SUMMARY STATEMENT

ROBERT FINKELSTEIN
301-496-5745
finkelsr@ninds.nih.gov

(Privileged Communication) ***Release Date:*** **11/04/2004**

Application Number: **1 R01 NS051439-01**

OYESIKU, NELSON M MD, PHD
EMORY UNIVERSITY
DEPT OF NEUROSURGERY
1365B CLIFTON ROAD
SUITE 6400
ATLANTA, GA 30322

Review Group: **ZRG1 CNBT (01)**
Center for Scientific Review Special Emphasis Panel

Meeting Date: **10/14/2004**
Council: **JAN 2005**
Requested Start: **04/01/2005**

PCC: **FINKERNG**
Dual PCC: **R1DI**
Dual IC(s): **CA**

Project Title: **Molecular Targeting and Imaging of Pituitary Adenomas**

SRG Action: **Priority Score: 141 Percentile: 1.6**
Human Subjects: **30-Human subjects involved - Certified, no SRG concerns**
Animal Subjects: **30-Animals involved - no SRG comments or concerns noted**
Gender: **1A-Both genders, scientifically acceptable**
Minority: **1A-Minorities and non-minorities, scientifically acceptable**
Children: **1A-Both Children and Adults, scientifically acceptable**
Clinical Research - not NIH-defined Phase III Trial

Project Year	Direct Costs Requested	Estimated Total Cost
1	250,000	382,500
2	250,000	382,500
3	250,000	382,500
4	250,000	382,500
TOTAL	1,000,000	1,530,000

ADMINISTRATIVE BUDGET NOTE: The budget shown is the requested budget and has not been adjusted to reflect any recommendations made by reviewers. If an award is planned, the costs will be calculated by Institute grants management staff based on the recommendations outlined below in the COMMITTEE BUDGET RECOMMENDATIONS section.

NEW INVESTIGATOR

1R01NS051439-01 OYESIKU, N

RESUME AND SUMMARY OF DISCUSSION: This application from a well trained new investigator, a clinician scientist, proposes to examine the functional significance of folate receptor over-expression in diagnosis and therapy of non-functional pituitary adenomas which cause hypopituitarism or blindness in patients. The research plan stems from the principal investigator's recent observation that folate receptor alpha (FRα) is significantly overexpressed in clinically non-functional pituitary adenomas and the applicant now proposes to confirm the utility of FRα expression as a putative molecular marker for the diagnosis, investigate the contribution of FRα in pituitary tumorigenesis, and explore the possible application of FRα over-expression to imaging and tumor therapy. The research plan is elegantly organized, adequately detailed, cohesive and highly focused. High quality and compelling preliminary results strongly support the core rationale, hypotheses and feasibility of the proposed research. The principal investigator is well-versed with the methodology and has collected impressive array of tumor samples to facilitate the project. Excellent clinical resources, competent collaborators and outstanding research environment lend additional strengths to the application. Minor weaknesses include the use of transformed murine cell line that dilutes the relevance to human pathogenicity and sparse description of the cell line in the design of the experiments. Overall, it is contended that this translational research with desirable clinical significance has a greater potential to yield novel molecular insights leading to possible imaging biomarker and functional therapy for pituitary adenomas. The application is supported with high enthusiasm.

DESCRIPTION (provided by applicant): The pituitary gland is the pivotal endocrine organ. Pituitary tumors occur in -20% of the population and comprise 10% of all brain tumors. Functional pituitary tumors result in life-threatening diseases, infertility and impotence. Clinically non-functional (NF) tumors cause hypopituitarism or blindness and there is no available medical treatment or specific imaging technique for these tumors. The PI's long-term goal is to determine the molecular factors controlling their proliferation, and to exploit these insights to develop novel therapy and imaging. The focus of this proposal is the folate receptor (FRα) in NF tumors, because a) NF tumors are the commonest pituitary tumors, b) we discovered that FRα mRNA is uniquely overexpressed in NF tumors, c) the FRα holds significant promise for medical treatment for NF tumors by enabling molecular imaging and targeting of NF tumors to identify and select tumors that may respond to folate targeted therapy, and d) the PI has a large bank of human pituitary adenomas for the studies needed to execute this proposal. Our hypotheses are that, i) FRα overexpression enhances tumor proliferation, ii) FRα receptor targeting with folate coupled cytotoxic agents can inhibit tumor proliferation, iii) a FRα targeted imaging agent can identify FRα - expressing pituitary tumors by radionuclide imaging in vivo. The non-invasive diagnosis of tumor receptor expression to allow selection of NF tumors that may be treatable by targeted therapy opens up novel opportunities. Similar discoveries and applications of receptor biology led to new drugs for the treatment of prolactin-secreting tumors (bromocriptine, carbegoline) and growth-hormone secreting tumors (somatostatin, pegvisomant) with less need for surgery.

