DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 EY 00003-15 LMOD

PERIOD COVERED: October 1, 1986 to September 30, 1987

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:	Yoshio Akagi	M.D. Ph.D.	Visiting Scientist
	Sanai Sato	M.D.	Visiting Associate
	Tsuyoshi Tanimoto	Ph.D.	Visiting Scientist
	Gurley, Rebecca	M.S.	Biologist
	Katrina Armstrong	B.A.	Guest Worker

COOPERATING UNITS (if any)

None

LAB/BRANCH: Laboratory of Mechanisms of Ocular Disease

SECTION: Section of Molecular Pharmacology

INSTITUTE AND LOCATION: NEI, NIH, Bethesda, Maryland 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
5.5	4.0	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.)

The events leading to the onset of various ocular complications are being studied in addition to methods for their potential pharmacological control. Specifically, the relationships between the enzymes aldose reductase and aldehyde reductase and the progression of retinopathy, cataract, pupil function and iris changes, and keratopathy induced by diabetes or galactosemia are being investigated. Methods for either delaying or preventing the onset of these complications through the pharmacological control of these enzymes are also being developed.

The biochemical progression of several types of cataracts are also being studied as well as methods for controlling their onset through pharmacological intervention.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 EY 00011-13 CB

PERIOD COVERED
October 1, 1986 to September 30, 1987

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.	Head, Section on Ophthalmic Genetics and Pediatric Ophthalmology	CB, NEI
Others:	Carl Kupfer	M.D.	Director	NEI
	Lessie McCain	R.N.	Clinical Technician	CB, NEI
	Sandeep Jain	M.D.	Visiting Fellow	CB, NEI

COOPERATING UNITS *(if any)*

LAB/BRANCH
Clinical Branch

SECTION
Section on Ophthalmic Genetics and Pediatric Ophthalmology

INSTITUTE AND LOCATION
NEI, NIH, Bethesda, Maryland 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
1.35	1.25	.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 compare patients with and without glaucoma having pigment dispersion syndrome. The data acquired may enable a determination of the risk of patients with pigment dispersion syndrome to developing glaucoma as well as add to 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 00015-22 LRCMB

PERIOD COVERED

October 1, 1986 to September 30, 1987

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:	Robert St. Jules	Ph.D.	Staff Fellow	LRCMB, NEI

COOPERATING UNITS *(if any)*

Department of Anatomy, University of Toronto (M. J. Irons)

LAB/BRANCH

Laboratory of Retinal Cell and Molecular Biology

SECTION

Section on Cell Biology

INSTITUTE AND LOCATION

NEI, NIH, Bethesda, Maryland 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.)*

The post-translational 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. The role of the palmitate residues is unknown but could be related to membrane assembly. The addition of the vitamin A chromophore seems to be essential for intracellular transport of the opsin protein to the Golgi and to the outer segments. The addition of galactose residues may be a requirement for normal outer segment disc formation as it appears to be present only in the rhodopsin molecules found in the plasma membrane and basal folds.

The polyphosphoinositide pathway has been detected in rat rod outer segments thus extending the known distribution of this pathway from invertebrates and cold-blooded vertebrates to warm-blooded vertebrates. The role of this pathway in either transduction or light adaptation may be universal.

A manganese-dependent 5'-nucleotidase that cleaves cytidine monophosphate has been found to become highly active in rod outer segment tips at the time of disc shedding. It has been isolated, partially purified and characterized and could provide insight into new mechanisms related to the shedding process.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 EY 00016-20 LRCMB

PERIOD COVERED
October 1, 1986 to September 30, 1987

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

COOPERATING UNITS *(if any)*

School of Veterinary Medicine, University of Pennsylvania (G. Aguirre)

LAB/BRANCH
Laboratory of Retinal Cell and Molecular Biology

SECTION
Section on Cell Biology

INSTITUTE AND LOCATION
NEI, NIH, Bethesda, Maryland 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.)*

This project examines biochemical events unique to the retina, particularly the synthesis and modification of photoreceptor membrane components, in the retinas of vertebrates which can be affected by inherited retinal degenerations. The synthesis of the visual pigment, rhodopsin, occurs at a normal rate as measured by radioactive leucine incorporation following intravitreal injection in the eyes of miniature poodles affected with progressive rod-cone degeneration. Similarly, the glycosylation and acylation of rhodopsin were found to be normal following intravitreal injection of labeled fucose or palmitic acid, respectively. However, phospholipid synthesis or degradation, measured by radioactive palmitic acid incorporation, appears to be different in the affected dogs, suggesting a possible metabolic defect in this inherited disorder. The evidence suggests a significant diminution in the esterification of palmitic acid but not of arachidonic acid. Moreover, glycerol incorporation into phospholipid is not decreased in the affected animals, thus the defect may specifically involve palmitate.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 EY 00045-09 LSR

PERIOD COVERED
October 1, 1986, to September 30, 1987

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 Investigator.) (Name, title, laboratory, and institute affiliation)*

PI:	David Lee Robinson	Ph.D.	Research Physiologist	LSR NEI
Others:	John W. McClurkin	Ph.D.	Guest Worker	LSR NEI
	Caroline Kertzman	Ph.D.	IRTA	LSR NEI
	Irene Letvin	M.D.	Clinical Fellow	NINCDS
	Edmond FitzGibbon	M.D.	Clinical Fellow	LSR NEI
	Lance M. Optican	Ph.D.	Research Engineer	LSR NEI
	Barry J. Richmond	M.D.	Senior Surgeon, PHS	LNP NIMH
	Timothy Gawne	Ph.D.	Physiologist	LNP NIMH

COOPERATING UNITS *(if any)*

LAB/BRANCH
Laboratory of Sensorimotor Research

SECTION
Visuomotor Integration Section

INSTITUTE AND LOCATION
NEI, NIH, Bethesda, Maryland 20205

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
2.2	1.0	1.2

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.)*

We studied the responses of neurons to stimulus movement: that generated by real motion in the environment, by saccadic eye movements, and by smooth pursuit eye movements. Cells in the pulvinar discharge to real movement during periods of fixation but not when a saccadic eye movement causes the visual stimulation. However, these same cells do respond to the visual stimulation induced with pursuit eye movements. Many of these cells have a pause in their activity when an animal makes eye movements in total darkness, and it may be this inhibitory process which prevents them from responding with eye movements in the light. Neurons in the lateral geniculate nucleus respond in all three conditions: during fixation and with both types of eye movements. Cells in the superior colliculus are similar to those in the pulvinar, they respond to real motion during fixation and with pursuit movements but not with saccadic eye movements. These data show that some parts of the brain are influenced by the behavioral context in which visual stimulation occurs whereas others are not. We tested other pulvinar cells for their excitability after saccadic eye movements. Many respond better to light just after an eye movement than during fixation. Such changes may be related to the analysis of new data with each change in eye position. Other pulvinar cells are very selective for the frequency of stroboscopic stimulation; they respond very strongly to pulses at 4 to 6 per second. Frequently, they respond better to later stimuli in a train than to the first stimulus. Cells in the lateral geniculate nucleus have a wide variety of temporal response patterns which encode the details of visual stimulus patterns. Normal humans respond faster to a visual target when its spatial location is correctly indicated by a cuing light than when the location is incorrectly cued. The hypothesis is that the cue draws attention to its location and thereby facilitates reaction times. Patients with progressive supranuclear palsy who cannot make vertical eye movements are nonetheless able to move their attention in that direction.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 EY 00049-09 LSR

PERIOD COVERED
October 1, 1986, to September 30, 1987

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:	Mark A. Segraves	Ph.D.	Senior Staff Fellow	LSR, NEI
	Rolf Boch	Ph.D.	Visiting Fellow	LSR, NEI
	Edmond J. FitzGibbon	M.D.	Senior Staff Fellow	LSR, NEI
	Gregory B. Stanton	Ph.D	Guest Researcher	LSR, NEI

COOPERATING UNITS *(if any)*

LAB/BRANCH
Laboratory of Sensorimotor Research

SECTION
Neuro-Ophthalmologic Mechanisms Section

INSTITUTE AND LOCATION
NEI, NIH, Bethesda, Maryland 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
5.0	3.0	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.)*

The activity of single neurons in the prefrontal cortex that projects to the frontal eye fields has been studied in a number of visual and oculomotor tasks. Neurons in this region are visually responsive and show two sorts of activity before the beginning of a saccade: presaccadic enhancement and presaccadic reactivation. These results suggest that the prefrontal cortex participates in the planning of visually guided saccades.

Monkeys trained on a short saccadic adaptation paradigm learn quickly to change the amplitude of their saccades. Stimulation of the superior colliculus in the short term adapted case yields the same saccades as the unadapted case. The activity of some single neurons in the superior colliculus shows evidence of this adaptation: When a monkey makes a saccade of adjusted amplitude in response to a visual stimulus, some collicular neurons discharge before saccades ordinarily not associated with activity from those neurons. These observations were extended to a longer-term adaptation paradigm. One or more extraocular muscles were weakened by injection of botulinum toxin, and the non-paretic eye masked. The monkeys adapted the gain of their eye movements so that the seeing, weak eye made close to normal saccades and the non-seeing, normal eye made saccades of much larger amplitude than normal. Stimulation of the superior colliculus resulted in the production here too of saccades that did not reflect the adaptation process.

A class of patients with formal reading scores within the normal range who nonetheless consider themselves to be poor readers were found to have a higher than normal amount of unwanted rapid eye movements (square wave jerks) during visual fixation, and a higher than normal amount of backward eye movements during reading. Fixational instability did not correlate with performance on a quantitative assessment of skeletal motor functions which correlates with attentional deficit disorder in children.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 EY 00060-09 CB

PERIOD COVERED
October 1, 1986 to September 30, 1987

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.	Head, Section on Ophthalmic Genetics and Pediatric Ophthalmology	CB, NEI
Others:	Lessie McCain	R.N.	Clinical Technician	CB, NEI
	Rafael Caruso	M.D.	Visiting Scientist	CB, NEI
	Doris J. Collie	A.A.	Health Technician	CB, NEI

COOPERATING UNITS *(if any)*

LAB/BRANCH
Clinical Branch

SECTION
Section on Ophthalmic Genetics and Pediatric Ophthalmology

INSTITUTE AND LOCATION
NEI, NIH, Bethesda, Maryland 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
.65	.35	.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.)*

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 in these conditions and to evaluate its course over time. Family members are evaluated to attempt to determine factors which may identify the hetrozygous state.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 EY 00062-11 CB

PERIOD COVERED
October 1, 1986 to September 30, 1987

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:	Muriel I. Kaiser-Kupfer	M.D.	Head, Section on Ophthalmic Genetics and Pediatric Ophthalmology	CB, NEI
Others:	Carl Kupfer	M.D	Director	NEI
	Lessie McCain	R.N.	Clinical Technician	CB, NEI
	Manuel Datiles	M.D.	Visiting Scientist	CB, NEI

COOPERATING UNITS *(if any)*

LAB/BRANCH
Clinical Branch

SECTION
Section on Ophthalmic Genetics and Pediatric Ophthalmology

INSTITUTE AND LOCATION
NEI, NIH, Bethesda, Maryland 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
.35	.25	.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.)*

This project was formerly titled "Progressive Essential Iris Atrophy." Patients are being recruited with progressive essential iris atrophy with or without associated corneal disease. 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 00065-10 OSD

PERIOD COVERED

October 1, 1986, to September 30, 1987

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	OSD, NEI
Others:	Edna P. McCrane	B.S.	Biologist	OSD, NEI

COOPERATING UNITS *(if any)*

Lions of District 22C Eye Bank and Research Foundation, Inc (Seabrook, Maryland).

LAB/BRANCH

Office of the Scientific Director

SECTION

INSTITUTE AND LOCATION

NEI, NIH, Bethesda, Maryland 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
1.00	0.50	0.50

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. We have completed a study of the variation of functional properties of macaque ganglion cells with increasing eccentricity, which shows that color-opponent ganglion cells form a heterogenous group with respect to both spectral and non-spectral cell properties. The receptive-field size variation of these cells will be compared with dendritic-field variation of Golgi-impregnated ganglion cells, to assess if physiological differences reflect anatomical differences. In a separate study, we are comparing published data on the decline of human visual acuity with increasing eccentricity with the decline of cone and ganglion cell densities (cells/sq. degree) at various eccentricities of the retina of human donor eyes. Finally, we are completing analyses of prior studies for their publication.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 EY 00069-10 LI

PERIOD COVERED
October 1, 1986 to September 30, 1987

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:	Shigeto Hirose	M.D.	Visiting Fellow	LI, NEI
	Hiroki Sanui	M.D.	Visiting Fellow	LI, NEI
	Takao Tanaka	M.D.	Visiting Fellow	LI, NEI
	LiHong Hu	M.D.	Visiting Fellow	LI, NEI
	Roberto de Bara	M.D.	Senior Staff Fellow	LI, NEI

COOPERATING UNITS (if any)

LAB/BRANCH
Laboratory of Immunology

SECTION
Section on Experimental Immunology

INSTITUTE AND LOCATION
NIH, NEI, Bethesda, Maryland 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
7.95	7.84	0.11

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 which are designated "uveitis". In experiments with human material we have found that by using a sensitive assay, lymphocytes from a portion of healthy donors react in culture to retinal-specific antigens, S-antigen (S-Ag) and interphotoreceptor retinoid-binding protein (IRBP). Furthermore, clones of lymphocytes with specificity toward S-Ag were cultivated from the blood of a healthy donor. It is proposed that such lymphocytes, when activated, could play a pivotal role in the pathogeneis of uveitic conditions. The major segment of this project has focused on the animal disease, experimental autoimmune uveitis (EAU), which is considered a model for certain human conditions. Main findings: (1) Bovine IRBP is highly uveitogenic in primates, while monkey IRBP did not induce EAU at similar doses. Antibodies from monkeys immunized with bovine IRBP cross reacted well with monkey IRBP but the cross reaction was poorly detected by cellular reactions. (2) Fragments of IRBP of known amino acid sequence were found highly uveitogenic in rats, thus making it possible to identify the uveitogenic site(s) of this molecule. (3) A cell line of rat lymphocytes specific for IRBP was established in culture. The line cells produced EAU at numbers as low as 500,000/rat and will be useful for future studies on the pathogenesis of this disease. (4) Rats of the W/F inbred strain are poor responders to S-Ag induced EAU. This low susceptibility was found to be due to a poorly developed cellular immune response to S-Ag. (5) EAU development was found to be markedly enhanced by local damage to rat eyes. The data suggest that local injury could facilitate immune-mediated inflammation in the human eye as well. (6) Animals immunized with IRBP or S-Ag develop pinealitis, in addition to uveitis. The type of inflammation is different, however, in the two organs of affected rats and we report here that the "acute" inflammation in the eye disappears within 10 days while the "chronic" infiltration in the pineal lasts for at least 3 months.

