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TITLE: Continuation of a Postdoctoral Research Associateship Program with USAMRMC

PRINCIPAL INVESTIGATOR: Judith K. Nyquist, Ph.D.

CONTRACTING ORGANIZATION: National Academy of Sciences
Washington, DC 20418

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Fort Detrick, Maryland 21702-5012

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Continuation of a Postdoctoral Research Associateship Program with USAMRMC

Judith K. Nyquist, Ph.D.

National Academy of Sciences
Washington, DC 20418

U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

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Postdoctoral Research, Associateship Program, USAMRMC

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FOREWORD

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In conducting research using animals, the investigator(s) adhered to the "Guide for the Care and Use of Laboratory Animals," prepared by the Committee on Care and use of Laboratory Animals of the Institute of Laboratory Resources, national Research Council (NIH Publication No. 86-23, Revised 1985).

For the protection of human subjects, the investigator(s) adhered to policies of applicable Federal Law 45 CFR 46.

In conducting research utilizing recombinant DNA technology, the investigator(s) adhered to current guidelines promulgated by the National Institutes of Health.

In the conduct of research utilizing recombinant DNA, the investigator(s) adhered to the NIH Guidelines for Research Involving Recombinant DNA Molecules.

In the conduct of research involving hazardous organisms, the investigator(s) adhered to the CDC-NIH Guide for Biosafety in Microbiological and Biomedical Laboratories.

Judith K. Nyquist, Ph.D. 15 Nov 96
PI - Signature  Date

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NATIONAL RESEARCH COUNCIL

Cooperative Research Associateship Program

with the

US ARMY MEDICAL RESEARCH AND MATERIEL COMMAND

Status Report

October 1, 1995, through September 30, 1996

PUBLICITY

The NRC Research Associateship Programs for 1996 were announced to the scientific community in the Fall of 1995. Publicity materials describing the 1995 Programs were distributed in November to presidents, graduate deans, and heads of appropriate science and engineering departments of all academic degree-granting institutions in the United States. These materials were also sent to Program Representatives and Associateship Advisers at the participating laboratories and to other interested persons.

REQUESTS

Application materials were distributed in response to specific requests for information about the 1996 NRC-AMRMC Associateship Program or as a result of general requests by persons whose fields of specialization appeared to be appropriate for the research opportunities available in the AMRMC laboratories.

COMPETITION

Panel reviews of applicants for the Associateship Programs, including that with the US Army Medical Research and Materiel Command, are conducted in February, June and October of each year.

Enclosed as Attachment 1 and Attachment 2 is information on the awardees. Attachment 3 and Attachment 4 contain information on the status of the recommended candidates for reviews held during the period of this report.
OCTOBER 1995 REVIEW

Thirteen applications were received for this review. Prior to the review two applications were incomplete due to missing supporting documents, one application was ineligible, and four applications were not approved by the laboratory. Six applications were presented to the board for review and six were recommended for awards. Two applicants were not given awards due to lack of funding. Four applicants were offered awards of which three accepted and one declined.

FEBRUARY 1996 REVIEW

Eighteen applications were received for this review. Prior to the review three were not approved by the laboratory. Fifteen applications were presented to the board for review. Two were not recommended for awards. Ten were recommended for awards of which three were not offered awards due to lack of funding. Ten applicants were offered awards of which nine accepted and one declined.

JUNE 1996 REVIEW

Nine applications were received for this review. Prior to the review two were not approved by the laboratory. Seven applications were presented to the board for review and all seven were recommended for awards. Four were not offered awards due to lack of funding. Three were offered awards and accepted.

ASSOCIATES' ACTIVITIES

Termination Reports

Attachment 1 is a list of Associates, who terminated their appointments during the period of October 1, 1995, and September 30, 1996. It includes their laboratories, their starting and termination dates, and the names of their Advisers. Associates are required to submit reports upon termination (attached to this report), and Advisers are asked to submit final evaluations of each Associate. Associates who have not submitted a termination report have received a follow-up letter.
# Associates Who Ended Tenure 10/1/95 - 9/30/96

## U.S. Army Medical Research & Materiel Command

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* Indicates that the associate started tenure between 10/2/95 and 9/30/96.
(S) Associate is a Senior.
## Associates On Tenure

**October 1, 1996**

**U.S. Army Medical Research & Materiel Command**

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</tr>
<tr>
<td>Pushko, Peter Dr. Jonathan Fowler Smith</td>
<td>Medical Research Institute for Infectious Diseases Latvia</td>
<td>5/20/94</td>
<td>5/19/97</td>
</tr>
<tr>
<td>Ryu, Hyoik (S) Dr. Frederick J. Cassels</td>
<td>Walter Reed Army Institute of Research Republic Of Korea</td>
<td>10/03/94</td>
<td>10/02/97</td>
</tr>
<tr>
<td>Saikh, Kamal Uddin (S) Dr. Robert Glenn Ulrich</td>
<td>Medical Research Institute for Infectious Diseases India</td>
<td>4/03/95</td>
<td>4/02/97</td>
</tr>
<tr>
<td>Santhanam, Kausalya Dr. Jayasree Nath</td>
<td>Walter Reed Army Institute of Research India</td>
<td>7/05/95</td>
<td>7/04/97</td>
</tr>
<tr>
<td>* Shitzer, Avraham (S) Dr. Richard R Gonzalez</td>
<td>U.S. Army Research Institute of Environmental Med Israel</td>
<td>8/12/96</td>
<td>8/11/97</td>
</tr>
<tr>
<td>Stewart, V Ann Dr. D Gray Heppner, Jr</td>
<td>Research Institute of Medical Sciences United States</td>
<td>1/03/95</td>
<td>1/02/97</td>
</tr>
<tr>
<td>Wasielski, Leonard P Dr. Kevin Anderson</td>
<td>Medical Research Institute for Infectious Diseases United States</td>
<td>4/24/95</td>
<td>4/23/97</td>
</tr>
<tr>
<td>Woody, Mary Alice Dr. Bradley Gene Stiles</td>
<td>Medical Research Institute for Infectious Diseases United States</td>
<td>9/21/94</td>
<td>10/20/96</td>
</tr>
<tr>
<td>* Wyatt, James Kelley Dr. Harris Ritchie Lieberman</td>
<td>U.S. Army Research Institute of Environmental Med United States</td>
<td>7/01/96</td>
<td>6/30/97</td>
</tr>
<tr>
<td>* Yadava, Anjali</td>
<td>Walter Reed Army Institute of Research India</td>
<td>1/02/96</td>
<td>1/01/97</td>
</tr>
<tr>
<td>Zhang, Xiaoyan Dr. Marti Jett</td>
<td>Walter Reed Army Institute of Research People's Republic of China</td>
<td>4/10/95</td>
<td>4/09/97</td>
</tr>
</tbody>
</table>

* Indicates that the associate started tenure between 10/2/95 and 9/30/96.
+ (S) Associate is a Senior.
## Associates On Tenure

October 1, 1996

<table>
<thead>
<tr>
<th>Name + Adviser</th>
<th>Center Citizenship</th>
<th>Starting Date</th>
<th>Ending Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zhao, Bangti (S) Dr. Joseph Robert Putnak</td>
<td>Walter Reed Army Institute of Research People's Republic of China</td>
<td>1/10/94</td>
<td>1/09/97</td>
</tr>
</tbody>
</table>

Total for Lab: 55

* Indicates that the associate started tenure between 10/2/95 and 9/30/96.
+ (S) Associate is a Senior.
<table>
<thead>
<tr>
<th>Name</th>
<th>Research Title</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kurtis, Jonathan David</td>
<td>Correlation between Phenotypic T &amp; B Cell Immune Responses against Liver Stage Antigen 1 and the Expression of Naturally Acquired Resistance to Falciparum Malaria in Western Kenya</td>
</tr>
<tr>
<td>Luo, Chunyuan</td>
<td>Investigation of Ligand Modulation Mechanism on Reactivation of Phosphonyl Conjugate of Bispypiridinium Oximes</td>
</tr>
<tr>
<td>Yadava, Anjali</td>
<td>Cloning, Characterization and Immunogenicity of Sequestrin, a Cytoadherence Protein of Malaria</td>
</tr>
<tr>
<td>Name/Research Title</td>
<td>Project Description</td>
</tr>
<tr>
<td>---------------------</td>
<td>---------------------</td>
</tr>
<tr>
<td>Chakrabarti, Arun Kumar</td>
<td>Biochemical and Molecular Biological Aspects of Vesicating Agents Induced Protease Stimulation</td>
</tr>
<tr>
<td>Feaster, Shawn Ray</td>
<td>Determining the Mechanistic Pathway for Product Release in Acetylcholinesterase Catalysis</td>
</tr>
<tr>
<td>Guebre Xabier, Mimi</td>
<td>The Role of Liver Stage Antigen 1-specific T Cells in Protective Immunity Induced by Attenuated Plasmodium Falciparum Sporozoites</td>
</tr>
<tr>
<td>Kamrud, Kurt Iver</td>
<td>Development and Comparison of Three Recombinant Vaccines to Puumala Virus</td>
</tr>
<tr>
<td>Kovach, Ildiko M</td>
<td>Molecular Dynamics Simulation of the Inhibition of Cholinesterases</td>
</tr>
<tr>
<td>Lewis, Steven Fred</td>
<td>Effect of Caffeine on Rate of Muscle Fatigue and Recovery during Dynamic Leg Exercise</td>
</tr>
<tr>
<td>Li, Guo</td>
<td>Imaging Photoreceptors in the Primate Eye in vivo</td>
</tr>
<tr>
<td>Peel, Sheila Anne</td>
<td>Utilize in vitro Biological and Molecular Models to (1) Identify Molecular Determinants which Function in Drug Resistance, thereby Facilitating Drug Development against Multidrug Resistant Strains of P.falciparum, and to (2) Determine whether the Parasite Remodels the structure/function of pfmdr1 to Mediate Residstance to Zenobiotic</td>
</tr>
<tr>
<td>Name</td>
<td>Research Title</td>
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<tr>
<td>-----------------------------</td>
<td>-------------------------------------------------------------------------------</td>
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<tr>
<td>Dailey, Frank</td>
<td>Construction and Testing of Live Vaccine Candidates for Yersinia Pestis, the Causative Agent of Bubonic Plague</td>
</tr>
<tr>
<td>Das, Rina</td>
<td>Signal Transduction Pathways for Bioactive Lipids in Breast Cancer</td>
</tr>
<tr>
<td>Korte, William D</td>
<td>The Development and Evaluation of Liquid Chromatography-Mass Spectroscopy, Capillary Electrophoresis, or Fluoroimmunoassay Methods For the Detection of Sulfur Mustard Derivatives at Low Concentrations in Biological Samples</td>
</tr>
<tr>
<td>Shitzer, Avraham</td>
<td>Development of Mathematical Algorithms for Simultaneous Finger-tip Temperatures and Blood Perfusion Rates during Cold Stress</td>
</tr>
</tbody>
</table>
Accepted Award

KURTIS, JONATHAN DAVID
Citizenship: United States
Adviser: Dr. Patrick Emmet Duffy
Research Field: Tropical Medicine
Research Title: Correlation between Phenotypic T & B Cell Immune Responses against Liver Stage Antigen 1 and the Expression of Naturally Acquired Resistance to Falciparum Malaria in Western Kenya

LUO, CHUNYUAN
Citizenship: People's Republic Of China
Adviser: Dr. Bhupendra P. Doctor
Research Field: Biochemical Pharmacology
Research Title: Investigation of Ligand Modulation Mechanism on Reactivation of Phosphonyl Conjugate of Bispyridinium Oximes

YADAVA, ANJALI
Citizenship: India
Adviser: J Nehru University
Research Field: Immunology
Research Title: Cloning, Characterization and Immunogenicity of Sequestrin, a Cytoadherence Protein of Malaria

