Department of Defense
US Army Medical Research and Materiel Command

Fiscal Year 2003
Neurofibromatosis and Tuberous Sclerosis Research Programs
Awards Lists

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Introduction

The US Army Medical Research and Materiel Command is pleased to present the award list of funded projects for the fiscal year 2003 (FY03) Neurofibromatosis Research Program. Award negotiations were completed by September 30, 2004. The awards listed in this document were selected by a competitive two-tiered review process. Funding decisions were based upon scientific excellence evaluated in the first tier of review, followed by programmatic relevance judged in the second tier. These projects represent a diverse portfolio of scientific research directed toward the program's overall goal of promoting studies toward the understanding, diagnosis, and treatment of neurofibromatosis (NF), as well as the enhancement of the quality of life for persons with the disease.

Congressional direction for FY03 specified $20 million for NF research. Following the receipt of funds, a programmatic strategy was developed, proposals were solicited and evaluated, award recommendations were made, and contract negotiations were completed. The FY03 programmatic strategy called for Clinical Trial Development, New Investigator, Idea, Investigator-Initiated Research (with or without Nested Postdoctoral Traineeships), Therapeutic Development, and Clinical Trial Awards. The Clinical Trial Development Award was offered for the first time in FY03, and is designed to provide support to establish the necessary collaborations and develop the necessary infrastructure for the foundation of a multi-institutional NF-related clinical trial. The intent of the New Investigator Award is to help investigators at early stages of their careers become established in NF research. The Idea Award is intended to encourage innovative approaches to NF research. New Investigator Awards and Idea Awards do not require preliminary or pilot data. The intent of the Investigator-Initiated Research Award is to sponsor research that will elucidate the molecular mechanisms underlying the development of NF and related diseases and improve current approaches to the diagnosis and/or treatment of those diseases. Nested Postdoctoral Traineeships, offered as an optional component of the Investigator-Initiated Research Award, are intended to enable doctoral degree graduates to either extend ongoing research related to NF or broaden the scope of their research to include work relevant to NF. The intent of the Therapeutic Development Award is to develop and evaluate preclinical model systems for NF1, NF2 and/or Schwannomatosis. The Clinical Trial Award is intended to sponsor clinical studies that determine the toxicity (Phase 1) or investigate the efficacy (Phase 2) of any novel therapeutic approach for NF1, NF2 and/or Schwannomatosis. A total of 13 studies was funded in FY03.

As the funded scientists embark on these projects, the Department of Defense and the US Army gratefully acknowledge the participation of their scientific advisors, people living with NF, and the NF advocacy community. The expertise, vision, and diversity of perspectives of all individuals who contributed to this program were vital to developing a sound investment strategy on behalf of all persons living with NF. It is with great anticipation and excitement that we await the outcomes of this research.

Clinical Trial Development Award

Log Number	Last Name	First Name	Institution	Proposal Title	Award Amount
NF030032	Gusella	James	Massachusetts General Hospital	A Prospective, Randomized Clinical Trial of Celecoxib for the Control of Symptomatic Plexiform Neurofibroma in Neurofibromatosis 1	$150,000
NF030073	Viskochil	David	University of Utah	Malignant Peripheral Nerve Sheath Tumors in Neurofibromatosis Type 1: A Multicenter Project with 3 Clinical Trials	$146,014

Therapeutic Development Awards

Log Number	Last Name	First Name	Institution	Proposal Title	Award Amount
NF030039	Martuza	Robert	Massachusetts General Hospital	HSV Vector Therapy for NF2 Lesions in Mouse Models	$2,647,746
NF030009	Kloog	Yoel	Tel Aviv University	Drug Treatments Targeting Active Ras: A Novel Class of Ras Inhibitors as a Potential Therapeutic Approach for Neurofibromatosis Type 1	$599,773

Idea Award

Log Number	Last Name	First Name	Institution	Title	Award Amount
NF030078	Heitman	Joseph	Duke University	Novel Gbeta Mimic Kelch Proteins Gpb1 and Gpb2 Connect G-Protein Signaling to Ras via Yeast Neurofibromin Homologs Ira1 and Ira2: A Model for Human NF1	$693,000

