

SCIENCE IN THE PUBLIC INTEREST

ANTIOXIDANT THERAPY IN THE AMELIORATION OF ROCKY MOUNTAIN SPOTTED FEVER

David J. Silverman, Ph.D.

Rocky Mountain spotted fever is a bacterial infection transmitted from ticks to humans. While its incidence is significantly less than that of other well-known tick-borne diseases in the United States, it has the distinction of being one of the most severe and a potentially fatal infection. The disease is caused by a unique group of bacteria called "Rickettsia." These bacteria are different from most bacteria in that they require a living cell in which to survive and grow. In the human, the endothelial cells that line the blood vessels of veins, arteries, and also smaller vessels provide this special niche. Upon entering the bloodstream following the bite of a tick (usually the dog tick or wood tick), these bacteria are capable of gaining entry into the endothelial cells, multiplying, and causing irreversible damage. Destruction of endothelial cells ultimately can lead to vascular collapse, multi-organ system failure within the body, and subsequent death. Fortunately, when diagnosed properly and treated early following the development of clinical symptoms, this disease effectively responds to antibiotics such as tetracycline. Unfortunately, the symptomatology of this disease closely mimics other types of bacterial infections as well as some viral infections, and as a result, is often treated inappropriately. Consequently, the mortality rate of Rocky Mountain spotted fever as a result of misdiagnosis can be as high as 15 - 20%.

Studies in our research laboratory over the past several years using human endothelial cells growing in culture dishes and infected with these bacteria as a closely representative model of human infection, have shown that the damage produced in endothelial cells by these bacteria most likely occurs through the production of toxic oxygen molecules that accumulate during multiplication of the bacteria within the cells. These "toxic oxygen species" include hydrogen peroxide, which is capable of causing damage to lipids in membranes, DNA, RNA, and proteins.

As a result of our studies, we have established that a specific antioxidant, alpha-lipoic acid, is effective in preventing damage to the cells if administered during infection with the bacteria. We have further determined that this antioxidant is important in the protection of animals infected with these bacteria, and therefore, when extrapolated to human infection, this antioxidant could potentially abrogate the severity of the disease. The central theme of our hypothesis is that in misdiagnosed cases of Rocky Mountain spotted fever, especially when antibiotic therapy is not properly instituted in a timely manner, antioxidant therapy may prove beneficial in preventing some of the pathological sequelae that occur following cellular injury, and consequently, reduce the incidence of the more severe forms of the disease. As a result, our current focus is to identify other potential compounds or substances that may effectively protect human endothelial cells from infection by this group of bacteria and to understand the specific pathways that lead to the generation of toxic oxygen molecules in this disease.

DEPARTMENT INFORMATION

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SPOTLIGHT ON STUDENTS

MEET OUR ADVANCED STUDENTS



Laurel Burall (Mobley), from Camp Springs, MD, received her BA in biology from St. Mary's College of Maryland. Laurel's previous research experience includes studying the effects of pesticides on the water flea, *Ceriodaphnia*; work at the National Cancer Institute involving

B cell protection from apoptosis; and studies on the connection between sperm cell morphology and sexual competition in birds. Her thesis work involves using signature-tagged mutagenesis to identify attenuated mutants of *Proteus mirabilis* in the mouse model of ascending urinary tract infection. She is now in the process of defining phenotypes that might be responsible for the observed attenuation. In her spare time, Laurel enjoys crocheting and working on her house with her husband, Kyle. She also enjoys spending time with her large family, most of whom live in the area.



Riham El-Asady (Hadley) was born and raised in Kuwait. While living in Cairo, Egypt, she attended medical school and graduate school, obtaining a medical degree and an MS in Microbiology and Immunology. While pursuing her

PhD here, Riham is on sabbatical from a faculty position at the School of Medicine at Ain Shams University in Cairo. Her thesis involves the role of T lymphocyte-expressed adhesion molecules in targeting lymphocytes to epithelial sites, hence promoting epithelial cell destruction. Her work has included the delineation of various aspects of cell migration to the intestine and to epithelial targets in graft-versus-host disease. Riham is in the process of finalizing her thesis work, after which she plans to return to Egypt. Her hobbies include reading and swimming. Riham and her husband, Samy, have two children, Sarah and Rudy.