In Aim 1, we will test hypothesis (i) by cell culture of a pituitary tumor cell line, αT3-1, which is a model of human NF tumors. An expression vector containing the FRα cDNA or a dominant negative mutant FRα cDNA will be transfected into αT3-1 cells. Cell proliferation will be measured by cell counts, BrdUrd-PI, and proliferating cell antigen flow cytometry. The transforming property of FRα will be evaluated in soft agar. Tumorigenicity will be assayed by inoculating FRα transfected cells into nude mice and measuring tumor growth. In Aim 2, we will test hypothesis (ii) by culturing human pituitary tumor cells with folate-PEG-liposomes carrying the antineoplastic drug doxorubicin. We will determine the cytotoxicity efficacy of doxorubicin on human tumor cells in vitro by the MTT cytotoxicity assay. In Aim 3, we will test hypothesis (iii) by using a FRα targeted technetium-99 labeled radionuclide imaging molecule to identify FRα - expressing pituitary tumors in human subjects (in vivo). These experiments capitalize on our findings of selective overexpression of functional FRa in NF adenomas, thereby translating basic research into clinical application.

CRITIQUE 1:

SIGNIFICANCE: Pituitary tumors make up 10% of brain tumors and occur in 20% of the population (really?). Non-functional pituitary adenomas (those adenomas that do not cause clinical hormone hyper secretion) are the most common pituitary tumors. While most of these tumors are benign, 35% are invasive and are treated with surgery and radiation. Approximately 20% of treated patients have serious side effects, suggesting the need for better therapy. The present proposal intends to develop an improved folate receptor-based therapy for non-functional pituitary adenomas, and as such is of significance.

APPROACH: This proposal intends to use the discovery of folate receptor over-expression on non-functional pituitary adenomas (NFPA) as the basis for determining the significance of the over-expression and its potential use in diagnosis and therapy. As background the PI presents a very nice (although slightly cluttered) series of figures clearly showing that 1) folate receptor is over-expressed and functional in NFPA but not other pituitary tumors or normal tissue, 2) that a functional folate receptor can be expressed in cultured pituitary tumor cells, 3) that NFPA selectively take up folate and folate-linked liposomes, 4) that doxorubicin-loaded folate-linked liposomes are selectively toxic to FR+ cells, and 5) that FR+ NFAP can be very nicely imaged using a folate-based radioimaging agent. The preliminary data presented are a real strength of this proposal, as are the clarity of presentation, the attention to data analysis, and clear dedication of the PI to the problem at hand. The preliminary data sets the stage for the studies proposed, which are logical and necessary extensions. In these studies the applicant will determine if folate receptor expression enhances the growth of cells derived from NFPA, if folate receptor expression is key for cellular transformation, if folate targeted cytotoxic molecules can block growth of pituitary cells in vitro, and if folate-targeted imaging agents can detect NFPA. These studies are all very nicely described and the applicant has spent considerable time designing the studies and considering what the results will tell him, which is commendable. The clinical trial of the folate-based radioimaging agents proposed in aim 3 is also very nice and it is fortuitous that such an agent already exists for the applicant's purpose. There is, however, one main concern with this application and this focuses on the use of the T3-1 cell line as a model cell line for use in aims 1 and 2. The description of this cell line is very sketchy and the reader is forced to piece together the fact that this cell line is derived from pituitary tumors in SV40 infection mice, that these cells do not over-express folate receptor, and that they do not grow well in low folate media. The fact that these cells are murine and FR negative is an immediate concern as the human tumors of interest are importantly FR+. It's not clear why the applicant didn't use cultured human FR+ NFPA material and assess the consequences of FR on growth by employing siRNA or antisense techniques to block FR. Similarly the use of what appears to be a transformed cell to assess the contribution of FR to transformation seems very puzzling. If the T3-1 cells already grow in soft agar, will FR over-expression in a soft agar assay measure degree of transformation or merely effects on growth? Aim 2 is a slight improvement in that the studies address primarily folate-mediated targeting. In this aim, however, the exact cells to be used are somewhat unclear, as is how the PI will assess killing of the targeted cells in a mixed FR+/FR- cell culture. Aim 3 is the strength of the proposal and is a very solid, very interesting, and very clinically relevant study which should be done