Investigator-Initiated Research Awards

Log Number	Last Name	First Name	Institution	Title	Award Amount
NF030006	Stern	Michael	Rice University	Control of Growth within Drosophila Peripheral Nerves by Ras and Protein Kinase A	$1,210,566
NF030008	Dumanski	Jan	Uppsala University	Identification of the NF2 Phenotype Modifying Gene(s) and Detailed Functional Characterization of the NF2 Locus	$1,717,800
NF030010	Ratner	Nancy	University of Cincinnati	Therapeutic Targets for Neurofibromas: Identification by Cross-Species Gene Expression Analysis	$3,867,779
NF030012	Kadesch	Tom	University of Pennsylvania School of Medicine	Notch Signaling and Schwann Cell Transformation: Development of a Model System and Application to Human MPNSTs	$976,981
NF030056	Bernards	Andre	Massachusetts General Hospital	Functional Analysis of Drosophila NF1	$1,419,553
NF030020	Gutmann	David	Washington University	Functional Analysis of Protein 4.1 Tumor Suppressors	$1,183,129

New Investigator Awards

Log Number	Last Name	First Name	Institution	Title	Award Amount
NF030058	Hannan	Frances	New York Medical College	Functional Analysis of Human NF1 by Expression in Drosophila Melanogaster	$681,435
NF030063	Tang	Shao-Jun	University of California, Irvine	A Functional Genomic Analysis of NF1-Associated Learning Disabilities	$675,623
NF030086	Wu	Gang-Yi	Baylor College of Medicine	The Role of the Neurofibromin-Syndecan-CASK Complex in the Regulation of Synaptic Ras-MAPK Signaling and Dendritic Spine Plasticity	$677,250

Fiscal Year 2003 Neurofibromatosis Research Program
Peer Reviewers

Peer Reviewers	Degree	Institution/Affiliation
Barald, Katharine	Ph.D.	University of Michigan Medical School
Bidichandani, Sanjay	M.D., Ph.D.	University of Oklahoma Health Sciences Center
Buono, Susan		Illinois Chapter National Neurofibromatosis Foundation, Inc.
Clapp, David	M.D.	Cancer Research Institute, Indiana University, School of Medicine
Fernandez-Valle, Cristina	Ph.D.	University of Central Florida
Gobel, Stephen	D.D.S.	Scientific Review Administrator
Greenwood, Robert	M.D.	University of North Carolina School of Medicine
Haber, Roberta	Ph.D.	Scientific Review Administrator
Kwiatkowski, David	M.D., Ph.D.	Brigham and Women's Hospital
Largaespada, David	Ph.D.	University of Minnesota Twin Cities
MacCollin, Mia	M.D.	Massachusetts General Hospital
Mahacek, Rhonda		Neurofibromatosis, Inc.
Mattingly, Raymond	Ph.D.	Wayne State University
Moore, Bartlett	Ph.D.	University of Texas M.D. Anderson Cancer Center
Parker, Sandra		Texas Neurofibromatosis Foundation
Rao, Mahendra	Ph.D.	StemCell, LNS, GRC, NIH, National Institute of Aging
Ratner, Nancy	Ph.D.	College of Medicine, University of Cincinnati
Reilly, Karlyne	Ph.D.	MCGP, National Cancer Institute-Frederick
Rodenhiser, David	Ph.D.	University of Western Ontario
Rojiani, Amyn	M.D., Ph.D.	University of South Florida-H Lee Moffitt Cancer Center and Research Institute
Sampson, John	M.D., Ph.D.	Duke University Medical Center
Schoppet, Roxie		Neurofibromatosis, Inc.
Scoles, Daniel	Ph.D.	University of California, Los Angeles, School of Medicine
Shannon, Kevin	M.D.	University of California, San Francisco

Peer Reviewers	Degree	Institution/Affiliation
Sherman, Lawrence	Ph.D.	Oregon Health Sciences University
Stephens, Karen	Ph.D.	University of Washington
Viskochil, David	M.D., Ph.D.	University of Utah
Vogel, Kristine	Ph.D.	University of Texas Health Science Center at San Antonio
Walker, Cheryl	Ph.D.	University of Texas M.D. Anderson Cancer Center
Wallace, Margaret	Ph.D.	University of Florida
Welling, D. Bradley	M.D., Ph.D.	The Ohio State University
Yu, John	M.D.	Cedars-Sinai Medical Center
Zhong, Yi	Ph.D.	Cold Spring Harbor Laboratory

Fiscal Year 2003 Neurofibromatosis Research Program
Integration Panel (IP) Members

IP Members	Degree	Institution/Affiliation
Adamson, Peter	M.D.	University of Pennsylvania School of Medicine
Bellermann, Peter (Chair Emeritus)	M.P.A.	The National Neurofibromatosis Foundation, Inc.
Duffy, Brenda	M.A.	Neurofibromatosis, Inc.
Finkelstein, Robert	Ph.D.	National Institute of Neurological Disorders and Stroke
Fisher, Nancy	R.N., M.D., M.P.H.	University of Washington, Seattle
Gibbs, Jackson	Ph.D.	Merck Research Laboratories
Johnson, William	M.D.	University of Medicine and Dentistry of New Jersey Robert Wood Johnson Medical School
Korf, Bruce	M.D., Ph.D.	University of Alabama, Birmingham
Legius, Eric	M.D., Ph.D.	Catholic University Leuven
Small, Judy (Chair)	Ph.D.	The National Neurofibromatosis Foundation, Inc.