GPO 914-918

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 EY 00070-10 LRCMB

PERIOD COVERED

October 1, 1986 to September 30, 1987

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
	Michael Redmond	Ph.D.	Staff Fellow	LRCMB, NEI
	Umi Hirose	M.D.	Guest Worker	LRCMB, NEI
	Gerald J. Chader	Ph.D.	Chief	LRCMB, NEI

COOPERATING UNITS *(if any)*

LSU Eye Center, New Orleans, LA (N. Bazan, T. Reddy)

LAB/BRANCH

Laboratory of Retinal Cell and Molecular Biology

SECTION

Section on Biochemistry

INSTITUTE AND LOCATION

NEI, NIH, Bethesda, Maryland 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
2.8	1.8	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.)*

Enzyme-linked immunosorbent assay (ELISA) was used to quantitate interphotoreceptor retinoid-binding protein (IRBP) in retinoblastoma tumors and in human subretinal fluid (SRF) samples. In retinoblastoma tumors there was a direct correlation between the degree of differentiation of the tumors and IRBP concentration. Higher concentrations of IRBP were found only in the more recent rhegmatogenous detachments, and IRBP was absent from SRF of patients with retrolental fibroplasia. Cyanogen bromide peptides from purified bovine IRBP were purified by high performance liquid chromatography (HPLC) and several peptides were found to produce experimental autoimmune uveitis (EAU) in rats. IRBP was shown to be phosphorylated in a crude bovine interphotoreceptor matrix (IPM) wash, and the phosphorylation was of serine and/or threonine residues. Intravitreal injection of radiolabeled retinol or fatty acids into frog eyes showed both retinol and fatty acids to be bound to IRBP.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 EY 00075-09 LI

PERIOD COVERED
October 1, 1986 to September 30, 1987

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:	Alan G. Palestine	M.D.	Head, Section on Clinical Immunology	LI, NEI
	Chi-Chao Chan	M.D.	Senior Staff Fellow	LI, NEI
	William Leake	M.S.	Biologist	LI, NEI
	Shigeto Hirose	M.D.	Visiting Fellow	LI, NEI

COOPERATING UNITS (if any)

LAB/BRANCH
Laboratory of Immunology

SECTION
Section on Immunoregulation

INSTITUTE AND LOCATION
NEI, NIH, Bethesda, Maryland 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.91	0.21	0.7

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), 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 to ocular tissues. In addition, purified antigens from the toxoplasmosis organism are also 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. These results 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 00078-10 LOP

PERIOD COVERED

October 1, 1986, to September 30, 1987

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

Histopathology of Human Dystrophies and Degeneration

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

PI:	Merlyn M. Rodrigues	M.D.,Ph.D.	Head, Section on Ophthalmic Pathology	LOP, NEI
Others:	Joseph Hackett	B.S.	Biologist	LOP, NEI

COOPERATING UNITS *(if any)*

Department of Ophthalmology, University of Iowa, Iowa City

LAB/BRANCH

Laboratory of Ophthalmic Pathology

SECTION

Section on Ophthalmic Pathology

INSTITUTE AND LOCATION

National Eye Institute, NIH, Bethesda, MD 20205

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.)*

Human corneal dystrophies and degenerations which have been clinically documented are studied as keratoplasty specimens with histochemical stains, scanning and transmission electron microscopy, and immunologic techniques in an attempt to elucidate pathogenetic mechanisms. This approach has provided insight into cell-to-cell relationships in the normal and diseased states. In patients with primary and recurrent macular corneal dystrophy, intercellular and extracellular accumulation of fibrillogranular material was observed in the corneal stroma, Descemet's membrane, and corneal endothelium. The presence and production of collagen, glycoconjugates, and collagenase have been investigated with immunofluorescent electrophoretic, and chromatographic methods. The lectin binding patterns were compared in corneas from patients with macular dystrophy and control. The characterization of amyloid in lattice corneal dystrophy and corneal amyloid degeneration was performed using immunohistochemical stains and biochemical analysis. Lack of AA reactivity was observed in corneal amyloid deposits. Keratoplasty specimens from granular corneal dystrophy and controls were examined by combinations of immunohistological stains, transmission electron microscopy, and SDS gel electrophoresis. In granular dystrophy, the deposits consisted of phospholipid with microfibrillar protein at the edges. Corneal buttons from patients with Fuchs' dystrophy had varying degrees of clinical edema measured in most cases by preoperative optical ultrasonic pachymetry. Histologically, marked thickening of Descemet's membrane and abnormal corneal endothelium corresponded to areas of severe clinical edema and were usually located in the central and paracentral regions. Clinical edema was not present unless accompanied by marked thickening of Descemet's membrane with multiple guttata and attenuation of corneal endothelium. The peripheral cornea was relatively clear clinically and showed minimal histologic changes.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 EY 00083-10 CB

PERIOD COVERED

October 1, 1986 to September 30, 1987

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

Gyrate Atrophy of the Choroid and Retina

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

PI:	Muriel I. Kaiser-Kupfer	M.D.	Head, Section on Ophthalmic Genetics and Pediatric Ophthalmology	CB, NEI
Others:	Lessie McCain	R.N.	Clinical Technician	CB, NEI
	Rafael Caruso	M.D.	Visiting Scientist	CB, NEI
	Kent Higgins	Ph.D.	Expert	CB, NEI

COOPERATING UNITS *(if any)*

The Howard Hughes Medical Institute Laboratory and the Department of Pediatrics, Johns Hopkins University, School of Medicine, Baltimore, Maryland (David L. Valle, M.D.)

LAB/BRANCH

Clinical Branch

SECTION

Section on Ophthalmic Genetics and Pediatric Ophthalmology

INSTITUTE AND LOCATION

NEI, NIH, Bethesda, Maryland 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
1.3	.8	.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.)*

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

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 EY 00084-09 CB

PERIOD COVERED
October 1, 1986 to September 30, 1987

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, Section on Ophthalmic Genetics and Pediatric Ophthalmology	CB, NEI
	Lessie McCain	R.N.	Clinical Technician	CB, NEI
	Manuel B. Datiles	M.D.	Visiting Scientist	CB, NEI
	Paul Edwards	M.D.	Visiting Fellow	CB, NEI

COOPERATING UNITS *(if any)*

LAB/BRANCH
Clinical Branch

SECTION
Section on Ophthalmic Genetics and Pediatric Ophthalmology

INSTITUTE AND LOCATION
NEI, NIH, Bethesda, Maryland 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.60	0.40	.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.)*

With recent embryological research indicating the role of the neural crest in contributing to all connective tissues anterior to the lens epithelium, 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 00092-09 LI

PERIOD COVERED
October 1, 1986 to September 30, 1987

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

COOPERATING UNITS (if any)
Center for Drugs and Biologics, Food and Drug Administration (Kamal Mittal, M.D.)

LAB/BRANCH
Laboratory of Immunology

SECTION
Section on Immunoregulation

INSTITUTE AND LOCATION
NEI, NIH, Bethesda, Maryland 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.03	0.03	0

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.)

Patients with ocular toxoplasmosis, pars planitis, Behcet's disease, chorioretinitis of unknown origin, are being studied to determine the phenotype frequency of the HLA, ABO, and B-cell alloantigens. Because the B-cell alloantigens or DR antigens are thought to play a role in the immunologic response to antigens, these findings will complement other immune uveitis studies being simultaneously carried out.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 EY 00094-09 LI

PERIOD COVERED
October 1, 1986 to September 30, 1987

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:	Alan G. Palestine	M.D.	Head, Section on Clinical Immunology	LI, NEI
	William Leake	M.S.	Biologist	LI, NEI
	Rashid Mahdi		Biologist	LI, NEI

COOPERATING UNITS (if any)

LAB/BRANCH
Laboratory of Immunology

SECTION
Section on Immunoregulation

INSTITUTE AND LOCATION
NEI, NIH, Bethesda, Maryland 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.69	0.24	0.45

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.)

Lewis rats and non-human primates, immunized at a site distant to the eye with the retinal soluble antigen (S-antigen) in complete Freund's adjuvant, develop experimental autoimmune uveitis (EAU). Lymph node cells and peripheral lymphocytes from immunized animals manifested significant cellular immune responses measured by the lymphocyte culturing technique. The cyclosporines, a family with specific anti-T-activity, have been found to be exceptionally effective in protecting rats with EAU. Attempts at local immunosuppressive therapy in order to prevent EAU have begun. Topical and periocular CsA have been used in order to evaluate its effectiveness in EAU. Newer cyclosporines, particularly D&G, have been evaluated in this model, with their efficacy compared to that of cyclosporine A. Ciamexone, a drug with immunopotentiating characteristics, has always been utilized in this model. An in vitro model of specific S-antigen antibody production is being developed.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 EY 00096-09 LOP

PERIOD COVERED
October 1, 1986, to September 30, 1987

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Clinicopathologic Studies of Human Ocular Diseases

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

PI:	Merlyn M. Rodrigues	M.D., Ph.D.	Head, Section on Ophthalmic Pathology	LOP, NEI
Others:	Joseph Hackett	B.S.	Biologist	LOP, NEI
	Reginald Gaskins		Histologist	LOP, NEI

COOPERATING UNITS *(if any)*

LAB/BRANCH
Laboratory of Ophthalmic Pathology

SECTION
Section on Ophthalmic Pathology

INSTITUTE AND LOCATION
National Eye Institute, NEI, Bethesda, MD 20205

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.3	0.2	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.)*

Patients with localized ocular diseases or with ocular manifestations of systemic disease are examined clinically, and photographic documentation is made of significant findings. Biopsy specimens or autopsy eyes from these patients are examined by electron microscopy and histochemical stains. Studies are performed on patients with ocular manifestations of systemic diseases.

Forty patients with acquired immunodeficiency syndrome (AIDS) were examined for ocular abnormalities. Twenty of these patients died and the eyes were obtained for culture and histologic examination. These patients have multiple opportunistic infections and neoplasms as the result of a severe depression of cellular immunity. Fifty percent of all patients with AIDS and 75% of the autopsy group have ocular signs attributable to AIDS. Ocular findings were confined to four major categories: cytomegalovirus (CMV) retinitis (10 patients), retinal cotton wool spots (11 patients), conjunctival Kaposi's sarcoma (2 patients), and neuro-ophthalmic motility abnormalities (3 patients). Cytomegalovirus retinitis was a significant cause of visual loss. Seven of 40 autopsy eyes had hand-motion or worse vision prior to the patient's death because of CMV and progressed to involve the entire retina in three to six months resulting in a gliotic retina membrane. Disseminated systemic histoplasmosis was observed in a patient with AIDS. In 3 patients, the effect of argon laser treatment was shown to be ineffective in halting the spread of cytomegalovirus in patients with AIDS.

Immunohistochemical stains are performed on patients with retinitis pigmentosa and retinoblastoma to test for the presence of neuronal and glial proteins. Electron microscopy is also performed in selected cases.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 EY 00105-08 LMOD

PERIOD COVERED
October 1, 1986 to September 30, 1987

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:	Valerie A. Lucas	Ph.D.	Visiting Fellow	LMOD, NEI
	Qing-ling Huang	M.D.	Visiting Fellow	LMOD, NEI
	Xinyu Du	M.D.	Visiting Fellow	LMOD, NEI

COOPERATING UNITS *(if any)*
Jules Stein Eye Institute, UCLA Medical School (J. Horwitz); Department of Chemistry, Adelphi University (F. Bettelheim); Department of Ophthalmology, University of Tennessee (H. M. Jernigan, Jr.)

LAB/BRANCH
Laboratory of Mechanisms of Ocular Diseases

SECTION
Section on Cataract

INSTITUTE AND LOCATION
NEI, NIH, Bethesda, Maryland 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
2.6	2.6	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 crystallins are the basic structural elements of the ocular lens. These globular, structural proteins are evolutionarily conservative proteins with structures uniquely suited to their functional role, ie, to form highly organized and densely packed protein matrices which are optically transparent. Our studies are oriented toward elucidation of the mechanisms of cataract development and the role of changes either in the structure or the composition of the crystallins in opacification of the lens.

With respect to structural modifications to crystallins, we are particularly interested in the modifications induced by oxidative stress since the lens is exposed in vivo to an unusual level of such stress. We have previously investigated the potential effects of the high concentration of H_2O_2 in the aqueous humor on intact lenses in organ culture, finding that H_2O_2 is toxic whereas stronger but short-lived oxidants (free radicals) derived from it show little toxicity when produced in the fluids surrounding the lens. In model systems we have now shown that when generated intracellularly the reverse is true. H_2O_2 itself causes little damage, but upon conversion to hydroxyl radicals or related species the crystallins are rapidly oxidized. Thus not only the oxidizing species, but the location in which it is generated is critical in determining its potential for producing lens damage.