INNOVATION: The PI notes that in other pituitary tumors, an understanding of receptor biology has opened up new opportunities for diagnosis and therapy. The application of the same concept to NF pituitary adenomas is therefore not new, but is based on the applicant's observation of folate receptor over-expression in these tumors, and is innovative. The application of existing folate-based therapeutics to the problem is also novel and very interesting. As such this proposal is very innovative.

INVESTIGATOR: The PI is an Associate Professor in the Dept. of Neurological Surgery at Emory University and a new investigator. He has a modest number of publications, the majority of which directly relate to the clinical management of pituitary adenomas or the biology of these tumors. As noted, one of these publications was the first to note over-expression of folate receptor in pituitary adenomas. The applicant also sees approximately 80 pituitary adenoma cases per year and as such

has direct access to material. The applicant has also enlisted the help of a variety of consultants and collaborators who will help in pathologic evaluation of samples, handling of cells, and drug creation and delivery. In all this is a very strong, very competent team.

ENVIRONMENT: The research environment at Emory University is well suited for the work proposed. The applicant has access to patients and samples, has good collaborators, and has adequate lab facilities to carry out all studies.

OVERALL EVALUATION: This is an interesting and innovative application that is built on the PIs previous observations and has direct clinical application. The strengths of the application are its preliminary data, the attention to detail, and the careful consideration of the studies proposed and their potential results. The proposal is slightly weakened by the limited number of patients the work might ultimately help, and more importantly by the choice of cell lines in aim 1 and 2. The work is nonetheless interesting and generates enthusiasm.

CRITIQUE 2:

This is an application from a new investigator who has developed much of the preliminary data with a K Award. This is a highly focused study on nonfunctional pituitary tumors. The application is focused on the folate receptor which is uniquely overexpressed in these tumors. The first aim is to determine the biological affect of folate receptor overexpression on pituitary tumors. These will be carried out predominantly with the murine pituitary tumor cell line αT3-1. Appropriate experiments with transfection of dominant negative mutants will be carried out as well as determining transformation ability of the folate receptor by its ability to transform αT3-1 cells both with appropriate *in vitro* and *in vivo* studies. The next hypothesis will pursue the effects of inhibiting folate receptor with doxorubicin. They will be delivered with folate-targeted lysosomes loaded with doxorubicin. The success of these experiments would lead to rapid translational ability of these findings. Doxorubicin may have broader effects than simple suppression of the folate receptor, although an understanding of the total mechanism would not be necessary for success of these experiments. The third aim will be an actual clinical set of experiments using Technetium-labeled folate receptor ligand. This would be a highly promising approach to identify folate receptor-expressing tumors that might respond to subsequent chemotherapy. The only minor criticism I have of this grant is that these last experiments are not controlled with regard to nonspecific uptake of tumor by an imaging agent. It would greatly enhance these latter experiments if a nonspecific control such as Technetium-labeled human serum albumin or another peptide that would not bind to the folate receptor could be used and compared in the quantitative SPECT analysis.

This is a highly dedicated investigator who has excellent collaboration with appropriate nuclear medicine physicians and physicists. Moreover, there are consultants within in-depth experience in folate biochemistry and a highly qualified neuropathologist who will be collaborating.

CRITIQUE 3:

SIGNIFICANCE: Pituitary tumors constitute ≈10% of all brain tumors and occur in ≈ 20% of the population. Clinically, non-functional pituitary tumors are not amenable to medical treatment and have not been amenable to specific imaging techniques. The P.I. proposes to exploit the fact that the majority of non-functional pituitary tumors (but not a majority of functional pituitary tumors) express a membrane folate receptor and wishes to develop a folate-receptor imaging biomarker and folate targeted therapy. The significance of the proposal is the potential that new molecular insights will be developed for this type of pituitary tumor and that a potential imaging biomarker and functional therapy will be developed.