Declined

BHUSHAN, REVA
Citizenship: United States
Adviser: Dr. Susan Lee Welkos
Research Field: Microbiology
Research Title: Mechanism of Action of Plasminogen Activator in Systemic Infection by Virulent Y. Pestis

Recommended/No Funding

LI, JIA
Citizenship: People's Republic Of China
Adviser: Dr. Antoinette B. Hartman
Research Field: Infectious Diseases
Research Title: Development of Reagents to Aid in the Study of Cytokine Responses to Shigella Infection in the Guinea Pig Keratoconjunctivitis Model

MALAVASIC, MICHAEL JOHN
Citizenship: United States
Adviser: Dr. Charles Hearn Hoke, Jr
Research Field: Virology
Research Title: Cloning of Dengue Virus-specific, Display-phage Encoded Mimitopes as Tools to Investigate Dengue Virus Neutralization

Ph.D. Date: 1996
Brown University/RI
7/01/96
6/30/97

Ph.D. Date: 1993
China Unknown
3/12/96
3/11/97

Ph.D. Date: 1991
J Nehru University
1/02/96
1/01/97

Ph.D. Date: 1995
State Univ of New York-Buffalo

Ph.D. Date: 1994
Pennsylvania State U Central Off

Ph.D. Date: 1988
University of Chicago/IL
Recommended Candidates  10/1/95 - 9/30/96

U.S. Army Medical Research & Materiel Command

February 1996

Recommended

SHALEV, ARIEH YOEL
Citizenship: Israel
Adviser: Dr. Gregory L. Belenky
Research Field: Behavioral Biology
Research Title: Prospective Study of Treatment Intervention Following Exposure to Extreme Stress
Ph.D. Date: 1972
Montpellier I, U

Accepted Award

CHAKRBARTI, ARUN KUMAR
Citizenship: India
Adviser: Dr. Prabhati Ray
Research Field: Toxicology
Research Title: Biochemical and Molecular Biological Aspects of Vesicating Agents Induced Protease Stimulation
Ph.D. Date: 1984
Calicut, U Of
Actual Starting Date: 5/30/96
Termination Date: 1/29/97

CRISE, BRUCE JEFFREY
Citizenship: United States
Adviser: Dr. Michael D Parker
Research Field: Virology
Ph.D. Date: 1993
Yale University/CT
Expected Starting Date: 11/15/96
Termination Date: 11/14/97

FEASTER, SHAWN RAY
Citizenship: United States
Adviser: Dr. Bhupendra P. Doctor
Research Field: Biophysical Chemistry
Research Title: Determining the Mechanistic Pathway for Product Release in Acetylcholinesterase Catalysis
Ph.D. Date: 1995
University of Iowa
Expected Starting Date: 2/01/97
Termination Date: 1/31/98

GUEBRE XABIER, MIMI
Citizenship: Ethiopia
Adviser: Dr. Urszula Krzych
Research Field: Immunology
Research Title: The Role of Liver Stage Antigen 1-specific T Cells in Protective Immunity Induced by Attenuated Plasmodium Falciparum Sporozoites
Ph.D. Date: 1988
France Unknown
Actual Starting Date: 5/20/96
Termination Date: 5/19/97

KAMRUD, KURT IVER
Citizenship: United States
Adviser: Dr. Connie Sue Schmaljohn
Research Field: Virology
Research Title: Development and Comparison of Three Recombinant Vaccines to Puumala Virus
Ph.D. Date: 1996
Colorado State University
Actual Starting Date: 8/05/96
Termination Date: 8/04/97

KOVACH, ILDIKO M
Citizenship: United States
Adviser: Dr. Bhupendra P. Doctor
Research Field: Biochemistry Biophysics
Research Title: Molecular Dynamics Simulation of the Inhibition of Cholinesterases
Ph.D. Date: 1974
University of Kansas
Actual Starting Date: 5/28/96
Termination Date: 9/27/96
<table>
<thead>
<tr>
<th>Accepted Award</th>
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<tbody>
<tr>
<td>LEWIS, STEVEN FRED</td>
<td>Ph.D. Date: 1977</td>
</tr>
<tr>
<td>Citizenship: United States</td>
<td>Stanford University/CA</td>
</tr>
<tr>
<td>Adviser: Dr. Harris Ritchie Lieberman</td>
<td>Actual Starting Date: 5/16/96</td>
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<tr>
<td>Research Field: Nutrition</td>
<td>Termination Date: 9/15/97</td>
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<tr>
<td>Research Title: Effect of Caffeine on Rate of Muscle Fatigue and Recovery during Dynamic Leg Exercise</td>
<td></td>
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<tr>
<td>LI, GUO</td>
<td>Ph.D. Date: 1993</td>
</tr>
<tr>
<td>Citizenship: People's Republic Of China</td>
<td>University of Mass-Lowell</td>
</tr>
<tr>
<td>Adviser: Dr. Harry Zwick</td>
<td>Actual Starting Date: 9/16/96</td>
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<tr>
<td>Research Field: Medical Research</td>
<td>Termination Date: 9/15/97</td>
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<tr>
<td>Research Title: Imaging Photoreceptors in the Primate Eye in vivo</td>
<td></td>
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<tr>
<td>PEEL, SHEILA ANNE</td>
<td>Ph.D. Date: 1991</td>
</tr>
<tr>
<td>Citizenship: United States</td>
<td>U of North Carolina-Chapel Hill</td>
</tr>
<tr>
<td>Adviser: Dr. Edwin O. Nuzum</td>
<td>Actual Starting Date: 8/01/96</td>
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<tr>
<td>Research Field: Parasitology</td>
<td>Termination Date: 7/31/97</td>
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<tr>
<td>Research Title: Utilize in vitro Biological and Molecular Models to (1) Identify Molecular Determinants which Function in Drug Resistance, thereby Facilitating Drug Development against Multidrug Resistant Strains of P.falciparum, and to (2) Determine whether the Parasite Remodels the structure/function</td>
<td></td>
</tr>
</tbody>
</table>

| Declined |  |
| GIRALDO, LUIS ERNESTO | Ph.D. Date: 1996 |
| Citizenship: United States | Tulane University of Louisiana |
| Adviser: Dr. Alan J. Magill |  |
| Research Field: Pathology |  |
| Research Title: Isolation and Characterization of a Define Leishmania DTH Antigen and Serological Diagnosis of Leishmania |  |

| Withdrew after Review/Recommend |  |
| OSORIO, JORGE EMILIO | Ph.D. Date: 1996 |
| Citizenship: Colombia | University of Wisconsin-Madison |
| Adviser: Dr. George V Ludwig |  |
| Research Field: Virology |  |
| Research Title: Effectiveness of the New Generation of Alphavirus Vaccines against Current or newly Emerging Strains |  |

| Recommended/No Funding |  |
| MUKHTAR, MAOWIA MOHAMED | Ph.D. Date: 1989 |
| Citizenship: United States | Cornell University/NY |
| Adviser: Dr. Alan J. Magill |  |
| Research Field: Immunology |  |
| Research Title: Cloning of Recombinant Leishmania Antigens for the Diagnosis and the Development of Vaccines for Visceral Leishmaniasis |  |
## Recommended Candidates 10/1/95 - 9/30/96

### U.S. Army Medical Research & Materiel Command

#### June 1996

<table>
<thead>
<tr>
<th><strong>Recommended</strong></th>
<th><strong>Ph.D. Date:</strong></th>
<th><strong>Citizenship:</strong></th>
<th><strong>Adviser:</strong></th>
<th><strong>Research Field:</strong></th>
<th><strong>Research Title:</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>TSAREV, SERGEI ANATOLYEVICH</td>
<td>1989</td>
<td>Russia</td>
<td>Dr. Bruce Lamont Innis</td>
<td>Virology</td>
<td>Refining the Strategy of Hepatitis E Virus Vaccination through Molecular Virology Studies</td>
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<tr>
<th><strong>Accepted Award</strong></th>
<th><strong>Ph.D. Date:</strong></th>
<th><strong>Citizenship:</strong></th>
<th><strong>Adviser:</strong></th>
<th><strong>Research Field:</strong></th>
<th><strong>Research Title:</strong></th>
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<tbody>
<tr>
<td>DAILEY, FRANK</td>
<td>1986</td>
<td>United States</td>
<td>Dr. Arthur Michael Friedlander</td>
<td>Infectious Diseases</td>
<td>Construction and Testing of Live Vaccine Candidates for Yersinia Pestis, the Causative Agent of Bubonic Plague</td>
</tr>
<tr>
<td>DAS, RINA</td>
<td>1987</td>
<td>India</td>
<td>Dr. Marti Jett</td>
<td>Biochemistry</td>
<td>Signal Transduction Pathways for Bioactive Lipids in Breast Cancer</td>
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<table>
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<tr>
<th><strong>KORTE, WILLIAM D</strong></th>
<th><strong>Ph.D. Date:</strong></th>
<th><strong>Citizenship:</strong></th>
<th><strong>Adviser:</strong></th>
<th><strong>Research Field:</strong></th>
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<tr>
<td></td>
<td>1966</td>
<td>United States</td>
<td>Dr. Ming L. Shih</td>
<td>Analytical Chemistry</td>
<td>The Development and Evaluation of Liquid Chromatography-Mass Spectroscopy, Capillary Electrophoresis, or Fluoroimmunoassay Methods For the Detection of Sulfur Mustard Derivatives at Low Concentrations in Biological Samples</td>
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<tr>
<th><strong>SHITZER, AVRAHAM</strong></th>
<th><strong>Ph.D. Date:</strong></th>
<th><strong>Citizenship:</strong></th>
<th><strong>Adviser:</strong></th>
<th><strong>Research Field:</strong></th>
<th><strong>Research Title:</strong></th>
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<tr>
<td></td>
<td>1971</td>
<td>Israel</td>
<td>Dr. Richard R Gonzalez</td>
<td>Bioengineering</td>
<td>Development of Mathematical Algorithms for Simultaneous Finger-tip Temperatures and Blood Perfusion Rates during Cold Stress</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Withdrew after Review/Recommend</strong></th>
<th><strong>Ph.D. Date:</strong></th>
<th><strong>Citizenship:</strong></th>
<th><strong>Adviser:</strong></th>
<th><strong>Research Field:</strong></th>
<th><strong>Research Title:</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>ZANARDI, ALBERT THOMAS</td>
<td>1996</td>
<td>United States</td>
<td>Dr. Kevin Anderson</td>
<td>Virology</td>
<td>The Role of Secreted and Membrane-anchored Forms of the Ebola Virus Glycoprotein in Providing Protective Immunity to Virus Challenge</td>
</tr>
<tr>
<td>Name</td>
<td>Citizenship</td>
<td>Adviser</td>
<td>Research Field</td>
<td>Research Title</td>
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<tr>
<td>ZUBER, MOHAMMED</td>
<td>United States</td>
<td>Dr. Arthur Michael Friedlander</td>
<td>Bacteriology</td>
<td>Development of Attenuated Live Vaccine Strains for Plague</td>
<td>1981</td>
</tr>
</tbody>
</table>

Additional note: June 1996
Final report for NRC Senior Associateship Program

1. Date:

April 28, 1996

2. Name:

Gabriel Amitai, Ph.D.

