chronic anterior uveitis (formation of cyclitic and pupillary membranes) and posterior uveitis (formation of cyclitic and epiretinal membranes) were evaluated immunohistochemically. Glial cells and proliferating Müller cells were the major cellular components in these membranes. Basement membrane-like components and new collagens were the major extracellular membrane components. In vitro studies of the Müller cell may help to elucidate the mechanism of action in its involvement of uveoretinitis.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 EY 00226-04 LI

PERIOD COVERED
October 1, 1989 to September 30, 1990

TITLE OF PROJECT (*80 characters or less. Title must fit on one line between the borders.*)
Immunopathology of Ocular Onchocerciasis and Other Parasitic Diseases

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation.)*

PI:	Chi-Chao Chan	M.D.	Medical Officer	LI, NEI
Others:	Robert B. Nussenblatt	M.D.	Clinical Director	NEI

COOPERATING UNITS *(if any)*
National Institute of Allergy and Infectious Diseases, Clinical Parasitic Diseases Section (Eric A. Ottesen, M.D.); World Health Organization (K. Awadzi, M.D.)

LAB/BRANCH
Laboratory of Immunology

SECTION
Section on Immunoregulation

INSTITUTE AND LOCATION
NEI, NIH, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.33	0.33	0.0

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☒ (b) Human tissues ☐ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

This project has been terminated.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 EY 00241-04 LI

PERIOD COVERED

October 1, 1989 to September 30, 1990

TITLE OF PROJECT (*80 characters or less. Title must fit on one line between the borders.*)

Immunopathology of Ocular Diseases in Humans

PRINCIPAL INVESTIGATOR (*List other professional personnel below the Principal Investigator.*) (*Name, title, laboratory, and institute affiliation.*)

PI:	Chi-Chao Chan	M.D.	Medical Officer	LI, NEI
Others:	Robert B. Nussenblatt	M.D.	Clinical Director	NEI
	Ming Ni	M.D.	Visiting Fellow	LI, NEI
	Marc de Smet	M.D.	Visiting Associate	LI, NEI
	Benjamin Rubin	M.D.	Senior Staff Fellow	LI, NEI

COOPERATING UNITS (*if any*)

University of Minnesota, Department of Ophthalmology (Edward J. Holland, M.D.); Institute of Ophthalmology, University of London (Susan Lightman, M.D.); L'Hôpital de la Pitié, Paris, France (Phuc LeHoang, M.D.)

LAB/BRANCH

Laboratory of Immunology

SECTION

Section on Immunoregulation

INSTITUTE AND LOCATION

NEI, NIH, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.82	0.82	0.0

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☒ (b) Human tissues ☐ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK (*Use standard unreduced type. Do not exceed the space provided.*)

Specimens from human ocular tissues with various diseases, such as uveitis, conjunctival and corneal diseases, metabolic genetic diseases, and tumors were studied using immunoperoxidase technique as well as light and electron microscopic evaluation. In uveitis, immunocompetent cells and lymphokines are critical in the reflection of clinical diagnosis, disease course, and prognosis. In non-uveitis conditions, alteration of cellular membrane surface markers and intracytoskeleton on the ocular resident cells may imply damage and abnormalities in these diseases. Elucidating the role of the relationships between infiltrating inflammatory cells and other cells in the clinical behavior of various diseases will increase our understanding of human ocular disorders.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 EY 00264-01 LI

PERIOD COVERED

October 1, 1989 to September 30, 1990

TITLE OF PROJECT (*80 characters or less. Title must fit on one line between the borders.*)

Cytokines and Ocular Antigens in the Eye

PRINCIPAL INVESTIGATOR (*List other professional personnel below the Principal Investigator.*) (*Name, title, laboratory, and institute affiliation.*)

PI:	Chi-Chao Chan	M.D.	Medical Officer	LI, NEI
Others:	Robert B. Nussenblatt	M.D.	Clinical Director	NEI
	Igal Gery	Ph.D.	Head, Section on Experimental Immunology	LI, NEI
	Ming Ni	M.D.	Visiting Fellow	LI, NEI
	Quian Li	M.D.	Visiting Fellow	LI, NEI

COOPERATING UNITS (*if any*)

Laboratory of Immunoregulation, National Cancer Institute (Kouji Matsushima, M.D., Ph.D.)

LAB/BRANCH

Laboratory of Immunology

SECTION

Section on Immunoregulation

INSTITUTE AND LOCATION

NEI, NIH, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
1.7	1.7	0.0

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☒ (b) Human tissues ☒ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK (*Use standard unreduced type. Do not exceed the space provided.*)

Cytokines are communication signals between leukocytes and organ resident cells. Interleukin 1 (IL-1) a pleiotropic cytokine produced by many cell types, most notably macrophages, can stimulate a general inflammatory reaction by causing the activation of a variety of cells which then, among their other functions, release a cascade of other cytokines. One of them is Interleukin 8 (IL-8), which has more direct action of activating the neutrophils and T lymphocytes. Intravitreal injection of IL-8 was compared to that of IL-1 in both Lewis and Fischer rats. IL-8 induced milder inflammation than IL-1. Lewis rats show a higher inflammatory response to the injections than do Fischer rats. These data suggest that IL-8 may be active as one component in neutrophil-mediated ocular disease. Further understanding of the role of each cytokine in ocular inflammation, will require study of the production of endogenous cytokines in the eye.

Ocular antigens play an important role in autoimmune diseases. S-antigen (S-Ag), a retinal soluble antigen, can induce experimental autoimmune uveoretinitis. In situ, study of S-Ag expression in human fetal eyes demonstrated an embryonic development pattern similar to that of other mammals. The expression of S-Ag in RNA of non-retinal fetal tissues may suggest its involvement in certain ocular diseases. Lens crystallin proteins α, β and γ were also found in human fetal iris and retinoblastoma cells. The roles of their expression in non-lenticular tissue require further investigation.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 EY 00251-03 LMDB

PERIOD COVERED
October 1, 1989 to September 30, 1990

TITLE OF PROJECT (*80 characters or less. Title must fit on one line between the borders.*)
Regulation of the αA-Crystallin Promoter and Its Use for Genetically Engineering the Lens

PRINCIPAL INVESTIGATOR (*List other professional personnel below the Principal Investigator.*) (*Name, title, laboratory, and institute affiliation.*)

PI:	Ana B. Chepelinsky	Ph.D.	Research Biologist	LMDB, NEI
Others:	Teresa I. Limjoco	M.D.	Visiting Fellow	LMDB, NEI
	Jorge M. Sztein	D.V.M.	Visiting Fellow	LMDB, NEI
	Graeme J. Wistow	Ph.D.	Visiting Scientist	LMDB, NEI

COOPERATING UNITS (*if any*)

Gerontological Research Unit, Natl. Inst. of Health and Medical Research, Paris (Yves Courtois, Ph.D., Maryvonne Laurent, Ph.D.); Imperial Cancer Research Fund, London (Clive Dickson, Ph.D., Susan Jamieson, Ph.D.); Lab. of Neurobiology, Natl. Inst. of Neurological Diseases and Stroke (Carolyn A. Bondy, M.D.)

LAB/BRANCH
Laboratory of Molecular and Developmental Biology

SECTION
Section on Molecular Genetics

INSTITUTE AND LOCATION
NEI, NIH, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
2.3	2.3	0.0

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK (*Use standard unreduced type. Do not exceed the space provided.*)

The *cis* regulatory elements of the αA-crystallin promoter responsible for the lens-specific expression of this gene and for its developmental regulation were further characterized. The results indicated that sequence -88 to +46 of the murine αA-crystallin gene contains the *cis* regulatory elements for lens-specific expression and for correct developmental regulation of this gene in vivo. The αA-crystallin promoter (-366/+46) which has become a very useful tool to target gene expression to the lens, is being used to study how foreign gene expression in the lens affects the phenotype of the lens or the rest of the eye.

Aldose reductase mRNA levels were found to be significantly increased in the lens of a transgenic mouse line that carries the αA-crystallin promoter fused to the SV40 large T antigen. That mouse line develops a complete cataract as early as embryonic day 14.

Several fusion genes containing the αA-crystallin promoter fused to growth factors, oncogenes, interferon, or ribozymes are currently being used to study the effect of their expression in the eye.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 EY 00253-02 LMDB

PERIOD COVERED
October 1, 1989 to September 30, 1990

TITLE OF PROJECT (*80 characters or less. Title must fit on one line between the borders.*)
Regulation of Expression of Lens Fiber Membrane Genes

PRINCIPAL INVESTIGATOR (*List other professional personnel below the Principal Investigator.*) (*Name, title, laboratory, and institute affiliation.*)

PI:	Ana B. Chepelinsky	Ph.D.	Research Biologist	LMDB, NEI
Others:	M. Michele Pisano	Ph.D.	Staff Fellow	LMDB, NEI
	Teresa I. Limjoco	M.D.	Visiting Fellow	LMDB, NEI
	Gabriela M. Tobal		Summer Student	LMDB, NEI

COOPERATING UNITS (*if any*)
Harvard Medical School (David Paul, Ph.D.)

LAB/BRANCH
Laboratory of Molecular and Developmental Biology

SECTION
Section on Molecular Genetics

INSTITUTE AND LOCATION
NEI, NIH, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
1.8	1.8	0.0

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☒ (b) Human tissues ☐ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK (*Use standard unreduced type. Do not exceed the space provided.*)

This project studies the regulation of expression of genes encoding lens fiber membrane proteins that may be involved in cell-cell communication. Particular emphasis is put on the study of major intrinsic protein (MIP). We have cloned the MIP gene and have begun to analyze the *cis* regulatory elements responsible for its lens-specific expression.

A recombinant clone containing the human MIP gene was isolated from a human leukocyte genomic library using a bovine MIP cDNA (Gorin et al., *Cell* 39:49, 1984). This is the first lens-specific non-crystallin gene that has been cloned. Sequencing data indicates that this gene is 3.6 kbp long and contains four exons. The 5' flanking sequence of the gene contains a TATA box, two CCAAT boxes, and potential binding sites for the transcription factors Sp1, NF-kB, and glucocorticoid receptor. Alu repeats are present in the 5' flanking region and third intron of the gene. In order to characterize the elements regulating expression of the MIP gene, 5' flanking DNA fragments of different lengths, synthesized by the polymerase chain reaction, were introduced upstream of the chloramphenicol acetyltransferase (CAT) reporter gene.

Transfection of these gene constructs into explanted embyonic chicken lens epithelia and analysis of transient gene expression indicated that 253 bp of 5' flanking sequence contains an active promoter. The human MIP gene promoter functions with approximately the same efficiency as the promoter for the mouse γ2 crystallin gene (also expressed specifically in lens fibers). We are presently mapping the various *cis* regulatory elements responsible for the discrete temporal and tissue-specific expression of the MIP gene during lens fiber cell differentiation.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 EY 00254-01 LMDB

PERIOD COVERED
October 1, 1989 to September 30, 1990

TITLE OF PROJECT (*80 characters or less. Title must fit on one line between the borders.*)
Regulatory Elements of the Opsin Promoter

PRINCIPAL INVESTIGATOR (*List other professional personnel below the Principal Investigator.*) (*Name, title, laboratory, and institute affiliation.*)

PI:	Ana B. Chepelinsky	Ph.D.	Research Biologist	LMDB, NEI
Others:	Teresa I. Limjoco	M.D.	Visiting Fellow	LMDB, NEI

COOPERATING UNITS (*if any*)

LAB/BRANCH
Laboratory of Molecular and Developmental Biology

SECTION
Section of Molecular Genetics

INSTITUTE AND LOCATION
NEI, NIH, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.35	0.35	0.0

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
- ☐ (a1) Minors
- ☐ (a2) Interviews

SUMMARY OF WORK (*Use standard unreduced type. Do not exceed the space provided.*)

This project has been terminated.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 EY 00259-01 LMDB

PERIOD COVERED

October 1, 1989 to September 30, 1990

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Molecular Biology of the Cornea

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation.)*

PI:	R. Andrew Cuthbertson	M.B. B.S., Ph.D.	Visiting Associate	LMDB, NEI
Others:	Joram Piatigorsky	Ph.D.	Chief	LMDB, NEI

COOPERATING UNITS *(if any)*

LAB/BRANCH

Laboratory of Molecular and Developmental Biology

SECTION

Section on Molecular Genetics

INSTITUTE AND LOCATION

NEI, NIH, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.8	0.8	0.0

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The cornea depends on a high degree of cellular differentiation to fulfill its unique functions as an optically clear barrier and refractive surface at the front of the eye. The deceptively simple overall structure of the corneal epithelium, stroma, and endothelium is ultimately dictated by the spatial and temporal regulation of gene expression in these cells. The molecular events that control phenotypic expression in the layers of the cornea are very poorly understood; we have therefore undertaken to isolate and characterize cDNAs that are preferentially (and perhaps uniquely) expressed in the corneal epithelium and endothelium, using subtractive hybridization and subsequent differential screening.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 EY 00062-14 OGCS

PERIOD COVERED

October 1, 1989 to September 30, 1990

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Irido-Corneal-Endothelial (ICE) Syndrome

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation.)*

PI:	Manuel B. Datiles	M.D.	Visiting Scientist	OGCS, NEI
Others:	Muriel I. Kaiser-Kupfer	M.D.	Chief	OGCS, NEI
	Lessie McCain	R.N.	Nurse Specialist	OGCS, NEI

COOPERATING UNITS *(if any)*

LAB/BRANCH

Ophthalmic Genetics and Clinical Services Branch

SECTION

Section on Cataract and Corneal Diseases

INSTITUTE AND LOCATION

NEI, NIH, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.15	0.10	0.05

CHECK APPROPRIATE BOX(ES)

☒ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

This project was formerly titled "Progressive Essential Iris Atrophy." Patients with progressive essential iris atrophy with or without associated corneal disease are being recruited. Information is being gathered to evaluate the clinical features and course of the disease process and to investigate aqueous humor dynamics in both affected and unaffected eyes.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 EY 00187-07 OGCS

PERIOD COVERED
October 1, 1989 to September 30, 1990

TITLE OF PROJECT (*80 characters or less. Title must fit on one line between the borders.*)
The Effects of Corneal Contact Lenses on the Cornea

PRINCIPAL INVESTIGATOR (*List other professional personnel below the Principal Investigator.*) (*Name, title, laboratory, and institute affiliation.*)

PI:	Manuel B. Datiles	M.D.	Visiting Scientist	OGCS, NEI
Others:	Maria Elena Sibug	M.D.	Visiting Fellow	OGCS, NEI
	Lessie McCain	R.N.	Nurse Specialist	OGCS, NEI
	Juan Lopez	M.D.	Visiting Associate	OGCS, NEI

COOPERATING UNITS (*if any*)

LAB/BRANCH
Ophthalmic Genetics and Clinical Services Branch

SECTION
Section on Cataract and Corneal Diseases

INSTITUTE AND LOCATION
NEI, NIH, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.65	0.40	0.25

CHECK APPROPRIATE BOX(ES)

☒ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK (*Use standard unreduced type. Do not exceed the space provided.*)

Short-term as well as long-term effects of contact lens wear on the cornea are being investigated. Changes in corneal curvature, changes in corneal epithelial morphology, and changes in corneal endothelial cell morphology are being studied by specular microscopy.

Analysis of the data obtained will help us understand the dynamics involved in the interaction between a contact lens and the cornea, the risk to corneal tissues, and how a systemic or local disorder may increase these risks.