APPROACH: The approach has been well thought out by the P.I. and the preliminary results demonstrate that not only can the P.I. accomplish the methods proposed, but that meaningful and significant results will probably be forthcoming.

INNOVATION: While none of the techniques are innovative by themselves, what is innovative is the translational application of these techniques to an important brain tumor molecular biology problem.

INVESTIGATOR: Dr. Nelson Oyesiku, earned his MB, BS in medicine from the University of Ibadan, Nigeria. He completed his M.Sc. in Occupational Medicine from the University of London and his Ph.D. in Neuroscience from Emory University. Currently Dr. Oyesiku serves as Associate Professor, Neurosurgery and Director, Laboratory of Molecular & Biotechnology at Emory university

ENVIRONMENT: Excellent.

OVERALL EVALUATION: Approve with excellent outstanding enthusiasm.

THE FOLLOWING RESUME SECTIONS WERE PREPARED BY THE SCIENTIFIC REVIEW ADMINISTRATOR TO SUMMARIZE THE OUTCOME OF DISCUSSIONS OF THE REVIEW COMMITTEE ON THE FOLLOWING ISSUES:

PROTECTION OF HUMAN SUBJECTS: Acceptable.

INCLUSION OF WOMEN PLAN: Acceptable.

INCLUSION OF MINORITIES PLAN: Acceptable.

INCLUSION OF CHILDREN PLAN: Acceptable.

VERTEBRATE ANIMAL AND WELFARE: Acceptable.

BIOHAZARD: No concerns.

COMMITTEE BUDGET RECOMMENDATIONS: The budget was recommended as requested.

BUDGETARY OVERLAP: None.

NOTICE: The NIH has modified its policy regarding the receipt of amended applications. Detailed information can be found by accessing the following URL address: http://grants.nih.gov/grants/policy/amendedapps.htm

NIH announced implementation of Modular Research Grants in the December 18, 1998 issue of the NIH Guide to Grants and Contracts. The main feature of this concept is that grant applications (R01, R03, R21, R15) will request direct costs in $25,000 modules, without budget detail for individual categories. Further information can be obtained from the Modular Grants Web site at http://grants.nih.gov/grants/funding/modular/modular.htm

MEETING ROSTER

Center for Scientific Review Special Emphasis Panel
CENTER FOR SCIENTIFIC REVIEW
ZRG1 CNBT (01) Q
October 14, 2004 - October 15, 2004

CHAIRPERSON

BENVENISTE, ETTY (TIKA) N, PHD
PROFESSOR AND CHAIR
DEPARTMENT OF CELL BIOLOGY
THE UNIVERSITY OF ALABAMA AT BIRMINGHAM
BIRMINGHAM, AL 352940005

MEMBERS

BAKSHI, ROHIT , MD
ASSOCIATE PROFESSOR
DEPARTMENT OF NEUROLOGY
BRIGHAM AND WOMEN'S HOSPITAL
HARVARD MEDICAL SCHOOL
BOSTON, MA 02115

BANIK, NAREN L, PHD
PROFESSOR
DEPARTMENT OF NEUROLOGY
MEDICAL UNIVERSITY OF SOUTH CAROLINA
CHARLESTON, SC 29425

BARGER, STEVEN W, PHD
ASSOCIATE PROFESSOR OF GERIATRICS,
NEUROBIOLOGY, AND INTERNAL MEDICINE
CENTRAL ARKANSAS VETERANS HEALTHCARE SYSTEM
DEPARTMENT OF VETERANS AFFAIRS
UNIVERSITY OF ARKANSAS FOR MEDICAL SCIENCES
LITTLE ROCK, AR 72205

BIGNER, DARELL D, MD, PHD
JONES CANCER RESEARCH PROFESSOR
DEPARTMENT OF PATHOLOGY
SCHOOL OF MEDICINE
DUKE UNIVERSITY
DURHAM, NC 27710

BIZZOZERO, OSCAR A, PHD
PROFESSOR
DEPARTMENT OF CELL BIOLOGY
AND PHYSIOLOGY
UNIVERSITY OF NEW MEXICO
HEALTH SCIENCES CENTER
ALBUQUERQUE, NM 87131

BOST, KENNETH L., PHD
BELK DISTINGUISHED PROFESSOR
DEPARTMENT OF BIOLOGY
UNIVERSITY OF NORTH CAROLINA
CHARLOTTE, NC 282230001