Fiscal Year 2003 Neurofibromatosis Research Program
Ad Hoc Programmatic Reviewers

Ad Hoc Reviewers	Degree	Institution/Affiliation
Cichowski, Karen	Ph.D.	Harvard Medical School
Perry, Arie	M.D.	Washington University School of Medicine
Young Poussaint, Tina	M.D.	Harvard Medical School

Glossary of Terms

Clinical Trial Award: The intent of this award mechanism is to sponsor clinical studies that determine the toxicity (Phase 1) or investigate the efficacy (Phase 2) of any novel therapeutic approach for neurofibromatosis (NF) 1, NF2, or Schwannomatosis. Applicants must include preliminary data to support the feasibility of their hypotheses and approaches, along with a detailed plan to conduct a Phase 1 or 2 clinical trial during the course of the award. Ultimately, the goal of this award mechanism is to sponsor novel research that will substantially improve today's approach to the treatment of NF1, NF2, and/or Schwannomatosis.

Clinical Trial Development Award (CTDA): The intent of this award is to provide support to establish the necessary collaborations and develop the necessary infrastructure, including a coordination core, for the foundation of a multi-institutional NF-related clinical trial. The goal of the CTDA is the development of clinical trials with the potential to have a major impact on the treatment of NF1, NF2, and/or Schwannomatosis. Applicants from all academic levels are eligible to submit proposals. Products of the CTDA mechanism include a detailed clinical trial protocol and a Clinical Trial Award submission in the following fiscal year (pending receipt of funds by the Neurofibromatosis Research Program).

Idea Award: The intent of this award mechanism is to encourage innovative approaches to NF research. These proposals may represent a new paradigm in the study of NF, challenge existing paradigms, or look at an existing problem from a new perspective. The proposed studies may be untested, but present a high probability of revealing new avenues of investigation. Although this research is inherently risky in nature, the research plan must demonstrate solid scientific judgment and rationale. Preliminary or pilot data is not required for this award mechanism.

Investigator-Initiated Research Award: The intent of this award mechanism is to sponsor basic and clinical research that will (1) provide insight into the molecular mechanisms underlying the development of NF and related diseases, (2) result in substantial improvement(s) over today's approach to the diagnosis and treatment of NF1, NF2, and/or Schwannomatosis, and (3) enhance the quality of life for persons with those diseases. These awards are intended to fund independent investigators across a broad spectrum of disciplines. This award mechanism also supports the establishment of synergistic, goal-focused, and non-exclusionary consortia. Preliminary data relevant to NF research, as well as a clear statistical plan of analysis, are required for these awards. Nested Postdoctoral Traineeships are offered as an optional part of the Investigator-Initiated Research Award. The intent of the Nested Postdoctoral Traineeship is to enable doctoral degree graduates to either extend ongoing research related to NF or broaden the scope of their research to include work relevant to NF under the guidance of a designated mentor who is participating in the proposal.

***New Investigator Award*:** The intent of this award mechanism is to help investigators at early stages of their careers become established NF researchers. This research may represent a new paradigm, challenge existing paradigms, or look at an existing problem from a new perspective. A new investigator is defined as an independent investigator below the level of Associate Professor (or equivalent) with access to appropriate research facilities. Preliminary or pilot data is not required for this award mechanism.

Therapeutic Development Award: The intent of this award mechanism is to sponsor the development and evaluation of preclinical model systems for NF1, NF2 and/or Schwannomatosis. The overall goal of this award mechanism is to allow NF investigators to develop the skills and generate the preclinical data necessary to conduct clinical trials after completion of the research. The proposed studies are expected to be empirical in nature and product-driven rather than hypothesis-driven. It is anticipated that the agents and model systems generated from these awards will lead to the development of a broad platform on which to test future therapies. The submission of preliminary data relevant to the phase(s) of the preclinical drug development process covered by the research is required for this award mechanism. If appropriate, the proposal should include a clear statistical plan of analysis.