Animal models showing abnormalities in corneal endothelium similar to those in long-term contact lens wearers are also being explored. These are diabetic and galactosemic animal models. Treatment with aldose reductase inhibitors helps prevent these corneal abnormalities.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 EY 00188-07 OGCS

PERIOD COVERED
October 1, 1989 to September 30, 1990

TITLE OF PROJECT (*80 characters or less. Title must fit on one line between the borders.*)
Documentation and Monitoring of Opacities in the Human Lens

PRINCIPAL INVESTIGATOR (*List other professional personnel below the Principal Investigator.*) (*Name, title, laboratory, and institute affiliation.*)

PI:	Manuel B. Datiles	M.D.	Visiting Scientist	OGCS, NEI
Others:	Rafael C. Caruso	M.D.	Visiting Scientist	OGCS, NEI
	Benjamin Magno	M.D.	Visiting Associate	OGCS, NEI
	James Schumer	M.D.	Staff Fellow	OGCS, NEI
	Maria E. Sibug	M.D.	Visiting Scientist	OGCS, NEI
	Lessie McCain	R.N.	Clinical Technician	OGCS, NEI
	Juan Lopez	M.D.	Visiting Associate	OGCS, NEI

COOPERATING UNITS (*if any*)

Image Processing and Analysis Laboratory, Division of Computer Research and Technology, NIH (Benes Trus, Ph.D., Chief); Clinical and Diagnostic Trials Section, National Cancer Institute, NIH (Sylvan Green, M.D.); Nuclear Medicine, Clinical Center, NIH (Joseph Frank, M.D.)

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Ophthalmic Genetics and Clinical Services Branch

SECTION
Section on Cataract and Corneal Diseases

INSTITUTE AND LOCATION
NEI, NIH, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
1.275	1.250	0.025

CHECK APPROPRIATE BOX(ES)

☒ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK (*Use standard unreduced type. Do not exceed the space provided.*)

This project uses different systems to develop objective and subjective methods to monitor and document opacities in the human lens. We are actively recruiting patients with and without cataracts for reproducibility studies on the objective system—the Scheimpflug cameras (Zeiss and Topcon), retroillumination camera (Neitz), specular microscope (Keeler) and laser light-scattering spectroscope (Kowa). Tests of other systems will use sound (ultrasonography) and nuclear magnetic resonance (magnetic resonance imaging). Our study of subjective systems or methods such as the effects of cataracts on visual perception, contrast sensitivity, and glare may be useful in identifying additional parameters for monitoring cataract presence, progression, or regression.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 EY 00212-05 OGCS

PERIOD COVERED
October 1, 1989 to September 30, 1990

TITLE OF PROJECT (*80 characters or less. Title must fit on one line between the borders.*)
Model Program for Collaboration Between Cataract Surgeons and Ophthalmic Researchers

PRINCIPAL INVESTIGATOR (*List other professional personnel below the Principal Investigator.*) (*Name, title, laboratory, and institute affiliation.*)

PI:	Manuel B. Datiles	M.D.	Visiting Scientist	OGCS, NEI
Others:	D. James Schumer	M.D.	Staff Fellow	OGCS, NEI
	Benjamin Magno	M.D.	Visiting Associate	OGCS, NEI
	Juan Lopez	M.D.	Visiting Associate	OGCS, NEI

COOPERATING UNITS (*if any*)

LAB/BRANCH
Ophthalmic Genetics and Clinical Services Branch

SECTION
Section on Cataract and Corneal Diseases

INSTITUTE AND LOCATION
NEI, NIH, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.95	0.95	0.0

CHECK APPROPRIATE BOX(ES)

☒ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
- ☐ (a1) Minors
- ☐ (a2) Interviews

SUMMARY OF WORK (*Use standard unreduced type. Do not exceed the space provided.*)

There is an extreme scarcity of human cataract material because of an abrupt shift of cataract surgical technique from intracapsular (intact lens) to extracapsular (fragmented lens), primarily because of advent of the use of intraocular lens. We are exploring ways by which fragmented lens materials can be maximally used in cataract basic research through close collaboration with cataract surgeons and basic researchers and through modification of techniques by both groups.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 EY 00249-02 LI

PERIOD COVERED

October 1, 1989 to September 30, 1990

TITLE OF PROJECT (*80 characters or less. Title must fit on one line between the borders.*)

Cytokines in Human Intraocular Fuids

PRINCIPAL INVESTIGATOR (*List other professional personnel below the Principal Investigator.*) (*Name, title, laboratory, and institute affiliation.*)

PI:	Janet L. Davis	M.D.	Senior Staff Fellow	LI, NEI
Others:	Robert B. Nussenblatt	M.D.	Clinical Director	NEI

COOPERATING UNITS (*if any*)

Eye Research Institute, Boston, MA (Alex E. Jalkh, M.D., Charles Schepens, M.D.); University of Miami, Miami, FL (Harry W. Flynn, Jr., M.D.)

LAB/BRANCH

Laboratory of Immunology

SECTION

Section on Immunoregulation

INSTITUTE AND LOCATION

NEI, NIH, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.32	0.32	0.0

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☒ (b) Human tissues ☐ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK (*Use standard unreduced type. Do not exceed the space provided.*)

This project has been terminated.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 EY 00065-13 IRP

PERIOD COVERED

October 1, 1989 to September 30, 1990

TITLE OF PROJECT (*80 characters or less. Title must fit on one line between the borders.*)

Physiological Studies of the Primate Visual System

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation.)*

PI: Francisco M. de Monasterio M.D., D.Sc. Medical Officer IRP, NEI

COOPERATING UNITS *(if any)*

LAB/BRANCH

Office of the Director of Intramural Research

SECTION

INSTITUTE AND LOCATION

NEI, NIH, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.3	0.3	0.0

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

This project involves the study of the physiological organization of neurons of the visual system of primates, with emphasis on the chromatic properties of color-opponent ganglion cells and of cells from the lateral geniculate nucleus and the primary visual cortex of macaques.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 EY 00122-10 IRP

PERIOD COVERED

October 1, 1989 to September 30, 1990

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Anatomical Studies of the Primate Visual System

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation.)*

PI: Francisco M. de Monasterio M.D., D.Sc. Medical Officer IRP, NEI

COOPERATING UNITS *(if any)*

LAB/BRANCH

Office of the Director of Intramural Research

SECTION

INSTITUTE AND LOCATION

NEI, NIH, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.7	0.7	0.0

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☒ (b) Human tissues ☐ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

This project involves the study of the anatomical properties and organization of cells in the visual system of primates, with emphasis on the retina and the visual cortex. The studies include (1) the electroretinogram (ERG) mediated by blue-sensitive cone signals before and after the staining of putative blue-sensitive cones by tissue-reactive dyes, (2) the distribution patterns of cones in the human donor retinas with a diagnosis of diabetic retinopathy, and (3) the anatomical association of outer-retinal cells selectively stained with tissue-reactive dyes.

(1) Evaluation of the spectral properties of the macaque monkey cones selectively stained with tissue-reactive dyes, which have been tentatively identified as the "blue" cones, has been hindered by the fact that the dye itself alters the spectral transmission of the ocular media. The study of ERG sensitivity of the same animals before and after the selective labeling of the putative blue cones with the clear monochlorotriazinyl reagent Sandospace S, which can be marked with a secondary dye, has continued. This reagent produced a sharp reduction of the test and field sensitivity of the ERG b-wave mediated by blue cone signals, providing further evidence that the above tentative identification is correct.

(2) Evidence of a cone population with a point pattern resembling that of cones selectively stained by tissue-reactive dyes was obtained in initial studies of the retinas of diabetic human donors. Although such dyes were not injected into the eyes of these donors, in vitro staining with more conventional dyes showed a differential receptor labeling, in which cones with the pattern mentioned above were found to be more densely stained than other cones.

(3) A systematic light-microscope study of the anatomical association of blue cones and horizontal and bipolar cells that have been selectively stained by several tissue-reactive dyes has been initiated in the macaque retina. These studies provide information on the probable retinal circuitry of the blue-sensitive cone pathway of primate retina.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: ZO1 EY 00218-05 LI

PERIOD COVERED

October 1, 1989 to September 30, 1990

TITLE OF PROJECT (*80 characters or less. Title must fit on one line between the borders.*)

Acquired Immune Deficiency Syndrome

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation.)*

PI:	Marc D. de Smet	M.D.	Visiting Scientist	LI, NEI
Others:	Robert B. Nussenblatt	M.D.	Clinical Director	NEI
	Benjamin I. Rubin	M.D.	Senior Staff Fellow	LI, NEI
	Scott Whitcup	M.D.	Senior Staff Fellow	LI, NEI
	Rubens Belfort	M.D.	Visiting Scientist	LI, NEI
	Juan Lopez	M.D.	Visiting Fellow	LI, NEI

COOPERATING UNITS *(if any)*

Lab. of Cellular and Molecular Biology, Natl. Cancer Inst. (Dharam Ablashi, D.V.M.); Dept. of Critical Care Medicine, Clinical Center (Henry Masur, M.D.); Lab. of Tumor Cell Biology, Natl. Cancer Inst. (Robert C. Gallo, M.D.); Lab. of Immunoregulation, Natl. Inst. of Allergy and Infectious Diseases (H. Clifford Lane, M.D.); Natl. Inst. of Allergy and Infectious Diseases (Anthony Fauci, M.D.); Pediatric Branch, Natl. Cancer Inst. (Phil A. Pizzo, M.D.)

LAB/BRANCH

Laboratory of Immunology

SECTION

Section on Immunoregulation

INSTITUTE AND LOCATION

NEI, NIH, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
1.2	1.2	0.0

CHECK APPROPRIATE BOX(ES)

☒ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Patients with AIDS are at risk of developing significant ocular problems, some of which can lead to blindness. Left untreated, CMV retinitis is a major cause of blindness in AIDS patients. We have looked at the effect of the new antiviral drug foscarnet and determined its ability to inhibit progression of the virus. We have also started investigating the usefulness of adjunctive therapy with laser photocoagulation in preventing progression of the disease.

In the course of our studies, we have also identified new manifestations of known infectious agents in patients with AIDS, namely, HZV retinitis. In conjunction with the Pediatric Branch of the National Cancer Institute, we have been following about 125 children with symptomatic HIV to determine the natural history of the disease and to determine the probability of significant ocular disease in these children.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 EY 00266-01 LI

PERIOD COVERED
October 1, 1989 to September 30, 1990

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Characterization of Immune Responses to S-antigen

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation.)*

PI:	Marc D. de Smet	M.D.	Visiting Scientist	LI,NEI
Other:	Igal Gery	Ph.D.	Head, Section on Experimental Immunology	LI, NEI
	Robert B. Nussenblatt	M.D.	Clinical Director	NEI
	Scott Whitcup	M.D.	Senior Staff Fellow	LI,NEI
	Xiao Yan Zhang	M.D.	Guest Worker	LI,NEI

COOPERATING UNITS *(if any)*
Department of Ophthalmology, Kurume Univ., Japan (M. Mochizuki, M. D.); INSERM-86, Laboratory of Ocular Immunopathology, Paris (J-P Faure, Ph.D.); Hadassah Hospital, Jerusalem, Israel.

LAB/BRANCH
Laboratory of Immunology

SECTION
Section on Clinical Immunoregulation

INSTITUTE AND LOCATION
NEI, NIH, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.44	0.44	0.0

CHECK APPROPRIATE BOX(ES)
☒ (a) Human subjects ☒ (b) Human tissues ☐ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Experimental autoimmune uveitis (EAU) is a disease model induced in genetically susceptible animals by injection of various soluble retinal antigens in adjuvant. The best characterized of these antigens is S-Ag. The uveitis it induces is critically dependent on the presence of activated T cells. It has been established that T cells become activated as a result of their interaction with primed antigen-presenting cells, a process through which the immunogenic protein is internalized and partially digested. Fragments from the original protein are then reexpressed on the cell surface where they can interact with T cells. Work is being carried out to identify and characterize those fragments which are responsible for the clinical response in animals as well as in humans.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 EY 00267-01 LI

PERIOD COVERED
October 1, 1989 to September 30, 1990

TITLE OF PROJECT (*80 characters or less. Title must fit on one line between the borders.*)
Modulation of Immune Functions Using the Immunotoxin IL2-PE40

PRINCIPAL INVESTIGATOR (*List other professional personnel below the Principal Investigator.*) (*Name, title, laboratory, and institute affiliation.*)

PI:	Marc D. de Smet	M.D.	Visiting Scientist	LI,NEI
Others:	Stefan S. Thurau	M.D.	Special Volunteer	LI,NEI
	Carl P. Herbort	M.D.	Special Volunteer	LI,NEI
	Robert B. Nussenblatt	M.D.	Clinical Director	NEI

COOPERATING UNITS (*if any*)
Laboratory of Molecular Biology, National Cancer Institute (Ira Pastan, M.D.); University of Montreal, School of Medicine (Francois G. Roberge, M.D.)

LAB/BRANCH
Laboratory of Immunology

SECTION
Section on Immunoregulation

INSTITUTE AND LOCATION
NEI, NIH, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.6	0.6	0.0

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK (*Use standard unreduced type. Do not exceed the space provided.*)

IL-2-PE40 is a recombinant chimeric protein composed of interleukin-2 (IL-2) and of *Pseudomonas* endotoxin (PE40), minus its cell-binding domain. This toxin, once internalized, kills cells by irreversibly inhibiting protein synthesis. Hence, cells bearing IL-2 receptors on their surface, which are prime targets for this toxin, can be effectively removed from an organism without producing too many untoward side effects.

In experimental autoimmune uveitis (EAU), T cells play a major role. Once activated, these T cells express on their cell surface IL-2 receptors, which can be targeted by the chimeric toxin and eliminated. We have demonstrated that this toxin is able to reduce significantly the incidence and severity of experimentally induced uveitis. IL-2PE40 is also able to reduce the incidence and severity of corneal graft rejection following systemic administration of the toxin.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 EY 00231-04 LI

PERIOD COVERED
October 1, 1989 to September 30, 1990

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Cell Surface Antigens on Retinoblastoma Cells

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation.)*

PI:	Barbara Detrick	Ph.D.	Expert	LI, NEI
Others:	John J. Hooks	Ph.D.	Head, Section on Immunology and Virology	LI, NEI
	Gerald J. Chader	Ph.D.	Chief	LRCMB, NEI
	Caroline Percopo	B.S.	Biologist	LI, NEI

COOPERATING UNITS *(if any)*
Tumor Biology Section, Laboratory of Biology, National Cancer Institute (Charles Evans, M.D.); Walter Reed Army Medical Center (Norman Katz, M.D.); University of Maryland, Baltimore (Meryln Rodrigues, M.D.)

LAB/BRANCH
Laboratory of Immunology

SECTION
Section on Immunoregulation

INSTITUTE AND LOCATION
NEI, NIH, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.6	0.4	0.2

CHECK APPROPRIATE BOX(ES)
☒ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

This project has been terminated.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 EY 00235-04 LI

PERIOD COVERED

October 1, 1989 to September 30, 1990

TITLE OF PROJECT (*80 characters or less. Title must fit on one line between the borders.*)

Identification and Modulation of Class II Antigens

PRINCIPAL INVESTIGATOR (*List other professional personnel below the Principal Investigator.*) (*Name, title, laboratory, and institute affiliation.*)

PI:	Barbara Detrick	Ph.D.	Expert	LI, NEI
Others:	John J. Hooks	Ph.D.	Head, Section on Immunology and Virology	LI, NEI
	Chi-Chao Chan	M.D.	Medical Officer	LI, NEI
	Caroline Percopo	B.S.	Biologist	LI, NEI
	Robert B. Nussenblatt	M.D.	Clinical Director	NEI

COOPERATING UNITS (*if any*)

University of Pennsylvania (G. Aguirre, D.D.S., Ph.D.); Duke University (Barton F. Haynes, M.D.); Paris, France (Laurence Boumsell, M.D.).

LAB/BRANCH

Laboratory of Immunology

SECTION

Section on Immunoregulation

INSTITUTE AND LOCATION

NEI, NIH, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.44	0.34	0.10

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK (*Use standard unreduced type. Do not exceed the space provided.*)

This project has been terminated.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 EY 00261-01 LI

PERIOD COVERED
October 1, 1989 to September 30, 1990

TITLE OF PROJECT (*80 characters or less. Title must fit on one line between the borders.*)
Identification of Pathogens in Ocular Tissues by PCR

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation.)*

PI:	Charles E. Egwuagu	M.P.H., Ph.D.	Scientist	LI, NEI
Others:	Antoine P. Brezin	M.D.	Visiting Fellow	LI, NEI
	Robert B. Nussenblatt	M.D.	Clinical Director	LI, NEI
	Rubens Belfort, Jr.	M.D.	Visiting Scientist	LI, NEI
	Rashid Mahdi		Biologist	LI, NEI

COOPERATING UNITS *(if any)*

Department of Ophthalmic Pathology, Armed Forces Institute of Pathology, Washington, DC, and Brazilian Registry of Ophthalmic Pathology, São Paulo, Brazil (Miguel Burnier, Jr., M.D., Brazilian Registry of Medicine); Clinica Silveira, Erexim, Brazil (Claudio Silveira, M.D.); Laboratory of Parasitology, National Institute of Allergy and Infectious Diseases (Ricardo T. Gazzinelli, Ph.D.)