BURNS, JAMES B, MD
PROFESSOR
DEPARTMENT OF NEUROLOGY
UNIVERSITY OF UTAH
SCHOOL OF MEDICINE
SALT LAKE CITY, UT 84132

CORY-SLECHTA, DEBORAH A., PHD
DIRECTOR
ENVIRONMENTAL AND OCCUPATIONAL
HEALTH SCIENCES INSTITUTE
ROBERT WOOD JOHNSON MEDICAL SCHOOL
RUTGERS UNIVERSITY
PISCATAWAY, NJ 08854

DAVIES, PETER , PHD
RESNICK PROFESSOR
DEPARTMENT OF PATHOLOGY
ALBERT EINSTEIN COLLEGE OF MEDICINE
BRONX, NY 10461

DEVRIES, GEORGE H, PHD
CAREER RESEARCH HEALTH SCIENTIST
EDWARD HINES, JR. VA HOSPITAL
PROFESSOR OF CELL BIOLOGY AND ANATOMY
UNIVERSITY OF ILLINOIS AT CHICAGO
CHICAGO, IL 60612

DUNN, ADRIAN J, PHD
BOYD PROFESSOR AND DEPARTMENT HEAD
DEPARTMENT OF PHARMACOLOGY
LOUISIANA STATE UNIVERSITY MEDICAL CENTER
SHREVEPORT, LA 71130

EISENBERG, DAVID S, PHD
PROFESSOR
DEPARTMENT OF CHEMISTRY
COLLEGE OF LETTERS AND SCIENCES
UNIVERSITY OF CALIFORNIA
LOS ANGELES, CA 90024

FIGLEWICZ, DENISE A., PHD
ASSOCIATE PROFESSOR
DEPARTMENT OF NEUROLOGY
UNIVERSIY OFMICHIGAN
KRESGE BUILDING
ANN ARBOR, MI 48109

FRASER, NIGEL W., PHD
PROFESSOR
DEPT. OF MICROBIOLOGY
MEDICAL SCHOOL, UNIVERSITY OF PENNSYLVANIA
PHILADELPHIA, PA 19104

FULTS, DANIEL W, MD
PROFESSOR
DEPARTMENT OF NEUROSURGERY
UNIVERSITY OF UTAH
SCHOOL OF MEDICINE
SALT LAKE CITY, UT 841322303

GANEA, DOINA , PHD
PROFESSOR
RUTGERS UNIVERSITY
DEPT OF BIOLOGICAL SCIENCES
NEWARK, NJ 07102

GASSER, DAVID L., PHD
PROFESSOR
DEPARTMENT OF GENETICS
UNIVERSITY OF PENNSYLVANIA SCHOOL OF MEDICINE
PHILADELPHIA, PA 191046145

GELLER, ALFRED I, PHD
ASSISTANT PROFESSOR OF NEUROLOGY
HARVARD MEDICAL SCHOOL
WEST ROXBURY VA HOSPTIAL
WEST ROXBURY, MA 02132

GENAIN, CLAUDE P, MD
ASSOCIATE PROFESSOR
DEPARTMENT OF NEUROLOGY
UNIVERSITY OF CALIFORNIA, SAN FRANCISCO
SAN FRANCISCO, CA 94143

GILMORE, WENDY , PHD
ASSOCIATE PROFESSOR
DEPARTMENT OF NEUROLOGY
USC SCHOOL OF MEDICINE
LOS ANGELES, CA 90033

GOTTSCHALL, PAUL E, PHD
PROFESSOR
DEPARTMENT OF PHARMACOLOGY
& THERAPEUTICS
UNIVERSITY OF SOUTH FLORIDA
TAMPA, FL 336124799

GUTMANN, DAVID H., MD, PHD
DONALD O. SCHNUCK FAMILY PROFESSOR OF
NEUROLOGY
DEPARTMENT OF NEUROLOGY
WASHINGTON UNIVERSITY SCHOOL OF MEDICINE
ST. LOUIS, MO 63110

ILYAS, AMJAD A, PHD
ASSOCIATE PROFESSOR
DEPARTMENT OF NEUROSCIENCE
UMDNJ-NEW JERSEY
MEDICAL SCHOOL
NEWARK, NJ 07103

JAMES, CHARLES D, PHD
PROFESSOR
DEPARTMENT OF LABORATORY MEDICINE AND
PATHOLOGY
MAYO CLINIC AND FOUNDATION
ROCHESTER, MN 55905