We have recently found that zeta-crystallin, a lens protein unique to guinea pigs which we discovered and partially characterized, is absent or present in sharply reduced amounts in the lenses of guinea pigs with hereditary congenital nuclear cataracts. This finding gives us an ideal opportunity to investigate in an animal model system the effect of a major change in crystallin composition.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 EY 00109-07 LSR

PERIOD COVERED

October 1, 1986, to September 30, 1987

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

Visual Motion Processing in the Primate Brain

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

PI:	Robert H. Wurtz	Ph.D.	Chief	LSR, NEI
Others:	Hidehiko Komatsu	Ph.D.	Visiting Scientist	LSR, NEI
	Dwayne S. G. Yamasaki	Ph.D.	Guest Researcher	LSR, NEI
	Jean-Pierre Roy	M.D. Ph.D.	Guest Researcher	LSR, NEI

COOPERATING UNITS *(if any)*

LAB/BRANCH

Laboratory of Sensorimotor Research

SECTION

Visuomotor Integration Section

INSTITUTE AND LOCATION

NEI, NIH, Bethesda, Maryland 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
4.0	2.0	2.0

CHECK APPROPRIATE BOX(ES)

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

☐ (a1) Minors

☐ (a2) Interviews

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

We have continued our study of visual motion processing in the cerebral cortex. Our investigations concentrated on two areas of cortex that are largely devoted to motion processing, the middle temporal area (MT) and the medial superior temporal area (MST). In area MST we investigated the response of cells to motion of the visual background as the monkey made a pursuit eye movement. We could identify two types of cells. One type responded vigorously to large field stimulation and this response frequently was synergistic with the pursuit response. Another group of cells respond to small moving spots and are largely insensitive to motion of the background. In area MT, we have investigated changes in the receptive field size of cells adjacent to a region damaged by a neurotoxin that impairs the monkey's ability to generate a pursuit eye movement. We found that the receptive fields did not expand selectively to cover the area of the visual field previously covered by the cells damaged by the neurotoxin. Many cells did, however, show an expansion of their field size in all directions.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 EY 00114-07 LOP

PERIOD COVERED
October 1, 1986, to September 30, 1987

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Histopathologic Studies of Animal Models of Human Ocular Disease

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

PI:	Merlyn M. Rodrigues	M.D., Ph.D.	Head, Section on Ophthalmic Pathology	LOP, NIH
Others:	Joseph Hackett	B.S.	Biologist	LOP, NIH
	Barbara Wiggert	Ph.D.	Research Chemist	LVR, NIH
	Geraldn Chader	Ph.D.	Chief, Laboratory of Vision Research	

COOPERATING UNITS *(if any)*

LAB/BRANCH
Laboratory of Ophthalmic Pathology

SECTION
Section on Ophthalmic Pathology

INSTITUTE AND LOCATION
National Eye Institute, 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.)*

Immunocytochemical staining of fresh frozen rhesus monkey retinas was performed using indirect immunofluorescence and immunoperoxidase (avidin-biotin-complex). Affinity-purified antibodies to interphotoreceptor retinoid-binding protein (IRBP) obtained from rabbits was used to localize IRBP on frozen sections. Fresh frozen pineal glands from the same species were stained by the avidin-biotin-peroxidase method. In addition, retinas from rod-dominant and cone-dominant species were examined. Immunocytochemical staining revealed localization of IRBP in the interphotoreceptor space of peripheral equatorial and posterior retina, with marked decrease in staining in the fovea. A transition zone was noted at the ora serrata, where staining was present in the peripheral retina up to the ora serrata, but was absent in ciliary epithelium. Cone-dominant retinas (chick and turtle) showed lack of reactivity to IRBP. Rod-dominant rat retina showed localization of IRBP to the interphotoreceptor space. Primate and rat pineal showed immunocytochemical localization of IRBP. Spontaneously occurring anterior chamber segment anomalies in DBA/2 mice were studied by slit-lamp biomicroscopy and light and transmission electron microscopy (TEM). The opacities consisted of aggregates of basophilic material in the superficial stroma which stained positively for elastin TEM revealed that they were electron dense and extracellular. Iris abnormalities consisted of stromal atrophy and proliferation of corneal endothelium and basement membrane across the iris surface and trabecular meshwork. The corneal opacities seen in DBA/2 mice show a striking similarity to those which characterize familial band-shaped nodular keratopathy, a form of corneal elastosis.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 EY 00115-07 LI

PERIOD COVERED
October 1, 1986 to September 30, 1987

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:	Alan G. Palestine	M.D.	Head, Section on Clinical Immunology	LI, NEI
	Edward J. Holland	M.D.	Senior Staff Fellow	LI, NEI
	Roberto de Bara	M.D.	Senior Staff Fellow	LI, NEI
	Francois Roberge	M.D.	Visiting Associate	LI, NEI
	Richard P. Wetzig	M.D.	Senior Staff Fellow	LI, NEI

COOPERATING UNITS (if any)

LAB/BRANCH
Laboratory of Immunology

SECTION
Section on Immunoregulation

INSTITUTE AND LOCATION
NEI, NIH, Bethesda, Maryland 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
1.49	1.48	0.01

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 will be done to test cyclosporine's efficacy in the treatment of uveitis. Within the context of these ongoing studies, the effect of hydergine on reversing cyclosporine induced nephrotoxicity is being evaluated in a randomized, masked, cross-over study. Additionally, selected patients whose uveitis is well controlled on cyclosporine for one year or more are undergoing kidney biopsies to evaluate the long term effects of this agent.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 EY 00117-07 CB

PERIOD COVERED
October 1, 1986 to September 30, 1987

TITLE OF PROJECT (80 characters or less. Title must fit on one line between the borders.)
Oculomotor Disorders in Human Subjects

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

PI:	James Carl	M.D.	Senior Staff Fellow	CB, NEI
Others:	Edmond FitzGibbon	M.D.	Senior Staff Fellow	LSR, NEI
	Reuben Gellman	Ph.D.	Staff Fellow	CB, NEI

COOPERATING UNITS (if any)

LAB/BRANCH
Clinical Branch

SECTION
Neuro-ophthalmology Section

INSTITUTE AND LOCATION
NEI, NIH, Bethesda, Maryland 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
1.7	1.7	

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 continuing emphasis of this project has been to collaborate with the Laboratory of Sensorimotor Research in studying oculomotor disorders in human subjects. The computerized methods for recording and analysing eye movements pioneered by the LSR have been applied to a variety of clinical eye movement disorders.

An ongoing series of experiments established a set of normative values for human performance of several of the oculomotor subsystems, particularly the saccadic and pursuit systems. The major advances in these areas were extensions of neurophysiological work done in the LSR on non-human primates. The major findings included a description of the motion processing needed to keep the eyes following a moving target by saccades and pursuit movements. The human brain requires about 75 milliseconds to begin to follow moving stimuli, but an accurate assessment of the stimulus velocity develops over an additional 100 milliseconds.

Studies on the role of the basal ganglia in eye movement processing continued with a study of patients with progressive supranuclear palsy, with particular attention to the abnormalities of vertical eye movements in spite of relatively preserved horizontal eye movements. These patients were also examined for attentional deficits.

Additional ongoing projects included following patients with a variety of neurological disorders of metabolism such as Gaucher's, Fabry's and Niemann-Pick disease.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 EY 00122-07 OSD

PERIOD COVERED

October 1, 1986, to September 30, 1987

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	OSD, NEI
Others:	Edna P. McCrane	B.S.	Biologist	OSD, NEI
	Marvin B. Shapiro	M.S.	Research Mathematician	LSM, DCRT
	Catherine J. Szeliga		Normal Volunteer	CC

COOPERATING UNITS *(if any)*

Howe Laboratory, Harvard Medical School, Massachusetts Eye and Ear Infirmary, (Boston, Massachusetts), and Laboratory for Statistical Methodology, DCRT.

LAB/BRANCH

Office of the Scientific Director

SECTION

INSTITUTE AND LOCATION

NEI, NIH, Bethesda, Maryland 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
1.20	0.50	0.70

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 blue-sensitive cones of the macaque retina were selectively labelled using tissue-reactive dyes injected into the vitreous humour, and the spatial properties of the retinal point pattern of these cones was examined. We have developed a model describing the degree of regularity and structure of the cone pattern. To evaluate the topographical relationship between the cones and ganglion cells of the area centralis of human and macaque retina, especially in the fovea, we have also studied and quantified the radial displacement between photoreceptors and postreceptoral cells, and measured the density of both cones and ganglion cells. Correction for such displacement permits the topographical comparison of the densities of these two cell types in terms of visual angle; this comparison allows for an estimate of the overall degree of convergence of cones to ganglion cells, and provides boundaries for the areal coverage factor of these cells. We have also compared the density of ganglion cells to that of cells of the lateral geniculate nucleus (LGN), both for the parvocellular and the magnocellular streams; this comparison provides information about central magnification properties in this nucleus.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 EY 00123-07-CB

PERIOD COVERED
October 1, 1986 to September 30, 1987

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:	Muriel I. Kaiser-Kupfer	M.D.	Head, Section on Ophthalmic Genetics and Pediatric Ophthalmology	CB, NEI
Others:	Rafael C. Caruso	M.D.	Visiting Scientist	CB, NEI
	Kent E. Higgins	Ph.D.	Expert	CB, NEI
	Ralph D. Gunkel	O.D.	Ophthalmic Physicist	CB, NEI

COOPERATING UNITS *(if any)*

LAB/BRANCH
Clinical Branch

SECTION
Section on Ophthalmic Genetics and Pediatric Ophthalmology

INSTITUTE AND LOCATION
NEI, NIH, Bethesda, Maryland 20892

TOTAL MAN-YEARS	PROFESSIONAL:	OTHER:
.65	.35	.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.)*

The visual function of patients with ocular diseases or lesions in the visual pathways and of normal subjects is measured with psychophysical techniques. These data are correlated with those obtained with electrophysiological 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 effect 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 00124-07 LRCMB

PERIOD COVERED
October 1, 1986 to September 30, 1987

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:	Marlissa Campbell	Ph.D.	Staff Fellow	LRCMB, NEI
	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, Maryland 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
2.2	2.2	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.)*

Internal and external messengers have been studied which code for aspects of growth, development and function of normal retinal cells and also which affect differentiation of retinoblastoma cells in culture. Insulin receptors are present in high concentration in normal retinal cells and in retinoblastoma cells indicating a role for insulin in retinal function. Also, extracellular matrix components such as laminin have been found to affect differentiation of cultured human retinoblastoma cells.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 EY 00126-06 LMDB

PERIOD COVERED

October 1, 1986 to September 30, 1987

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
	Ana B. Chepelinsky	Ph.D.	Expert	LMDB, NEI
	Graeme J. Wistow	Ph.D.	Visiting Associate	LMDB, NEI
	Cynthia Jaworski	M.S.	Chemist	LMDB, NEI
	Diana Parker	B.A.	Chemist	LMDB, NEI
	Ilana Keshet	Ph.D.	Fogarty Fellow	LMDB, NEI
	Bernd Sommer	Ph.D.	Guest Worker	LMDB, NEI

COOPERATING UNITS *(if any)*

See next page.

LAB/BRANCH

Laboratory of Molecular and Developmental Biology

SECTION

INSTITUTE AND LOCATION

NEI, NIH, Bethesda, Maryland 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
12.6	12.6	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.)*

We have continued to characterize crystallin gene structure although greater emphasis was placed on expression. Sequences have been completed, or nearly completed, for the human and chicken αA- and the chicken βB1-crystallin genes. Intron 1 of the human αA-crystallin gene has been shown to encode an insert exon found so far only in rodents. The 5' flanking sequence of the murine αA-crystallin gene has been dissected into a distal, enhancer-like element and a proximal element. Both elements bind specifically to different nuclear proteins of embryonic lens cells, as judged by gel retardation experiments. Transfection studies using the pSVOCAT expression plasmid have shown that the 5' flanking sequence of the chicken δ1-crystallin gene contains an upstream region (-603 to -120) that appears to down-regulate promoter activity. Strong promoter activity has been identified in the 5' flanking sequence of the chicken βB1-crystallin gene, initiating our efforts to study the regulation of this class of crystallins. The human and murine αB-crystallin genes have been isolated; the promoter has been identified in the murine gene. A transgenic mouse facility has been established, and several progeny carrying hybrid genes using crystallin promoters have been born. Numerous crystallins have been shown to be enzymes: ε-crystallin is lactate dehydrogenase, δ-crystallin is argininosuccinate lyase and τ-crystallin is enolase, indicating the pragmatism of lens evolution, i.e., the use of enzymatic proteins in a new structural role. Finally three crystallin polypeptides have been identified in the jellyfish lens; one (35K) has been purified and partially sequenced.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 EY 00127-11 LMDB

PERIOD COVERED

October 1, 1986 to September 30, 1987

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

Plasma Membrane Composition and Biosynthesis in Chick Lens Fibers and Epithelia

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

PI:	Peggy Zelenka	Ph.D.	Geneticist	LMDB, NEI
	Luke Pallansch	Ph.D.	Staff Fellow	LMDB, NEI
	John Talian	Ph.D.	IRTA Fellow	LMDB, NEI

COOPERATING UNITS *(if any)*

Flora de Pablo	M.D.	Diabetes Branch/NIDDK
Paul Russell	Ph.D.	LMOD, NEI
David Beebe	Ph.D.	USUHS, Bethesda, MD

LAB/BRANCH

Laboratory of Molecular and Development Biology

SECTION

Section on Cellular Differentiation

INSTITUTE AND LOCATION

NEI, NIH, Bethesda, Maryland 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
2.0	1.3	0.7