3. Name and Location of Laboratory and Center:

Division of Biochemistry
Walter Reed Army Institute of Research
Washington DC 20307-5100

4. Dates of Tenure:

January 7 - July 7 1995
October 1 - October 16, 1995

5. Title of Research Project:

Studies on Inhibitors and Reactivators of Acetylcholinesterase

6. Research Advisor’s Name:

Dr. B.P. Doctor
Director, Division of Biochemistry
Walter Reed Army Institute of Research

7. Are you on leave from a professional post?

I was on leave from the Israel Institute for Biological Research, Ness Ziona
Israel, where I am currently serving as Head, Division of Medicinal
Chemistry.
8. International posts held during tenure

N/A

9. Programmatic travel during tenure

1) Travel to IIBR, Ness Ziona, Israel, March 1995

2) Travel to University of Pittsburgh, Chemical Engineering, Center for Biotechnology and Bioengineering, University of Pittsburgh, PA. May 1995. Working in the laboratory of Dr. Alan J. Russell on covalent binding of AChE to polyurethane foam.

3) Travel to UCSD, La Jolla, CA. Department of Pharmacology, May 1995. Working with Dr. Zoran Radic and Prof. Palmer Taylor on mouse AChE mutants.

10. Scientific seminars, meetings, and/or consultations

1) APBI Meeting in Columbia, Md., organized by the DOD, March 95.

2) Fourth Meeting on Chemical Protection, ERDEC, APG, Md., April 95.

3) Meetings with Dr. Ken Dretchen, Assistant Dean for Research, Georgetown University. Discussions on oximes and human BChe and visit at the Department of Pharmacology, Georgetown University (March, May, 95).

4) Meetings with Napoleon Monroe, Vice President STI, Inc., Rockville, Md. Discussions, preparation and submission of preproposal (by IIBR) on the improvement of HI-6 stability in automatic combined syringe of STI. (March, April, May, June and October 95).

5) Consultation with Dr. Palmer Taylor on Fasciculin II inhibition kinetics and mouse AChE mutants, (March-July 95, see also programmatic travel).
6) 5th International Symposium on Protection against Chemical and Biological Warfare Agents, Stockholm, Sweden, June 1995 (invited lecturer).

11. Seminars or lectures delivered at universities and/or institutes:

N/A

12. Meetings attended by specific invitation

5th International Symposium on Protection against Chemical and Biological Warfare Agents, Stockholm, Sweden, June 1995 (invited lecturer).

13. Teaching, if any as an associate:

N/A

14. Work in progress:

1) Kinetics of inhibition of human plasma cholinesterase and erythrocyte AChE by pyridostigmine

2) Kinetics of inhibition of AChE from various species and AChE mutants by fasciculin II.

3) Delineation of the selectivity and kinetics of inhibition of BChE and AChE by Chlorpyrofos-oxon (CPO).

4) Binding of FBS-AChE to Polyurethane foams and use of insoluble AChE matrix together with oximes for degradation of Nerve Agents.

15. Summary of research during tenure

During my tenure as a senior NRC fellow at the WRAIR I have been involved in four different projects: 1. Construction of kinetic model for the analysis of the time-course of inhibition of human plasma BChE and erythrocyte AChE by pyridostigmine (PYR). 2. Kinetics of inhibition of AChE from various species and AChE mutants by fasciculin II (FAS II).
3. Delineation of the inhibition of BChE and AChE by Chlorpyrofos-oxon (CPO). 4. Covalent binding of FBS-AChE to polyurethane foams and its application for the degradation of nerve-agents. The inhibition of human blood ChE's by pyridostigmine was studied in normal volunteers and outpatients of the Walter Reed hospital in order to find abnormal ChE sensitivity towards PYR. Mouse AChE mutants H287R, D280V, D283N and the double mutant D280V/D283N were prepared to delineate which amino acids affect the affinity of FAS II for FBS and human AChE and are located close to the PAS. Kinetics of inhibition of H287R mutant with FAS II yields K_F value 6 fold higher than that obtained for the wild type. The K_F obtained for the double mutant D280V/D283N is 3 fold larger than that of the wild type. CPO, a metabolite of the widely used insecticide chlorpyrifos, inhibits human plasma BChE and rHBChE with exceptionally high bimolecular rate constant (k_i) 1.3x10^9 and 1.6x10^9 M^-1 min^-1, respectively. These values are 140 and 180 fold larger than the k_i value obtained for the inhibition of rHAChe and 340 and 420 fold larger than for human erythrocyte AChE, respectively. The double mutant of the acyl pocket residues of rHAChe F295L/F297V, that display characteristics of BChE active center, shows a 7.5 fold enhanced inhibition rate with CPO as compared to the wild type. These results provide a rationale for higher efficacy of CPO scavanging by BChE as compared to AChE. Furthermore, CPO may serve for differential quantitative determination of BChE active-site concentration especially at low enzyme levels.

16. Publications and papers resulting from research as an associate


National Research Council Associateship Program Final Report

1. Date: March 18, 1996

2. Name (ID): Julianne Claire Maloney Clifford

3. Dates of Tenure: April 9, 1994 to April 9, 1995
   April 9, 1995 to April 9, 1996

4. Title of Research Project: Ricin intoxication in a cell-free system.

5. Research Advisor: Dr. Thomas H. Hudson

6. On leave from a professional post? No

7. International posts held during tenure: NA

8. Programmatic Travel during tenure: NA

9. Scientific seminars, meetings and/or consultations:
   3. February 1996, Annual Meeting of American Association for the Advancement of Science

10. Seminars or Lectures delivered at Universities and/or Institutes: NA

11. Meetings attended by specific invitation: NA

12. Teaching, if any, as an associate:
    I was responsible for the training and laboratory supervision of a student hire from May 1995 through February 1996.
13. Work in Progress:
I am currently examining the effects of nonhydrolyzable analogs GTP and GDP on ricin translocation in a permeabilized cell system utilizing the system I have developed for detecting the enzymatic effects of translocated ricin on ribosomal RNA.

14. Summary of Research During Tenure:
In accordance to the proposed goals of this research project I have 1) developed a system for detecting the enzymatic effects of translocated ricin toxin on ribosomal RNA, 2) optimized conditions for generating a permeabilized cell system utilizing the pore forming toxin Staphyloccocal alpha oxin and 3) used this unique detection system to investigate the organelle and energy requirements for ricin translocation in the intact and permeabilized cell systems.

15. Publications:

16. Patents: NA

17. Future position and address:
Staff Fellow
Laboratory of Bacterial Toxins
Building 29 Rm. 103
Center for Biologics Evaluation & Research
Food and Drug Administration
Bethesda, MD 20892

18. Appraisal of associateship programs:
I consider myself fortunate to have had the opportunity to participate as a postdoctoral fellow in the associateship program. On the whole I have found the system to be responsive to my needs but has allowed pursue my research interests unheeded by administrative distractions. I cannot comment specifically on the performance of any one staff member since I have not experienced any circumstances, complications or problems within the system which required any considerable interaction with the staff. I feel that the associateship program has given me a chance to work in a
unique research environment (Walter Reed Army Institute of Research) and for that I am grateful. The WRAIR liaison office has always been helpful and responsive to my inquiries and needs. The only critical comment I can think of is that I found the system for making travel arrangements and reimbursements to be both confusing and complicated (but I have not had to make arrangements through the travel office since December 1994, so the complaint is a bit outdated).
FINAL REPORT

(1) DATE
7-26-1996

(2) NAME (AND ID NUMBER IF KNOWN)
Jose Diaz Romero

(3) NAME AND LOCATION OF LABORATORY CENTER
Department of Bacterial Diseases
Walter Reed Army Institute of Research
Washington, DC 20307-5100

(4) DATES OF TENURE
9-1-1995/8-31-1996

(5) TITLE OF RESEARCH PROJECT
"DEVELOPMENT OF NEW METHODS TO STUDY THE IMMUNE RESPONSE TO NEISSERIA MENINGITIDIS GROUP B"

(6) RESEARCH ADVISER'S NAME
Dr. Wendell D. Zollinger

(7) ARE YOU ON LEAVE FROM A PROFESSIONAL POST?
No

(8) INTERNATIONAL POSTS HELD DURING TENURE
N/A
(9) PROGRAMMATIC TRAVEL DURING TENURE

N/A

(10) SCIENTIFIC SEMINARS, MEETINGS, AND/O CONSULTATIONS

NATO ASI "Vaccine Design: The Role of Cytokine Networks" 24 June - 5 July 1996, Cape Sounion Beach, Greece.

(11) SEMINARS OR LECTURES DELIVERED AT UNIVERSITIES AND/ OR INSTITUTES

N/A

(12) MEETINGS ATTENDED BY SPECIFIC INVITATION

N/A

(13) TEACHING, IF ANY, AS AN ASOCIATE

N/A

(14) WORK IN PROGRESS.

N/A

(15) SUMMARY OF RESEARCH DURING TENURE

A problem in obtaining a Neisseria meningitidis B vaccine is the lack of capsular polysaccharide immunogenicity. This homopolymer of N-acetyl neuraminic acid residues in alpha 2-8 linkage, polysialic acid, is also present on the surface of animal cells as a unique glycosylation of the neural cellular adhesion molecule (NCAM). NCAM is expressed on hematopoietic cells and recognized by anti-CD56 mAb, a marker of NK cells and lymphocytes that mediate MHC-unrestricted cytotoxicity. A previous report exits about the presence of polysialic acid in NK cells. In this work we reexamine this point by the use of different monoclonal antibodies polysialic acid-specific.

(16) PUBLICATIONS AND PAPERS RESULTING FROM RESEARCH AS AN ASSOCIATE

Cross-reaction Between Human NK Cells and Group B Meningococci. Yong Q Wang, Jose Diaz Romero, Craig A. Hammack and Wendell D. Zollinger. (manuscript in preparation)

(17) PATENTS APPLIED FOR AS A RESULT OF RESEARCH AS AN ASSOCIATE

N/A
FUTURE POSITION AND ADDRESS OR CURRENT FORWARDING ADDRESS

C/ Oviedo 13, 1 D
28020 Madrid
SPAIN
Tel. and Fax: (34) 1-5343811

APPRAISAL OF THE ASSOCIATESHIP PROGRAMS

Under Article 22(1) of the tax treaty between the United States and Spain, my research grant qualifies for exemption from withholding of federal income tax, but I was not aware of this point until I filled my federal income-tax return; the handbook of Policies, Practices, and Procedures of the N.R.C. in the chapter about tax does not any mention to the possibility of exemptions:

6.3 Federal Tax Liability of Nonresident Aliens
(Exchange Visitors)

6.3.1 — If you are a nonresident alien who holds an Exchange Visitor (J1) Visa, the Research Council is required by the US Tax Code to withhold an amount from your stipend of 30% per month and to report this deduction to the Internal Revenue Service annually.

6.3.2 — Although taxes will be withheld at the 30% level, actual tax liability is determined when you file a federal income-tax return. In the event the tax liability is less than the amount withheld, you will receive a tax refund directly from the IRS.

6.3.3 — As a nonresident alien, you should file Form 1042 NR as early as possible, but not later than the 15th day of June following the close of the tax (calendar) year. For other filing options, you should consult a tax professional and/or the IRS.
FINAL REPORT

(1) DATE: 29 July 1996

(2) NAME: Catherine L.V. Gabarée, Ph. D.

(3) NAME AND LOCATION OF LABORATORY:
U.S. Army Research Institute of Environmental Medicine
Kansas Street
Natick, Massachusetts 01760-5007

(4) DATES OF TENURE: 1 June 1993 to 15 July 1996

(5) TITLE OF RESEARCH PROJECTS:
A) Assessment of Intra- and Inter-individual Metabolic and Hormonal Variation in Special Operations Forces (SOF) Soldiers.

B) Effects of Topical Skin Protectant on Heat Exchange in Humans.