LAB/BRANCH
Laboratory of Immunology

SECTION
Section of Experimental Immunology

INSTITUTE AND LOCATION
NEI, NIH, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
2.0	1.9	0.1

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☒ (b) Human tissues ☐ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

We have used the polymerase chain reaction (PCR) to amplify fragments specific to *Toxoplasma gondii* from two cases of ocular toxoplasmosis. In both cases, PCR revealed the presence of toxoplasmic DNA although optical microscopy showed toxoplasmic cysts in only one eye. Our success in identifying the parasite in these samples indicates the usefulness of this technique as an adjunct to currently available diagnostic methods.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 EY 00262-01 LI

PERIOD COVERED

October 1, 1989 to September 30, 1990

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

TCR Gene Usage in Experimental Autoimmune Uveoretinitis (EAU)

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation.)*

PI:	Charles E. Egwuagu	M.P.H., Ph.D.	Scientist	LI, NEI
Others:	Igal Gery	Ph.D.	Head, Section on Experimental Immunology	LI, NEI
	Robert B. Nussenblatt	M.D.	Clinical Director	LI, NEI
	Christopher Chow	B.A.	HHMI-NIH Scholar	LI, NEI
	Evelyne Beraud	Ph.D	Visiting Associate	LI, NEI
	Rachel Caspi	Ph.D.	Visiting Associate	LI, NEI
	Rashid Mahdi		Biologist	LI, NEI
	Antoine P. Brezin	M.D.	Visiting Fellow	

COOPERATING UNITS *(if any)*

LAB/BRANCH

Laboratory of Immunology

SECTION

Section of Experimental Immunology

INSTITUTE AND LOCATION

NEI, NIH, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
1.4	1.1	0.3

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

This project is aimed at learning about the T cell receptors (TCR) expressed by T cells that mediate a group of inflammatory eye diseases referred to as "uveitis". Most emphasis in FY 1990 has been on the isolation and characterization of the genes that code for these surface proteins used by T cells for antigen recognition.

We have investigated the TCRs expressed on T cell lines and clones specific for S-antigen and interphotoreceptor retinoid-binding protein (IRBP) and compared V-region gene usage between T cells capable of transferring EAU (uveitogenic) and non-pathogenic T cells. Our analyzsis of the Vβ8 gene locus for genomic rearrangements demonstrated the predominant Vβ8 gene rearrangement, even in our most pathogenic T cell lines, suggesting that small proportions of the cells in our T cell lines that induce EAU use the Vβ8 gene element. On the other hand, our detection of Vβ8 transcripts in uveitogenic T cell lines and the level of Vβ8 gene expression could be correlated with the abilities of our various T cell lines and clones to induce EAU, which suggests that T cells expressing the Vβ8 phenotype may be involved in the etiology of EAU. However, Northern analysis using a probe specific to Vβ8.2 revealed that, unlike the pathogenic T cells involved in other experimental autoimmune diseases, uveitogenic T cell lines express a member of the Vβ8 TCR family that appears to be similar to but distinct from Vβ8.2. We have cloned and sequenced the Vβ8.2-like cDNAs derived from S-antigen and IRBP-specific uveitogenic T cell lines. The gene from the IRBP line shows approximately 99% sequence homology within rat Vβ8.2, while the gene from the S-antigen line is only 90% homologous to Vβ8.2.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 EY 00189-07 LMOD

PERIOD COVERED
October 1, 1989 to September 30, 1990

TITLE OF PROJECT (*80 characters or less. Title must fit on one line between the borders.*)
Oxidation of Proteins in Cataractogenesis

PRINCIPAL INVESTIGATOR (*List other professional personnel below the Principal Investigator.*) (*Name, title, laboratory, and institute affiliation.*)

PI:	Donita L. Garland	Ph.D.	Research Chemist	LMOD, NEI
Others:	Jose Jimenez	Ph.D.	Visiting Fellow	LMOD, NEI
	Lorenzo Merola	M.S.	Chemist	LMOD, NEI

COOPERATING UNITS (*if any*)

LAB/BRANCH
Laboratory of Mechanisms of Ocular Diseases

SECTION
Section on Cataracts

INSTITUTE AND LOCATION
NEI, NIH, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
3.0	3.0	0.0

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK (*Use standard unreduced type. Do not exceed the space provided.*)

Oxidative changes of lens proteins are thought to occur with aging and to contribute to the development of cataracts. The goals of this project are to determine (1) the extent of oxidative modification of crystallins and metabolic enzymes in both normal and cataractous lenses, (2) the nature of the modifications and mechanisms leading to the changes, and (3) the effect of the modifications on the structure and function of lens proteins. Bovine and rat lenses are used. The approach is to study the modifications of lens proteins after treatment in vitro by metal-catalyzed oxidation systems.

Structural alterations induced by these oxidative systems were examined by circular dichroism and peptide mapping. Trace metal analysis of bovine aqueous and rat and bovine lenses indicated that copper and iron are both present in micromolar concentrations. Further studies on fetal bovine lenses demonstrated that copper and iron are not associated with any crystallin to an appreciable extent in vivo. In vitro, copper appears to interact specifically with some of the bovine gamma-crystallins and at greater than stoichiometric levels induces protein aggregation. These results support the possibility that metal-catalyzed oxidative reactions may contribute to age-related changes in lens.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 EY 00069-13 LI

PERIOD COVERED

October 1, 1989 to September 30, 1990

TITLE OF PROJECT (*80 characters or less. Title must fit on one line between the borders.*)

Immune Responses to Ocular Antigens

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation.)*

PI:	Igal Gery	Ph.D.	Head, Section on Experimental Immunology	LI, NEI
Others:	Satoshi Kotake	M.D.	Visiting Fellow	LI, NEI
	Yoichi Kawano	M.D.	Visiting Fellow	LI, NEI
	Yoichi Sasamoto	M.D.	Visiting Fellow	LI, NEI
	Xiao-Yan Zhang	M.D.	Guest Worker	LI, NEI
	William Lipham	B.A.	HHMI-NIH Scholar	LI, NEI
	Barbara Vistica	B.A.	Microbiologist	LI, NEI
	Gerald J. Chader	Ph.D.	Chief	LRCMB, NEI
	Barbara Wiggert	Ph.D.	Head, Section on Biochemistry	LRCMB, NEI
	T. Michael Redmond	Ph.D.	Senior Staff Fellow	LRCMB, NEI

COOPERATING UNITS *(if any)*

Metabolism Branch, Division of Cancer Biology and Diagnosis, National Cancer Institute (Jay A. Berzofsky, M.D.)

LAB/BRANCH

Laboratory of Immunology

SECTION

Section on Experimental Immunology

INSTITUTE AND LOCATION

NEI, NIH, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
3.2	3.0	0.2

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

This project is aimed at learning about the pathogenesis of inflammatory eye diseases grouped under the term "uveitis." Our effort in FY1990 focused on studies in experimental animals and has yielded the following main achievements:

1. The active site of the immunodominant and highly uveitogenic determinant of bovine interphotoreceptor retinoid-binding protein (IRBP) was localized to a nonapeptide at sequence 1182-1190. Four of the amino acids of this peptide were identified to be pivotal to its immunological activities; residues 1182 and 1190 are essential for its binding to the antigen presenting cell while 1188 and 1189 interact with the T cell receptor.

2. Lymphocytes become highly uveitogenic by their activation in culture. Data collected this period show dissociation between the generation of uveitogenicity and the proliferation of activated lymphocytes.

3. Concanavalin A (Con A), which stimulates vigorous proliferation responses in spleen (Sp) and lymph node (LN) cell cultures, also generates uveitogenicity in Sp cells, but not in LN cells. This lack of Con A effect in LN cultures was found to result from a deficiency in an accessory cell population present in the Sp.

4. Lymphocytes sensitized to non-dominant IRBP peptides do not recognize whole IRBP in culture as they do in the eye when mediating uveitis in rats. However, these lymphocytes do recognize IRBP following its digestion by endopeptidases. This finding provides an explanation for the aforementioned discrepancy and suggests that the recognition of IRBP in the eye is facilitated by its cleavage by tissue enzymes.

5. Rats injected with the uveitogenic peptide 1177-1191 in aqueous solution were found to be resistant to EAU induction by this peptide when it was injected in its uveitogenic form, in adjuvant emulsion. Furthermore, the treated rats were also resistant to induction of EAU by whole IRBP.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 EY 00049-12 LSR

PERIOD COVERED
October 1, 1989 to September 30, 1990

TITLE OF PROJECT (*80 characters or less. Title must fit on one line between the borders.*)
Cerebral Cortical Mechanisms for Eye Movements and Visual Attention

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation.)*

PI:	Michael E. Goldberg	M.D.	Chief, NMS	LSR, NEI
Others:	Edmond J. FitzGibbon	M.D.	Senior Staff Fellow	LSR, NEI
	Carol L. Colby	Ph.D.	Senior Staff Fellow	LSR, NEI
	Jean-Rene Duhamel	Ph.D.	Visiting Scientist	LSR, NEI
	Carl R. Olsen	Ph.D.	Guest Researcher	LSR, NEI
	Suzanne Y. Musil	Ph.D.	NRSA Fellow	LSR, NEI
	Edward L. Keller	Ph.D.	Guest Researcher	LSR, NEI

COOPERATING UNITS *(if any)*

LAB/BRANCH
Laboratory of Sensorimotor Research

SECTION
Section on Neuro-Ophthalmologic Mechanisms

INSTITUTE AND LOCATION
NEI, NIH, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
5.6	4.5	1.1

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Two different lines of inquiry were followed to determine how the cerebral cortex and its efferent regions control eye movements and visuospatial attention.

In one, activity of movement neurons of the superior colliculus was studied in relation to saccades evoked by electrical stimulation of either the frontal eye field or the superior colliculus and modified by their temporal proximity to visually evoked saccades. In the other, visual neurons in the posterior parietal cortex were studied using double-step tasks to see how this cortex might maintain spatial accuracy when there was a dissonance between the retinal location of a stimulus and the saccade necessary to acquire that stimulus. Neurons in this region discharged when the monkey made a saccade of the proper direction to acquire a stimulus, whether or not that stimulus lay in the neuron's receptive field as studied in a routine fixation task. Such neurons required the presence of a visual stimulus, suggesting that in the posterior parietal cortex, spatial accuracy is maintained by coordinate transformation of a visual map rather than by the explicit coding of target position in space.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 EY 00246-03 OGCS

PERIOD COVERED
October 1, 1989 to September 30, 1990

TITLE OF PROJECT (*80 characters or less. Title must fit on one line between the borders.*)
Molecular Genetics of Retinal Degenerations

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation.)*

PI:	Michael B. Gorin	M.D., Ph.D.	Medical Officer	OGCS, NEI
Others:	Steven Snyder	M.D.	Staff Fellow	OGCS, NEI
	Tatiana Putilina	Ph.D.	Special Volunteer	OGCS, NEI

COOPERATING UNITS *(if any)*

Retinitis Pigmentosa Foundation; Northwestern Univ. (Larry Pinto, Ph.D.); Univ. of Linkoping, Linkoping, Sweden (Kristina Narfstrom, V.M.D.); Dept. of Biochemistry, UCLA (David Sigman, Ph.D.); Lab. of Molecular Microbiology, Natl. Inst. of Allergy and Infectious Diseases (Christine Kozak, Ph.D.)

LAB/BRANCH
Ophthalmic Genetics and Clinical Services Branch

SECTION
Section on Ophthalmic Genetics

INSTITUTE AND LOCATION
NEI, NIH, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
1.3	1.3	0.0

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The purpose of this project is to identify the genes responsible for different inherited retinal disorders in animal models and to establish the genetic relationship of these animal disorders to forms of human retinal degenerations and conditions.

"Reverse" genetic approaches are being applied to specific animal models of retinal dysfunction, including new methods for cloning regions associated with a mapped genetic disorder. Polymerase chain amplification methods are being used to evaluate interspecies differences in specific genetic transcripts.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 EY 00135-18 IRP

PERIOD COVERED
October 1, 1989 to September 30, 1990

TITLE OF PROJECT (*80 characters or less. Title must fit on one line between the borders.*)
Biochemistry of Retina and Pigmented Epithelium in Health and Disease

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation.)*

PI: Helen H. Hess M.D. Medical Officer (Research) IRP, NEI

COOPERATING UNITS *(if any)*

LAB/BRANCH
Office of the Director of Intramural Research

SECTION

INSTITUTE AND LOCATION
NEI, NIH, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
1.0	1.0	0.0

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The effects of nutrition, oxidation, and other environmental factors (light intensity or darkness) on incidence and progress of posterior subcapsular opacities (PSO) associated with retinal degeneration are being studied in pink-eyed Royal College of Surgeons (RCS) rats, in which rod photoreceptor outer segment debris accumulates secondary to a phagocytic defect in retinal pigmented epithelium. Evidence was obtained that oxidative changes in polyunsaturated fatty acids in debris led to water-soluble toxic aldehydes, detectable in the vitreous and toxic to lens cells and membranes. Dystrophic rats fed a natural ingredient diet (NIH-07) are highly susceptable to retinal light damage, beginning at 1-4 footcandles (fc) intensity: 27% of the rats develop mature cataracts by 7-12 months. Increased light intensity (cyclic or constant) increased the percentage of rats with mature cataracts, while dark-rearing from birth prevented PSO and mature cataracts. A purified diet (AIN-76A), fortified with 0.4% β-carotene + 0.01% BHT, also prevented PSO and mature cataracts.

Rhodopsin bleaching appears to be essential for retinal light damage and PSO. A 100% incidence of bilateral mature cataracts occurred in dystrophic rats given 48 hours of 700-fc constant light between postnatal days 22 and 28, when rhodopsin is increased 70% in debris. A similar incidence of bilateral cataracts occurred in congenic control RCS rats given 18 days of dark adaptation to increase rhodopsin by 50%, followed by the same constant light exposure. In vitro, free retinaldehyde can act as a photosensitizer to generate singlet oxygen, an extremely energetic oxidant. Present results suggest a similar effect in vivo, with damage to both lipids and proteins. Current studies are directed toward exploring how many days retinal degeneration can be delayed by different antioxidant-containing diets. Antioxidants may slow or prevent cataracts in some human retinal diseases.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 EY 00232-05 LI

PERIOD COVERED
October 1, 1989 to September 30, 1990

TITLE OF PROJECT (80 characters or less. Title must fit on one line between the borders.)
Interferon System in Cellular Function and Disease

PRINCIPAL INVESTIGATOR (List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation.)

PI:	John J. Hooks	Ph.D.	Head, Section on Immunology and Virology	LI, NEI
Others:	Caroline Percopo	M.S.	Biologist	LI, NEI
	Christian Hamel	M.D.	Visiting Fellow	LI, NEI
	Shirin Barer	M.D.		LI, NEI
	Gerald Chader	Ph.D.	Chief	LRCMB, NEI

COOPERATING UNITS (if any)
New York University, School of Medicine (Jan Vilcek, M.D.); Tumor Biology Section, Laboratory of Biology, Division of Cancer Etiology, National Cancer Institute (Charles Evans, M.D.); Vaccine Research and Development Branch, Division of AIDS, National Institute of Allergy and Infectious Diseases (Barbara Detrick, Ph.D.)

LAB/BRANCH
Laboratory of Immunology

SECTION
Section on Immunology and Virology

INSTITUTE AND LOCATION
NEI, NIH, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
1.1	0.7	0.4

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK (Use standard unreduced type. Do not exceed the space provided.)