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 seeks to determine whether lens fiber differentiation is associated with alterations in plasma membrane lipids or proteins. Previous results have indicated that phosphatidlyinositol degradation ceases when lens epithelial cells differentiate to form lens fiber cells. Since phosphatidylinositol is rich in arachidonic acid, a precursor of prostaglandins and leukotrienes, the metabolites of arachidonic acid produced by lens cells are being characterized. Comparison of metabolites synthesized before and after the onset of fiber cell formation demonstrates that the loss of a lipoxygenase pathway metabolite is associated with differentiation and the concommitant increase in c-myc mRNA. Plasma membrane proteins being investigated include the insulin and IGF receptors, and the membrane associated protein calpactin I. Specific insulin and IGF receptors have been demonstrated on both lens epithelial cells and lens fiber cells throughout embryonic development; a marked decrease in insulin receptors is associated with fiber cell formation. Calpactin I has been shown to be a major component of the EDTA extractable protein (EEP) of lens membranes. This protein binds both phospholipids and actin, and may thus be involved in anchoring the cytoskeleton of the lens to the membrane.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 EY 00132-06 LMDB

PERIOD COVERED

October 1, 1986 to September 30, 1987

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

Molecular Biology of Photopigments

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

PI:	Toshimichi Shinohara	Ph.D.	Head	LMDB, NEI
Others:	Masahiko Tsude	M.D., Ph.D.	Visiting Fellow	LMDB, NEI
	Benjamin Amaladoss	Ph.D.	Visiting Assoc.	LMDB, NEI
	Kunihiko Yamaki	M.D., Ph.D.	Visiting Fellow	LDN, NICHD
	Viji Singh	Ph.D.	Visiting Assoc.	LMDB, NEI

COOPERATING UNITS *(if any)*

Larry Donoso	M.D., Ph.D.	Wills Eye Hospital Philadelphia, PA

LAB/BRANCH

Laboratory of Molecular and Developmental Biology

SECTION

Section on Molecular Biology

INSTITUTE AND LOCATION

NEI, NIH, Bethesda, Maryland 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
4	4	0.0

CHECK APPROPRIATE BOX(ES)

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

☐ (a1) Minors

☐ (a2) Interviews

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

We have investigated the structure, function, evolution and immunogenic sites of the retinal S-antigen (48 K protein) and its gene. The complete amino acid sequences of human, bovine and murine retinal S-antigen have been determined by partial protein sequencing and cDNA sequencing. Coding sequences of S-antigen cDNAs from human, bovine and murine retinas have approximately 80% similarity. In contrast, noncoding sequences of these cDNAs have at most only 30% similarity. The polypeptide sequences of S-antigen from human, bovine and murine retinas are also very similar (~83%). Immunogenic sites of bovine S-antigen were determined, as were two monoclonal antibody binding sites (epitopes) and two uveitopathogenic sites (named M and K) using 20 different chemically synthesized oligopeptides. The minimum size required for EAU induction was also determined. M peptide was 12 and K peptide was 20 amino acids long. These small peptides contain all the necessary information for the induction of EAU. EAU was also observed following the adaptive transfer of T cell lymphocytes from Lewis rats which were previously immunized with M peptide, indicating that experimental autoimmune uveitis (EAU) induced by M was also a T cell mediated autoimmune response. The clinical and histopathologic features of EAU induced with M peptide were similar to those developed with native S-antigen. The M12 peptide of S-antigen from humans and mice has an identical sequence to that of bovine S-antigen. Searching the NBRF data bank revealed no extensive sequence homology between S-antigen and other proteins, although some sequence similarity was apparent with α-transducin. Interestingly, these include the sites subject to ADP-ribosylation by petussis toxin and the phosphoryl binding sites.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 EY 00135-15

PERIOD COVERED

October 1, 1986 to September 30, 1987

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) OSD, NEI

COOPERATING UNITS *(if any)*

Veterinary Resources Branch, DRS, NIH

LAB/BRANCH

Office of the Scientific Director, NEI

SECTION

INSTITUTE AND LOCATION

National Eye Institute, NIH, Bethesda, Maryland 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
1.3	1.0	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.)*

The effects of nutrition, oxidation, and other environmental factors (light intensity or darkness) on the incidence and progress of posterior subcapsular opacities (PSO) associated with retinal degeneration are being studied in Royal College of Surgeons (RCS) rats, in which rod photoreceptor outer segment debris accumulates secondary to a phagocytic defect in the retinal pigmented epithelium. Evidence has been obtained that oxidative changes in polyunsaturated fatty acids in the debris lead to water-soluble toxic aldehydes that can be detected in the vitreous, and are toxic to lens membranes. Several diets prevent the mature cataracts, and dark-rearing prevents the PSO detectable microscopically. Pink-eyed dystrophic rats exposed to constant light of 25 footcandles beginning (1) at 20-23 postnatal days or (2) at birth, had histopathological changes similar to those in some naturally occurring human posterior subcapsular cataracts (PSC), such as in retinitis pigmentosa. Many mature cataracts also occur with cyclic light of low intensity at a time when a large amount of rhodopsin debris is present. In the RCS dystrophic rat, freed retinal may have a prolonged lifetime (owing to slowed conversion of retinal to retinol and to poor regeneration of rhodopsin). Freed retinal may act as a photosensitizer to generate singlet oxygen, a highly energetic oxidant for polyunsaturated lipids. Prevention of the cataracts by dark rearing or by feeding a purified diet with lipid-soluble antioxidants (vitamin E, BHT ‡ Beta-carotene) supports the hypothesis of lipoperoxidative damage to the lens. Principles established with this readily manipulated animal model may have significance for slowing or preventing human PSC and mature cataracts.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 EY 00144-06-CB

PERIOD COVERED
October 1, 1986 to September 30, 1987

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:	Muriel I. Kaiser-Kupfer	M.D.	Head, Section on Ophthalmic Genetics and Pediatric Ophthalmology	CB, NEI
Others:	Rafael Caruso	M.D.	Visiting Scientist	CB, NEI
	Kent E. Higgins	Ph.D.	Expert	CB, NEI
	Doris J. Collie	A.A.	Health Technician	CB, NEI

COOPERATING UNITS *(if any)*

LAB/BRANCH
Clinical Branch

SECTION
Section on Ophthalmic Genetics and Pediatric Ophthalmology

INSTITUTE AND LOCATION
NEI, NIH, Bethesda, Maryland 20892

TOTAL MAN-YEARS	PROFESSIONAL:	OTHER
.65	.35	.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.)*

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 00148-14 LRCMB

PERIOD COVERED

October 1, 1986 to September 30, 1987

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:	Susan Gentleman	Ph.D.	Expert	LRCMB, NEI
	R. Theodore Fletcher	M.S.	Chemist	LRCMB, NEI
	Robert L. Somers	B.S.	Chemist	LRCMB, NEI
	C. Lal Kapoor	Ph.D.	Guest Worker	LRCMB, NEI

COOPERATING UNITS *(if any)*

Section on Medical Genetics, School of Veterinary Medicine, University of Pennsylvania (G. Aguirre); Department of Anatomy, Erasmus University, Rotterdam, The Netherlands (S. Sanyal)

LAB/BRANCH

Laboratory of Retinal Cell and Molecular Biology

SECTION

Section on Gene Regulation

INSTITUTE AND LOCATION

NEI, NIH, Bethesda, Maryland 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
2.7	0.7	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.)*

It has been shown that cyclic nucleotides (cGMP, cAMP) mediate many of the normal functions of the neural retina, especially as related to the visual process. Moreover, protein kinases (cAMP-dependent protein kinase, C-kinase) mediate the function of these nucleotides as well as transduce other important signals (eg, calcium, lipids, etc.). We have evidence that (1) abnormalities in cAMP-dependent protein kinase may be involved in human retinoblastoma, (2) cyclic GMP accumulation and distribution is abnormal in photoreceptor cells of an animal model of inherited retinal degeneration and (3) C-kinase could be involved in normal light/dark mechanisms in the photoreceptor outer segment.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 EY 00149-14 LMOD

PERIOD COVERED
October 1, 1986 to September 30, 1987

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.	Chief, Section on Pathophysiology	LMOD, NEI
Others:	Masao Nagata	Ph.D., 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 Pathophysioloy

INSTITUTE AND LOCATION
NEI, NIH, Bethesda, Maryland 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
5.2	5.0	.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 loss of mural cells from capillary walls is the earliest histopathological lesion reported in diabetic retinas. Like several other diabetic complications, this lesion appears to be related to aldose reductase activity. Mural cells were cultured from capillaries of human retinas. Verification that contaminating cells had been removed was made on the basis of the mural cell's distinctive appearance in culture, inability to internalize acetylated-low-density lipoprotein, and immunoreactivity for muscle actin. Using pure cultures of human mural cells, the presence of aldose reductase was demonstrated immunohistochemically with antibodies directed against human placental aldose reductase, and aldose reductase activity was shown biochemically by monitoring the accumulation of xylitol in cells incubated with 30 mM xylose. Bovine and canine as well as human mural cells and endothelial cells from retinal capillaries have been grown in cell culture so that the role of aldose reductase in alterations of cell structure and function in the diabetic state could be studied under chemically defined conditions. Aldose reductase inhibitors are useful for studies of the possible prevention of diabetic retinopathy.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 EY 00152-05 LSR

PERIOD COVERED

October 1, 1986, to September 30, 1987

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

Adaptive Changes in Saccadic Innervation

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

PI:	Lance Optican	Ph.D.	Res. Biomedical Engineer	LSR, NEI
Others:	Zoi Kapoula	Ph.D.	Guest Researcher	LSR, NEI
	Paolo Inchingolo	Ph.D.	Visiting Scientist	LSR, NEI
	Michael E. Goldberg	M.D.	Chief, NMS	LSR, NEI
	Edward J. FitzGibbon	M.D.	Senior staff fellow	LSR, NEI

COOPERATING UNITS *(if any)*

LAB/BRANCH

Laboratory of Sensorimotor Research

SECTION

Oculomotor Control Section

INSTITUTE AND LOCATION

NEI, NIH, Bethesda, Maryland 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
1.3	0.9	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.)*

Saccades are the rapid eye movements used to change visual fixation. These eye movements are very acurate and end without drift. Our previous experiments have shown that the brain controls saccadic accuracy and actively suppresses post-saccadic drift by altering the levels of innervation sent to the muscles during and after a saccade. The adaptive mechanism for suppression of post-saccadic drift is sensitive to optically-imposed post-saccadic retinal slip. Our previous work in primates showed that the cerebellum was required for altering the gain and time constants of the neural components of saccadic innervation. After ablation of the midline vermis and fastigial nuclei saccades became hypermetric, and the adaptive control of saccadic accuracy was lost. After bilateral flocculectomy, monkeys developed post-saccadic ocular drift and became insensitive to optically-imposed retinal slip.

The current work studies two aspects of saccadic adaptation. First, we are extending the work on post-saccadic drift suppression to human subjects. We have already found that human subjects, like monkeys, respond to optically-induced post-saccadic slip by developing post-saccadic ocular drift. In addition, this mechanism appears binocular, and can not adjust the innervation to the two eyes differently. The second study attempts to determine the neural mechanisms underlying adaptive control of saccadic accuracy. By comparing details of the saccadic waveform before and after adaptation with possible models for saccade generation, it can be shown that saccadic accuracy must be controlled upstream from the superior colliculus, by changing the size of the saccadic command. Preliminary evidence suggests that the innervation changes come from a second, parallel pathway that contributes to the main visual pathway of the saccade command.

DEPARTMENT OF HEALTH AND HUMAN SERVICES · PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 EY 00153-05 LSR

PERIOD COVERED

October 1, 1986, to September 30, 1987

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

Adaptive Regulation in Primate Oculomotor System

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

PI:	Frederick A. Miles	D.Phil	Chief, OCS	LSR, NEI
Others:	Hubert Kimmig	M.D.	Visiting Fellow	LSR, NEI
	Urs Schwarz	M.D.	Visiting Fellow	LSR, NEI
	James R. Carl	M.D.	Senior Staff Fellow	CB, NEI
	Reuben S. Gellman	Ph.D.	Visiting Fellow	CB, NEI

COOPERATING UNITS *(if any)*

LAB/BRANCH

Laboratory of Sensorimotor Research

SECTION

Oculomotor Control Section

INSTITUTE AND LOCATION

NEI, NIH, Bethesda, Maryland 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
2.5	1.0	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.)*

Experiments were concerned with the ocular following responses of human subjects elicited by transient ramp movements of the visual scene. Such tracking movements normally aid the stabilization of gaze and thereby help to maintain clear vision. Responses were consistent, although varied in form from one subject to another. Latencies were invariably short, a typical value with a good stimulus being about 75 msec. Tracking was transiently enhanced after saccadic eye movements, the responses generated in the immediate wake of a saccade being on average about twice the amplitude of those generated half a second later: postsaccadic enhancement. A small part of this enhancement was shown to result from the visual disturbance created by the antecedent saccade since ocular following responses were also slightly enhanced after saccade-like shifts of the scene. These saccade-like shifts also elicit transient ocular following responses while the visual disturbance associated with real saccades do not, suggesting the existence of an extraretinal mechanism that prevents the tracking of saccades. Partitioning the scene into separate central and peripheral regions showed that en masse movement was not the best stimulus: the inphase motion in the surround had a suppressive effect. This indicates that the system has developed some special features to facilitate the tracking of objects.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 EY 00162-05 CB

PERIOD COVERED
October 1, 1986 to September 30, 1987

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)

None

LAB/BRANCH
Clinical Branch

SECTION
Section on Retinal and Vitreal Diseases

INSTITUTE AND LOCATION
NEI, NIH, Bethesda, Maryland 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.3	0.3	0,00

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.)