(6) RESEARCH ADVISER'S NAME:
A) John F. Patton III, Ph.D. 1 June 1993-31 May 1994

B) Michael N. Sawka, Ph. D. 1 June 1994-15 July 1996

(7) ARE YOU ON LEAVE FROM A PROFESSIONAL POST? N/A

(8) INTERNATIONAL POSTS HELD DURING TENURE: N/A

(9) PROGRAMMATIC TRAVEL DURING TENURE:
Pennington Biomedical Research Institute, Baton Rouge, LA:
March 1993 (2 days for study preparation)
May 1993 (2 days for study preparation)
June 1993 (3 weeks for data collection)
July 1993 (3 weeks for data collection)

(10) SCIENTIFIC SEMINARS, MEETINGS, AND/OR CONSULTATIONS:
Interagency Committee on Human Nutrition Research, Bethesda, MD, February 23-24, 1994
Experimental Biology '94, Anaheim, CA, April 24-28, 1994
New England American College of Sports Medicine, May 6, 1994
American College of Sports Medicine, Indianapolis, IN, June 1-4, 1994
Experimental Biology '95, Atlanta, GA, April 1995
Experimental Biology '96, Washington D.C., April 1996
American College of Sports Medicine, Cincinnati, Ohio, May 31-June 1, 1996
(11) SEMINARS OR LECTURES DELIVERED AT UNIVERSITIES AND/OR INSTITUTES: N/A

(12) MEETINGS ATTENDED BY SPECIFIC INVITATION: N/A

(13) TEACHING, IF ANY, AS AN ASSOCIATE: N/A

(14) WORK IN PROGRESS: I am currently working on a research study to determine daily variation in skin blood flow in healthy individuals and individuals who smoke and individuals with high cholesterol. Additionally I am continuing to collect data for a methodological study comparing two methods of determining skin blood flow.

(15) SUMMARY OF RESEARCH DURING TENURE:
Study 1: Metabolic and hormonal intra- and inter-individual variation during repeated bouts of prolonged, treadmill exercise was determined in order to evaluate substrate utilization during exercise and recovery. Diet, hydration status, energy expenditure, and ambient conditions were controlled. Extremely low variation in respiratory and biochemical variables indicated insignificant variation between individuals in substrate utilization during exercise.

Study 2: The effects of application of a Topical Skin Protectant (TSP) on heat exchange during exercise in the heat were determined. Esophageal temperature, skin temperature, heart rate, and pre- and post-experimental weights were measured. Mean skin temperature, mean body temperature, changes in esophageal temperature per min of exercise, evaporative heat loss, and sweating rate were calculated. TSP application minimally affected heat exchange under the conditions of this study.

(16) PUBLICATIONS AND PAPERS RESULTING FROM RESEARCH AS AN ASSOCIATE:


(17) PATENTS APPLIED FOR AS A RESULT OF RESEARCH AS AN ASSOCIATE: N/A

(18) FUTURE POSITION AND ADDRESS OR CURRENT FORWARDING ADDRESS:
Research Physiologist
U.S. Army Research Institute of Environmental Medicine
Kansas Street
Natick, MA 01760-5007

(19) APPRAISAL OF THE ASSOCIATESHIP PROGRAM: My tenure as an NRC associate was most beneficial to me. I have had the opportunity to pursue my interests in basic metabolism as well as thermal effects on metabolism. I particularly appreciated the travel funds available for scientific conferences and presentations.
Final Report

1. DATE:  3/17/96

2. NAME: Bruce W. Hart #916533

3. NAME AND LOCATION OF LABORATORY:
USAMRICD, APG-EA, MD 21010

4. DATES OF TENURE: 4/93-4/96

5. TITLE OF RESEARCH PROJECT:
The role of p34cdc2 in sulfur mustard-induced G2 block of human epidermal keratinocytes.

6. RESEARCH ADVISER’S NAME: Dr. John Schlager

7. ON LEAVE FROM PROFESSIONAL POST?: no

8. INTERNATIONAL POSTS HELD DURING TENURE: N/A

9. PROGRAMMATIC TRAVEL DURING TENURE:

10. SCIENTIFIC SEMINARS, MEETINGS, AND/OR CONSULTATIONS:
American Association for Cancer Research Annual Meeting, San Francisco, CA, April 1994
Society of Toxicology Annual Meeting, Baltimore, MD, March 1995
American Association for Cancer Research Annual Meeting, Toronto, ON, April 1995
Society of Toxicology Annual Meeting, Anaheim, CA, March 1996

11. SEMINARS OR LECTURES DELIVERED AT UNIVERSITIES AND/OR INSTITUTES:
Georgetown University, March 1996

12. MEETING ATTENDED BY SPECIFIC INVITATION: NONE

13. TEACHING: none

14. WORK IN PROGRESS:
This work is being continued on a new contract. Studies will focus on the production of reactive oxygen species by the protein phosphatase 2A inhibitors and reversal of the G2/M cell cycle block.
15. SUMMARY OF RESEARCH DURING TENURE:

Nitrogen and sulfur mustards, both DNA alkylating agents, were shown to produce a $G_s/M$ cell cycle block in normal and transformed human cells. This cell cycle block was completely reversed by substantial inhibition of protein phosphatase 2A. This resulted in an abnormal mitotic state, accompanied by marked changes in protein phosphorylation and DNA integrity. Inhibiton of protein phosphatase 1 had no effect on the mustards-induced $G_s/M$ block. These results suggest that protein phosphatase 2A is involved in the $G_s/M$ block produced by exposure of human cells to low concentrations of nitrogen or sulfur mustard.

16. PUBLICATIONS AND PAPERS RESULTING FROM RESEARCH AS AN ASSOCIATE:


Hart, B.W. and Schlager, J.J. Abrogation of nitrogen mustard-induced $G_s/M$ block by inhibitors of protein phosphatase 2A. (Submitted to *J. Biol. Chem.*).


17. PATENTS APPLIED FOR: none

18. CURRENT FORWARDING ADDRESS:

30-L Greystone Ct.
Annapolis, MD, 21403

19. APPRAISAL OF THE ASSOCIATESHIP PROGRAMS:

I have been very pleased with the NRC program overall. I have had no problems with any aspect of the program directly controled by the NRC. I believe that the program is a great alternative to the traditional academic postdoc. I do, however, have reservations about the USAMRICD program. There is overwhelming pressure at the Institute to generate large numbers of manuscripts. The quality of the manuscripts (or the journals they are submitted to) is not considered, only the number. This is not a healthy attitude for a scientific institution. The credibility of an organization is dictated by the quality of it’s work, and I believe that this “bean counter” attitude sends a bad message to young and growing scientists.
FINAL REPORT (using attached format)

1. January 12, 1996

2. Mark Andrew Hebert

3. Division of Neurosciences
   Walter Reed Army Institute of Research
   Walter Reed Army Medical Center
   Washington, DC
   20307-5100


5. Defeat-induced pathology in golden hamsters

6. Research Advisor: James L. Meyerhoff

7. No

8. N/A

9. Programmatic Travel: The University of Georgia: May 7-15, 1994

10. Scientific Meetings:

    23rd annual meeting of the Society for Neuroscience
    Washington, DC
    Nov. 7-12, 1993

    24th annual meeting of the Society for Neuroscience
    Miami Beach, FLA
    Nov. 13-18, 1994

    25th annual meeting of the Society for Neuroscience
    San Diego, CA
    Nov. 11-16, 1995

    Annual meeting of the International Behavioral Neuroscience Society
    Satellite symposium: The Neurobiology of Defensive Behavior
    Santiago de Compostela, Spain
    May 16-21, 1995

11. N/A
12. N/A
13. N/A
14. Current Work:

Studying effects of acute defeat on immobility in mice. Psychopharmacological drugs are being evaluated to delineate the underlying neuropharmacology of the effect.

15. Summary of Research During Tenure:

Conditioned defeat (CD), an animal model of combat-related psychopathologies such as CSR or PTSD, was examined extensively. Experimental procedures were developed for the acute induction of CD in both Syrian hamsters and DBA/2 mice. Tests were devised for assessing changes in social and non-social behavior following CD acquisition. Benzodiazepines, stress-related neuropeptides, antidepressants, and other compounds were screened for possible effects on CD. None of the drugs tested were found to reverse CD, but diazepam potentiated the syndrome. Neuroendocrine, immunological, and cardiovascular responses were also characterized and neuroanatomical studies were initiated using the CD models.

16. Peer-reviewed Published Papers


Potegal, M., Ferris, C., Hebert, M., Meyerhoff, J.L. & Skaredoff, L. Attack priming in female Syrian golden hamsters is mediated by a c-fos coupled process within the corticomedial amygdala (in prep).

Published abstracts


Hebert, M.A., Potegal, M., Moore, T. & Meyerhoff, J.L. Diazepam enhances conditioned

17. Patents: Automated activity monitor for activity of rodents in a water medium
    Patent application initiated by WRAIR.

18. Future address:

    University of Hawaii at Manoa
    Pacific Biomedical Research Center
    Bekesy Laboratory of Neurobiology
    1993 East-West Road
    Honolulu
    Hawaii
    96822

19. Appraisal of Associateships Program:

    I was pleased with the program overall. I was disappointed at times with the slowness of the staff
    in processing travel expense forms. I waited 4 months for reimbursement for one trip. I was also
    disappointed with the manner in which NRC stipends were increased for new NRCs at WRAIR in
    the fall of 1993. Second and third year NRCs did not get an increase at that time, which I feel
    was unfair. The NRC should implement a fair, universal policy with regard to stipend increases
    with which all laboratories must comply.
FINAL REPORT

(1) **Date:** 12/20/95.

(2) **Name:** Vadim Joseph Levenson.

(3) **Name and location of laboratory:** Walter Reed Army Institute of Research, Washington, D.C.

(4) **Dates of tenure:** 1/03/93 - 1/02/96

(5) **Title of Research Project:** Ribosome as a vaccine vector.

(6) **Research adviser's name:** T.L.Hale.

(7) **Are you on leave from a professional position:** No.

(8) **International posts held during tenure:** No.

(9) **Programmatic travel during tenure:** No.

(10) **Scientific seminars, meetings, consultations:**

    Vaccines: Novel Strategies. Eilat, Israel,

(11) **Seminars or lectures delivered at universities.**

    NIH, August 9, 1995.

(12) **Meetings attended by specific invitation:** No.

(13) **Teaching, if any, as an associate:** No.

(14) **Work in progress:** N/A
(15) **Summary of the research during tenure:**

Nucleoprotein subcellular (NPS) vaccine from *S. sonnei* was established as a candidate vaccine for humans. Several bench lots were prepared and tested. They elicited in mice an intensive IgG antibody response and the early protection against intranasal challenge with homologous shigellae. In guinea pigs, one parenteral injection of NPS vaccine induced an intensive response of IgA-ASC and about 70% protection against keratoconjunctival challenge. Protocol for the large-scale production of the NPS *S. sonnei* vaccine was elaborated, and the vaccine was produced in 1995 under GMP conditions for clinical trial. Experimental NPS vaccine from *S. flexneri* was obtained to be further tested as a component of the bivalent *Shigella* vaccine.

(16) **Publications and papers resulting from research as associate:**


Levenson V.J. 1995. Subcellular dysentery vaccine. 39th OHOLO Conference, Eliat, Israel, p.7P.


(17) **Patents applied for as a result of research as an associate.** No.

(18) **Future position and address.**

Will participate in the WRAIR CRADA project as an employee of the SBL (Swedish Biological Laboratories). Laboratory of Enteric Infections, WRAIR, Washington, D.C. 20307-5100.

(19) **Appraisal of the associateship programs.**

The program was very helpful as an opportunity to demonstrate the protective efficacy of parenteral vaccination against shigellosis and to make further steps in the development of parenteral NPS vaccine as a candidate vaccine for humans. It also gave the better understanding of the vaccine research and development practice in the U.S.
FINAL REPORT

(1) DATE
   October 16, 1995

(2) NAME (ID#)
   Natalya P. Matylevich (9189650)

(3) NAME AND LOCATION OF LABORATORY OR CENTER
   Laboratory Department, US Army Institute of Surgical
   Research, Fort Sam Houston, San Antonio, TX 78234

(4) DATES OF TENURE
   May 18, 1992 - November 17, 1995

(5) TITLE
   Mechanism of antimicrobial activity of silver nylon
   dressing.