The interferon (IFN) protein, which can modify a variety of biological activities, is considered one of the body's regulatory proteins. Numerous studies have indicated that the IFNs are potent immunoregulators. During the past year, we have been studying the ways in which IFN proteins interact with cells of the immune system and with cells in the ocular microenvironment.

Using immunocytochemical analysis, we have developed a sensitive method of identifying the lymphokines IFN-γ and interleukin 2 (IL-2) at the site of tissue damage. We have identified these lymphokines in inflammatory eye diseases. The presence of these lymphokines is associated with lymphocyte infiltrate predominantly of T cell origin and with the expression of major histocompatibility complex (MHC) class II antigens on both the infiltrating cells and retinal pigment epithelial (RPE) cells.

Experimentally, we have shown that this direct intravitreal inoculation of recombinant rat IFN-γ results in the expression of MHC Class II antigen (Ia) in a variety of ocular cells. In conjunction with Ia expression, two striking changes were noted: an iritis and infiltrating cells in the inner retinal layers. Both of these phenomena have been observed in certain inflammatory eye diseases.

IFN-γ is known to be a potent regulator of gene expression. We found that IFN-γ enhances the expression of retinal S-antigen, a specific neuronal cell marker. Preliminary studies indicate this IFN-γ is acting at the level of transcription.

These observations indicate that IFN-γ induced MHC class II antigen expression may serve as a local amplification system in autoimmune and inflammatory eye disease. A better understanding of the role of lymphokines in the mechanisms involved in the development of autoimmunity and inflammation may be beneficial in developing treatments for these diseases.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 EY 00233-05 LI

PERIOD COVERED
October 1, 1989 to September 30, 1990

TITLE OF PROJECT (*80 characters or less. Title must fit on one line between the borders.*)
Studies on the Bioregulatory Aspects of the Retinal Pigment Epithelial Cell

PRINCIPAL INVESTIGATOR (*List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation.)*

PI:	John J. Hooks	Ph.D.	Head, Section on Immunology and Virology	LI, NEI
Others:	Caroline Percopo	M.S.	Biologist	LI, NEI
	Laura Caspers-Velu	M.D.	Visiting Associate	LMOD, NEI
	Shuji Suzuki	M.D.	Visiting Associate	LI, NEI

COOPERATING UNITS (*if any*)

Hôpital St. Louis, Paris, France (Lawrence Boumsell, M.D.); Univ. of Nice, France (Alain Bernard, M.D.); NRID, NIH (Reuben Sigraganian, M.D.); Univ. of Virginia, Charlottesville, VA (Stanley A. Vinores, Ph.D., Peter Campochiaro, M.D.); Oregon Health Sciences Univ., Portland, OR (Stephen R. Planck, Ph.D., James T. Rosenbaum, M.D.); Division of AIDS, National Institute of Allergy and Infectious Diseases (Barbara Detrick, Ph.D.)

LAB/BRANCH
Laboratory of Immunology

SECTION
Section on Immunology and Virology

INSTITUTE AND LOCATION
NEI, NIH, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
1.96	1.76	0.20

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☒ (b) Human tissues ☐ (c) Neither
- ☐ (a1) Minors
- ☐ (a2) Interviews

SUMMARY OF WORK (*Use standard unreduced type. Do not exceed the space provided.)*

The retinal pigment epithelial (RPE) cell has a major regulatory function in the eye, in a variety of ways influencing the maintenance of retinal integrity and function. In order to study this cell more effectively in vivo and in vitro, we have produced monoclonal antibodies directed against human RPE cells.

Using immunoperoxidase assays (ABC), we have identified two mouse IgG monoclonal antibodies that react with the human RPE cell. The monoclonal antibodies are both specific for the RPE cell within the eye because they do not react with any other ocular structures. Moreover, these antibodies do not cross-react with human skin, kidney, or peripheral mononuclear cells. These antibodies recognize cell surface molecules that must be highly conserved, being found in man, monkey, rat, mouse, cow, chicken, and frog.

These antibodies, which detect epitopes present solely on RPE cells, provide us with the unique opportunity to evaluate a variety of aspects of RPE cell development and function. Studies of RPE cell development indicate that the epitopes appear only after the cells have begun terminal differentiation. Moreover, these studies indicate that a very specific product of the RPE cell is synthesized as the photoreceptor outer segment starts to develop, suggesting that this product could be involved in an essential step of the outer segment development. Studies on RPE migration also demonstrate the value of these antibodies in evaluating epiretinal membrane formation.

These are the first monoclonal antibodies directed solely at the human RPE cell. Further characterization and studies of these antibodies should prove useful in the identification of RPE cells in situ and in vitro. This immunoglobulin will allow us to probe the bioregulatory functions of the cells.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 EY 00234-05 LI

PERIOD COVERED

October 1, 1989 to September 30, 1990

TITLE OF PROJECT (*80 characters or less. Title must fit on one line between the borders.*)

MHC Class II Antigens in the Pathogenesis of Inflammatory Diseases

PRINCIPAL INVESTIGATOR (*List other professional personnel below the Principal Investigator.*) (*Name, title, laboratory, and institute affiliation.*)

PI:	John J. Hooks	Ph.D.	Head, Section on Immunology and Virology	LI,NEI
Other:	Caroline Percopo	M.S.	Biologist	LI,NEI
	Robert B. Nussenblatt	M.D.	Clinical Director	NEI

COOPERATING UNITS (*if any*)

Vaccine Research and Development, Division of AIDS, National Institute of Allergy and Infectious Diseases (Barbara Detrick, Ph.D.)

LAB/BRANCH

Laboratory of Immunology

SECTION

Section on Immunology and Virology

INSTITUTE AND LOCATION

NEI, NIH, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.4	0.3	0.1

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK (*Use standard unreduced type. Do not exceed the space provided.*)

MHC class II antigens, HLA-DR in the human and Ia in the mouse, are membrane-bound glycoproteins encoded by genes of the major histocompatibility complex. Expression of these antigens is of great functional importance for the initiation and perpetuation of immune responses. In a number of immunopathologic conditions, HLA-DR antigen-negative cells are stimulated to express class II antigens. In these cases, an immunologic role has been postulated for the class II antigen expression.

We showed that cytokine-activated RPE cells express MHC class II antigens. These Ia-positive cells can both process retinal antigens and present them to specifically sensitive T-helper lymphoctyes. These studies indicated that cytokine activated RPE cells may be a basic component of ocular immunity.

These studies on MHC class II antigen expression in localized autoimmune diseases provide evidence that the activation of these antigens may contribute to the immunopathogenesis of these diseases.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 EY 00240-04 LI

PERIOD COVERED
October 1, 1989 to September 30, 1990

TITLE OF PROJECT (*80 characters or less. Title must fit on one line between the borders.*)
Virus Infections in the Eye

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation.)*

PI:	John J. Hooks	Ph.D.	Head, Section on Immunology and Virology	LI, NEI
Others:	Susan Robbins	Ph.D.	Postdoctoral Fellow	LI, NEI
	Christian Hamel	M.D.	Visiting Fellow	LI, NEI
	Caroline Percopo	M.S.	Biologist	LI, NEI
	Charles Evans	M.D., Ph.D.	Medical Officer	LB, NCI

COOPERATING UNITS *(if any)*

Div. of AIDS, Natl. Inst. of Allergy and Infectious Diseases; (Barbara Detrick, Ph.D.); Wilmer Eye Institute, Johns Hopkins Hospital, Baltimore (W. Richard Green); Dept. of Pathology, Uniformed Services Univ. for Health Sciences, Bethesda, MD (Katherine Holmes, Ph.D.); Dept. of Ophthalmology, Ruprecht-Karl's Univ., Heidelberg, Germany (Ellen Kraus-Mackiw, M.D.); Dept. of Ophthalmology, Univ. of Munich, Germany (Otto F. Scheiffarth, M.D.)

LAB/BRANCH
Laboratory of Immunology

SECTION
Section on Immunology and Virology

INSTITUTE AND LOCATION
NEI, NIH, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
1.0	0.9	0.1

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☒ (b) Human tissues ☐ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

During the past year, we have studied various virologic and immunopathologic processes that occur when viruses replicate in the ocular microenvironment. This project consists of three areas: (1) studies on coronavirus infection in ocular and optic nerve cells; (2) determination of the possible roles of viruses in human diseases; (3) antiviral therapeutic actions of cytokines and drugs.

We have established that murine coronavirus can induce ocular disease and thus may be used as a model system for studying retinal degenerative diseases. This model has many unique features. The virus is capable of inducing an acute infection in the presence of mild inflammation. The initial retinal damage is followed by clearance of the virus and progressive retinal destruction, even months after the virus is gone. This disease may be considered a model for degenerative diseases of the pigment epithelium and photoreceptors in humans.

The need for effective drug treatment and prevention of herpes virus and other viral diseases has assumed growing importance. We found that leukoregulin, a naturally occurring immunologic cytokine, increases the antiviral actions of the drug acyclovir. These findings which demonstrate that combination immunotherapy and chemotherapy can produce substantial inhibition of herpes virus replication, provide a rationale for the application of this approach to the treatment of virus infections.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 EY 00193-06 LMOD

PERIOD COVERED

October 1, 1989 to September 30, 1990

TITLE OF PROJECT (*80 characters or less. Title must fit on one line between the borders.*)

Molecular Biology of Hereditary Eye Diseases

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation.)*

PI:	George Inana	M.D., Ph.D.	Head, Section on Molecular Pathology	LMOD, NEI
Others:	Carmelann Zintz	Ph.D.	Staff Fellow	LMOD, NEI
	Yoshihiro Hotta	M.D.	Visiting Associate	LMOD, NEI
	Carolyn Chambers	Ph.D.	IRTA Fellow	LMOD, NEI
	Tetsuo Sasabe	M.D., Ph.D.	Visiting Associate	LMOD, NEI

COOPERATING UNITS *(if any)*

LAB/BRANCH

Laboratory of Mechanisms of Ocular Diseases

SECTION

Section on Molecular Pathology

INSTITUTE AND LOCATION

NEI, NIH, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
5.0	5.0	0.0

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☒ (b) Human tissues ☐ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

This project has been terminated.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 EY 00003-17 LMOD

PERIOD COVERED
October 1, 1989 to September 30, 1990

TITLE OF PROJECT (*80 characters or less. Title must fit on one line between the borders.*)
Pharmacology of Ocular Complications

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation.)*

PI:	Peter F. Kador	Ph.D.	Research Chemist	LMOD, NEI
Others:	Julia Derr	B.A.	Biologist	LMOD, NEI
	Kosei Karino	M.D.	Visiting Associate	LMOD, NEI
	Tadashi Mizoguchi	Ph.D.	Visiting Scientist	LMOD, NEI
	Yukio Takahashi	M.D.	Visiting Associate	LMOD, NEI
	Sanai Sato	M.D.	Visiting Scientist	LMOD, NEI

COOPERATING UNITS *(if any)*

LAB/BRANCH
Laboratory of Mechanisms of Ocular Diseases

SECTION
Section on Molecular Pharmacology

INSTITUTE AND LOCATION
NEI, NIH, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
4.1	4.1	0.0

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The role of the enzymes aldose reductase and aldehyde reductase in the onset and progression of complications associated with diabetes are being investigated. In the eye these complications include retinopathy, cataract, keratopathy, changes in pupil function, and iris and ciliary process structure changes. Under development are methods of pharmacological control of these enzymes to either delay or prevent the onset and progression of these complications.

Events leading to the formation of several types of cataracts, as well as methods for controlling the onset of these cataracts through pharmacological intervention, are also being investigated.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 EY 00011-16 OGCS

PERIOD COVERED

October 1, 1989 to September 30, 1990

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Pigment Dispersion With and Without Glaucoma

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation.)*

PI:	Muriel I. Kaiser-Kupfer	M.D.	Chief	OGCS, NEI
Others:	Lessie McCain	R.N.	Nurse Specialist	OGCS, NEI

COOPERATING UNITS *(if any)*

LAB/BRANCH

Ophthalmic Genetics and Clinical Services Branch

SECTION

Section on Ophthalmic Genetics

INSTITUTE AND LOCATION

NEI, NIH, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.2	0.1	0.1

CHECK APPROPRIATE BOX(ES)

☒ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither

☒ (a1) Minors

☒ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The purpose of this project is to determine the risks of patients with pigment dispersion syndrome to developing glaucoma. Comparisons of patients with and without glaucoma will be made on the basis of diagnostic tests, genetic screening, aqueous humor dynamics, and pupillary responses to light. The data acquired may enable a determination of the risk of patients with pigment dispersion syndrome to developing glaucoma, as well as adding to the understanding of the pathology of the disease.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 EY 00060-12 OGCS

PERIOD COVERED
October 1, 1989 to September 30, 1990

TITLE OF PROJECT (*80 characters or less. Title must fit on one line between the borders.*)
Visual Function and Ocular Pigmentation in Albinism

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation.)*

PI:	Muriel I. Kaiser-Kupfer	M.D.	Chief	OGCS, NEI
Others:	Lessie McCain	R.N.	Nurse Specialist	OGCS, NEI
	Rafael Caruso	M.D.	Visiting Scientist	OGCS, NEI

COOPERATING UNITS *(if any)*

LAB/BRANCH
Ophthalmic Genetics and Clinical Services Branch

SECTION
Section on Ophthalmic Genetics

INSTITUTE AND LOCATION
NEI, NIH, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.20	0.15	0.05

CHECK APPROPRIATE BOX(ES)

☒ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
- ☒ (a1) Minors
- ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Patients with hypomelanotic disorders such as ocular albinism, oculocutaneous albinism, Chediak-Higashi disease, Hermansky-Pudlak syndrome, and iris transillumination defects are being recruited to determine visual function with these conditions and to evaluate the changes in visual function over time. Family members are evaluated to attempt to determine factors which may identify the heterozygous state.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 EY 00083-13 OGCS

PERIOD COVERED
October 1, 1989 to September 30, 1990

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Gyrate Atrophy of the Choroid and Retina and Other Retinal Degenerations

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation.)*

PI:	Muriel I. Kaiser-Kupfer	M.D.	Chief	OGCS, NEI
Others:	Michael B. Gorin	M.D., Ph.D.	Medical Officer	OGCS, NEI
	Lessie McCain	R.N.	Nurse Specialist	OGCS, NEI
	Rafael Caruso	M.D.	Visiting Scientist	OGCS, NEI
	Doris Collie	A.A.	Ophthalmic Health Technician	OGCS, NEI

COOPERATING UNITS *(if any)*
The Howard Hughes Medical Institute, Laboratory and the Department of Pediatrics, The Johns Hopkins University, School of Medicine, Baltimore, MD (David L. Valle, M.D.).

LAB/BRANCH
Ophthalmic Genetics and Clinical Services Branch

SECTION
Section on Ophthalmic Genetics

INSTITUTE AND LOCATION
NEI, NIH, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
1.1	0.5	0.6

CHECK APPROPRIATE BOX(ES)

☒ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
- ☐ (a1) Minors
- ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Patients with gyrate atrophy of the choroid and retina are examined systematically to confirm the diagnosis. Skin fibroblasts of affected patients and family members are grown in tissue culture and assayed for ornithine aminotransferase activity. The results are evaluated for correlation with the presence of homozygosity or heterozygosity for the disease trait. Each patient is given a trial of pyridoxine to see if serum concentration of ornithine can be reduced; if so, the patient is classified as a "responder" and treatment with pyridoxine is continued. Nonresponder and responder patients are then placed on a low-arginine, low-protein diet with supplemental amino acids and observed for arrest or improvement of the disease. If patients are not considered eligible for the diet, or if they appear unable to comply with the dietary regimen, they are followed to record the natural progression of the condition. Patients with other forms of retinal degeneration such as retinitis pigmentosa, fundus flavimaculatus, juvenile retinoschisis, and Usher's syndrome, are also examined and their courses are compared with those of gyrate atrophy patients.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 EY 00163-08 OGCS

PERIOD COVERED
October 1, 1989 to September 30, 1990

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
NIH Interinstitute Genetics Program: The Genetics Clinic

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation.)*

PI:	Muriel I. Kaiser-Kupfer	M.D.	Chief	OGCS, NEI
Others:	Michael B. Gorin	M.D., Ph.D.	Medical Officer	OGCS, NEI
	Lessie McCain	R.N.	Nurse Specialist	OGCS, NEI

COOPERATING UNITS *(if any)*
Interinstitute Medical Genetics Program, NIH

LAB/BRANCH
Ophthalmic Genetics and Clinical Services Branch

SECTION
Section on Ophthalmic Genetics

INSTITUTE AND LOCATION
NEI, NIH, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.3	0.1	0.2

CHECK APPROPRIATE BOX(ES)

☒ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
☒ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The Interinstitute Genetics Program and the Genetics Clinic, supported by the NIH Clinical Center, offer a multidisciplinary approach to patients with genetic disease (ZO1 CP 05139-05 CEB). Involved in the program are researchers from all Institutes. Patients evaluated in the clinic represent a broad spectrum of genetic diseases. During the last year, approximately 200 individuals seen represented about 60 distinct disease categories. Due to the high frequency of ocular involvement in many of the cases, almost all the patients were evaluated by Ophthalmic Genetics and Clinical Services Branch staff or were discussed in consultation. The Clinic serves as a source of interesting case material concerning patients with inherited or developmental abnormalities of the visual system.