Introduction

The US Army Medical Research and Materiel Command is pleased to present the award list of funded projects for the fiscal year 2003 (FY03) Tuberous Sclerosis Complex Research Program (TSCRP). Award negotiations were completed by September 30, 2004. The awards listed in this document were selected by a competitive two-tiered review process. Funding decisions were based on scientific excellence evaluated in the first tier of review, followed by programmatic relevance judged in the second tier. These projects represent scientific research directed toward the program's overall goal of promoting studies toward a better understanding of the role and function of proteins produced by the tuberous sclerosis complex 1 (TSC1) and TSC2 tumor suppressor genes.

Congressional direction for FY03 specified $2 million for research into the role and function of TSC1 and TSC2. Following the receipt of funds, a programmatic strategy was developed, proposals were solicited and evaluated, award recommendations were made, and contract negotiations were completed. The FY03 programmatic strategy called for a single award mechanism, the Idea Development Award. This award encourages innovative research aimed at understanding the role and function of proteins produced by the TSC1 and TSC2 tumor suppressor genes. Of the 13 proposals received, three proposals were funded. One additional proposal was placed on an alternate list to be funded as funds become available.

As the funded scientists embark on these projects, the Department of Defense and the US Army gratefully acknowledge the participation of their scientific advisors, people living with tuberous sclerosis, and the tuberous sclerosis advocacy community. The expertise, vision, and diversity of perspectives of all individuals who contributed to this program were vital to developing a sound investment strategy on behalf of all persons living with tuberous sclerosis. It is with great anticipation and excitement that we await the outcomes of this research.

Idea Development Award

Log Number	Last Name	First Name	Institution	Title	Final Budget
TS030004	Sabatini	Bernardo	Harvard Medical School	The Role of TSC1 in the Formation and Maintenance of Excitatory Synapses	$425,000.00
TS030008	Kaelin	William	DFCI, BWH	Hypoxia-Inducible Factor Regulation by the TSC2 Tumor Suppressor Protein	$356,600.00
TS030012	Krymskaya	Vera	University of Pennsylvania	The Role of TSC Proteins in Regulating Cell Adhesion and Motilit	$150,000.00
TS030017	Stokoe	David	University of California, San Francisco	The Role of GSK3 in Regulating Hamartin Phosphorylation and Activity in Response to Nutrients and Growth Factors	$425,000.00

Fiscal Year 2003 Tuberous Sclerosis Research Program
Peer Reviewers

Peer Reviewers	Degree	Institution/Affiliation
Chugani, Diane	Ph.D.	Wayne State University, Children's Hospital of Michigan
Gobel, Stephen	D.D.S.	Scientific Review Administrator
Guan, Kun-Liang	Ph.D.	University of Michigan
Henske, Elizabeth	M.D.	Fox Chase Cancer Center
Kwiatkowski, David	M.D., Ph.D.	Brigham and Women's Hospital
Mastbaum, Celia		Tuberous Sclerosis Alliance
Sherman, Lawrence	Ph.D.	Oregon Health Sciences University
Viskochil, David	M.D., Ph.D.	University of Utah
Vogel, Kristine	Ph.D.	University of Texas Health Science Center at San Antonio
Walker, Cheryl	Ph.D.	University of Texas, M.D. Anderson Cancer Center

Fiscal Year 2003 Tuberous Sclerosis Research Program
Ad Hoc Programmatic Reviewers

Ad Hoc Reviewers	Degree	Institution/Affiliation
Adamson, Peter	M.D.	University of Pennsylvania School of Medicine
Finkelstein, Robert	Ph.D.	National Institute of Neurological Diseases and Stroke
Gibbs, Jackson	Ph.D.	Merck Research Laboratories
Holets Whittemore, Vicky (Acting Chair)	Ph.D.	Tuberous Sclerosis Alliance
Johnson, William	M.D.	Robert Wood Johnson Medical School
Korf, Bruce	M.D., Ph.D.	Harvard-Partners Center for Genetics and Genomics
Legius, Eric	M.D., Ph.D.	Catholic University of Leuven, Belgium
Northrup, Hope	M.D.	University of Texas – Houston Medical School
Small, Judy	Ph.D.	The National Neurofibromatosis Foundation, Inc.

Glossary of Terms

Idea Development Award: The intent of Idea Development Awards is to encourage innovative research aimed at understanding the role and function of proteins produced by the TSC1 and TSC2 tumor suppressor genes. To be eligible for an Idea Development Award, the applicant must be an independent investigator at the level of Assistant Professor (or equivalent) or above. All Idea Development Award proposals must include preliminary data relevant to tuberous sclerosis research and the proposed project.