JANIGRO, DAMIR , PHD
PROFESSOR OF MOLECULAR MEDICINE
DIRECTOR OF CEREBROVASCULAR RESEARCH
CLEVELAND CLINIC FOUNDATION
CLEVELAND, OH 44195

KIELIAN, TAMMY L, PHD
ASSISTANT PROFESSOR
DEPARTMENT NEUROBIOLOGY & DEVELOPMENTAL
SCIENCES
UNIVERSITY OF ARKANSAS FOR MEDICAL SCIENCES
LITTLE ROCK, AR 72205

KUMAR, ANAND , MD
PROFESSOR IN RESIDENCE
UNIVERSITY OF CALIFORNIA, LOS ANGELES
NEUROPSYCHIATRIC INSTITUTE AND HOSPITAL
LOS ANGELES, CA 900951759

LATERRA, JOHN J, MD, PHD
PROFESSOR
DEPARTMENT OF NEUROLOGY
JOHNS HOPKINS UNIVERSITY
KENNEDY KRIEGER RESEARCH INSTITUTE
BALTIMORE, MD 21205

LIAU, LINDA M, MD, PHD
ASSOCIATE PROFESSOR OF NEUROSURGERY
DIRECTOR, MALIGNANT BRAIN TUMOR PROGRAM
DAVID GEFFEN SCHOOL OF MEDICINE AT UCLA
UNIVERSITY OF CALIFORNIA, LOS ANGELES
LOS ANGELES, CA 900956901

LIPTON, HOWARD L, MD
PROFESSOR
DEPARTMENTS OF NEUROLOGY, MICROBIOLOGY-
IMMUNOLOGY, AND BIOCHEMISTRY, MOLECULAR
AND CELLULAR BIOLOGY
NORTHWESTERN UNIVERSITY
EVANSTON, IL 60201

MEHTA, PANKAJ D., PHD
HEAD
DEPARTMENT OF CLINICAL IMMUNOLOGY
INSTITUTE FOR BASIC RESEARCH IN
DEVELOPMENTAL DISABILITIES
STATEN ISLAND, NY 103146399

NEVE, RACHAEL L., PHD
ASSOCIATE PROFESSOR
DEPARTMENT OF PSYCHIATRY
HARVARD MEDICAL SCHOOL
BELMONT, MA 02478

O'BANION, M. KERRY, MD, PHD
ASSOCIATE PROFESSOR
DEPARTMENTS OF NEUROBIOLOGY AND ANATOMY
AND NEUROLOGY
SCHOOL OF MEDICINE
UNIVERISTY OF ROCHESTER
ROCHESTER, NY 14642

O'HARA, RUTH M., PHD
ASSISTANT PROFESSOR
DEPARTMENT OF PSYCHIATRY AND BEHAVIORAL
SCIENCES
STANFORD UNIVERSITY SCHOOL OF MEDICINE
STANFORD UNIVERSITY
STANFORD, CA 94305

PASCUAL, DAVID W, PHD
ASSOCIATE PROFESSOR OF IMMUNOLOGY
VETERINARY MOLECULAR BIOLOGY
MONTANA STATE UNIVERSITY
BOZEMAN, MT 597173610

PETTEGREW, JAY W., MD
DIRECTOR, NEUROPHYSICS LABORATORY
PROFESSOR, DEPARTMENT OF PSYCHIATRY,
NEUROLOGY AND HEALTH SCIENCES ADMINISTRATION
UNIVERSITY OF PITTSBURGH MEDICAL CENTER/WPIC
PITTSBURGH, PA 15213

PHILIPP, MARIO T, PHD
CHAIR, DIVISION OF BACTERIOLOGY & PARASITOLOGY
PROFESSOR OF MICROBIOLOGY AND IMMUNOLOGY
TULANE NATIONAL PRIMATE RESEARCH CENTER
TULANE UNIVERSITY HEALTH SCIENCES CENTER
COVINGTON, LA 70433

PIEPER, RUSSELL O, PHD
PROFESSOR AND DIRECTOR OF BASIC SCIENCE
DEPARTMENT OF NEUROLOGICAL SURGERY
UCSF COMPREHENSIVE CANCER CENTER
UNIVERSITY OF CALIFORNIA-SAN FRANCISCO
SAN FRANCISCO, CA 941150875