In addition to the Genetics Clinic, patients are seen for genetic consultation at the Maryland School for the Blind. This experience has resulted the recruitment of patients into NEI intramural protocols.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 EY 00172-07 OGCS

PERIOD COVERED

October 1, 1989 to September 30, 1990

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Age-Related Macular Degeneration

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation.)*

PI:	Muriel I. Kaiser-Kupfer	M.D.	Chief	OGCS, NEI
Others:	Monique S. Roy	M.D.	Visiting Scientist	CB, NEI

COOPERATING UNITS *(if any)*

LAB/BRANCH

Ophthalmic Genetics and Clinical Services Branch

SECTION

Section on Ophthalmic Genetics

INSTITUTE AND LOCATION

NEI, NIH, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.05	0.05	0.0

CHECK APPROPRIATE BOX(ES)

☒ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

This project has been terminated.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 EY 00211-05 OGCS

PERIOD COVERED
October 1, 1989 to September 30, 1990

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
A Double-Masked Controlled Randomized Clinical Trial of Topical Cysteamine

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation.)*

PI:	Muriel I. Kaiser-Kupfer	M.D.	Chief	OGCS, NEI
Others:	Lessie McCain	R.N.	Clinical Technician	OGCS, NEI
	Manuel Datiles	M.D.	Visiting Scientist	OGCS, NEI

COOPERATING UNITS *(if any)*
Human Genetics Branch, National Institute of Child Health and Human Development (William Gahl, M.D., Ph.D.)

LAB/BRANCH
Ophthalmic Genetics and Clinical Services Branch

SECTION
Section on Ophthalmic Genetics

INSTITUTE AND LOCATION
NEI, NIH, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.50	0.25	0.25

CHECK APPROPRIATE BOX(ES)

☒ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Nephropathic cystinosis is an autosomal, recessively inherited storage disease in which nonprotein cystine accumulates within cellular lysosomes due to a defect in lysosomal cystine transport. Ocular manifestations include photophobia, crystal deposits in the cornea, conjunctiva, and iris, and depigmentation of the retina. Systemic complications include the Fanconi syndrome and renal failure.

Nine years ago cysteamine, a free thiol that depletes cystine from cells, was introduced in the therapy of cystinotic patients. Although patients had improved growth and stabilized renal function, there was no noticeable effect on the accumulation of corneal crystals. Recent studies showed that corneal cells in tissue culture are readily depleted of cystine by the introduction of cysteamine, making feasible the use of topical ophthalmic cysteamine to circumvent the humoral route. After appropriate animal studies to test for complications revealed none, we began a double-masked clinical trial to test the efficacy of topical cysteamine (0.1%) in humans. Fourteen patients of ages less than 3 years were enrolled and randomized to 0.1% cysteamine. Five patients showed a significant decrease in crystals in the cysteamine-treated eyes. In order to test the effects of increasing the concentration of cysteamine eye drops in humans, a toxicity study was performed in rabbits, showing no adverse reactions. The results permitted an increase in the concentration to 0.5% for human use, and all patients receiving 0.1% cysteamine were switched to 0.5%. An additional 5 young patients showed a significant decrease in treated eyes. Thus, of 18 young patients, 10 successfully had the code broken; of the remaining 8, 2 died, 3 discontinued medication, and 3 are still in the trial. Due to the success in the younger patients, this study was expanded to include older patients, 3-31 years of age. The findings have been most exciting: seven patients have shown a significant decrease in crystals in treated eyes as well as improvements in comfort, i.e, relief of pain and photophobia. This study has resulted in significantly improved quality of life for the successfully treated patients.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 EY 00084-12 OGCS

PERIOD COVERED

October 1, 1989 to September 30, 1990

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Anterior Chamber Anomalies Associated With Glaucoma or Ocular Hypertension

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation.)*

PI:	Carl Kupfer	M.D.	Director	NEI
Others:	Muriel I. Kaiser-Kupfer	M.D.	Head	OGCS, NEI
	Lessie McCain	R.N.	Nurse Specialist	OGCS, NEI
	Manuel B. Datiles	M.D.	Visiting Scientist	OGCS, NEI

COOPERATING UNITS *(if any)*

LAB/BRANCH

Ophthalmic Genetics and Clinical Services Branch

SECTION

Section on Cataract and Corneal Diseases

INSTITUTE AND LOCATION

NEI, NIH, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.05	0.05	0.0

CHECK APPROPRIATE BOX(ES)

☒ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Recent embryological research has indicated the role of the neural crest in contributing to all connective tissues anterior to the lens epithelium. Therefore, the group of developmental anomalies of the anterior chamber with glaucoma or ocular hypertension is being reviewed.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 EY 00153-08 LSR

PERIOD COVERED
October 1, 1989 to September 30, 1990

TITLE OF PROJECT (*80 characters or less. Title must fit on one line between the borders.*)
Visual Motion and the Stabilization of Gaze

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation.)*

PI:	Frederick A. Miles	D.Phil.	Senior Research Physiologist	LSR, NEI
Others:	Urs Schwarz	M.D.	Visiting Associate	LSR, NEI
	Thomas S. Collett	Ph.D.	Visiting Scientist	LSR, NEI
	Claudio Busettini	Ph.D.	Visiting Fellow	LSR, NEI
	James R. Carl	M.D.	Expert	LSR, NEI

COOPERATING UNITS *(if any)*

LAB/BRANCH
Laboratory of Sensorimotor Research

SECTION
Section on Oculomotor Control

INSTITUTE AND LOCATION
NEI, NIH, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
4.7	4.1	0.6

CHECK APPROPRIATE BOX(ES)

☒ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

We have done a series of studies concerned with the dependence of various oculomotor and perceptual phenomena on viewing distance. Our previous experiments on monkeys had shown that the visual and vestibular ocular responses to translational disturbances of the scene and of the observer are linear functions of the inverse of the viewing distance. Such dependence on proximity is appropriate for the vestibular reflexes that are stimulated by the linear acceleration of the head and must transform signals from cartesian to polar coordinates. We attributed the synergistic visual reflex sharing of this property to shared neural pathways secondary to shared function and frame of reference. We now report that smooth pursuit tracking in monkeys also shows this dependence on proximity, though somewhat less vigorously. We have begun similar studies in human subjects and have some preliminary data. Human responses to translational disturbances of the upper torso generated compensatory eye movements that were linear functions of the inverse of the viewing distance and that were virtually identical to those previously obtained in monkeys. However, in stark contrast to those of monkeys, human ocular following responses associated with translation of the visual scene showed no such dependence on proximity. We suspect that the insensitivity of human ocular following to viewing distance may result from the impoverished nature of the stimulus situation. Other studies on the scaling of size and depth cues with viewing distance by human subjects indicate that angular size is an important parameter in the scaling of depth, especially at greater distances when oculomotor cues are less reliable.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 EY 00196-07 LRCMB

PERIOD COVERED
October 1, 1989 to September 30, 1990

TITLE OF PROJECT (*80 characters or less. Title must fit on one line between the borders.*)
Molecular Genetics of the Eye and Ocular Diseases

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation.)*

PI:	John M. Nickerson	Ph.D.	Biologist	LRCMB, NEI
Others:	Diane Borst	Ph.D.	Staff Fellow	LRCMB, NEI
	Steven Bernstein	Ph.D., M.D.	Senior Staff Fellow	LRCMB, NEI
	Jing-Sheng Si	M.D.	Visiting Associate	LRCMB, NEI
	David Saperstein	M.D.	Extramural NRSA Fellow	LRCMB, NEI
	Fintan Steele	Ph.D.	NRC Fellow	LRCMB, NEI
	Gerald J. Chader	Ph.D.	Chief	LRCMB, NEI

COOPERATING UNITS *(if any)*

University of Maryland Medical School, Baltimore, MD (M. Rodrigues); Jules Stein Eye Institute, UCLA, Los Angeles, CA (D. Farber, B. Bateman, J. Ngo-Jones, R. Sparkes); Departments of Pathology and Ophthalmology, University of Virginia, Charlottesville, VA (F. Gonzalez-Fernandez)

LAB/BRANCH
Laboratory of Retinal Cell and Molecular Biology

SECTION
Section on Gene Regulation

INSTITUTE AND LOCATION
NEI, NIH, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
3.8	3.8	0.0

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☒ (b) Human tissues ☐ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Interphotoreceptor retinoid-binding protein (IRBP) is the first example of an extracellular matrix protein that plays a role in transporting, buffering, or mediating the actions of retinoids and fatty acids in the interphotoreceptor space. This laboratory has isolated and characterized recombinant DNA molecules necessary for the study of the structure and expression of IRBP. We determined the primary structure of the IRBP gene and its protein, prerequisites to thorough study of IRBP gene expression. The DNA clones are important substrates that provide the tools for studies of how IRBP is synthesized and functions. IRBP is a single polypeptide that contains four 300 amino acid long repeats, with 30%-40% identity among the repeats. These sequences have been helpful in the analysis of the uveitogenic peptides in IRBP. The cell in the retina that contains IRBP mRNA is the photoreceptor. IRBP mRNA is large and usually gives only one band on a Northern blot. But two sizes of IRBP mRNA are present in rat and mouse. Having analyzed the IRBP gene in many species, especially the human, we have determined that there is only one IRBP gene per haploid genome. The chromosomal location of the IRBP gene is 10q21.1 for human and 14 for mouse, chromosomal localizations that rule out IRBP as the defective gene in many inherited eye disorders. Moreover, we have demonstrated that IRBP cannot cause fundus albipunctatus, a rare autosomal recessive form of stationary night blindness with a defect in the vitamin A cycle. The IRBP gene structure, which is compact for the size of the protein, has only three introns. The remarkable quadruplication within the gene suggests an interesting evolution, possibly involving a processed gene intermediate and two unequal crossovers. We have begun to characterize the elements regulating IRBP gene expression, including both *cis*-elements (the DNA sequences) and *trans*-acting factors (DNA binding proteins). We find two homologous areas of sequence in the 5' flanking regions of the bovine and mouse IRBP genes, one from -1 to -350 and another at -1200 to -1410. At least two blocks of sequence (one in each homologous area) and at least one protein of 120,000 MW form DNA-protein complexes in this promoter by gel-shift assays, DNAse footprinting, and Southwestern blotting. A region including sequences 1.7 kb upstream from the start of transcription is important for maximum expression in transient assays. Shorter segments have lesser promoter activity.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 EY 00075-12 LI

PERIOD COVERED
October 1, 1989 to September 30, 1990

TITLE OF PROJECT (*80 characters or less. Title must fit on one line between the borders.*)
Immune Functions in Ocular Diseases of Obscure Etiology

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation.)*

PI:	Robert B. Nussenblatt	M.D.	Clinical Director	NEI
Others:	Marc de Smet	M.D.	Visiting Scientist	LI, NEI
	Benjamin Rubin	M.D.	Senior Staff Fellow	LI, NEI
	Barry Grubbs	B.Sc.	Biologist	LI, NEI
	Rashid Mahdi		Biologist	LI, NEI
	Scott Whitcup	M.D.	Senior Staff Fellow	LI, NEI
	Jan Lopez	M.D.	Visiting Fellow	LI, NEI
	Rubens Belfort	M.D.	Visiting Scientist	LI, NEI
	Alan G. Palestine	M.D.	Special Volunteer	LI, NEI

COOPERATING UNITS *(if any)*
University of Kurume, Kurume, Japan (Manabu Mochizuki, M.D.)

LAB/BRANCH
Laboratory of Immunology

SECTION
Section on Immunoregulation

INSTITUTE AND LOCATION
NEI, NIH, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
1.02	1.00	0.02

CHECK APPROPRIATE BOX(ES)

☒ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
- ☐ (a1) Minors
- ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

In vitro cellular immune functions and lymphocyte subsets are being studied in a masked method in patients with ocular toxoplasmosis, pars planitis, Behcet's disease, geographic choroiditis, and chorioretinitis of unknown origin. Crude ocular antigens, purified uveitogenic soluble antigen (S-antigen), interphotoreceptor-binding protein (IRBP) of the retina, and uveitogenic fractions of the retinal S-antigen are being used in a lymphocyte microculture technique to evaluate the presence of cellular immune memory in ocular tissues. In addition, purified antigens from the toxoplasmosis organism are being tested in this in vitro system. A subgroup of patients with posterior uveitis has been identified as having this immunologic memory. Lymphocyte subsets in the blood and in the eye are being defined in these patients by monoclonal antibodies, which may shed light on the basic mechanisms of uveitis and may be used as a guide for specific immunologic therapy. The serum from these patients is also being evaluated.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 EY 00092-11 LI

PERIOD COVERED
October 1, 1989 to September 30, 1990

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
HLA, ABO, and B-cell Alloantigens and Ocular Inflammatory Disease

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation.)*

PI:	Robert B. Nussenblatt	M.D.	Clinical Director	NEI
Others:	Charles Egwuagu	Ph.D.	Staff Fellow	LI, NEI

COOPERATING UNITS *(if any)*
L'Hôpital de la Pitié, Paris, France (Phuc Le Hoang, M.D.)