(6) RESEARCH'S ADVISER'S NAME
   Albert T. McManus, PhD

(7) ARE YOU ON LEAVE FROM A PROFESSIONAL POST?
   Research Scientist, Institute of Cell Biophysics, Russian
   Academy Of Sciences, Pushchino, Moscow Reg., 142292

(8) INTERNATIONAL POST HELD DURING TENURE
   Research Associate

(9) PROGRAMMATIC TRAVEL DURING TENURE
   N/A
(10) SCIENTIFIC SEMINARS, MEETINGS, AND/OR CONSULTATIONS

(1) National Meetings:
Wound Repair, Gordon Research Conference, June 1993, New London, NH
13th Annual Meeting of the Bioelectrical Repair and Growth Society (BRAGS), October 1993, Dana Point, CA
Galveston Conference on Burn Resuscitation, November 21-23, Galveston, TX
26th annual meeting of the American Burn Association, April 1994, Orlando, FL
27th annual meeting of the American Burn Association, Annual Meeting, April 1995, Albuquerque, NM
5th Annual Wound Healing Society Meeting, Minneapolis, MN, April 1995

(2) International Meetings:
New Approach in Wound Healing, Scientific Conference, December 18-21, 1993, Pushchino, Russia
9th Congress of the International Society for Burn Injuries, June 1994, Paris, France
6th Congress of European Burn Association, September 1995, Verona, Italy

(3) Seminars
University of Texas at Austin, Bioengineering Department, August 1992
US Army Institute of Surgical Research, Saturday Seminars, 1992-1995
City Trauma Conference, San Antonio, Quarterly, 1994-1995
University of Texas at San Antonio, Health Science Center, Biochemistry and Microbiology Dept., through 1992-1995
(11) SEMINARS OR LECTURES DELIVERED AT UNIVERSITIES AND/OR INSTITUTES

Pushchino State University, December 22, 1993
US Army Institute of Surgical Research, May 6, 1995

(12) MEETINGS ATTENDED BY SPECIFIC INVITATIONS

New Approach in Wound Healing, Scientific Conference, December 1993, Pushchino, Russia

(13) TEACHING, IF ANY, AS AN ASSOCIATE

N/A

(14) WORK IN PROGRESS

MRI study of the effect of silver nylon dressings and direct current on metabolic activity in the burn wound.

(15) SUMMARY OF RESEARCH DURING TENURE

Effect of application of weak direct electric current through silver nylon wound dressing on plasma extravasation in partial and full thickness scald burn wounds in rats have been studied. Fluorescent tracers FITC-albumin and Rhodamine-albumin were used to estimate quantitatively plasma volume and plasma protein concentration in wound tissue. We have used fluorometry and confocal fluorescence microscopy to measure fluorescence intensity signals in plasma and tissue. It was shown that direct current reduces plasma volume loss and decreases protein extravasation in burn wounds after the injury, reduces edema accumulation and induces reabsorption of edema fluid and plasma proteins from interstitium.

(16) PUBLICATIONS AND PAPERS RESULTING FROM RESEARCH AS AN ASSOCIATE

(1) Matylevich NP, McManus AT, Mason AD Jr, Pruitt BA Jr: Direct current treatment reduces plasma volume loss following


(6) Chu CS, McManus AT, Matylevich NP, Mason AD Jr, Pruitt BA Jr: Survival of Dermal allografts in composite (auto/allo) with partial thickness autografts using silver-nylon dressings and direct current. Presented at the 9th Congress of the


(13) Chu CS, McManus AT, Matylevich NP, Mason AD Jr, Pruitt BA Jr: Reduction of dermal ischemia and maintenance of hair


(17) PATENTS APPLIED FOR AS A RESULT OF RESEARCH AS AN ASSOCIATE N/A

(18) CURRENT FORWARDING ADDRESS
4031 Thousand Oaks Dr.
Apt. 312
San Antonio, TX 78217

(19) APPRAISAL OF THE ASSOCIATESHIP PROGRAMS
I found this program extremely useful and helpful for my professional growth, including experience as research investigator, communication skills, professional contacts, experience in participation in scientific conferences and discussions. US Army Institute of Surgical Research provides great opportunity for basic research in cell and tissue biology as well as in applied medical studies.

[Signature]
Final Report

(1) Date: March 20, 1996

(2) Name: M. Steven Oberste, Ph.D.

(3) Name and location of laboratory or center: Virology Division, US Army Medical Research Institute of Infectious Diseases, USAMRDC, Ft. Detrick, Frederick, MD.


(5) Title of research project: Development of candidate vaccines for enzootic strains of Venezuelan equine encephalitis (VEE) virus

(6) Research advisor: Jonathan F. Smith, Ph.D.

(7) Are you on leave from a professional post? N/A

(8) International posts held during tenure: N/A

(9) Programmatic travel during tenure: N/A

(10) Scientific seminars, meetings, or consultations:
    a. 43rd annual meeting, American Society of Tropical Medicine and Hygiene, Cincinnatti, OH, Nov. 13-17, 1994
    c. 44th annual meeting, American Society of Tropical Medicine and Hygiene, San Antonio, TX, Nov. 17-21, 1995.

(11) Seminars or lectures delivered at universities and/or institutes:
     Centers for Disease Control and Prevention, Aug. 25, 1995.

(12) Meetings attended by specific invitation: N/A

(13) Teaching, if any, as an Associate: N/A

(14) Work in progress:
     Three VEE IAB-IE chimeric viruses have been constructed by recombinant DNA techniques. The first of these is somewhat attenuated in virulence for mice, but it protects mice against subsequent lethal challenge with VEE IE. Additional animal work is in progress with this and the remaining two chimeric viruses. Others in the lab will continue my work by constructing additional chimeric viruses with which to map the viral determinants of differential animal virulence.
and mosquito vector competence. Subgenomic cDNA clones have been constructed to be used to construct a full-length VEE IE infectious clone. A mutant gene cassette with which to construct attenuated viruses has also been cloned. Studies on VEE sequence diversity are being completed, using the ns3 and PE2 coding regions to characterize VEE viruses both within a given serotype and among distantly related VEE strains.

(15) Summary of research during tenure: The complete sequence of Venezuelan equine encephalitis (VEE) virus subtype IE was determined. Sequence analysis showed that the nsP3 protein contains four conserved domains within a region which is generally hypervariable among alphaviruses. Preliminary animal studies using chimeric viruses, which express one or more VEE IE structural proteins in the context of VEE IAB, suggest that this approach may be useful in developing a live-attenuated VEE IE vaccine. Further sequencing studies have shown that at least three of the four conserved domains are maintained in all VEE strains. Partial sequencing of the structural genes of prototype and sample isolates (approximately 70 isolates) was used to identify VEE strains which were the cause of recent outbreaks in Mexico, Peru, Panama, Colombia, and Venezuela.

(16) Publications and papers resulting from research as an Associate:
(e) Oberste, M.S., S.C. Weaver, D.M. Watts, and J.F. Smith. Genetic identification of Panama-genotype Venezuelan equine encephalitis virus subtype ID in Peru: The first occurrence of the Panama genotype outside of the Republic of Panama. (manuscript in preparation).
(f) Oberste, M.S., S. Schmura, S.C. Weaver, and J.F. Smith. Genetic diversity among spatially and temporally separated isolates of Venezuelan equine encephalitis subtype IE. (manuscript in preparation).
(g) Oberste, M.S., S. Schmura, and J.F. Smith. Sequence conservation within the hypervariable C-terminal half of alphavirus nsP3 defines potential functional domains. (manuscript in preparation).

(17) Patents applied for as a result of research as an Associate: N/A
Future position and address or current forwarding address:
Research Microbiologist, GS-13, Respiratory and Enteric Viruses Branch,
Division of Viral and Rickettsial Diseases, National Center for Infectious
Diseases, Centers for Disease Control and Prevention, Mailstop G17, Atlanta,
GA 30333.
Home mailing address, as of 3/30/96: PO Box 95181, Atlanta, GA 30347.

Appraisal of the Associateship programs:
My two years as a Senior Associate have been very rewarding, both personally
and professionally. I have had the opportunity to be part of an exciting research
program and to develop research, managerial, and interpersonal skills which will
be invaluable throughout the rest of my career.
FINAL REPORT FORMAT

(1) Date March 6, 1996

(2) NAME Christopher Onyemaechi OUNJI Ph.D

(3) NAME AND LOCATION OF LABORATORY OR CENTER
Walter Reed Army Institute of Research, Washington DC

(4) DATES OF TENURE March 15, 1993 to March 14, 1996

(5) TITLE OF RESEARCH PROJECT: Antileishmanial Agents Based on Isolates from plants used in Traditional Medicine.

(6) RESEARCH ADVISER'S NAME Dr. Joan E. Jackson

(7) ARE YOU ON LEAVE FROM A PROFESSIONAL POST?
If so, list position or title and address of facilities
Senior Lecturer, University of Nigeria, Nsukka, Nigeria.

(8) INTERNATIONAL POSTS HELD DURING TENURE:
Secretary/Treasurer Bioresources Development and Conservation Program International (Non-profit Organization)

(9) PROGRAMMATIC TRAVEL DURING TENURE
List location(s) and date(s) N/A

(10) SCIENTIFIC SEMINARS, MEETINGS AND/OR CONSULTATIONS
List location(s) and date(s). List foreign meetings separately
Drug Discovery and Commercial Opportunities in Medicinal plants September 19-20, The Ritz Carlton, Pentagon City, Arlington, VA

National Institute of Allergy and Infectious Diseases (NIAID) International Centers for Tropical Diseases Research, Second Annual Meeting, April 28-30, 1993

National Institute of Allergy and Infectious Diseases (NIAID) International Centers for Tropical Diseases Research, Third Annual Meeting, April 27-29, 1994

National Institute of Allergy and Infectious Diseases (NIAID) International Centers for Tropical Diseases Research, Fourth Annual Meeting, April 26-28, 1995

HPLC Forum '95 Seminar, Mariot Hotel, Bethesda Maryland, May 15, 1995

Foreign meetings


Bioresources Development and Conservation Programme Second International Congress on the Utilization of Tropical Plants and Biodiversity Conservation Douala Cameroon, October 23-27, 1995

(11) SEMINARS OR LECTURES DELIVERED AT UNIVERSITIES AND/OR INSTITUTES. List location(s) and date(s)
Division of Experimental Therapeutics Chembio meeting - Screening Nigerian Medicinal Plants for Antileishmanial Activity 1994 Forest Glen, 1994

(12) MEETINGS ATTENDED BY SPECIFIC INVITATION
List location(s) and date(s)

American Chemical Society Meeting Chicago, Illinois August 20-25, 1995

Bioresources Development and Conservation Programme Second International Congress on the Utilization of Tropical Plants and Biodiversity Conservation Douala Cameroon, October 23-27, 1995

(13) TEACHING, IF ANY, AS AN ASSOCIATE N/A

(14) WORK IN PROGRESS.
Two pending patent applications  
Structural elucidation of some antileishmanial compounds

(15) SUMMARY OF RESEARCH DURING TENURE

Evaluation of the antileishmanial activity of 110 extracts representing 40 plants species implicated in traditional medicine enabled the identification of new antileishmanial chemotypes that proved highly active and are radically different from the existing drugs. A new bioassay technique was also developed. About 39% of the extracts possess significant in vitro antileishmanial activity compared to pentavalent antimonials. Bioassay-directed fractionation of active extracts using a combination of chromatographic techniques yielded lead compounds, from which ten chemically novel antileishmanial compounds were selected based on their chemical class and lack of known toxicity. These findings clearly demonstrate that medicinal plants hold high promise for the development of new antileishmanial drugs.