PLAUTZ, GREGORY E., MD
STAFF
CENTER FOR SURGERY RESEARCH
DEPARTMENT OF SURGERY
CLEVELAND CLINIC FOUNDATION
CLEVELAND, OH 44195

RAO, JASTI S, PHD
PROFESSOR AND HEAD
DEPARTMENT OF OF BIOMEDICAL & THERAPEUTIC SCIENCES
UNIVERSITY OF ILLINOIS COLLEGE OF MEDICINE
PEORIA, IL 61605

RASBAND, MATTHEW N, PHD
ASSISTANT PROFESSOR OF NEUROSCIENCE
DEPARTMENT OF NEUROSCIENCE
UNIVERSITY OF CONNECTICUT HEALTH CENTER
FARMINGTON, CT 06030

ROSTAMI, ABDOLMOHAMAD , MD, PHD
PROFESSOR AND CHAIR
DEPARTMENT OF NEUROLOGY
THOMAS JEFFERSON UNIVERSITY
PHILADELPHIA, PA 19107

SUPATTAPONE, SURACHAI , MD, PHD
ASSISTANT PROFESSOR OF BIOCHEMISTRY AND MEDICINE
DARTMOUTH MEDICAL SCHOOL
HANOVER, NH 03755

SWANBORG, ROBERT H, PHD
PROFESSOR
DEPARTMENT OF IMMUNOLOGY
AND MICROBIOLOGY
SCHOOL OF MEDICINE
WAYNE STATE UNIVERSITY
DETROIT, MI 48201

TYLER, KENNETH L, MD
REULER-LEWIN FAMILY PROFESSOR OF NEUROLOGY
PROFESSOR OF MEDICINE, MICROBIOLOGY & IMMUNOLOGY
UNIVERSITY OF COLORADO HEALTH SCIENCES CENTER
DENVER, CO 80262

VOSKUHL, RHONDA R, MD
PROFESSOR
DEPARTMENT OF NEUROLOGY
UCLA SCHOOL OF MEDICINE
DIRECTOR, UCLA MULTIPLE SCLEROSIS PROGRAM
LOS ANGELES, CA 90095

WISNIEWSKI, THOMAS M, MD
ASSOCIATE PROFESSOR
DEPARTMENTS OF NEUROLOGY, PSYCHIATRY AND PATHOLOGY
NEW YORK UNIVERSITY MEDICAL CENTER
NEW YORK, NY 10016

YAMAMOTO, BRYAN K., PHD
PROFESSOR
DEPT. OF PHARMACOLOGY & EXP. THERAPEUTICS
BOSTON UNIVERSITY SCHOOL OF MEDICINE
BOSTON, MA 02118

YOUNG, M. RITA I, PHD
ASSOCIATE CHIEF OF STAFF FOR RESEARCH
RALPH H. JOHNSON VA MEDICAL CENTER
PROFESSOR OF MEDICINE
MEDICAL UNIVERSITY OF SOUTH CAROLINA
CHARLESTON, SC 29403

MAIL REVIEWER(S)

ROBAKIS, NIKOLAOS K, PHD
PROFESSOR OF NEUROBIOLOGY
A.P. SLANER PROFESSOR OF ALZHEIMER DISEASE
MOUNT SINAI SCHOOL OF MEDICINE, NYU
NEW YORK, NY 10029

SCIENTIFIC REVIEW ADMINISTRATOR

JOSHI, JAY , PHD
SCIENTIFIC REVIEW ADMINISTRATOR
CENTER FOR SCIENTIFIC REVIEW
NATIONAL INSTITUTES OF HEALTH
BETHESDA, MD 20892

GRANTS TECHNICAL ASSISTANT

CHACON, PEDRO
GRANTS TECHNICAL ASSISTANT
CENTER FOR SCIENTIFIC REVIEW
NATIONAL INSTITUTES OF HEALTH
BETHESDA, MD 20892

WILLIAMS, LYNNE
GRANTS TECHNICAL ASSISTANT
CENTER FOR SCIENTIFIC REVIEW
NATIONAL INSTITUTES OF HEALTH
BETHESDA, MD 20892

Consultants are required to absent themselves from the room during the review of any application if their presence would constitute or appear to constitute a conflict of interest.