LAB/BRANCH
Laboratory of Immunology

SECTION
Section on Immunoregulation

INSTITUTE AND LOCATION
NEI, NIH, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.03	0.03	0.0

CHECK APPROPRIATE BOX(ES)

☒ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

This project has been terminated.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 EY 00094-11 LI

PERIOD COVERED

October 1, 1989 to September 30, 1990

TITLE OF PROJECT (*80 characters or less. Title must fit on one line between the borders.*)

Immune Mechanisms in Experimental Autoimmune Uveitis

PRINCIPAL INVESTIGATOR (*List other professional personnel below the Principal Investigator.*) (*Name, title, laboratory, and institute affiliation.*)

PI:	Robert B. Nussenblatt	M.D.	Clinical Director	NEI
Others:	Yujiro Fujino	M.D.	Visiting Associate	LI, NEI
	Stephan Thurau	M.D.	Special Volunteer	LI, NEI
	Rashid Mahdi		Biologist	LI, NEI
	Evelyn Beraud	M.D.	Visiting Associate	LI, NEI
	Benjamin Rubin	M.D.	Senior Staff Fellow	LI, NEI
	Phuc Le Hoang	M.D.	Visiting Scientist	LI, NEI

COOPERATING UNITS (*if any*)

LAB/BRANCH

Laboratory of Immunology

SECTION

Section on Immunoregulation

INSTITUTE AND LOCATION

NEI, NIH, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
1.35	1.25	0.10

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK (*Use standard unreduced type. Do not exceed the space provided.*)

This project has been terminated.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 EY 00115-12 LI

PERIOD COVERED
October 1, 1989 to September 30, 1990

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Cyclosporine Therapy in Uveitis

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation.)*

PI:	Robert B. Nussenblatt	M.D.	Clinical Director	NEI
Others:	Marc de Smet	M.D.	Senior Staff Fellow	LI, NEI
	Benjamin Rubin	M.D.	Senior Staff Fellow	LI, NEI
	Scott Whitcup	M.D.	Senior Staff Fellow	LI, NEI
	Juan Lopez	M.D.	Visiting Fellow	LI, NEI
	Chi-Chao Chan	M.D.	Medical Officer	LI, NEI

COOPERATING UNITS *(if any)*

LAB/BRANCH
Laboratory of Immunology

SECTION
Section on Immunoregulation

INSTITUTE AND LOCATION
NEI, NIH, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.68	0.68	0.0

CHECK APPROPRIATE BOX(ES)

☒ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Cyclosporine, an endecapeptide fungal product with specific anti-T cell characteristics, will be administered to patients with sight-threatening ocular inflammatory disease of non-infectious origin who have failed on either corticosteroid or cytotoxic agent therapy. This procedure will test cyclosporine's efficacy in the treatment of uveitis. Within the context of ongoing studies, the combined use of cyclosporine A and ketaconazole will be evaluated: Selected patients whose uveitis is well controlled on cyclosporine for 1 year or more are undergoing kidney biopsies for evaluatation of the long-term effects of this agent. The use of specific thromboxane A2 antagonists to inhibit the renal toxicity of cyclosporine is being considered. An ongoing phase I/II randomized trial using cyclosporine A and G nears completion.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 EY 00015-25 LRCMB

PERIOD COVERED
October 1, 1989 to September 30, 1990

TITLE OF PROJECT (*80 characters or less. Title must fit on one line between the borders.*)
The Cell Biology of the Vertebrate Retina

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation.)*

PI:	Paul J. O'Brien	Ph.D.	Head, Section on Cell Biology	LRCMB, NEI
Others:	Sylvia B. Smith	Ph.D.	Staff Fellow	LRCMB, NEI

COOPERATING UNITS *(if any)*

LAB/BRANCH
Laboratory of Retinal Cell and Molecular Biology

SECTION
Section on Cell Biology

INSTITUTE AND LOCATION
NEI, NIH, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.6	0.6	0.0

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
- ☐ (a1) Minors
- ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The posttranslational modifications of rhodopsin include acylation, glycosylation, and chromophore addition. All appear to take place in the rod inner segment. The resulting molecules exhibit a slightly higher molecular weight than the mature rhodopsin in the outer segment and thus can be distinguished. This higher molecular weight is attributable to the larger oligosaccharide normally found on nascent glycoproteins. Ordinarily, the large oligosaccharide is trimmed and modified as the glycoprotein passes through the Golgi complex. The glycoprotein acquires its mature molecular size by the time it reaches the cell surface. Rhodopsin behaves somewhat differently in that it still exhibits a slightly larger molecular weight after it has been inserted into the plasma membrane of the rod outer segment. Several lines of experimentation have shown that these molecules possess a galactose residue not present in rhodopsin molecules that have been further sequestered in isolated rod outer segment disc membranes. The experimental methods included sensitivity to galactose oxidase and β-galactosidase as well as affinity chromatography on galactose-specific lectin matrices. As the rhodopsin molecules migrated from the plasma membrane to the disc membranes, they lost labeled galactose and lectin-binding. Separation of plasma membrane and disc membrane fractions confirmed that galactose was trimmed from the oligosaccharide.

This unusual sequence of events may be related to disc morphogenesis insofar as tunicamycin blockage of oligosaccharide synthesis results in failure of the rhodopsin-containing membranes to form new discs.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 EY 00016-23 LRCMB

PERIOD COVERED

October 1, 1989 to September 30, 1990

TITLE OF PROJECT (*80 characters or less. Title must fit on one line between the borders.*)

The Biochemistry of Normal and Dystrophic Retinas

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation.)*

PI:	Paul J. O'Brien	Ph.D.	Head, Section on Cell Biology	LRCMB, NEI
Others:	Sylvia B. Smith	Ph.D.	Staff Fellow	LRCMB, NEI
	Jun Li	M.D.	IRTA Fellow	LRCMB, NEI

COOPERATING UNITS *(if any)*

School of Veterinary Medicine, University of Pennsylvania (G. Aguirre, D.V.M.); Cullen Eye Institute, Baylor College of Medicine (R.E. Anderson, Ph.D., M.D.)

LAB/BRANCH

Laboratory of Retinal Cell and Molecular Biology

SECTION

Section on Cell Biology

INSTITUTE AND LOCATION

NEI, NIH, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
1.6	1.6	0.0

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Previous studies on the metabolism of polyunsaturated fatty acids in the retinas of miniature poodles had suggested that the essential fatty acid, linolenic acid, having 18 carbon atoms and three double bonds, was not elongated and desaturated to docosahexaenoic acid (DHA) with 22 carbons and six double bonds in the rod outer segments (ROS). This analysis was made 24 hours after intravitreal injection of labeled linolenic acid. Further study revealed that some elongation and desaturation had taken place elsewhere in the retinas. A more detailed study in rats showed that there was rapid conversion of linolenic acid to several of the intermediates in the pathway, but that the final desaturation step was extremely slow, as was the appearance of labeled DHA in ROS. Thus, the mammalian retina appears to be capable of converting small amounts of linolenic acid to DHA but is probably dependent on extraocular sources for the DHA needed to replace large amounts of ROS disc membranes, which are uniquely enriched in this fatty acid.

Poodles affected with progressive rod-cone degeneration (prcd) have low blood levels of DHA, probably because of a defect in the final desaturating enzyme. Several types of retinitis pigmentosa patients also exhibit low blood levels of DHA, which could result in impaired ROS renewal. Attempts to identify the plasma proteins involved in transporting linolenic acid and DHA have revealed that labeled linolenic acid, administered by gavage, first enters the blood bound to very low density lipoprotein which transports it to the liver. After conversion to DHA, the labeled fatty acid then appears to be transported by albumin. Identification of the carrier proteins will target candidate genes for studies of inherited retinal degenerations.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 EY 00256-02 LSR

PERIOD COVERED
October 1, 1989 to September 30, 1990

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Information Processing by Visual System Neurons

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation.)*

PI:	Lance M. Optican	Ph.D.	Chief, NMS	LSR, NEI
Others:	John W. McClurkin	Ph.D.	Staff Fellow	LSR, NEI
	Arthur V. Hays	B.A.	Electronics Engineer	LSR, NEI
	Brad J. Zoltick	M.A.	Computer Programmer	LSR, NEI

COOPERATING UNITS *(if any)*
Laboratory of Neuropsychology, National Institute of Mental Health (Barry J. Richmond, M.D., Timothy J. Gawne, Ph.D., Emad N. Eskandar, B.A.)

LAB/BRANCH
Laboratory of Sensorimotor Research

SECTION
Section on Neural Modeling

INSTITUTE AND LOCATION
NEI, NIH, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
2.8	1.9	0.9

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Visual perception depends on rich interactions among individual neurons. These interactions depend on mechanisms that encode, process, and transmit information among different visual areas of the brain. We are applying information theory to neurophysiological studies of behavior to learn what role neurons play in forming perceptions. We have already shown that neurons in different areas of the brain encode and transmit information about stationary, two-dimensional pictures that vary in form, brightness, and duration. In all areas studied, neurons encode picture information using a multidimensional temporal code. Neurons can transmit at least three times as much information using a multivariate temporal code as could be transmitted using a univariate strength code. We are now recording from individual neurons during visual discrimination tasks. It appears that neurons in the inferior temporal cortex send two types of messages during a pattern recognition task. One type of message describes the picture, whereas the other type of message indicates that a certain response is called for, without describing the eliciting picture. These results suggest that behavioral and physical parameters of a stimulus may be coupled within a temporal code.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 EY 00217-04 LI

PERIOD COVERED
October 1, 1989 to September 30, 1990

TITLE OF PROJECT (*80 characters or less. Title must fit on one line between the borders.*)
Lymphocyte Migration in Experimental Autoimmune Uveitis

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation.)*

PI:	Alan G. Palestine	M.D.	Head, Section on Clinical Immunology	LI, NEI
Others:	Robert B. Nussenblatt	M.D.	Clinical Director	NEI
	Jeffrey N. Bloom	M.D.	Senior Staff Fellow	LI, NEI

COOPERATING UNITS *(if any)*

LAB/BRANCH
Laboratory of Immunology

SECTION
Section on Clinical Immunology

INSTITUTE AND LOCATION
NEI, NIH, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.26	0.26	0.0

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

This project has been terminated.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 EY 00219-04 LI

PERIOD COVERED

October 1, 1989 to September 30, 1990

TITLE OF PROJECT (*80 characters or less. Title must fit on one line between the borders.*)

The Effect of Bromocriptine on Human Uveitis

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation.)*

PI:	Alan G. Palestine	M.D.	Head, Section on Clinical Immunology	LI, NEI
Others:	Robert B. Nussenblatt	M.D.	Clinical Director	NEI
	Janet L. Davis	M.D.	Senior Staff Fellow	LI, NEI
	David C. Herman	M.D.	Senior Staff Fellow	LI, NEI
	Jeffrey N. Bloom	M.D.	Senior Staff Fellow	LI, NEI

COOPERATING UNITS *(if any)*

Metabolism Branch, National Cancer Institute (Marie C. Gelato, M.D.)

LAB/BRANCH

Laboratory of Immunology

SECTION

Section on Clinical Immunology

INSTITUTE AND LOCATION

NEI, NIH, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.91	0.91	0.0

CHECK APPROPRIATE BOX(ES)

☒ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

This project has been terminated.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 EY 00220-04 LI

PERIOD COVERED

October 1, 1989 to September 30, 1990

TITLE OF PROJECT (*80 characters or less. Title must fit on one line between the borders.*)

Endocrine Modulation of Immune-Mediated Eye Disease in Rats

PRINCIPAL INVESTIGATOR (*List other professional personnel below the Principal Investigator.*) (*Name, title, laboratory, and institute affiliation.*)

PI:	Alan G. Palestine	M.D.	Head, Section on Clinical Immunology	LI, NEI
Others:	Robert B. Nussenblatt	M.D.	Clinical Director	NEI
	David C. Herman	M.D.	Staff Fellow	LI, NEI

COOPERATING UNITS (*if any*)

LAB/BRANCH

Laboratory of Immunology

SECTION

Section on Clinical Immunology

INSTITUTE AND LOCATION

NEI, NIH, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.31	0.31	0.0

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK (*Use standard unreduced type. Do not exceed the space provided.*)

This project has been terminated.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 EY 00221-04 LI

PERIOD COVERED
October 1, 1989 to September 30, 1990

TITLE OF PROJECT (*80 characters or less. Title must fit on one line between the borders.*)
Intraocular Class II Antigen Expression in Endotoxin-Induced Uveitis

PRINCIPAL INVESTIGATOR (*List other professional personnel below the Principal Investigator.*) (*Name, title, laboratory, and institute affiliation.*)

PI:	Alan G. Palestine	M.D.	Head, Section on Clinical Immunology	LI, NEI
Others:	Robert B. Nussenblatt	M.D.	Clinical Director	NEI
	Horst Helbig	M.D.	Special Volunteer	LI, NEI
	Rebecca Gurley	M.S.	Biologist	LI, NEI

COOPERATING UNITS (*if any*)

LAB/BRANCH
Laboratory of Immunology

SECTION
Section on Clinical Immunology

INSTITUTE AND LOCATION
NEI, NIH, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.31	0.31	0.0

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK (*Use standard unreduced type. Do not exceed the space provided.*)

This project has been terminated.

GPO 914-918

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 EY 00230-04 LI

PERIOD COVERED
October 1, 1989 to September 30, 1990

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Modulation of Retinal Vascular Permeability by Inflammatory Mediators

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation.)*

PI:	Alan G. Palestine	M.D.	Head, Section on Clinical Immunology	LI, NEI
Others:	Rebecca Gurley	M.S.	Biologist	LI, NEI
	Benjamin Rubin	M.D.	Senior Staff Fellow	LI, NEI
	Horst Helbig	M.D.	Special Volunteer	LI, NEI

COOPERATING UNITS *(if any)*

LAB/BRANCH
Laboratory of Immunology

SECTION
Section on Clinical Immunology

INSTITUTE AND LOCATION
NEI, NIH, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.43	0.03	0.40

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

This project has been terminated.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 EY 00247-02 LI

PERIOD COVERED

October 1, 1989 to September 30, 1990

TITLE OF PROJECT (*80 characters or less. Title must fit on one line between the borders.*)

Autoimmunity to the Anterior Uvea in Patients with Uveitis

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation.)*

PI:	Alan G. Palestine	M.D.	Head, Section on Clinical Immunology	LI, NEI
Others:	Rebecca Gurley	M.S.	Biologist	LI, NEI

COOPERATING UNITS *(if any)*

LAB/BRANCH

Laboratory of Immunology

SECTION

Section on Clinical Immunology

INSTITUTE AND LOCATION

NEI, NIH, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.77	0.17	0.60

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☒ (b) Human tissues ☐ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

This project has been terminated.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 EY 00243-04 LMOD

PERIOD COVERED

October 1, 1989 to September 30, 1990

TITLE OF PROJECT (*80 characters or less. Title must fit on one line between the borders.*)

Ocular Cells Cultured Under Normal and Diabetic Conditions

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation.)*

PI:	Bruce A. Pfeffer	Ph.D.	Senior Staff Fellow	LMOD, NEI
Others:	W. Gerald Robison, Jr.	Ph.D.	Chief, Section on Pathophysiology	LMOD, NEI

COOPERATING UNITS *(if any)*

LAB/BRANCH

Laboratory of Mechanisms of Ocular Diseases

SECTION

Section on Pathophysiology

INSTITUTE AND LOCATION

NEI, NIH, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
1.5	1.0	0.5

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☒ (b) Human tissues ☐ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Biosynthesis of extracellular matrix molecules was studied using cultured monkey retinal pigment epithelial (RPE) cells. In one set of experiments, native interphotoreceptor matrix (IPM) was labeled in vivo to parallel the apical expression of putative IPM components by cultured RPE. By polyacrylamide gel electrophoresis and subsequent autoradiography, we found that cultured RPE produces several proteins whose electrophoretic mobility coincides with those of proteins in vivo. Therefore, cultured RPE may be a source of previously unidentified IPM constituents.

Also shown was cultured RPE synthesis of two well-characterized basement membrane components, the attachment glycoprotein laminin and heparan sulfate proteoglycan (HSPG). While the depositon of the former was polarized to the basal side of the cells, the latter was released in insoluble form as part of the extracellular matrix substrate and secreted in soluble form into the culture media. Cultured RPE cells do not proteolytically "chip" the precursor to the core protein of HSPC, but instead release an intact proteoglycan with glycosaminoglycan chains attached to the full-size 400 kD protein moiety.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 EY 00126-09 LMDB

PERIOD COVERED

October 1, 1989 to September 30, 1990

TITLE OF PROJECT (*80 characters or less. Title must fit on one line between the borders.*)

Crystallin Genes: Structure, Organization, Expression, and Evolution

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation.)*

PI: Joram Piatigorsky Ph.D. Chief LMDB, NEI

COOPERATING UNITS *(if any)*

Section on Mammalian Gene Regulation, Lab. of Molecular Genetics, Natl. Inst. of Child Health and Human Development (Heiner Westphal, M.D., Head); Section on Molecular Genetics of Immunity, Lab. of Developmental and Molecular Immunity, Natl. Inst. of Child Health and Human Development (Keiko Ozato, Ph.D., Head); Jules Stein Eye Institute, UCLA Medical School, Los Angeles, CA (Joseph Horwitz, Ph.D.); DNA Chemistry, Biotechnica International, Inc., Cambridge, MA (Abdul H. Ally, Ph.D.)