(16) PUBLICATIONS AND PAPERS RESULTING FROM RESEARCH AS AN ASSOCIATE


Okunji C.O., Jackson J.E., Tally J.D. and Iwu M.M., Cytosensor Microphysiometer System (CMS): A New Method of Screening Medicinal Plants for Antileishmanial Activity being an invited paper delivered at the IOCD International Symposium; Chemistry, Biological and Pharmacological Properties of African Medicinal

(17) PATENTS APPLIED FOR AS A RESULT OF RESEARCH AS AN ASSOCIATE
    - in draft

(18) FUTURE POSITION AND ADDRESS OR CURRENT FORWARDING ADDRESS

    Senior Research Associate,
    Division of Experimental Therapeutics,
    Walter Reed Army Institute of Research,
    Washington DC 20305-5100.

(19) APPRAISAL OF THE ASSOCIATESHIP PROGRAMS

    The project has been a phenomenal success in identifying
    new antileishmanial chemotypes as potential leads in the area
    where there has been no effective therapy. Because such leads have
    a lengthy history of human use, unacceptable toxicity would not be
    expected. The data on the in vitro and in vivo studies are
    significant especially to encourage further investigation.

    This program has offered us the opportunity of working as
    a team in the advancement of knowledge and research in the area of
    antileishmanial drugs from natural products. Although leishmaniasis
    is regarded as a major tropical disease affecting humankind, work
    in this direction has been of low priority due to limited
    market/investment profit. This important scientific contribution
    could not have been possible without the NRC program.

    The NRC program is an excellent program full of vision and
    foresight. I personally enjoyed the company of your staff, the
    interaction was cordial. You have the right calibre of scientific
    and administrative staff to administer this program. May I use
    this opportunity to express my appreciation to all of you managing
    this program. The program has been meaningful, exiting and
    rewarding. The experience gain during the tenure will obviously
    constitute an indispensable part of my career. However, arrangement
    with National Academies Travel concerning travels should be
    seriously reviewed.
In an effort to identify the ischemic "penumbra," the viable (and potentially salvagable) but compromised area of neuronal tissue circumscribing the core infarct, I have examined the distribution of markers of cellular viability (beta-actin and c-fos mRNA) in infarcted rat brains using the in situ hybridization technique. Rats received 2 hr of intraluminal middle cerebral artery occlusion and either 4 or 24 hr of reperfusion. In comparison to the contralateral hemisphere, infarcted brain regions exhibited only very low levels of beta-actin or c-fos mRNA. However, the ischemic penumbra exhibited consistently elevated c-fos mRNA at 4 hr, and elevated beta-actin mRNA at 24 hr. The elevated expression of beta-actin gene in the ischemic penumbra may represent a compensatory state of neuronal function following ischemic insults.
16: PUBLICATIONS AND PAPERS RESULTING FROM RESEARCH AS AN ASSOCIATE


17: PATENTS APPLIED FOR AS A RESULT OF RESEARCH AS AN ASSOCIATE
None

18: FUTURE POSITION AND ADDRESS OR CURRENT FORWARDING ADDRESS
Current forwarding address is:
James P. Ray
2445 Lyttonsville Rd., Apt. 402
Silver Spring, MD 20910

20: APPRAISAL OF THE ASSOCIATESHIP PROGRAM
The Associateship Programs serve a vital purpose, to support scholars doing critical research, and they do this very well
1. 6-4-1996

2. Paul F. Reid

3. Toxinology Department, USAMRIID, Fort Detrick, Frederick, MD 21702

4. 6-23-1993 to 6-23-1996

5. Cloning and expression of Dendrotoxins

6. Dr. Leonard A. Smith

7. N/A

8. None

9. N/A

    "Current topics in gene expression systems", San Diego, October 23-25 1994
    "5th International Society on Toxinology", Frederick, July 30-4 August 1995.

11. Work in progress seminars given annually at USAMRIID


13. Trained four military technicians to assist in projects.

14. Currently engaged in expression of Dendrotoxin mutants in order to complete additional experiments not possible prior to this time.
    Creating new mutant toxins by site-directed mutagenesis in an attempt to convert a mamba trypsin inhibitor to a ion channel blocker. Also investigating the possibility of testing the mamba trypsin inhibitor in the prevention of HIV replication. Subcloning other venom genes into the yeast vector, pPic9K, to test expression in yeast. It is
also planned to screen mouse T-cell library to isolate serum immune repressor genes whose protein sequence have some homology to short chain neurotoxins.

15. Forty mutant clones derived from dendrotoxins K and I had been constructed. These mutants were incorporated into a protein expression system as a fusion protein coupled to maltose binding protein. It was my function to solve the expression and purification problems which existed and isolate these mutant toxins. To this end protocols for expression and affinity purification were developed and a final chromatographic procedure was incorporated. Purified mutants were examined by polyacrylamide electrophoresis and N-terminal sequencing before being sent to a laboratory in England for analysis in binding assays. On receipt of binding data, new mutant toxins were designed and created permitting further investigation of toxin structure/function relationships.


17. none

18. Current address: 4610 Reels Mill road, Frederick, MD 21704

19. This program has been of tremendous benefit to post-doctoral people such as myself. It has presented me with the opportunity to work in a modern environment that would not have been possible elsewhere. Through
this position I have greatly expanded my knowledge of snake venoms and their future therapeutic potentials in the field of neurochemistry and in general medicine overall. Through your travel allowance scheme, my attendance of several meetings has given me exposure to experts in related fields which has been useful to us in the laboratory. My only grievance would be that the NRC do not allow their research fellows to attend workshop seminars which would allow them to acquire experience in the latest techniques. Over the course of two or more years new techniques arise and having these skills should aid progress in the laboratory. Aside from that, I consider myself fortunate to have participated in this programme. At this point, I would like to express my gratitude and wish you continuing success.
Final Report for National Research Council Associateship Program

1) September 23, 1996
2) Dr. Allen K. Sample
3) USAMRIID, Ft. Detrick, Maryland
4) October 4, 1994 to July 17, 1996
5) Role of YpkA protein kinase in the pathogenicity of Yersinia pestis.
6) Col. Arthur Friedlander
7) No
8) None
9) None
10) 95th ASM General meeting (Washington DC) May 1995
Chemotactic Cytokines (Philadelphia, PA) October 1995
96th ASM General Meeting (New Orleans, LA) May 19-22, 1996
11) None
12) None
13) None
14) None
15) I cloned the gene encoding the protein kinase from Yersinia pestis and expressed the protein in Escherichia coli. Antibody raised against the purified recombinant protein was used to detect kinase expression in Y. pestis and Y. pseudotuberculosis. In contrast to the literature, I demonstrated that the kinase was not secreted but was completely cell associated in both species. The entire gene was sequenced and showed little divergence from the published sequence of Y. pseudotuberculosis. Immunization of mice with purified recombinant protein kinase did not afford significant protection against challenge with wild-type Y. pestis.
16) Plasminogen Activator Protease of Yersinia pestis degrades proinflammatory cytokines
Allen K. Sample and Arthur M. Friedlander (Manuscript in preparation)
17) None
18) Manufacturing Scientist, IDEXX Labs, One IDEXX Drive, Westbrook, ME 04092
19) The Associateship Program gave me the opportunity to move out of the area of academic research and into a more applied industrial-type research. This undoubtedly was a major factor in obtaining my current position at IDEXX laboratories.
National Research Council Associateship Program
Final report

(1) Date 7 May, 1996

(2) Name Katherine Ann Schmidt

(3) Name and Location of Laboratory:
Walter Reed Army Institute of Research
Department of Bacterial Diseases
Bldg 40, Room 2085
Washington DC 20307-5100


(5) Title of Research Project: Neisseria gonorrhoeae opacity protein expression during infection in human male volunteers.

(6) Research Adviser: Carolyn Deal, Ph.D., Herman Schneider, Ph.D.

(7) Are you on leave from a professional post? no

(8) International posts held during tenure: none

(9) Programmatic travel during tenure:
USAMRIID, Ft. Detrich, Frederick MD. May 1994, Infectivity study
Kimbrough Hospital, Ft. Meade, MD. May 1995, Infectivity study

(10) Scientific Seminars, Meetings and other Consultations:
March 1994: Vaccine Conference, Alexandria VA.
May 1994: American Society for Microbiology, General Meeting, Las Vegas NV.
May 1995: American Society for Microbiology, General Meeting, Washington DC.
October 1995: IBC International Conference on Mucosal Immunization, Rockville MD.
May 1996: American Society for Microbiology, General Meeting, New Orleans, LA.
International meetings:
September 1994: Neisseria 94, Winchester, England

(11) Seminars or Lectures delivered at Universities and/or Institutes:

(12) Meetings attended by specific invitation: NA

(13) Teaching, if any, as an assistant: Mentor, SEAP program, summer 1993, 1994, 1995

(14) Work in progress: I am continuing study of the opacity protein of Neisseria gonorrhoeae.

(15) Summary of research during tenure:
I participated in 4 human volunteer infectivity studies, and analyzed N. gonorrhoeae recovered from infected volunteers for opacity protein content: size, and N-terminal sequence. When it became evident that no specific opacity protein was required for human infection, I redirected my studies towards identifying critical common epitopes in the opacity proteins. I showed that an oligopeptide homologous to COOH-terminal outer loop region of opacity protein was recognized by antibodies in the serum of an uninfected volunteer. Specific rabbit polyclonal and mouse monoclonal antibodies are currently being used to screen a panel of gonococcal isolates for the peptide.

(16) Publications and papers resulting from research as an associate:
Refereed Manuscripts:
Wylie, J. C. Sadoff, C. D. Deal, and A. S. Cross. 1996 Sialylation lessens the infectivity
of Neisseria gonorrhoeae MS11mkC. J. Infect. Dis. 173 In Press.
proteins expressed by strains recovered from volunteers infected with transparent
Skillman, C.-H. Zhou, J. W. Boslego, and H. Schneider. Differential antibody and
cytokine responses in male volunteers infected with Neisseria gonorrhoeae MS11mkC.
In preparation.
activity in urine of volunteers infected experimentally with Neisseria gonorrhoeae. In
preparation.

Abstracts and Presentations
1994. Relationship of the onset of symptoms and dysuria to opacity protein (protein
M. Feavers, ed., Neisseria 94: Proceedings of the Ninth International Pathogenic
Neisseria Conference, Winchester, UK.
A. S. Cross, and H. Schneider. 1995. Sialylation of lipooligosaccharide by CMP-NANA
does not enhance infectivity of Neisseria gonorrhoeae in a human male volunteer trial.
B173. American Society for Microbiology General Meeting, Washington DC.
Schneider, and J. W. Boslego. 1995. Antibody and cytokine production in human male
volunteers infected with Neisseria gonorrhoea. Eighth International Congress of
Mucosal Immunity. San Diego, CA.
gonorrhea infections in male volunteers? B312. American Society for Microbiology
General Meeting, New Orleans, LA.

(17) Patents applied for as a result of research as an associate: none

(18) Future position and address or current forwarding address:
contract employee, WRAIR, Dept. Bacterial Diseases, Washington DC
forwarding address: 9114 Piney Branch Road, Apt 202, Silver Spring MD 20903.

(19) Appraisal of the associateship programs:
The NRC fellowship program provided me with the opportunity to make the
transition from student to scientist. The program made it possible for me to meet many
of the other scientists involved in the field of STD research. Since my goals are to
continue in research, with limited teaching and mentoring, the program was ideal for
me.