Vitreous fluorophotometry has been performed in patients with diabetes mellitus without retinopathy, patients with diabetes mellitus with nonproliferative retinopathy, and normal volunteer subjects, age- and sex-matched to the patients. The amount of fluorescein leakage into the vitreous of patients has been compared to that of the normal subjects. Correlations with other features of diabetes, such as the quality of diabetic control, the existence of subclinical neuropathy and nephropathy, and others were sought.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 EY 00163-05 CB

PERIOD COVERED
October 1, 1986 to September 30, 1987

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
NIH Interinstitute Medical 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.	Head, Section on Ophthalmic Genetics and Pediatric Ophthalmology	CB, NEI
Others:	Lessie McCain	R.N.	Clinical Technician	CB, NEI

COOPERATING UNITS *(if any)*

LAB/BRANCH
Clinical Branch

SECTION
Section on Ophthalmic Genetics and Pediatric Ophthalmology

INSTITUTE AND LOCATION
NEI, NIH, Bethesda, Maryland 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER
.15	.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.)*

The Interinstitute Medical Genetics Program and the Genetics Clinic, supported by the Clinical Center, offer a multidisciplinary approach to patients with genetic disease (Z01 CP 05139-04 CEB). Involved in the program are researchers from all Institutes. Patients evaluated in the clinic reporsent a broad spectrum of genetic disease. During the last year, approximately 425 individuals were seen, representing approximately 100 different disease categories. Due to the high frequency of ocular involvement in many of the cases, almost all the patient were evaluated by Clinical Branch staff of 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 Clinical Branch protocols.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 EY 00172-05 CB

PERIOD COVERED

October 1, 1986 to September 30, 1987

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

Senile 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.	Head, Section on Ophthalmic Genetics	CB, NEI
Others:	Carl Kupfer	M.D.	Director	NEI
	Monique S. Roy	M.D.	Visiting Scientist	CB, NEI

COOPERATING UNITS (if any)

None

LAB/BRANCH

Clinical Branch

SECTION

Section on Ophthalmic Genetics and Pediatric Ophthalmology

INSTITUTE AND LOCATION

NEI, NIH, Bethesda, Maryland 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
.43	.43	0

CHECK APPROPRIATE BOX(ES)

- [X] (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.)

This study will determine if patients with severe visual loss because of senile macular degeneration in one eye and with good vision in the second eye can be protected from severe visual loss in the good eye by the administration of vitamin E and vitamin C when exposure of the retina to light below 500 nanometers is diminished. The recruited patients will be randomly assigned either to a treated or untreated control group and examined at four-month intervals. Follow-up will continue for five years, unless an early beneficial or detrimental effect causes the study to be terminated in less than five years.

DEPARTMENT OF HEALTH AND HUMAN SERVICES · PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 EY 00184-05 LI

PERIOD COVERED
October 1, 1986 to September 30, 1987

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 Caspi	Ph.D.	Visiting Associate	LI, NEI
Others:	Robert B. Nussenblatt	M.D.	Clinical Director	NEI
	Francois Roberge	M.D.	Visiting Associate	LI, NEI
	Chi-Chao Chan	M.D.	Senior Staff Fellow	LI, NEI
	William Leake	M.S.	Biologist	LI, NEI
	Myung Kim	M.D.	Visiting Fellow	LI, NEI
	Makoto Higuchi	M.D.	Visiting Fellow	LI, NEI

COOPERATING UNITS *(if any)*

LAB/BRANCH
Laboratory of Immunology

SECTION
Section on Immunoregulation

INSTITUTE AND LOCATION
NEI, NIH, Bethesda, Maryland 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
2.08	2.04	0.04

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 vivo functional long-term T-cell lines and T-cell clones are developed and maintained in vitro from both peripheral blood and ocular fluids of humans and animals. 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 will be to identify the immunoreactive cells and mediators involved in the intraocular inflammatory process.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 EY 00187-04-CB

PERIOD COVERED
October 1, 1986 to September 30, 1987

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	CB, NEI
Others:	Carl Kupfer	M.D.	Director	NEI
	Lessie McCain	R.N.	Clinical Technician	CB, NEI
	Muriel I. Kaiser-Kupfer	M.D.	Head, Section on Ophthalmic Genetics and Pediatric Ophthalmology	CB, NEI

COOPERATING UNITS *(if any)*

LAB/BRANCH
Clinical Branch

SECTION
Section on Ophthalmic Genetics and Pediatric Ophthalmology

INSTITUTE AND LOCATION
NEI, NIH, Bethesda, Maryland 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.2	0.10	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.)*

Short- 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.

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

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 EY 00188-04 CB

PERIOD COVERED
October 1, 1986 to September 30, 1987

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	CB, NEI
Others:	Carl Kupfer	M.D.	Director	NEI
	Robert Sperduto	M.D.	Head, Epidemiology Branch	BEP, NEI
	Peter Kador	Ph.D.	Head, Section on Molecular Pharmacology	LMOD, NEI
	Lessie McCain	R.N.	Clinical Technician	CB, NEI

COOPERATING UNITS *(if any)*
Image Processing and Analysis Laboratory, DCRT, NIH (Benes Trus, Ph.D., Chief)
Clinical and Diagnostic Trials Section, NCI, NIH (Sylvan Green, M.D.)
Nuclear Medicine, Clinical Center, NIH (Joseph Frank, M.D.)

LAB/BRANCH
Clinical Branch

SECTION
Section on Ophthalmic Genetics and Pediatric Ophthalmology

INSTITUTE AND LOCATION
NEI, NIH, Bethesda, Maryland 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER
0.9	0.7	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.)*

We are developing objective and subjective methods to monitor and document opacities in the human lens using different systems. We are presently actively recruiting patients with and without cataracts for reproducibility studies on the objective systems--the Scheimpflug cameras (Zeiss and topcon), Retroillumination camera (Neitz), Specular microscope (Keeler) and laser light-scattering spectroscope (KOWA). We will also test other systems using sound (ultrasonography), and nuclear magnetic resonance (magnetic resonance imaging). We are also studying subjective systems or method, such as the effects of cataracts on visual perception, contrast sensitivity, and glare, which may be useful as additional parameters in the monitoring of cataract presence, progression, or regression.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 EY 00189-04 LMOD

PERIOD COVERED

October 1, 1986 to September 30, 1987

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

Oxidation of Proteins in Cataractogenesis and Protein Kinases in Lens Function

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

Donita L. Garland, Ph.D. Expert LMOD, NEI

COOPERATING UNITS *(if any)*

None

LAB/BRANCH

Laboratory of Mechanisms of Ocular Disease

SECTION

Section on Cataracts

INSTITUTE AND LOCATION

NEI, NIH, Bethesda, Maryland 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.)*

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; 3) the effect of the modifications on structure function of lens proteins. Bovine and human lenses were used. The approach taken has been to study the modifications of lens proteins after treatment in vitro by mixed function oxidation systems. Such treatment of crystallins led to crosslinking, partial degradation, charge changes, and production of nontryptophan fluorescence. Similar studies are in progress on a human gamma crystallin expressed in mouse L cells; the goal is to identify the modified amino acids. Treatment of lens homogenates for several days resulted in brown pigment formation, crosslinking, and the introduction of carbonyls. The mechanisms of these reactions are being studied.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 EY 00193-04 LMOD

PERIOD COVERED
October 1, 1986 to September 30, 1987

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.	Section Head	LMOD, NEI
Others:	Carmelann Zintz	Ph.D.	Staff Fellow	LMOD, NEI
	Yoshihiro Hotta	M.D.	Visiting Associate	LMOD, NEI
	Lila Inouye	M.D.	Staff Fellow	LMOD, NEI

COOPERATING UNITS *(if any)*

See next page.

LAB/BRANCH
Laboratory of Mechanisms of Ocular Diseases

SECTION
Molecular Pathology Section

INSTITUTE AND LOCATION
NEI, NIH, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
3 1/2	3 1/2	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.)*

Ornithine Aminotransferase Deficiency in Gyrate Atrophy: Gyrate atrophy (GA) is a blinding, hereditary degenerative disease of the retina and choroid of the eye characterized by a generalized deficiency in the mitochondrial enzyme, ornithine aminotransferase (OAT). Using the OAT cDNA which we had characterized before, we have established the presence of an OAT gene family and mapped the functional OAT and other OAT-related gene sequences to chromosomes 10 and X, respectively. Restriction fragment length polymorphisms were found in the functional OAT gene sequence and in the OAT-related gene sequences on the X-chromosome which may potentially show a linkage to X-linked retinitis pigmentosa (XLRP) since the locus of these sequences is identical to that of the XLRP linkage marker L1.28. Analysis of the OAT gene, mRNA, and protein in GA patients identified a case with a partial heterozygous deletion of the OAT gene, no OAT mRNA, and essentially undetectable OAT protein. This finding is the first real demonstration of the OAT defect in GA at the gene level and establishes the molecular basis of the genetic defect present in GA. In order to determine whether our OAT cDNA clone contains all of the sequences necessary for expression of active OAT, we have also constructed a mammalian expression clone containing the OAT cDNA and expressed it in mouse fibroblasts. Ability to express OAT using our cDNA clone in mammalian cells opens up the possibility of considering a gene replacement therapy for GA.

Hereditary Retinoblastoma: Hybrids between Y79 retinoblastoma and NIH3T3 cells were previously shown to be non-malignant, confirming the recessiveness of retinoblastoma. Variants were isolated among the hybrids that show reversion to malignant phenotype, suggesting that additional human gene(s) besides the chromosome 13 gene may be important in the suppression of malignancy in these cells and that progressive loss of these human genes from the hybrids may result in malignant reversion. Hybrids were also made between the Y79 retinoblastoma cells and normal human fibroblasts, and shown to be non-malignant, confirming previous results.

GPO 814-918

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 EY 00196-04 LRCMB

PERIOD COVERED
October 1, 1986 to September 30, 1987

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.	Senior Staff Fellow	LRCMB, NEI
Others:	Diane Borst	Ph.D.	IRTA Fellow	LRCMB, NEI
	Shirley Rainier	Ph.D.	Staff Fellow	LRCMB, NEI
	T. Michael Redmond	Ph.D.	Staff Fellow	LRCMB, NEI
	Adriana Albini	Ph.D.	Visiting Associate	LRCMB, NEI
	Lila Inouye	M.D.	Staff Fellow	LRCMB, NEI

COOPERATING UNITS *(if any)*
Zoology Department, University of Lund, Lund, Sweden (Theo van Veen)

LAB/BRANCH
Laboratory of Retinal Cell and Molecular Biology

SECTION
Section on Gene Regulation

INSTITUTE AND LOCATION
NEI, NIH, Bethesda, Maryland 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
3.7	3.7	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.)*

My laboratory presently is isolating and characterizing recombinant DNA molecules necessary for the study of the structure and expression of IRBP (Interphotoreceptor Retinoid-Binding Protein). We have cloned many different cDNAs (copies of the IRBP messenger RNA) from bovine retina that correspond to 4.8 kb of the IRBP mRNA. We have sequenced portions of all of these overlapping cDNA clones and have about 3000 bases in continuous sequence. The IRBP mRNA is long (7000 bases) and gives only one band on a Northern blot; however, we have evidence that suggests that there is sequence heterogeneity near the 3' end of the IRBP mRNA. Two authentic cDNA clones show a striking divergence in their sequences, yet sequences both 5' and 3' to the divergence are identical. Both sequences in the divergence hybridize to one gene clone. Alternative splicing of the IRBP gene primary transcript could explain the origin of the two types of cDNA clones. The cDNA sequences have been used to predict the amino acid sequence of the protein. These sequences have been helpful in the analysis of the uveitogenic peptides in IRBP. The entire gene for bovine IRBP has been cloned. Partial DNA sequence analysis of the gene clone has identified the authentic N-terminus, the putative initiator methionine codon and a putative signal peptide sequence of the IRBP polypeptide. A second different complete bovine IRBP gene has been identified. In human, the IRBP gene is on chromosome 10, as determined by in situ hybridization of our bovine cDNA probe to human chromosome squashes. This result was verified by isolating genomic clones from a human chromosome 10 specific library. We have screened a human retinal cell cDNA library with the bovine IRBP cDNA probe and have identified several large cDNA clones up to 4.5 kb in length for human IRBP.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 EY 00198-04 CB

PERIOD COVERED
October 1, 1986 to September 30, 1987

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:	Manuel Datiles	M.D.	Staff Ophthalmologist	CB, NEI
	James R. Carl	M.D.	Senior Staff Fellow	CB, NEI

COOPERATING UNITS (if any)
Division of Diabetes, Endocrinology, and Metabolic Diseases, 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, Maryland 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
2.35	1.25	1.1

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.)

Oral sorbinil, an aldose reductase inhibitor, will be administered in a double-masked randomized trial to diabetics with no or minimal diabetic retinopathy. This will be done to evaluate the effects of sorbinil on the development of diabetic retinopathy and further investigate the safety and toleration of sorbinil. The study will be conducted simultaneously in 11 research centers in the USA.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 EY 00201-03 LMOD

PERIOD COVERED
October 1, 1986 to September 30, 1987

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Molecular Biology 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:	Chihiro Nishimura	M.D.	Visiting Associate	LMOD, NEI
	Caroline Graham	B.A.	Chemist	LMOD, NEI

COOPERATING UNITS *(if any)*

Wistar Institute, 3601 Spruce St., Philadelphia, PA (Dr. Bernard Dietzschold)

LAB/BRANCH
Laboratory of Mechanisms of Ocular Diseases

SECTION
Section on Cataracts

INSTITUTE AND LOCATION
NEI, NIH, Bethesda, Maryland 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
1.7	1.5	.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 enzyme, aldose reductase (AR), has been implicated in diabetic complications of the nerve, kidney, retina and lens. Currently, a variety of AR inhibitors are being tested as a possible new treatment modality for diabetics, although side effects are always a concern. In order to study the function and expression of AR, we initiated a study on the structure of aldose reductase using peptide and DNA sequencing. We have successfully sequenced over 85% of the aldose reductase protein.