LAB/BRANCH

Laboratory of Molecular and Developmental Biology

SECTION

Section on Molecular Genetics

INSTITUTE AND LOCATION

NEI, NIH, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
13.5	13.5	0.0

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The structure and expression of various crystallin genes have been investigated in humans, mice, chicken, squid, and jellyfish. The human and mouse αB-, the chicken βA3/A1- and the major squid crystallin genes have been fully sequenced; many other squid and one jellyfish crystallin genes have been cloned. Numerous *cis*-regulatory sites have been identified in the 5' flanking regions of αA-, αB-, βB1-, and squid crystallin genes, all of which include sequences known to bind transcription factors found in many tissues and involved in the regulation of other genes. In this connection, at least seven different cDNAs encoding zinc fingers have been cloned from the mouse lens. One of these cDNAs encoding a protein called αA-CRYBP1 is implicated in the lens-specific expression of the mouse αA-crystallin gene and is similar to human MBP-1 and PRDII-BF1, which bind to the MHC class I and the β-interferon gene regulatory elements, respectively. The αA-CRYBP1 binding site confers lens-preferred expression to the thymidine kinase promoter when tested in an SV40-transformed mouse lens epithelial cell line, but not in primary cultures of chicken lens cells. The chicken αA-crystallin gene was found to use at least one and possibly two different sequences further upstream than the αA-CRYBP1 site for its expresssion in the lens cells; one of these has a dyad of symmetry. The insert exon of the αA-crystallin gene was shown to be present among many mammals, indicating an early evolutionary appearance for this alternatively spliced coding sequence. The two δ-crystallin genes were shown to be differentially expressed in lens, heart and brain in chicken embryos. The δ1 gene is specialized for lens, while the δ2 gene is preferentially expressed in non-lens tissues, consistent with δ2 being the homologue of the argininosuccinate lyase gene. Finally, the chicken carbonic anhydrase II gene was shown to be regulated differently in lens and retina, and a functional promoter has been cloned.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 EY 00260-01 LRCMB

PERIOD COVERED
October 1, 1989 to September 30, 1990

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Molecular Biology of Outer Retina-Specific Proteins

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation.)*

PI:	T. Michael Redmond	Ph.D.	Research Biologist	LRCMB, NEI
Others:	Christian P. Hamel	M.D.	Visiting Associate	LRCMB, NEI
	Gerald J. Chader	Ph.D.	Chief	LRCMB, NEI

COOPERATING UNITS *(if any)*

LAB/BRANCH
Laboratory of Retinal Cell and Molecular Biology

SECTION
Section on Gene Regulation

INSTITUTE AND LOCATION
NEI, NIH, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
2.1	2.1	0.0

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Retinal pigment epithelial (RPE) cells and the photoreceptor (PR) cells are functionally and developmentally closely integrated. During development of the outer retina in rat, the determinant recognized by the RPE-specific monoclonal antibody RPE-9 is first expressed at post-natal day 3 whereas the PR outer segments (OS) appear at day 5. The OS first appears where RPE cells are already expressing their determinant. RPE-9 recognizes a 67-kDa protein specific to the RPE. This protein is found in mammalian and avian RPE. A membrane-associated protein, it is probably non-glycosylated. We have begun to screen a bovine RPE cDNA library for a cDNA for this protein.

We have subcloned DNA fragments corresponding to the first two repeats of bovine IRBP into a bacterial expression vector. IRBP is involved in the transport of retinoids, a functional relationship between the RPE and the PR. The resultant expressed protein fragments will be tested for their ligand-binding and immunological properties.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 EY 00228-04 LI

PERIOD COVERED
October 1, 1989 to September 30, 1990

TITLE OF PROJECT (*80 characters or less. Title must fit on one line between the borders.*)
Study of Ocular Glial Cell Involvement in Uveitis

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation.)*

PI:	Francois Roberge	M.D.	Visiting Associate	LI, NEI
Others:	Robert B. Nussenblatt	M.D.	Clinical Director	NEI
	Rachel Caspi	Ph.D.	Visiting Associate	LI, NEI

COOPERATING UNITS *(if any)*

LAB/BRANCH
Laboratory of Immunology

SECTION
Section on Immunoregulation

INSTITUTE AND LOCATION
NEI, NIH, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.82	0.82	0.0

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
- ☐ (a1) Minors
- ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

This project has been terminated.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 EY 00045-12 LSR

PERIOD COVERED
October 1, 1989 to September 30, 1990

TITLE OF PROJECT (*80 characters or less. Title must fit on one line between the borders.*)
Visuomotor Properties of Neurons in the Thalamus

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigetor.) (Name, title, laboratory, and institute affiliation.)*

PI:	David Lee Robinson	Ph.D.	Section Chief	LSR, NEI
Others:	Caroline Kertzman	Ph.D.	IRTA	LSR, NEI
	Verity J. Brown	Ph.D.	Visiting Fellow	LSR, NEI
	Eric M. Bowman	Ph.D.	NRSA Fellow	LSR, NEI
	Edmond J. FitzGibbon	M.D.	Senior Staff Fellow	LSR, NEI
	James R. Carl	M.D.	Expert	LSR, NEI

COOPERATING UNITS *(if any)*

Developmental Endocrinology Branch, National Institute of Child Health and Human Development (Richard Sherins, M.D.); Experimental Therapeutics Branch, National Institute of Neurological Disorders and Stroke (Irene Litvan, M.D.); Department of Anatomy, Howard University (Robert J. Cowie, Ph.D.)

LAB/BRANCH
Laboratory of Sensorimotor Research

SECTION
Section on Visual Behavior

INSTITUTE AND LOCATION
NEI, NIH, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
2.0	1.4	0.6

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

A visual stimulus appearing in the periphery causes a shift of attention. This change is not localized to the site of the visual stimulus, but facilitates adjacent regions. Parietal cortex neurons are modulated during this attentional behavior: cells with visual receptive fields at the focus of attention are suppressed, a mechanism thus leading to facilitation of the responses of cells not at the focus of attention. When animals respond to visual targets that alternate between locations in a predictable way, reaction times to expected targets are faster than to than unexpected targets. Parietal cells respond best to the unexpected stimulus. These observations are consistent with the parietal cortex's containing a signal to shift attention. We have tested a group of Parkinson's disease patients on complex reaction time tasks. Although the disease produces a general impairment on all tasks, treatment with L-dopa selectively improves performance on only one. Responses which are "compatible" with the visual stimulus signaling them are speeded with L-dopa; responses "arbitrarily" associated with the triggering stimulus are unaffected by this treatment. These studies suggest that the basal ganglia, using dopamine, function in the initiation of movement. We have discovered that when a brainstem region involved in the initiation of head movements is electrically stimulated, the animal makes a brisk head movement. The size and amplitude of this movement depends on the intensity of the current and the starting position of the head. Injecting chemical tracers, we discovered that areas sending information to this brainstem region include the deep layers of the superior colliculus, the primary motor cortex, and the premotor cortex. The axons of cells in these areas reach the cervical spinal cord as well as other premotor, brainstem sites. These studies help explain the organization of systems for initiating head movements.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 EY 00149-17 LMOD

PERIOD COVERED
October 1, 1989 to September 30, 1990

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Ultrastructure and Function of the Cells and Tissues of the Eye

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation.)*

PI:	W. Gerald Robison, Jr.	Ph.D.	Head, Section on Pathophysiology	LMOD, NEI
Others:	Nora Laver	M.D.	Visiting Associate	LMOD, NEI
	Bruce A. Pfeffer	Ph.D.	Senior Staff Fellow	LMOD, NEI

COOPERATING UNITS *(if any)*

LAB/BRANCH
Laboratory of Mechanisms of Ocular Diseases

SECTION
Section on Pathophysiology

INSTITUTE AND LOCATION
NEI, NIH, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
4.5	2.0	2.5

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☒ (b) Human tissues ☐ (c) Neither
- ☐ (a1) Minors
- ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

This laboratory has developed the first reliable and convenient animal model for the very distinct group of lesions characteristic of human background diabetic retinopathy. Taking advantage of the fact that aldose reductase has a higher affinity for galactose than for glucose, which results in more intracellular polyol accumulation in galactosemia, we fed rats galactose for extended periods in an effort to produce diabetic-like retinal lesions. Galactosemia indeed induced diabetic-like microangiopathies that were more advanced and more like human diabetic lesions than those which develop in long-term diabetic rats. The galactose-fed rat exhibits capillary basement membrane thickening within 28 weeks; selective pericyte loss, capillary dilation, endothelial cell proliferation, some tortuosity of vessels, and some acellularity within 33 weeks; microaneurysms, occlusions, and shunts within 66 weeks; and extensive regions of varicose capillary meshwork by 98 weeks, making the galactosemic rat a good model for diabetes-induced retinal microangiopathies that take longer to develop. This rat should also serve as a model for other polyol-related complications of diabetes. The galactose-fed rat model has distinct advantages over genetic or chemically induced models of diabetes for intervention studies: It shows lesions sooner, and upon removal from the galactose diet, it returns to a normal physiological state within a few days. We plan to determine appropriate times for intervention using different aldose reductase inhibitors, and to attempt, by dietary manipulation, to produce rat models that develop the diabetic-like retinal angiopathies sooner. Also, using cell culture, we will investigate possible mechanisms of endothelial cell proliferation and subsequent pathologies.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 EY 00162-07 CB

PERIOD COVERED

October 1, 1989 to September 30, 1990

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Vitreous Fluorophotometry

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation.)*

PI: Monique S. Roy M.D. Visiting Scientist CB, NEI

COOPERATING UNITS *(if any)*

Biomedical Engineering and Instrumentation Branch, Division of Research Services, NIH (Peter Bungay, Ph.D.)

LAB/BRANCH

Clinical Branch

SECTION

Section on Retinal and Vitreal Diseases

INSTITUTE AND LOCATION

NEI, NIH, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.4	0.4	0.0

CHECK APPROPRIATE BOX(ES)

☒ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

This project has been terminated.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 EY 00198-06 CB

PERIOD COVERED
October 1, 1989 to September 30, 1990

TITLE OF PROJECT (*80 characters or less. Title must fit on one line between the borders.*)
Sorbinil Retinopathy Trial

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation.)*

PI:	Monique S. Roy	M.D.	Visiting Scientist	CB, NEI
Others:	James R. Carl	M.D.	Senior Staff Fellow	CB, NEI

COOPERATING UNITS *(if any)*
National Institute of Diabetes and Digestive and Kidney Diseases, NIH (R. Silverman)

LAB/BRANCH
Clinical Branch

SECTION
Section on Retinal and Vitreal Diseases

INSTITUTE AND LOCATION
NEI, NIH, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.7	0.7	0.0

CHECK APPROPRIATE BOX(ES)

☒ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

This project has been terminated.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 EY 00263-01 LI

PERIOD COVERED
October 1, 1989 to September 30, 1990

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Comparison of Surgical Treatment in Uveitis Patients With Glaucoma

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation.)*

PI:	Benjamin I. Rubin	M.D.	Senior Fellow	LI, NEI
Others:	Robert B. Nussenblatt	M.D.	Clinical Director	NEI
	Marc de Smet	M.D.	Visiting Fellow	LI, NEI
	Chi-Chao Chan	M.D.	Medical Officer	LI, NEI

COOPERATING UNITS *(if any)*

LAB/BRANCH
Laboratory of Immunology

SECTION
Section of Clinical Immunology

INSTITUTE AND LOCATION
NEI, NIH, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.2	0.2	0.0

CHECK APPROPRIATE BOX(ES)

☒ (a) Human subjects ☒ (b) Human tissues ☐ (c) Neither
☒ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Four patients have been entered into the study. Three patients were randomized to trabeculectomy with 5-fluorouracil (5-FU) and one to the Molteno glaucoma implant. Two patients were black; two patients, white. Two patients are women; two, men. Three of the patients have aphakic uveitis, and one patient is phakic with uveitis. Intraocular pressure in all four patients has been maintained between 12 and 20 millileters of mercury. Complications occurring postsurgically have included serious choroidal detachments in the three aphakic patients.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 EY 00237-05 LMOD

PERIOD COVERED
October 1, 1989 to September 30, 1990

TITLE OF PROJECT (*80 characters or less. Title must fit on one line between the borders.*)
Characterization of the Lens

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation.)*

PI:	Paul Russell	Ph.D.	Research Chemist	LMOD, NEI
Others:	Takahiko Yamada	M.D.	Visiting Associate	LMOD, NEI

COOPERATING UNITS *(if any)*

LAB/BRANCH
Laboratory of Mechanisms of Ocular Diseases

SECTION
Section on Cataracts

INSTITUTE AND LOCATION
NEI, NIH, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
1.5	1.5	0.0

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☒ (b) Human tissues ☐ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The advent of transgenic animals has made possible study of the influence and regulation of various genes on the development of an organism. However, this technique has not generally been used to develop cell lines for use in tissue culture. Tissue culture of the lens epithelium has been a goal of lens researchers because it may afford an opportunity to develop in vitro systems to test the efficacy of anticataract agents, as well as to study some mechanisms of cataract formation.

A recently obtained transgenic animal has the T-antigen from the SV40 virus linked to the αA-crystallin promoter. Cells from the lens of this animal that proliferate in the tissue culture environment have been shown to produce all the α-crystallins. These cells also synthesize the enzyme aldose reductase, which is induced under conditions of hyperosmolarity. The cell line has been used to study metabolic alterations that occur during incubation with naphthalene metabolites, compounds chosen because of naphthalene cataracts' similarity to subcapsular age-related cataracts in humans. The specific-activity of the enzyme DT-diaphorase was increased when cells were exposed to high levels of naphthalene metabolites.

Extensive work with epithelial samples from human donor eyes has shown little difference between epithelium from various sites in the lens or between epithelium from young or old adult epithelium.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 EY 00252-02 LMOD

PERIOD COVERED
October 1, 1989 to September 30, 1990

TITLE OF PROJECT (*80 characters or less. Title must fit on one line between the borders.*)
Cataract in the Philly Mouse Strain

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation.)*

PI:	Paul Russell	Ph.D.	Research Chemist	LMOD, NEI
Others:	Carolyn Chambers	Ph.D.	Staff Fellow	LMOD, NEI

COOPERATING UNITS *(if any)*

LAB/BRANCH
Laboratory of Mechanisms of Ocular Diseases

SECTION
Section on Cataracts

INSTITUTE AND LOCATION
NEI, NIH, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
1.5	1.5	0.0

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The Philly mouse derived from the Swiss-Webster strain develops a cataract about 6 weeks after birth. The results of early studies have shown that in the lenses of these animals, the epithelial cells fail to undergo complete differentiation. Biochemically, a 27 kD protein apparently missing from the Philly lens was shown to be the βB2-crystallin, which in the normal lens is a heat-stable protein. Investigation of the Philly mouse revealed that mRNA with approximately the same size as the normal βB2 mRNA is present in the Philly lens. It was further shown that a protein present in the Philly lens is immunologically related to the βB2 protein in the normal lens. This protein shares the same amino terminal as the normal βB2 but lacks part of the carboxyl half of the protein. The altered protein is slightly smaller and has a more acidic isoelectric point than the normal lens βB2-crystallin.

cDNAs were cloned and sequenced for normal and Philly mouse βB2-crystallin. The normal mouse βB2 cDNA is 725 (bp) in length and has 618 bp of open reading frame. Deduced amino acid sequences suggest that the normal mouse βB2 lacks a phosphorylation site at the C-terminal that is found in other mammals. The Philly mouse has a deletion of 12 nucleotides in the area encoding its fourth motif. The properties of the protein encoded with this deletion appear to be consistent with the earlier protein findings and may be responsible for the cataract formation.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 EY 00250-03 LRCMB

PERIOD COVERED
October 1, 1989 to September 30, 1990

TITLE OF PROJECT (*80 characters or less. Title must fit on one line between the borders.*)
Molecular Biology of Experimental Autoimmune Uveitis

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation.)*

PI:	Toshimichi Shinohara	Ph.D.	Head, Section on Molecular Biology	LRCMB, NEI
Others:	Tohru Abe	M.D., Ph.D.	Visiting Associate	LRCMB, NEI
	Kotaro Eto	M.D., Ph.D.	Visiting Associate	LRCMB, NEI
	S. Sunil	M.D.	Visiting Fellow	LRCMB, NEI

COOPERATING UNITS *(if any)*
National Research Council, Division of Chemistry, Canada (H. Henry Mantsch, Ph.D.); Wills Eye Hospital, Philadelphia, PA (L.A. Donoso, M.D., Ph.D.)