However, the program might be improved by adding a teacher-track option: where
an NRC fellow could do research under an approved mentor at a participating university,
with a limited course-load (for example: no more than 1 course per semester, or 10
credit-hours per year). The teacher-track option would allow a young scientist to gain
experience teaching, while preventing the usual course overload most part time and even
tenure-track instructors face. It would make participants more competitive in the
limited job market: many of the universities, and even small colleges place a priority on
teaching experience.
1. Date:
   November 27, 1995

2. Name:
   Ashok Kumar Srivastava, DM, DTM, Ph.D.

3. Name and location of laboratory or center:
   Department of Virus Diseases
   Division of Communicable Diseases and Immunology
   Walter Reed Army Institute of Research, Washington DC

4. Dates of tenure:

5. Title of research project:
   Development of recombinant vaccine for dengue viruses.

6. Research advisor's name:
   Col. Charles H. Hoke, Jr. and Dr. J. Robert Putnak.

7. Are you on leave from a professional post:
   None

8. International post held during tenure:
   None

9. Programmatic travel during tenure:
   None
10. **Scientific seminars, meetings, and/or consultation:**


11. **Seminar or lectures delivered at Universities and/or institutes:**


12. **Meetings attended by specific invitation:**

None
13. Teaching, if any as an associate:

None

14. Work in progress:

1. Evaluation of dengue virus 1, 3 and 4 serotypes recombinant vaccine in monkeys.
2. Immunization of mice with dengue virus type-2 E and NS1 recombinant protein made in baculovirus.

15. Summary of research during tenure:

Srivastava A.K.: Dengue vaccine made in *Escherichia coli*.

A recombinant fusion protein encoding the C-terminus of structural envelope glycoprotein (E) and the N-terminus of non-structural protein (NS-1) of dengue-2 virus (DEN-2) was expressed in *Escherichia coli*, purified and characterized. This fusion protein was reactive with anti-DEN-2 polyclonal sera and monoclonal antibodies which recognize a linear epitope in E. The purified fusion protein was injected into mice subcutaneously. The immunized mice made anti-DEN-2 antibodies measured by the hemagglutination-inhibition (HAI) and neutralization (N) tests, and were protected against lethal challenge with DEN-2 virus administered by intracerebral inoculation. In a separate experiment, a group of Rhesus monkeys were immunized subcutaneously with three different concentration of fusion protein. The monkeys immunized with the higher concentration of protein (100 μg/dose) showed significant N and ELISA antibody titers 2 weeks after the second booster.

16. Publications and papers resulting from research as associate:


17. Patent applied for as a result of research as associate:

1. Filed to the Office of Patent Trademarks, Washington DC.

18. **Future position and address or current forwarding address:**

Head  
Viral Vaccine Production  
Department of Biologics Research  
Division of Communicable disease and Immunology, Building 40. Room Number 2053  
Walter Reed Army Institute of Research, Washington DC  
TEL:202-782-7019, TEL:301-427-6609; Fax:202-782-0442

19. **Appraisal of the associate programs:**

1. The young scientist should be given more chance for such fellowship.

2. NRC Associate program lacks the critical significance such as:

   .Lack of communication between NRC and fellows.

   .NRC does not care much about their fellows related to their progress in science.

   .NRC Associates are not entitled to obtain an Invention Award Money. Although the data have been generated from the original research proposal of an associate and evaluated as a novel finding, and then submitted as an Invention Disclosure followed by filing the patent application.

   .NRC does not provide any kind of document/certificate stating the tenure as associate.

3. NRC is requested to consider these comments carefully.
1/ DATE: 8/9/96

2/ NAME AND ID NUMBER: Janos Szebenni, 929212

3/ NAME AND LOCATION OF LABORATORY CENTER: Lab. Membrane Biochemistry, Walter Reed Army Institute of Research.

4/ DATES OF TENURE: 7/9/94-8/9/96

5/ TITLE OF RESEARCH PROJECT: The influence of hemoglobin-containing liposomes on the immune system

6/ RESEARCH ADVISER'S NAME: COL. Carl. R. Alving

7/ ARE YOU ON LEAVE FROM A PROFESSIONAL POST? no

8/ INTERNATIONAL POSTS HELD DURING TENURE: N/A

9/ PROGRAMMATIC TRAVEL DURING TENURE: N/A

10/ SCIENTIFIC SEMINARS, MEETINGS, AND/OR CONSULTATIONS:

Liposomes in Drug Delivery: The Nineties and Beyond. CDDR, School of Pharmacy, London University, London, Dec. 13-17, 1993

XI Congress of the International Society for Artificial Cells, Blood Substitutes and Immobilization Biotechnology, Boston, July 24-27, 1994

4) Complement activation by liposome-encapsulated hemoglobin (poster) Janos Szébeni, Nabila Wassef, Helmut H. Spielberg, Alan S. Rudolph and Carl R. Alving

5) The interaction of liposome-encapsulated hemoglobin with blood components: complement activation (invited lecture)

6) Complement activation by liposome-encapsulated hemoglobin (invited lecture)
Second annual Conference on "Current Issues in Blood Substitute Research -1995"
San Diego, March 30-April 1, 1995

1st World Meeting on Pharmaceutics, Biopharmaceutics and Pharmaceutical Technology
Budapest, May 9-11, 1995

The 9th International Congress of Immunology, San Francisco, 23-29 July, 1995

9) Complement activation in human serum by the red blood cell substitute, liposome-encapsulated hemoglobin. The roles of natural anti-phospholipid antibodies and of vesicle properties. (poster)
10) The interaction of liposome-encapsulated hemoglobin with human complement. (invited lecture) 
Janos Szébeni, Nabila M. Wassef, Alan S. Rudolph and Carl R. Alving 
The 6th International Symposium on Blood Substitutes, Montreal, 4-7, August, 1996

11/ SEMINARS OR LECTURES DELIVERED AT UNIVERSITIES AND/OR INSTITUTES:

N/A

12/ MEETINGS ATTENDED BY SPECIFIC INVITATION: Navy Review of the LEH Project, 
Bethesda, August 94

13/ TEACHING, IF ANY, AS AN ASSOCIATE:

No

14/ WORK IN PROGRESS:

Completion of 2-3 unfinished manuscripts

15/ SUMMARY OF RESEARCH DURING TENURE:

We have demonstrated the presence, and analyzed the mechanism of an adverse immune effect of liposome-encapsulated hemoglobin (LEH), which is currently being developed as an oxygen carrying blood substitute. The effect in question is complement (C) activation, a nonspecific inflammatory reaction of the immune system arising upon the exposure of foreign materials to the blood. The reaction results in increased elimination of activating particles along with numerous cardiovascular and hematological abnormalities. We have studied LEH-induced C activation in rats in vivo, and in rat and human serum, in vitro. It has been established that activation of C in rats proceeds through the alternative pathway, whereas in human serum it can proceed through both the classical and the alternative pathways. In human serum the reaction is mediated, in part, by naturally occurring anti-phospholipid antibodies displaying specific reactivity with LEH. Importantly, we have shown that the reaction can be effectively inhibited with soluble C receptor type 1 (sCR1), a recombinant, truncated form of the natural C inhibitor, CR1. Considering that C activation plays a key role in
the adverse consequences of polytrauma and/or hemorrhagic shock, particularly in the development of adult respiratory distress syndrome, demonstration of potential C activation by LEH and an efficient way to prevent it represents a significant progress in this research area.

16/ PUBLICATIONS AND PAPERS RESULTING FROM RESEARCH AS AN ASSOCIATE:

1) Complement activation in rats by liposomes and liposome-encapsulated hemoglobin: evidence for anti-lipid antibodies and alternative pathway activation.
   Janos Szabeni, Nabila M. Wassef, Helmut Spielberg, Alan S. Rudolph and Carl R. Alving

2) Complement activation by liposome-encapsulated hemoglobin in vitro: the role of endotoxin contamination.
   Janos Szabeni, Nabila M. Wassef, Alan S. Rudolph and Carl R. Alving

3) Complement activation in vitro by the red blood cell substitute, liposome-encapsulated hemoglobin: Mechanism of activation and inhibition by soluble complement receptor type 1.
   Transfusion, In press

   Janos Szabeni, Nabila M. Wassef, Alan S. Rudolph and Carl R. Alving
   Biophyrm Acta, Submitted for publication.

5) Complement activation and thromboxane secretion by liposome-encapsulated hemoglobin in rats in vivo: Inhibition by soluble complement receptor type 1.

17/ PATENTS APPLIED FOR AS A RESULT FROM RESEARCH AS AN ASSOCIATE:
   N/A
18/ FUTURE POSITION AND ADDRESS OR CURRENT FORWARDING ADDRESS:

According to plans I will be working at the National Institute of Hematology and Immunology in Budapest, at the following address:

Dr. Szebeni Janos  
Bone Marrow Transplantation Unit  
National Institute of Hematology and Immunology  
Budapest  
1502 Budapest Pf. 44., Hungary  
phone: 36-1-209-2311, fax: 36-1-209-2311

19/ APPRAISAL OF THE ASSOCIATESHIP PROGRAMS:

I am sincerely grateful for the opportunity provided by the NRC award I had the fortune to hold, for allowing me to pursue productive research without distraction. The program is excellently organized, the contact persons are nice and helpful, and my award has been generous in benefits in professional, as well as in financial matters.
FINAL REPORT

1. Date May 14, 1996
2. Name Surang Triteeraprapab
3. Laboratory DSD, USAMRIID, Ft. Detrick, Frederick, MD 21702-5011
4. Date of Tenure March 6, 1995 - June 14, 1996
5. Title of Research Project
   Molecular basis of dengue virus-2 S16803 attenuation after serial
   passage in primary dog kidney cells
6. Research advisor’s name Lieutenant Colonel Erik A. Henchal
7. I am on leave from a professional post.
   Faculty: Instructor and Physician
   Department of Parasitology
   Faculty of Medicine
   Chulalongkorn University
   Bangkok 10330, Thailand
   Telephone: (662)-252-5-944
8. International posts held during tenure
   Same as above (7.)
9. Programmatic travel during tenure
   N/A
10. Scientific seminars, meetings, and/or consultations
   10.1 The IVth International Congress on Positive Strand RNA
       Viruses held in Utrecht, the Netherlands during May 25-30, 1995.
   10.2 The 7th International Congress for Infectious Diseases to be
       held in Hong Kong during June 10-13, 1995.
11. Seminars or lectures delivered at universities and/or institutes
    N/A
12. Meetings attended by specific invitation
    N/A
13. Teaching, if any, as an associate
    N/A
14. Work in progress

Vaccinia virus/T7 RNA polymerase transient-expression system
and radio-immunoprecipitation assays were used to compare the levels
of expressed C-PrM/M proteins among D2NT57C (wild type clone),
D2NT57G, D2NT57A, and D2NT57T (attenuated clone) recombinants,
that contained dengue virus-2 5'UTR/C/PrM/M gene fragment with C,
G, A and T at nt57, respectively. At 24 hour-post infection, after 2-, 4-, 8-
and 12-hour labeling, the expression levels of D2NT57G were 45%,
96%, 74% and 45% of that of D2NT57C, respectively, and the expression
levels of D2NT57A were 44%, 43%, 66% and 64% of that of D2NT57C,
respectively. Interestingly, the lowest levels of expressed protein were
obtained from D2NT57T (attenuated clone), which were 29%, 39%, 29%
and 25% of that from D2NT57C, respectively.
To further confirm whether the point mutation at nt57 in the 5'UTR is important for the protein expression. We constructed the four recombinants containing 96-bp 5'UTR (with C, G, A or T at nt57) fused to luciferase gene of the pGEM-luc plasmid. The recombinant plasmid was named C-Luc, G-Luc, A-luc or T-luc, respectively. The levels of luciferase expression were compared among four constructs using vaccinia/SP6 polymerase transient-expression system and luciferase assays. At 3, 5, 8, 12, 24 and 48 hours post-transfection, G-Luc and A-Luc expressed luciferase at the similar level as C-Luc. The expression of C-Luc was significantly higher than that of T-Luc at all time points. All the recombinants expressed luciferase at the highest level at 24 hours post-transfection.