Fifteen λgt11 rat lens cDNA clones were isolated using oligonucleotide probes designed from partial amino acid sequence of purified rat lens AR. One of the clones gave hybridization with two separate probes and was subsequently sequenced. The insert is 1206 bp in length with an open reading frame encoding 284 amino acids (or a molecular size around 32,300 daltons). The sequences from six rat lens tryptic and cyanogen bromide-cleaved peptide fragments (totally 128 amino acids) are accounted for within the open reading frame of the cDNA insert, indicating that this insert encodes rat lens AR.

The sequence of AR has significant similarity (50%) with both human liver aldehyde reductase and frog lens rho crystallin. Local identities as high as 84% were observed. This degree of similarity suggests that all three proteins belong to the same superfamily with related structures and evolutionary origins.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 EY 00211-02 CB

PERIOD COVERED

October 1, 1986 to September 30, 1987

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.	Head, Section on Ophthalmic Genetics and Pediatric Ophthalmology	CB, NEI
Others:	Lessie McCain	R.N.	Clinical Technician	CB, NEI
	Manuel Datiles	M.D.	Visiting Scientist	CB, NEI

COOPERATING UNITS *(if any)*

Human Genetics Branch, NICHD, National Institutes of Health, Bethesda, Maryland (William Gahl, M.D., Ph.D.)

LAB/BRANCH

Clinical Branch

SECTION

Section on Ophthalmic Genetics and Pediatric Ophthalmology

INSTITUTE AND LOCATION

NEI, NIH, Bethesda, Maryland 20892

TOTAL MAN-YEARS	PROFESSIONAL:	OTHER:
.2	.10	.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.)*

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 cornea, conjunctiva iris and depigmentation of the retina. Systemic complications include the Fanconi syndrome, and renal failure.

Eight years ago cysteamine, a free thiol which 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 which revealed none, we have begun a double-masked clinical trial to test the efficacy of topical cysteamine in humans. Twelve patients have thus far been enrolled. Three patients have shown significant decrease in the cysteamine treated eyes and are now taking drops in both eyes.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 EY 00212-02 CB

PERIOD COVERED
October 1, 1986 to September 30, 1987

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	CB, NEI
Others:	Carl Kupfer	M.D.	Director	NEI
	Muriel I. Kaiser-Kupfer	M.D.	Head, Section on Ophthalmic Genetics and Pediatric Ophthalmology	CB, NEI

COOPERATING UNITS *(if any)*

See next page.

LAB/BRANCH
Clinical Branch

SECTION
Section on Ophthalmic Genetics and Pediatric Ophthalmology

INSTITUTE AND LOCATION
NEI, NIH, Bethesda, Maryland 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.65	0.65	

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 presently an extreme dearth 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 between cataract surgeons and basic researchers and modification of techniques by both groups.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 EY 00213-02 CB

PERIOD COVERED
October 1, 1986 to September 30, 1987

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Sensory and oculomotor contributions to ocular disorder

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

PI:	Kent E. Higgins	Ph.D.	Expert	CB, NEI
Others:	Rafael C. Caruso	M.D.	Visiting Scientist	CB, NEI
	Monique S. Roy	M.D.	Visiting Scientist	CB, NEI
	Francisco de Monasterio	M.D.	Medical Officer	OSD
	Robert Nussenblatt	M.D.	Clinical Director	CB, NEI

COOPERATING UNITS *(if any)*

None

LAB/BRANCH
Clinical Branch

SECTION
Office of the Clinical Director

INSTITUTE AND LOCATION
NEI, NIH, Bethesda, Maryland 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
1.4	1.0	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.)*

Spatial contrast sensitivity was used to assess losses or changes in overall visual resolution in patients having a variety of toxic, inflammatory, degenerative, or congenital retinal and neuro-ophthalmological disorders of the visual system. A criterion-free forced-choice physchophysical procedure was used, since this method was previously shown to minimize false positive or false negative diagnoses at initial test and to minimize spurious changes in sensitivity with repeated testing. Contrast sensitivity testing, while requiring more patient testing time, continued to be superior to conventional acuity measurements for the detection of early losses and for monitoring changes in visual resolution in patients undergoing treatment. Age-referenced normative data make it possible to distinguish contrast sensitivity loss due to ocular disorder from that expected on the basis of normal aging.

A retinal image stabilization system is under construction. This system is intended to permit focal electroretinography and high resolution microperimetry in small, localized regions of a patient's retina.

GPO 914-418

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 EY 00214-02 CB

PERIOD COVERED

October 1, 1986 to September 30, 1987

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

Acquired and Congenital Color Vision Deficiencies: Mechanisms and Diagnosis

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

PI:	Kent E. Higgins	Ph.D.	Expert	CB, NEI
Others:	Francisco M. deMonasterio	M.D.	Medical Officer	OSD, NEI
	Rafael C. Caruso	M.D.	Visiting Scientists	CB, NEI
	Robert B. Nussenblatt	M.D.	Clinical Director	CB, NEI

COOPERATING UNITS (if any)

None

LAB/BRANCH

Clinical Branch

SECTION

Office of the Clinical Director

INSTITUTE AND LOCATION

NEI, NIH, Bethesda, Maryland 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
1.1	1.0	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.)

This project involves the study of cone function in cases of color vision defects, with special emphasis on the acquired color deficiencies. Human subjects have been used for these studies which range from attempts to improve quantification of data from existing data for the purpose of designing better tests for detecting color defects secondary to ocular disorder.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 EY 00217-02 LI

PERIOD COVERED
October 1, 1986 to September 30, 1987

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
	Consuelo Muellenberg-Coulombre		Chemist	LI, NEI
	Myung Kim	M.D.	Visiting Fellow	LI, NEI
	Susan Lightman	M.D.	Visiting Fellow	LI, NEI

COOPERATING UNITS (if any)

LAB/BRANCH
Laboratory of Immunology

SECTION
Section on Clinical Immunology

INSTITUTE AND LOCATION
NEI, NIH, Bethesda, Maryland 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.30	0.20	0.1

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.)

Experimental autoimmune uveitis (EAU) is induced by immunization of rats and other experimental animals with S-antigen (a soluble antigen from the retina) is being investigated in this laboratory as a model of human intra-ocular inflammation. This experimental inflammation can be transferred from donor rats to naive recipients using lymphocytes harvested from the spleen or lymph nodes. Following harvesting of the cells from the donors and three days in culture with stimulating antigen, the cells are injected into the intra-peritoneal cavity and five to seven days later the recipient rats develop EAU. The disease can also be transferred using a T-helper cell line by intra-peritoneal or intra-ocular injection. The mechanism of transfer of disease is unclear. This work has used radioactively labeled lymphocytes to determine the fate of these lymphocytes after injection into the peritoneal cavity or blood during the process of the development of uveitis. The goal of this project is to understand the initiating mechanisms of inflammation in the hope that these mechanisms can be extended and applied to human inflammations. Cells from an S-Ag specific T cell line migrate into the retina and cause EAU. The kinetics of this migration are being studied. S-antigen specific cells reach the eye in greater numbers if the inflammation in the eye is induced by S-antigen than if it is induced by another mechanism.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 EY 00218-02 LI

PERIOD COVERED
October 1, 1986 to September 30, 1987

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:	Alan G. Palestine	M.D.	Head, Section on Clinical Immunology	LI, NEI
Others:	Robert B. Nussenblatt	M.D.	Clinical Director	NEI

COOPERATING UNITS *(if any)* Laboratory of Tumor Cell Biology, National Cancer Institute (S. Zaki Salahuddin, Ph.D.); Laboratory of Cellular & Molecular Biology, National Cancer Institute (Dharam Ablashi, D.V.M.); Department of Critical Care Medicine, Clinical Center (Henry Masur, M.D.); Laboratory of Tumor Cell Biology, National

LAB/BRANCH
Laboratory of Immunology

SECTION
Section on Clinical Immunology

INSTITUTE AND LOCATION
NEI, NIH, Bethesda, Maryland 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.09	0.09	0

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.)*

Cytomegalovirus retinitis is the major cause of blindness in AIDS patients. Although we have previously shown that DHPG is effective in treating this infection, the disease relapses without continued maintenance. Maintenance therapy requires intravenous infusion and is associated with marrow toxicity. A multi-center randomized trial is currently being planned to evaluate the use of this drug.

GPO 814-918

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 EY 00219-02 LI

PERIOD COVERED
October 1, 1986 to September 30, 1987

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 C. 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, Maryland 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
1.01	1.01	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.)

In recent years there has been increasing evidence in the literature that pituitary hormones are capable of regulating the immune system. There is evidence to suggest that prolactin is an immunostimulatory hormone and that reduction of serum prolactin levels in experimental animals by hypothesectomy or bromocriptine will result in a degree of immunosuppression.

This information has been applied to humans and two clinical studies have begun. Both of these are in early phase of patient recruitment. One study is a randomized trial between placebo and bromocriptine in recurrent anterior uveitis using the end point of the number of recurrences per year to determine whether or not bromocriptine is capable of regulating the immune system in these patients. The second trial focuses on the additive effects of cyclosporine plus bromocriptine in attempts to treat patients with posterior uveitis at lower doses of cyclosporine in order to reduce its concurrent renal toxicity while at the same time achieving an immunosuppressive effect. Cyclosporine and prolactin compete for binding sites on the lymphocyte.

Further studies in human disease will hopefully elucidate other aspects of the neuroendocrine axis which can be utilized to regulate the immune system to treat autoimmune diseases.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 EY 00220-02 LI

PERIOD COVERED
October 1, 1986 to September 30, 1987

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:	Consuelo Muellenberg-Coulombre		Chemist	LI, NEI
	Myung Kim	M.D.	Visiting Fellow	LI, NEI
	Robert B. Nussenblatt	M.D.	Clinical Director	NEI
	Stephanie A. Skolik	M.D.	Research 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, Maryland 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
1.19	0.49	0.7

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 recent years there has been increasing evidence in the literature that hormones are capable of regulating the immune system. There is evidence to suggest that prolactin is an immunostimulatory hormone and that reduction of serum prolactin levels in experimental animals by hypothesectomy or bromocriptine will result in a degree of immunosuppression.

An animal model of experimental autoimmune uveitis (EAU) induced by immunization of rats with S-antigen (a soluble antigen from the retina) is used as a model for intraocular inflammatory disease. We have demonstrated that concurrent antibody production in both males and females and the incidence of uveitis in female animals but did not have a significant effect on the immune responses measured by lymphocyte proliferation. As reported before, cyclosporine in high doses (10 mg/kg) there is only partial effect. We have demonstrated that the concurrent use of bromocriptine to suppress prolactin in combination with low dose cyclosporine is more effective than either drug separately in suppressing both the incidence of disease as well as the cellular and humoral immune responses to immunization. There is evidence in the literature to suggest that cyclosporine is able to compete for binding on the lymphocyte by prolactin and that reductions in prolactin level may therefore make cyclosporine more effective. Further studies in animal disease will hopefully elucidate other aspects of the neuroendocrine axis which can be utilized to regulate the immune system to treat autoimmune diseases.

The alpha adrenergic antagonist prazosin is also capable of modulating EAU in our laboratory. However, there is no decrease in cellular or humoral immune responses.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 EY 00221-02 LI

PERIOD COVERED
October 1, 1986 to September 30, 1987

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:	Myung Kim	M.D.	Visiting Fellow	LI, NEI
	Consuelo Muellenberg-Coulombre		Chemist	LI, NEI
	Robert B. Nussenblatt	M.D.	Clinical Director	NEI

COOPERATING UNITS (if any)

LAB/BRANCH
Laboratory of Immunology

SECTION
Section on Clinical Immunology

INSTITUTE AND LOCATION
NEI, NIH, Bethesda, Maryland 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.51	0.41	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.)

Endotoxin is a polysaccharide derived from the cell wall of gram negative bacteria. When injected into the footpad or the eye of a rat it will induce an inflammatory reaction within the eye. The mechanism of this inflammation is still unclear. However, since several types of anterior uveitis in humans appear to be linked to gram negative bacteria exposure, this is considered a relative model for anterior uveitis in humans such as Reiter's syndrome. In this study rats received E. coli endotoxin and the expression of class II antigens was studied within the eye using immunohistochemical techniques. We observed that the expression of class II antigens on the ciliary body and iris preceeded the influx of inflammatory cells into the eye and that the inflammatory cells that entered the eye were primarily neutrophils with some monocytes. No T-cells were present in the inflammatory infiltrate. The inflammatory cellular infiltrate could be inhibited by indomethacin or colchicine, however this did not alter the expression of class II antigens by the iris or ciliary body indicating that this expression is not simply a consequence of the inflammatory infiltrate but may be intimately involved with the mechanism of the expression of endotoxin induced uveitis. Corticosteroids were capable of suppressing both the cellular inflammatory infiltrate and the expression of class II antigens. The expression of class II antigens on nonlymphoid cells within the eye may be important in antigen presentation or may simply signal a phenotypic change on the cells due to the interaction of endotoxin with the cell membranes. The findings were compared with the expression of class II antigen in passive and active intraocular Arthus.

DEPARTMENT OF HEALTH AND HUMAN SERVICES · PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 EY 00222-02 LI

PERIOD COVERED
October 1, 1986 to September 30, 1987

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.	Senior Staff Fellow	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
	Barbara Detrick	Ph.D.	Expert	LI, NEI

COOPERATING UNITS *(if any)*
University of Tokyo, School of Medicine (Manabu Mochizuki, M.D.)