LAB/BRANCH
Laboratory of Retinal Cell and Molecular Biology

SECTION
Section on Molecular Biology

INSTITUTE AND LOCATION
NEI, NIH, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
1.0	1.0	0.0

CHECK APPROPRIATE BOX(ES)

☒ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
☒ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

We have previously determined amino acid sequences of human, mouse, rat and bovine retinal S-antigen and rat pineal gland S-antigen. Immunogenic sites and four uveitopathogenic sites of S-antigen were also determined. Two of the immunogenic sequences were highly conserved among these species.

There are many proteins which have a similar sequence with a uveitopathogenic site in the National Biomedical Research Foundation data base. We chemically synthesized many peptides, some of which induced experimental autoimmune uveitis (EAU) and experimental autoimmune pinealitis (EAP) in Lewis rats, including synthetic peptides from yeast (Saccharomyces cerevisiae) histone H3, *Escherichia coli* hypothetical protein, potato proteinase inhibitor, hepatitis virus protein, Moloney murine sarcoma virus protein, and Moloney murine leukemia virus protein. In addition, native yeast histone H3 was also capable of inducing EAU.

Interestingly, the animals that were administered the yeast histone orally suppressed the EAU and EAP induction by either yeast histone H3 peptide or a S-antigen peptide. Thus, the peptides that have molecular mimicry cross-induced the tolerance. These findings provide a basis for autoimmune inflammatory diseases of the eye in humans.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 EY 00132-09 LRCMB

PERIOD COVERED
October 1, 1989 to September 30, 1990

TITLE OF PROJECT (*80 characters or less. Title must fit on one line between the borders.*)
Molecular Biology of Phototransduction

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation.)*

PI:	Toshimichi Shinohara	Ph.D.	Head, Section on Molecular Biology	LRCMB, NEI
Others:	Kunihiko Yamaki	M.D., Ph.D.	Visiting Associate	LRCMB, NEI
	Thoru Abe	M.D., Ph.D.	Visiting Associate	LRCMB, NEI
	Shuji Suzuki	M.D., Ph.D.	Visiting Associate	LRCMB, NEI
	Takanobu Kikuchi	Ph.D.	Visiting Associate	LRCMB, NEI

COOPERATING UNITS *(if any)*
Division of Cancer Research, Mount Sinai Hospital, Toronto Ontario, Canada
(Martin Breitman, Ph.D.)

LAB/BRANCH
Laboratory of Retinal Cell and Molecular Biology

SECTION
Section on Molecular Biology

INSTITUTE AND LOCATION
NEI, NIH, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
4.2	4.2	0.0

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

We have characterized the S-antigen genes from human and mouse, a kinase cDNA from human; phosducin cDNAs from cow, rat, and human; Shuzin cDNAs from human and cow and a Shuzin gene from human. The gene sequences of the human and mouse S-antigens were determined. The S-antigen genes were approximately 50 kbp in length, contained 16 exons and 15 introns, and were comprised of 97% intron and 3% exon. The 5'-flanking regions of the genes, approximately 1.5 kbp long, have no known regulatory elements for transcription such as TATA, GC, or CCAAT boxes. Interestingly, the 5' flanking regions of the human and mouse genes expressed tissue specific promoter activity in both in vitro and in vivo transcription assays as well as in transgenic mice. Several cDNAs of the phosducin from human, rat, and cow were isolated, and we determined their DNA sequences. Each sequence contains a Ser73 for phosphorylation by A-kinase. Sequencing results show that the phosducin in the retina and pineal gland have the same sequences and the same phosphorylation sites. This suggests that the functional role of this protein is the same in the retina and pineal gland.

The functional role of the retinal protein Shuzin is unknown. We isolated several cDNAs and sequenced each of these from human and cow. The entire gene sequence of human Shuzin was also determined. This gene is composed of two introns and three exons and it has a highly repetitive sequence in the 5'-noncoding region.

We have constructed fusion genes containing a 5'-flanking S-antigen gene sequence upstream of the bacterial gene chloramphenicol acetyl transferase (CAT). A hybrid gene containing the 5'-flanking region of the mouse S-antigen gene and the CAT gene was microinjected into transgenic mice. Those mice expressed CAT activity in the retina and pineal gland, suggesting that the 1300 bp-long S-antigen promoter has a tissue specific enhancer and promoter.

S-antigen cDNAs were subcloned into two expression vector systems. The expressed protein was purified by gel filtration, and crystallization of this protein is now in progress.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 EY 00070-13 LRCMB

PERIOD COVERED
October 1, 1989 to September 30, 1990

TITLE OF PROJECT (*80 characters or less. Title must fit on one line between the borders.*)
Vitamin A and Ocular Tissues

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation.)*

PI:	Barbara Wiggert	Ph.D.	Head, Section on Biochemistry	LRCMB, NEI
Others:	Ling Lee	M.S.	Chemist	LRCMB, NEI
	Todd Duncan	M.S.	Biologist	LRCMB, NEI
	Gerald J. Chader	Ph.D.	Chief	LRCMB, NEI

COOPERATING UNITS *(if any)*

Boston Univ. School of Medicine (C. Cornwall, Ph.D., G. Jones, Ph.D.); The Johns Hopkins Univ., Baltimore (R. Adler. M.D.); Univ. of Lund, Lund, Sweden (T. van Veen, Ph.D.); Univ. of Illinois College of Medicine, Chicago (D. Pepperberg, Ph.D., H. Ripps, Ph.D.); Univ. of Pennsylvania School of Veterinary Medicine, Philadelphia (G. Aguirre, D.V.M., Ph.D., K. Long, Ph.D.)

LAB/BRANCH
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SECTION
Section on Biochemistry

INSTITUTE AND LOCATION
NEI, NIH, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
2.6	1.1	1.5

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☒ (b) Human tissues ☐ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

In the intact eye of the developing rd/rd, +/+ mutant mouse, interphotoreceptor-binding protein (IRBP), which is normally located extracellularly in the interphotoreceptor matrix, remains intracellular. However, when removed from the eye and placed in short-term organ culture, retinas from these mutant mice demonstrate the capacity to synthesize and secrete IRBP normally until postnatal day 11 - 12. There may then be regulatory factors which control IRBP secretion in the intact eye.

In studies of the physiological role of IRBP in the normal retina using the toad (*Bufo marinus*) eye-cup preparation, IRBP was shown to be capable of promoting regeneration of rhodopsin in bleached ROS. Serum albumin, however, did not promote regeneration. In addition, it was shown that 11-*cis* retinal was removed from the RPE by IRBP but not by serum albumin. It appears, then, that IRBP plays an active role in the vision process.

In initial studies on IRBP in mouse eyes inoculated with a murine coronavirus, there was a highly significant decrease in IRBP by day 3 following inoculation. In addition, IRBP was no longer restricted to its normal location in the interphotoreceptor matrix but had diffused in the direction of the vitreous, reaching as far as the inner nuclear layer.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 EY 00255-02 LMDB

PERIOD COVERED
October 1, 1989 to September 30, 1990

TITLE OF PROJECT (*80 characters or less. Title must fit on one line between the borders.*)
Origins, Structures, and Functions of Crystallins

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation.)*

PI:	Graeme J. Wistow	Ph.D.	Visiting Scientist	LMDB, NEI
Others:	Robert Kim	M.D.	Staff Fellow	LMDB, NEI
	Hyong Kim	B.A.	Guest Worker	LMDB, NEI
	Doug Lee	Ph.D.	NRC Fellow	LMDB, NEI
	Joram Piatigorsky	Ph.D.	Chief	LMDB, NEI

COOPERATING UNITS *(if any)*
Department of Biochemistry, Johns Hopkins University (G. Hart, L. Roquemore); Department of Biochemistry, Baylor University (W. O'Brien); Jules Stein Eye Institute, UCLA (J. Horwitz)

LAB/BRANCH
Laboratory of Molecular and Developmental Biology

SECTION
Section on Molecular Genetics

INSTITUTE AND LOCATION
NEI, NIH, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
2.9	2.4	0.5

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

We have continued to characterize novel taxon-specific crystallins including η-crystallin/aldehyde dehydrogenase in primitive placental mammals and μ-crystallin in marsupials. Both of these proteins appear to bind NAD(P) cofactors. We have also discovered that the αAins subunit of α-crystallin has a much more ancient origin than was expected; it is expressed in marsupials as well as in placental mammals. In an attempt to explain the anomalous subunit size of βB1 in birds, we have found that this major cytoplasmic protein is specifically glycylated in normal bird lenses but not in mammals. At the same time, we noted that a minor fraction of α-crystallin subunits in both birds and mammals is modified with an O-linked GlcNAc moiety, something which may have functional significance for the α-crystallin/small heat-shock protein superfamily. In the analysis of the gene for τ-crystallin/α-enolase we have found that the gene promoter is highly active in lens explants and in cultured liver and skin cells. This suggests that the basis for any lens-preferred expression of this gene must lie in other *cis* elements or in posttranscriptional events. Alternatively the promoter may be responding to the stressed condition of the cultured cells in these experiments.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 EY 00109-10 LSR

PERIOD COVERED

October 1, 1989 to September 30, 1990

TITLE OF PROJECT (*80 characters or less. Title must fit on one line between the borders.*)

Visuomotor Processing in the Primate Brain

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation.)*

PI:	Robert H. Wurtz	Ph.D.	Chief	LSR, NEI
Others:	Dwayne S. G. Yamasaki	Ph.D.	Staff Fellow	LSR, NEI
	Charles J. Duffy	M.D.,Ph.D.	Staff Fellow	LSR, NEI
	David M. Waitzman	M.D., Ph.D.	Staff Fellow	LSR, NEI
	Terence P. Ma	Ph.D.	Guest Researcher	LSR, NEI
	Douglas Munoz	Ph.D.	Guest Researcher	LSR, NEI

COOPERATING UNITS *(if any)*

LAB/BRANCH

Laboratory of Sensorimotor Research

SECTION

Section on Visuomotor Integration

INSTITUTE AND LOCATION

NEI, NIH, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
4.9	3.1	1.8

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Experiments have concentrated on the investigation of the smooth pursuit eye movement system, which keeps the fovea of the eye centered on a moving target, and of the rapid or saccadic eye movement system, which moves the fovea of the eye from one object of interest to another in the visual field. The pursuit system studies concentrated on the recovery of the ability to make pursuit eye movements following punctate lesions in the middle temporal cerebral cortical area (MT) as a model for studying the recovery of function following cerebral cortical damage. We found that large lesions that eliminated multiple areas related to visual motion processing produced deficits in the generation of pursuit that did not recover fully in 7 months. The contribution of other cortical areas beyond these motion-related areas was found to be limited. A neuronal correlate of this recovery is expansion of receptive fields in areas of MT cortex adjacent to the lesion. This receptive field expansion could provide information about the region of the visual field previously served by the damaged cells.

Studies of the saccadic system concentrated on neuronal activity in the superior colliculus. Altering saccadic eye movements by electrical stimulation of the colliculus further supports the model showing that superior colliculus activity is part of a feedback control system in the brainstem that controls the amplitude and the velocity in saccadic eye movement. Cells in the rostral pole of the colliculus were found to be related to the fixation of gaze by the monkey, suggesting that these cells may be related to a neural system that controls when the monkey makes a saccadic eye movement.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 EY 00238-05 LMDB

PERIOD COVERED
October 1, 1989 to September 30, 1990

TITLE OF PROJECT (*80 characters or less. Title must fit on one line between the borders.*)
Proto-Oncogene Expression During Lens Differentiation and Development

PRINCIPAL INVESTIGATOR (*List other professional personnel below the Principal Investigator.*) (*Name, title, laboratory, and institute affiliation.*)

PI:	Peggy Zelenka	Ph.D.	Geneticist	LMDB, NEI
Others:	Barbara Brewitt	Ph.D.	Staff Fellow	LMDB, NEI
	Anita Dash		Howard Hughes Scholar	LMDB, NEI
	Jo Ann Rinaudo	Ph.D.	IRTA Fellow	LMDB, NEI
	John Talian	Ph.D.	Staff Fellow	LMDB, NEI

COOPERATING UNITS (*if any*)
Department of Surgery, New Jersey Medical and Dental College (Thomas Lysz, Ph.D.)

LAB/BRANCH
Laboratory of Molecular and Developmental Biology

SECTION
Section on Cellular Differentiation

INSTITUTE AND LOCATION
NEI, NIH, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
4.9	3.9	1.0

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK (*Use standard unreduced type. Do not exceed the space provided.*)

This project investigates the expression of proto-oncogenes during the differentiation of embryonic lens epithelial cells to form lens fiber cells and seeks to determine the specific function of the corresponding gene products in the developing lens. The normal developmental profile of each of three nuclear proto-oncogenes, c-myc, c-fos, and c-jun, has been investigated in order to correlate expression of these genes with cell growth, differentiation, and expression of lens-specific genes. Information concerning proto-oncogene action in the lens is provided by studies of the exact timing of proto-oncogene expression in relation to cell division, cell differentiation, and expression of specific genes. In particular, we have attempted to correlate expression of specific proto-oncogene mRNAs with expression of mRNAs for proteins such as heat-shock protein (HSP70) and calpactin, whose expression and/or activity has been shown to be regulated by specific proto-oncogenes in other cell types. Finally, the effects of growth factors on proto-oncogene expression are being studied to provide a basis for organ culture of lenses.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 EY 00105-11 LMOD

PERIOD COVERED

October 1, 1989 to September 30, 1990

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Structure and Composition of Lens Crystallins with Respect to Cataractogenesis

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation.)*

PI:	J. Samuel Zigler, Jr.	Ph.D.	Research Biologist	LMOD, NEI
Others:	Xinyu Du	M.D.	Visiting Fellow	LMOD, NEI
	Guo-Tong Xu	M.D.	Special Volunteer	LMOD, NEI
	Vasantha Rao	Ph.D.	Visiting Fellow	LMOD, NEI
	Padmini Rao	Ph.D.	Visiting Fellow	LMOD, NEI
	Xiao-lan Cui	M.D.	Special Volunteer	LMOD, NEI

COOPERATING UNITS *(if any)*

Department of Ophthalmology, University of Tennessee (H.M. Jernigan, Jr.); Oakland University, Rochester, MI (V.N. Reddy); Alcon Laboratories (M. Lou); National Cancer Institute, (M. Krishna and P. Riesz); Centre for Cellular and Molecular Biology, Hyderabad, India (D. Balasubramanian).

LAB/BRANCH

Laboratory of Mechanisms of Ocular Diseases

SECTION

Section on Cataracts

INSTITUTE AND LOCATION

NEI, NIH, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
2.7	2.7	0.0

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☒ (b) Human tissues ☐ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Lens crystallins are structural proteins that comprise over 90% of the dry mass of the lens. In cataracts, the crystallins are found to be heavily modified, particularly via oxidation. This oxidative damage is thought to be a critical factor in the etiology of lens opacification. This laboratory is working toward elucidation of the actual functions of crystallins in the normal lens. We are studying how normal lens function is affected by modification of crystallin structure (e.g., by oxidation) or by change in the composition of crystallins through the loss by mutation of a particular crystallin.

In the guinea pig model we are studying, a mutation in the ζ-crystallin gene causes cataract. We have now shown that ζ-crystallin is an enzyme/crystallin which specifically binds NADPH and which is capable of functioning catalytically while the mutant form of zeta is enzymatically inactive. ζ-crystallin, which catalyzes the reduction of a class of quinones, appears to be distinct from previously described quinone reductases. This system provides a unique opportunity to investigate the effects on the lens of a defined structural change in a major lens protein. Use of this system also allows us to address fundamental questions concerning the function(s) of enzyme/crystallins.

Two major potential mechanisms of oxidative damage to the lens are photochemical processes and Fenton reactions involving metal ions and hydrogen peroxide (H_2O_2). In collaboration with Dr. D. Balasubramanian, we have quantitated the capacities of various photosensitizers present in the lens to produce singlet oxygen and superoxide anion. In addition, we have evaluated the effects of H_2O_2 and copper on lens crystallins.