The Northern and dot (RNA) blots were performed to evaluate the transcription messages of D2NT57C, D2NT57G, D2NT57A, and D2NT57T using vaccinia virus/T7 RNA polymerase transient-expression system. There was no significant difference of levels of RNA expression from four recombinants at 3, 5, 8, 12, 24 and 48 hours post-transfection.

These data are consistent with the hypothesis that point mutation at nt57 from C to U reduces the protein expression at the translational level.

15. **Summary of research during tenure (100 words)**
Attenuated dengue virus-2 S16803 (PDK50) contained a point mutation, nt57 (C to U), that may disrupt the 5'UTR stem-loop structure, which is conserved and important for transcription and translation in other positive RNA viruses. We used a vaccinia/T7 RNA polymerase transient-expression system, radio-immunoprecipitation, Northern and dot (RNA) blots to show that this mutation reduced the dengue protein expression. Data from luciferase reporter system confirmed that the mutation effected protein translation. These data provide the basic knowledge of molecular basis of dengue virus attenuation that may help to generate safe and effective vaccines for other flaviviruses.

16. **Publications and papers resulting from research as an associate**
Molecular basis of dengue virus-2 S16803 attenuation after serial passage in primary dog kidney cells. (in preparation)

17. **Patents applied for as a result of research as an associate**
N/A
18. Future position and address or current forwarding address
   Faculty: Instructor and Physician

   Before December 15, 1996, please send mail to:
   Surang Triteeraprapab
   1107A, Donnington Circle,
   Towson, MD 21204

   After December 15, 1996, please send mail to:
   Dr. Surang Triteeraprapab
   Department of Parasitology
   Faculty of Medicine
   Chulalongkorn University
   Bangkok 10330, Thailand

19. Appraisal of the associateship programs
   The associateship programs consist of exemplary programs that
   provide opportunities for talented researchers to perform their
   researches on interesting problems in the distinguished institutes. The
   program help me to gain more experience in doing research under the
   superb guidance of talented scientists. During the tenure, I also have
   opportunities to attend scientific meetings, where I can discuss and
   exchange knowledge with other renowned scientists in various fields.
   This will definitely enhance the future collaborations between
   laboratories.

   I myself deeply appreciate my advisor, Dr. Erik Henschal, for his
   guidance, confidence, patience and support during this project. His
   insight and constructive criticism have made this project a rich and
   rewarding experience. I am thankful to Dr. Connie Schmaljohn and Dr.
   Kevin Anderson for the constructive criticism.

   I would like to thank Dr. Carol Linden, Dr. Judith Nyquist,
   Suzanne Polo and Debbie Daugherty for their kindness and helping me
   with the administrative problems.
1) Date: 28 March 1996

2) Name and ID Number: Jefferson Archer Vaughan, (idnumber 938912)

3) Laboratory: USAMRIID
Diagnostic Systems Division
Fort Detrick
Frederick, MD 21702

4) Dates of Tenure: 3 January 1994 to 3 April 1996

5) Title of Research Project: Filaria-mediated enhancement of arboviral transmission

6) Research Advisor: Michael J. Turell, Ph.D.

7) Are you on leave from a professional post? NO

8) International posts held during tenure: N/A

9) Programmatic travel during tenure: N/A

10) Scientific seminars, meetings and/or consultations:

1. 13-17 November 1994
   43rd Annual Meeting of American Society of Tropical Medicine & Hygiene
   Cincinnati, OH

2. 15-23 March 1995
   61st Annual Meeting of American Mosquito Control Association
   Portland, OR

3. 17-21 November 1995
   44th Annual Meeting of American Society of Tropical Medicine & Hygiene
   San Antonio, TX

4. 24-28 March 1996
   62nd Annual Meeting of American Mosquito Control Association
   Norfolk, VA
11) Seminars or lectures delivered at universities and/or institutes:

1. 21 March 1996  
   Heska, Corp.  
   Fort Collins, CO

2. 11 December 1995  
   USAMRIID  
   Fort Detrick, Frederick, MD

3. 3 February 1995  
   Johns Hopkins University  
   Baltimore, MD

4. 2 June 1994  
   Biting Fly Workshop  
   Easton, MD

5. 12 April 1994  
   Tropical Medicine Dinner Club  
   Baltimore, MD

12) Meetings attended by specific invitation: N/A

13) Teaching as an Associate:

   Guest lectures in Medical Entomology Course  
   Johns Hopkins University  
   Baltimore, MD

14) Work in progress: Planned computer simulation studies

15) Summary of research during tenure:

   Two groups of mosquito-borne parasites enhanced mosquito transmission of arboviruses. Microfilarial parasites enhanced viral transmission from vertebrate to vector (= mosquito acquisition) by disrupting mosquito midgut barriers to viral dissemination. Malaria sporozoites enhanced viral transmission from vector to vertebrate (= mosquito transmission) by disrupting salivary gland barriers to oral secretion of virus. Because of its greater epidemiological potential, parameters of microfilarial enhancement were further defined. Parameters included; species differences in the capacity of microfilariae to penetrate the mosquito midgut, the amount of virus passing into the mosquito hemocoel during microfilarial penetration, and the innate susceptibility of mosquitoes to hemocoelomically-introduced virus.
16) Publications and papers resulting from research as an Associate:


17) Patents applied for as a result of research as an Associate: N/A

18) Current forwarding address:

Jefferson A. Vaughan
605 West 39th Street
Baltimore, MD 21211

19) Appraisal of the Associateship Programs:

The NRC Associateship Programs was very useful to me for the following reasons: 1) provided me the opportunity to conduct research in one of the worlds' foremost arbovirology facility; 2) allowed me to expand my scientific network to include workers in military preventive medicine; 3) provided me the opportunity to gather sufficient data to apply for long-term (5 yr) NIH funding. The Program is good and I have been recommending it to both junior and mid-level scientists that are seeking new research experiences.

cc: Dr. Michael J. Turell, Research Advisor
    Dr. Carol D. Linden, Laboratory Program Representative
(1) DATE 22 AUGUST 1996

(2) NAME YONGQIANG WANG

(3) NAME AND LOCATION OF LABORATORY OR CENTER
DEPARTMENT OF MOLECULAR PATHOLOGY
WALTER REED ARMY INSTITUTE OF RESEARCH
WASHINGTON, DC 20307-5100

(4) DATES OF TENURE
14 JUNE 1993 TO 13 SEPTEMBER 1996

(5) TITLE OF RESEARCH PROJECT
STUDY OF CROSS REACTION BETWEEN NEURAL CELL ADHESION
MOLECULE (N-CAM) ON HUMAN NK CELLS AND CAPSULAR
POLYSACCHARIDE OF GROUP B MENINGOCOCCI
HETEROPOLYAINS DO NOT INDUCE P-GLYCOPROTEIN ASSOCIATED
WITH MULTIDRUG RESISTANCE IN HUMAN BREAST CANCER CELLS

(6) RESEARCH ADVISER’S NAME
DR. WENDELL D. ZOLLINGER
DR. MARTI JETT

(7) ARE YOU ON LEAVE FROM A PROFESSIONAL POST?
ASSISTANT RESEARCH PROFESSOR
CANCER INSTITUTE (HOSPITAL)
CHINESE ACADEMY OF MEDICAL SCIENCES
BEIJING 100021
P.R.CHINA

(8) INTERNATIONAL POSTS HELD DURING TENURE
N/A

(9) PROGRAMMATIC TRAVEL DURING TENURE
N/A
(10) SCIENTIFIC SEMINARS, MEETINGS, AND/OR CONSULATIONS
NEISSERIA 94, SEPTEMBER 1994, WINCHESTER, ENGLAND
THIRD ANNUAL VACCINES: NEW TECHNOLOGIES & APPLICATIONS,
MARCH 20-22, 1995, ALEXANDRIA, VIRGINIA.

(11) SEMINARS OR LECTURES DELIVERED AT UNIVERSITIES AND/OR
INSTITUTES
N/A

(12) MEETINGS ATTENDED BY SPECIFIC INVITATION
N/A

(13) TEACHING, IF ANY, AS AN ASSOCIATE
N/A

(14) WORK IN PROGRESS
TWO NEW ENZYME-LINKED IMMUNOSORBENT ASSAYS (ELISA)
THAT USE MONOCLONAL ANTIBODIES FOR DETECTION OF
LIPOPOLYSACCHARIDE AND OUTER MEMBRANE PROTEIN OF NEISSERIA
MENINGITIDIS HAVE BEEN ESTABLISHED.

    CELLS EXPRESSING THE EMBRYONIC FORMS OF N-CAM, SUCH AS NK
    CELLS AND ATT20 CELLS REACTED WITH MONOCLONAL ANTIBODIES TO
    GROUP B CAPSULAR POLYSACCHARIDE ON MENINGOCOCCI WAS
    OBSERVED BY INDIRECT IMMUNOFLOURESCENCE, DOT BLOT, WESTERN
    BLOT AND FLOW CYTOMETRY.

    A 170 kDa GLYCOPROTEIN WAS DETECTED FROM THE MCF/ADR
    (MULTIDRUG RESISTANCE) CELLS BUT NOT THE MCF/WT (DRUG
    SENSITIVE) CELLS AND HETEROPOLYANIONS (HPA) TREATED CELLS. HPA
    WHICH DO NOT INDUCE P-GLYCOPROTEIN ASSOCIATED MULTIDRUG
    RESISTANCE MAY BE A GROUP OF HIGH POTENTIAL COMPOUNDS IN
    HUMAN BREAST CANCER TREATMENT.
(15) SUMMARY OF RESEARCH DURING TENURE
A CROSS-REACTION BETWEEN NEURAL CELL ADHESION MOLECULE
(N-CAM) ON HUMAN NK CELLS AND CAPSULAR POLYSACCHARIDE OF
GROUP B MENINGOCOCCI WAS OBSERVED. CELLS EXPRESSING THE
EMBRYONIC FORMS OF N-CAM, SUCH AS NK CELLS AND ATT20 CELLS
REACTION WITH MONOCLONAL ANTIBODIES TO GROUP B CAPSULAR
POLYSACCHARIDE ON MENINGOCOCCI WAS OBSERVED BY INDIRECT
IMMUNOFLUORESCENCE, FLOW CYTOMETRY AND WESTERN BLOT
ANALYSIS.

MULTIDRUG-RESISTANCE (MDR) IS A MAJOR OBSTACLE TO BREAST
CANCER TREATMENT. HETEROPOLYANIONS (HPA) ARE FREE-RADICAL
SCAVENGERS AND SHOWED EXCELLENT ANTIPROLIFERATIVE EFFECTS
AND DO NOT INDUCE P-GLYCOPEPTIDE ASSOCIATED MULTIDRUG
RESISTANCE DETECTED BY MDR1 GENE PRODUCTS ON WESTERN BLOT
AND PCR ANALYSIS.

(16) PUBLICATIONS AND PAPERS RESULTING FROM RESEARCH AS AN
ASSOCIATE
IN PREPARATION

(17) PATENTS APPLIED FOR AS A RESULT OF RESEARCH AS AN
ASSOCIATE
N/A

(18) FUTURE POSITION AND ADDRESS OR CURRENT FORWARDING
ADDRESS
3007 HUNTINGDON AVE
BALTIMORE, MD 21211

(19) APPRAISAL OF THE ASSOCIATESHIP PROGRAMS
VERY GOOD PROGRAM.