LAB/BRANCH
Laboratory of Immunology

SECTION
Section on Immunoregulation

INSTITUTE AND LOCATION
NEI, NIH, Bethesda, Maryland 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.43	0.43	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 marker on ocular resident cells in rodents with experimental autoimmune uveoretinitis by active immunization or adoptive transfer were analyzed by immunohistochemical studies. The lymphocyte population at the inflammatory sites was found to change markedly during the course of disease. In the early stage, T-helper/inducers are the predominant cells in the eye. A relative increase of T-suppressor/cytotoxic cells in the late stage were observed. Expression of major histocompatibility complex class II antigens on ocular resident cells such as RPE, retinal endothelium, keratocytes, fibroblast and ciliary epithelium was observed in different models of EAU. This antigen expression may play a certain role in the pathogenesis of EAU. Both infiltrating and alteration of class II antigens cell subpopulation can be modulated by cyclosporine and dexamethosone treatment.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 EY 00224-02 LI

PERIOD COVERED
October 1, 1986 to September 30, 1987

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.	Senior Staff Fellow	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.	Head, Laboratory of Ophthalmic Pathology	LOP, NEI

COOPERATING UNITS (If any)

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Laboratory of Immunology

SECTION
Section on Immunoregulation

INSTITUTE AND LOCATION
NEI, NIH, Bethesda, Maryland 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.12	0.12	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.)

Immunocompetent cells and ocular resident cells in the ocular tissues from patients with a clinical diagnosis of sympathetic ophthalmia were examined using the immunohistochemical technique. The choroidal infiltrates were composed primarily of T-lymphocytes. Different amounts of macrophages and B lymphocytes were present in each case. A varied spectrum of immunopathological and histopathological findings may occur in clinically diagnosed sympathetic ophthalmia. The immunopathology resembles EAU induced by retinal soluble model. Exposure of uveal tissue outside the eye and adjuvant effect may be important in the pathogenesis of this disease in humans.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 EY 00225-02 LI

PERIOD COVERED
October 1, 1986 to September 30, 1987

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.	Senior Staff Fellow	LI, NEI
Others:	Robert B. Nussenblatt	M.D.	Clinical Director	NEI
	Richard P. Wetzig	M.D.	Senior Staff Fellow	LI, NEI
	Francois Roberge	M.D.	Visiting Associate	LI, NEI

COOPERATING UNITS (if any)

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Laboratory of Immunology

SECTION
Section on Immunoregulation

INSTITUTE AND LOCATION
NEI, NIH, Bethesda, Maryland 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.16	0.16	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.)

Complications of post-inflammation in uveitis patients included destruction of photoreceptors, gliosis, choroidal scar, and formations of cyclitic membrane, snowbanking and preretinal membrane. Eyes enucleated from patients with end stages of chronic anterior uveitis (formation of cyclitic membrane), pars planitis (formation of preretinal membrane) were evaluated. Glial cells and proliferating Muller cells were the major components in these membranes.

GPO 814-818

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 EY 00226-02 LI

PERIOD COVERED
October 1, 1986 to September 30, 1987

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.	Senior Staff Fellow	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:
0.3	0.3	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.)*

Ocular specimens and sera from 12 patients with onchocerciasis and 10 controls were studied. A mild to moderate chronic inflammatory cellular infiltration was present in the conjunctiva of the onchocerciasis patients. T-lymphocytes were the predominant inflammatory cells with the T-suppressor subset being significantly increased in the onchocerciasis patients when compared to controls. In the onchocerciasis patients, the nonlymphoid cells in the conjunctiva and iris, such as vascular endothelia, pericytes and fibroblasts, showed an increase in expression of class II antigens. The anti-onchocerca Volvulus antibodies in the sera and aqueous humor were significantly higher in the patients compared to the controls. These findings suggest that T-cells are important in the ocular immune response to onchocerca and that expression of class II antigens on nonlymphoid cells and the humoral factors may all play a critical role in ocular onchocerciasis. Using the indirect immunoperoxidase method, autoimmune antibodies against outer segments of photoreceptors and inner neural layers of retina were identified in sera and ocular fluids from patients with onchocerciasis. These antibodies could not be absorbed by S-Ag nor IRBP. They may play a role in the retinal degeneration in onchocerciasis.

GPO 914-918

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 EY 00227-02 LI

PERIOD COVERED
October 1, 1986 to September 30, 1987

TITLE OF PROJECT (80 characters or less. Title must fit on one line between the borders.)
Histopathology of Pars Planitis and Experimental Autoimmune Uveitis

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

PI:	Richard P. Wetzig	M.D.	Senior Staff Fellow	LI, NEI
Others:	Robert B. Nussenblatt	M.D.	Clinical Director	NEI
	Chi-Chao Chan	M.D.	Senior Staff Fellow	LI, NEI
	Barbara Detrick	Ph.D.	Expert	LI, NEI
	John J. Hooks	Ph.D.	Head, Section on Immunology and Virology	LI, NEI

COOPERATING UNITS (If any)

LAB/BRANCH
Laboratory of Immunology

SECTION
Section on Immunoregulation

INSTITUTE AND LOCATION
NEI, NIH, Bethesda, Maryland 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.58	0.58	0

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.)

Studies in animals and in patients are being carried out to determine factors influencing ocular immune responses. In an animal model, rats are immunized with S-retinal antigen to produce experimental autoimmune uveitis. Animals in one group received anti-Ia antibody intraperitoneally and developed the onset of uveitis significantly later and to a lesser extent than controls. Histopathologically, the anti-Ia treated animals had much less inflammation than did controls. A human eye with pars planitis was also studied immunohistologically. In the pars plana region there was an elevated helper to suppressor T-cell ratio. In addition, the snowbank area showed staining for glial fibrillary acid protein Muller cells, type IV collagen and laminin. There was staining for HLA-DR throughout the globe. The results of these studies shed light on how surface antigens effect and are transmitted by ocular immune responses.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 EY 00228-02 LI

PERIOD COVERED
October 1, 1986 to September 30, 1987

TITLE OF PROJECT (80 characters or less. Title must fit on one line between the borders.)
Study of Ocular Glial Cells 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)

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Laboratory of Immunology

SECTION
Section on Immunoregulation

INSTITUTE AND LOCATION
NEI, NIH, Bethesda, Maryland 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.92	0.92	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 work extended our ongoing study of interactions between the retinal glial Müller cell and T lymphocytes. In an in vitro co-culture system, Müller cells had been shown to exert a profound inhibitory influence on antigen and IL-2 driven proliferation of T helper cell lines. Investigations of the nature of the inhibitory moiety revealed that it was sensitive to proteinase. In further studies, we demonstrated that Müller cells can produce interleukin 1 (IL-1) activity and that in conditions where their inhibitory action is removed they display the capacity to efficiently function as antigen presenting cells.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 EY 00229-02 LI

PERIOD COVERED
October 1, 1986 to September 30, 1987

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Assessment of the Size of the Leak Induced in Retinal Vessels Using PITC-Dextrans

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:	Susan Lightman	M.D.	Visiting Fellow	LI, NEI

COOPERATING UNITS *(if any)*
Laboratory of Ophthalmic Pathology, National Eye Institute (Toichiro Kuwabara);
Laboratory of Ophthalmic Pathology, National Eye Institute (Laura Caspers-Velu)

LAB/BRANCH
Laboratory of Immunology

SECTION
Section on Clinical Immunology

INSTITUTE AND LOCATION
NEI, NIH, Bethesda, Maryland 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.3	0.3	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.)*

Uveitis was induced in two monkeys by immunization with IRBP and serial fluorescein angiograms performed using different sized dextrans linked to fluorescein. The aim of these studies is to provide data on the retinal vessels and toxicology data to enable these agents to be used in humans. We have demonstrated that the larger molecular weight dextrans are less permeable than sodium fluorescein in the inflamed retina. The sites of large molecule leakage show ultrastructural evidence of open tight junctions whereas the areas that leak only sodium fluorescein have closed tight junctions.

GPO 814-818

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 EY 00230-02 LI

PERIOD COVERED
October 1, 1986 to September 30, 1987

TITLE OF PROJECT (80 characters or less. Title must fit on one line between the borders.)
Quantitative Assessment of Retinal Vascular Permeability

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:	Stephanie Skolik	M.D.	Research Fellow	LI, NEI

COOPERATING UNITS (if any) Laboratory of Neurosciences, National Institute on Aging (Emanuel Rechthand, M.D.); Laboratory of Neurosciences, National Institute on Aging (Stanley Rapoport, M.D.); Laboratory of Mechanisms of Ocular Diseases, Section on Molecular Pharmacology (Peter Kador, Ph.D.)

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Section on Clinical Immunology

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NEI, NIH, Bethesda, Maryland 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.33	0.33	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.)

A sensitive quantitative method was set up for examining the permeability of retinal vessels in the rat. Baseline values for normal rat retinal vessels were established and the method will be applied to pathological situations. Increased leakage was observed in clinically and acutely hypertensive rats. Increased leakage was also observed in galactosemic rats. This leakage was reversed by treatment with an aldose reductase inhibitor.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 EY 00231-02 LI

PERIOD COVERED
October 1, 1986 to September 30, 1987

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	LVR, NEI
	Merlyn Rodrigues	M.D., Ph.D.	Head, Section on Clinical Eye Pathology	LOP, NEI
	Caroline Percopo	A.B.	Biologist	LI, NEI

COOPERATING UNITS (if any) Walter Reed Army Medical Center, Washington, D.C. (Magda Tomaszewski, M.D.); Walter Reed Army Medical Center, Washington, D.C. (David Katz, M.D.); Duke University, Durham, North Carolina (Barton Haynes, M.D.); Ruprecht-Karl's University, Heidelberg, Germany (Ellen Kraus-Mackiw, M.D.)

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Laboratory of Immunology

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Section on Immunoregulation

INSTITUTE AND LOCATION
NEI, NIH, Bethesda, Maryland 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.65	0.45	0.2

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.)

Class II antigens (HLA-DR and HLA-DQ) are membrane bound glycoproteins encoded by genes in the major histocompatibility complex. In addition to their well established role as regulatory molecules of the immune response, these determinants are now suspected of playing an influencial part in cellular differentiation.

In exploring the cellular composition of a popular childhood tumor, retinoblastoma, we identified the presence of HLA-DR and HLA-DQ antigens on a population of undifferentiated malignant cells of the retina. This study provides the initial description of these class II antigens on retinoblastoma cells. Furthermore, HLA-DR antigen was found to be coexpressed on cells that contained both neuronal and glial markers. This study also identifies for the first time the presence of class II antigens on cells of neuronal origin.

Based on these initial studies, additional investigations are in progress. One approach focuses on the possible role of class II antigens in cellular differentiation or immune reactivity. A second examines the prognostic significance of these molecules on retinoblastoma cells and the possible relationship class II proteins may have to the modulation and management of this tumor. Finally, a third study will examine the role of IFN-gamma as a differentiating agent of this tumor.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 EY 00232-02 LI

PERIOD COVERED
October 1, 1986 to September 30, 1987

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:	Barbara Detrick	Ph.D.	Expert	LI, NEI
	Caroline Percopo	A.B.	Biologist	LI, NEI
	Christian Hamel	M.D.	Visiting Fellow	LI, NEI
	Muriel Kaiser-Kupfer	M.D.	Head, Section on Ophthalmic Genetics and Pediatrics	CB, NEI

COOPERATING UNITS (if any)
New York University, School of Medicine, Department of Microbiology (Jan Vilcek, M.D.)

LAB/BRANCH
Laboratory of Immunology

SECTION
Section on Immunology and Virology

INSTITUTE AND LOCATION
NEI, NIH, Bethesda, Maryland 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
1.15	0.75	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 IFN proteins can modify a variety of biological activities and are considered one of the body's regulatory proteins. Numerous studies now indicate that the IFN's 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 how this interaction may modify immune responses and immunologically related disorders.

Using immunocytochemical analysis we have developed a sensitive method of identifying lymphokines, IFN-gamma and IL2, at the site of tissue damage. We have identified the lymphokines, IFN-gamma and IL2 in inflammatory eye diseases. The presence of these lymphokines is associated with a lymphocyte infiltrate predominantly of a T-cell origin and with the expression of MHC class II antigens on both the infiltrating cells and in the retinal pigment epithelial (rpe) cells.

This is the first demonstration of lymphokines, IFN-gamma and Il2 at the site of a localized autoimmune disease. These observations may indicate that IFN-gamma 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 the treatment of these diseases.

GPO 914-918

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 EY 00233-02 LI

PERIOD COVERED
October 1, 1986 to September 30, 1987

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:	Barbara Detrick	Ph.D.	Expert	LI, NEI
	Caroline Percopo	A.B.	Biologist	LI, NEI
	Susan Robbins	Ph.D.	Postdoctoral Fellow	LI, NEI
	Laura Caspers-Velu	M.D.	Visiting Associate	LOP, NEI

COOPERATING UNITS (if any) Hopital St. Louis, Paris, France (Lawrence Bowsell, M.D.); Institute Gustave Rowsse, Villjuif, France (Alain Bernard, M.D.); National Institute of Dental Research, Laboratory of Microbiology & Immunology (Reuben Siraganian, M.D.)

LAB/BRANCH
Laboratory of Immunology

SECTION
Section on Immunology and Virology

INSTITUTE AND LOCATION
NEI, NIH, Bethesda, Maryland 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
1.45	1.25	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 retinal pigment epithelial (rpe) cell is a major regulatory cell in the eye. That is, the rpe cell exerts a variety of actions in maintaining retinal integrity and function. In order to more effectively study this cell 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 which react with the human rpe cell. The monoclonal antibodies are both specific for the rpe cell within the eye, since they do not react with any other ocular structures. Moreover, these antibodies do not cross react with human skin, kidney or peripheral mononuclear cells.

This is the first monoclonal antibody which is directed solely at the human rpe cell. Further characterization and studies with this antibody should prove useful in the identification of rpe cells in situ and in vitro. Moreover, this immunoglobulin will allow us to probe the bioregulatory functions of the cell.

DEPARTMENT OF HEALTH AND HUMAN SERVICES · PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 EY 00234-02 LI

PERIOD COVERED
October 1, 1986 to September 30, 1987

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
Others:	Barbara Detrick	Ph.D.	Expert	LI, NEI
	Christian Hamel	M.D.	Visiting Fellow	LI, NEI
	Chi-Chao Chan	M.D.	Senior Staff Fellow	LI, NEI
	Robert B. Nussenblatt	M.D.	Clinical Director	NEI

COOPERATING UNITS (if any)
Ioannina School of Medicine, Ioannina, Greece (Haralampos M. Moulsopoulos, M.D.)

LAB/BRANCH
Laboratory of Immunology

SECTION
Section on Immunology and Virology

INSTITUTE AND LOCATION
NEI, NIH, Bethesda, Maryland 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.65	0.65	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.)

MHC class II antigens, HLA-DR in the human and Ia in the mouse, are membrane bound glycoproteins that are 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.

During the past year, we have determined if class II antigens are expressed in certain diseases and we have evaluated their possible role in autoimmune and inflammatory diseases. Initial studies identified cells in the anterior segment and cells in the retina (rpe cell) which express class II antigens during inflammatory eye diseases. Treatment with monoclonal anti-Ia antibodies diminished the clinical disease and the expression of MHC class II antigens. These studies have been extended to evaluate Sjogren's syndrome. We found that the salivary gland in Sjogren's syndrome is infiltrated predominantly by T-lymphocytes and that this is associated with class II antigen expression on glandular epithelial cells. Moreover, we evaluated the effect of cyclosporin A on the immunopathological lesions in Sjogren's syndrome. We found that cyclosporin treatment resulted in a decrease in both T cell infiltration and a decrease in HLA-DR antigen expression.

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 disease.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 EY 00235-02 LI

PERIOD COVERED
October 1, 1986 to September 30, 1987

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
	Richard Wetzig	M.D.	Senior Staff Fellow	LI, NEI
	Chi-Chao Chan	M.D.	Senior Staff Fellow	LI, NEI
	Caroline Percopo	A.B.	Biologist	LI, NEI
	Robert B. Nussenblatt	M.D.	Clinical Director	NEI

COOPERATING UNITS (if any) Eye and Ear Infirmary, University of Illinois, Chicago, Illinois (M.O.M. Tso, M.D.); Duke University, Durham, North Carolina (Barton F. Haynes, M.D.); Paris, France (Laurence Boumsell, M.D.); and Paris, France (Alain Bernard, M.D.)

LAB/BRANCH
Laboratory of Immunology

SECTION
Section on Immunoregulation

INSTITUTE AND LOCATION
NEI, NIH, Bethesda, Maryland 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.43	0.33	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.)

Class II antigens are membrane bound glycoproteins encoded by genes in the mixed histocompatibility complex. Their expression is critical to immune reactivity. Although most immune cells constitutively express class II antigens, some non-immune cell types can be induced to demonstrate these molecules under selected conditions, such as an immunologic or degenerative event. Based on our earlier data, which demonstrated that retinitis pigmentosa patients had an alteration in IFN-gamma production and class II antigen expression and rpe cells can, in special instances, express class II antigens, we expanded our studies to evaluate class II antigen expression in a variety of ocular situations. We found that the rpe cell does not express class II antigen in the normal eye. In contrast, the rpe cell did express these molecules in a retinal degenerative disorder (retinitis pigmentosa) and in two ocular inflammatory diseases (sympathetic ophthalmia and uveitis). Using the EAU animal model of ocular autoimmune disease we demonstrated that the rpe cell is activated to express class II antigens prior to clinical and histopathological evidence of the disease. Finally, we demonstrated that EAU could be altered with anti-Ia therapy. In this study EAU animals receiving monoclonal anti-Ia antibodies experience not only less ocular inflammation but also a delay in the onset of EAU. Moreover, immunocytochemistry analysis revealed that eyes from these animals expressed less Ia antigen as well as a diminution of infiltrating macrophages and lymphocytes. These data show that anti-Ia treatment significantly modifies the course of EAU in the rat. We are continuing to investigate the effects of other potent modulators such as IFN-gamma and cyclosporine on class II antigen expression with the hope that an alteration in activation or expression of these molecules may modify the disease process to the benefit of the host.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 EY 00237-02 LMOD

PERIOD COVERED
October 1, 1986 to September 30, 1987

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Characterization of the Primate 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:	Masao Nakamura	M.D.	Visiting Associate	LMOD, NEI

COOPERATING UNITS *(if any)*
Division of Cancer Research, University of Toronto (S. Meakin, M. Breitman, L.-C. Tsui)

LAB/BRANCH
Laboratory of Mechanisms of Ocular Diseases

SECTION
Section on Cataract

INSTITUTE AND LOCATION
NEI, NIH, Bethesda, Maryland 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.)*

The most prevalent proteins in the human lens are the crystallins. One of the major groups of these proteins are called gamma crystallins. Because of alterations in these crystallins upon aging in the lens and the difficulty in getting purified polypeptide, the protein sequences of these crystallins are not known. The nucleotide sequences of the γ-crystallin family are known, however. As an alternate approach for assigning these genes to specific polypeptides, the genes for three of the γ-crystallins were stably integrated into mouse L-cells, a fibroblast cell line. The products of these genes that were expressed in the fibroblasts could then be compared to the proteins found in the human lens. Three of the human gamma crystallins expressed in the mouse cells have been shown to have properties identical to the γ-crystallins found in the human lens.

The aging of crystallins in vivo has been difficult to study because the exact mechanism for the alterations is not known. By using the γ-crystallins expressed in vitro in a mixed-function oxidation system, the microheterogeneity and shift to more acidic crystallin components found in the aging lens has been duplicated in vitro.

In addition to the work on the γ-crystallins, studies with lens membrane have also been done. A major protein in the membrane fraction of cell lenses has been identified as calpactin I. This protein is known to associate with actin in the presence of calcium and phospholipid. This protein may play a major role in the process of differentiation of lens epithelium to lens fiber.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 EY 00238-02 LMDB

PERIOD COVERED

October 1, 1986 to September 30, 1987

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:	Luke Pallansch	Ph.D.	Staff Fellow	LMDB, NEI
	Howard Beswick	Ph.D.	Visiting Fellow	LMDB, NEI

COOPERATING UNITS *(if any)*

Ilana Keshet	Ph.D.	Visiting Fellow	LMDB, NEI

LAB/BRANCH

Laboratory of Molecular and Developmental Biology

SECTION

INSTITUTE AND LOCATION

NEI, NIH, Bethesda, Maryland 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
2.3	2.0	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 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. Using radioactively labeled DNA probes we have demonstrated that levels of c-myc mRNA are transiently elevated during the first few hours after the initiation of differentiation in vitro. The elevation of c-myc mRNA seems to be post-transcriptionally regulated, as determined by a small-scale nuclear run-on transcription assay developed in this laboratory, which allows measurements to be made on as few as 10^6 cells. Inhibitors of the lipoxygenase pathway of arachidonic acid metabolism produce a similar elevation of c-myc mRNA, which also seems to be post-transcriptionally regulated. Analysis of the arachidonic acid metabolites synthesized by differentiating lens epithelial explants has confirmed that elevated c-myc mRNA levels are correlated with the disappearance of a specific lipoxygenase pathway metabolite.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 EY 00239-01 LI

PERIOD COVERED
October 1, 1986 to September 30, 1987

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

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

PI:	Edward J. Holland	M.D.	Senior Staff Fellow	LI, NEI
Others:	Chi-Chao Chan	M.D.	Senior Staff Fellow	LI, NEI
	Richard P. Wetzig	M.D.	Senior Staff Fellow	LI, NEI
	Robert B. Nussenblatt	M.D.	Clinical Director	NEI

COOPERATING UNITS *(if any)*

LAB/BRANCH
Laboratory of Immunology

SECTION
Section on Immunoregulation

INSTITUTE AND LOCATION
NEI, NIH, Bethesda, Maryland 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.38	0.38	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.)*

A rat penetrating keratoplasty model was developed to evaluate the corneal allograft rejection reaction. Using Brown Norway rats as donor for Lewis rats and by not removing sutures, a rejection rate of approximately 90% could be seen by the third week. Inflammation of the grafts could be seen in the second week followed by vascularization. Monoclonal antibodies to T-lymphocyte subsets and major histocompatibility complex (MHC) antigenic markers in the rat are now available which allow for the delineation of the acute corneal rejection reaction.

GPO 814-918

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 EY 00240-01 LI

PERIOD COVERED
October 1, 1986 to September 30, 1987

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
	Barbara Detrick	Ph.D.	Expert	LI, NEI
	Caroline Percopo	A.B.	Biologist	LI, NEI
	Robert B. Nussenblatt	M.D.	Clinical Director	NEI

COOPERATING UNITS (if any)
See attached

LAB/BRANCH
Laboratory of Immunology

SECTION
Section on Immunology and Virology

INSTITUTE AND LOCATION
NEI, NIH, Bethesda, Maryland 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.96	0.86	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 initiated studies to evaluate the various virologic and immunopathologic processes which occur when viruses replicate in the ocular microenvironment. This is a new project which is presently composed of three areas. (1) Evaluation of virus spread in HSV-1 induced retinitis. (2) Studies on coronavirus infection in ocular and optic nerve cells. (3) Possible role of viruses in human eye diseases.

Retinitis following anterior chamber inoculation of herpes simplex virus (HSV-1) is an interesting model of viral spread and virus induced disease. During the past year we have elucidated some of the pathologic mechanisms involved in this disease. We found that footprints of the immune system (IFN-gamma and MHC class II antigen expression) can be identified in the protected retina strongly indicating that it is the immune system which protects the retina from virus destruction. Moreover, we identified the virus in the ciliary body and ciliary nerves suggesting that this may be the mode of spread of the virus to the uninjected eye. Elucidation of virus spread and activation in the retina may provide insight into these same mechanisms in human disease, such as ARN.

We have initiated studies to evaluate coronarvirus infections in the eye and optic nerve. Preliminary studies using monoclonal anti-virus receptor antibody has identified selected cells within the eye which express virus receptors. These studies will be extended to evaluate virus induced ocular damage.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 EY 00241-01 LI

PERIOD COVERED
October 1, 1986 to September 30, 1987

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

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

PI:	Chi-Chao Chan	M.D.	Senior Staff Fellow	LI, NEI
Others:	Robert B. Nussenblatt	M.D.	Clinical Director	NEI
	Alan G. Palestine	M.D.	Head, Section on Clinical Immunology	LI, NEI
	Edward J. Holland	M.D.	Senior Staff Fellow	LI, NEI

COOPERATING UNITS (if any) Zhongshan Ophthalmic Center, Guangzhon, China (Winifred Mao, M.D.); University of Iowa (Jay H. Krachmer, M.D.); Georgetown University Center for Sight (Michael Lemp, M.D. and Garth Stevens, Jr., M.D.)

LAB/BRANCH
Laboratory of Immunology

SECTION
Section on Immunoregulation

INSTITUTE AND LOCATION
NEI, NIH, Bethesda, Maryland 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
1.52	1.52	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.)

Ocular specimens from human ocular tissues with various diseases, such as uveitis, conjunctival and corneal diseases, and ocular metabolic genetic diseases 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, course and prognosis. In non-uveitis, alteration of cellular membrane surface markers and intracytoskeleton on the ocular resident cells may imply damages and abnormalities in these diseases.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 EY 00242-01 LSR

PERIOD COVERED

October 1, 1986, to September 30, 1987

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

Visual Motor Control of Saccadic Eye Movements

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:	Lance M. Optican	Ph.D.	Res. Biomed. Engineer	LSR, NEI
	David M. Waitzman	M.D., Ph.D.	Staff Fellow	LSR, NEI
	Terence Paul Ma	Ph.D.	Guest Researcher	LSR, NEI

COOPERATING UNITS *(if any)*

LAB/BRANCH

Laboratory of Sensorimotor Research

SECTION

Visuomotor Integration Section

INSTITUTE AND LOCATION

NEI, NIH, Bethesda, Maryland 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
2.1	1.3	0.8

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.)*

We recorded single cell activity in the superior colliculus of monkeys trained to make rapid or saccadic eye movements. As reported previously, some cells discharged in relation to saccades made to targets in one area of the visual field, others with only saccadic eye movement made to a given part of the visual field. In addition, other cells have been identified that discharge only before saccades made to the location of a remembered target. Detailed information on the relation of cell discharge and the metrics of the saccade were collected for use in refining a neural model of the saccadic system.

GPO 914-918

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 EY 00243-01 LMOD

PERIOD COVERED
October 1, 1986 to September 30, 1987

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Ocular Cells Cultured under Normal 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, Maryland 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
1.0	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.)*

Evidence exists that the retinal pigment epithelium (RPE) is one of the affected tissues in diabetic ocular disease. Specifically, the integrity of the blood-retinal barrier at the level of the RPE may be compromised. We are utilizing cultured human retinal pigment epithelium as a potential in vitro model system to study the effects of elevated hexose on these cells. RPE incubated with medium containing 30 mM galactose accumulates sugar alcohol (polyol) and loses myo-inositol, and these effects are reversed when an aldose reductase inhibitor is present in the high galactose medium. This suggests that aldose reductase may be active in RPE and that the polyol accumulation may contribute to impairment of RPE function in diabetes. The deficit does not appear to be at the level of the sodium, potassium-ATPase.