Laura Quinn Leverton (Kaper) was born in North Carolina and raised in Virginia Beach, VA. She earned a BS in biology from James Madison University and an MS in microbiology from Old Dominion University. In her Masters research,

Laura studied the genetic regulation of a twocomponent system in *Streptococcus pyogenes*. Her PhD work involves the investigation of virulence gene regulation in Enteropathogenic *E. coli*. She enjoys seeing movies, doing yoga, and camping with her husband, Jeff.



Jean Lim (Devico) was born in Pennsylvania and raised here in Baltimore. She earned her undergraduate degree from Loyola College, during which time she worked at the Immunogenetics Laboratory at Johns Hopkins

University. Jean's thesis work involves the anti-HIV chemokine RANTES, focusing on the production and characterization of N-terminally processed isoforms. Her hobbies include tennis, oil painting, traveling, and cooking. She also enjoys spending time with her grandmother, who is 81.



Mariola Sadowska (Reitz) was born and raised in Minsk Mazowiecki, Poland. She received her MS in Microbiology from the University of Warsaw. Her prior research experience was at the University of Montpellier II in France, working on acute

promyelocytic leukemia; at the AIDS Institute in Warsaw; and in the Laboratory of Tumor Cell Biology at NIH. In Dr. Reitz's lab, Mariola works on Kaposi's sarcoma-associated herpesvirus. She is studying the role of viral cyclin D, a homologue of cellular cyclin, in virus replication. Outside of work, she enjoys hiking, listening to music, reading, gardening and taking care of her two cats.



Brian Taylor (Reitz) is originally from Baltimore. He obtained his BS in Biology and French at Hampden-Sydney College in Virginia. Brian previously worked as a research assistant in Dr. Barbara Hansen's lab (the Obesity and Diabetes Research Center)

here on campus. His thesis project involves looking at the basic science of HIV-1 entry. Brian studies virus mutants that are capable of entering cells that have a low number of coreceptors, even in the presence of antagonists. He is in the process of writing his thesis and hopes to finish soon. Brian says he is getting used to being a new parent with his wife, Christine, to their nine-month-old daughter, Anna. He is an avid fisherman and hunter, and he is also a karate instructor (Uechi-Ryu style) with a second-degree black belt.

DEPARTURES & ARRIVALS

DEPARTING STAFF

James (Adam) Crawford (Kaper) is now employed by Antex Biologics in Gaithersburg, MD. He is a senior scientist in Dr. Sukjoon Park's research group involved in vaccine development.

Xin Zhou (Kaper) is now working for the Food and Drug Administration. He is an Interdisciplinary Scientist/Microbiologist at the Office of New Drugs in the Center for Drug Evaluation and Research in Rockville, MD.

NEW RESEARCH TECHNICIAN

Anju Kadavil (Farber) was born in India and raised in Kuwait. She earned her undergraduate degree in General Microbiology and her Masters Degree in Applied Microbiology from the University of Madras in India. Her previous research experience was at the Indian Institute of Science in the department of Cell Biology and Microbiology, working on the analysis of microarray data related to the RNA polymerase of Saccharomyces cerevisiae. In Dr. Farber's lab, Anju is working on CD4 memory T-cells. Her hobbies include pinball, badminton, and baking. Her husband, John, recently earned his PhD from the Department of Pharmacology and Experimental Therapeutics (UMB) and now works at the FDA.

NEW LAB HELPER

Evets Morgan (Kaper) was born and raised in Timonium, MD. She previously worked as production manager for an advertising agency in Towson. Evets is a single mother with a seven-month-old son, Nicholas. When she has spare time, she enjoys playing guitar.

MEETINGS, TRAVEL & AWARDS

The **2003** International Meeting of the Institute of Human Virology was held in Baltimore, MD, September 29 – October 3. **Dr. Robert Gallo**, director of the IHV, has organized this annual conference for more than 20 years. Numerous IHV Faculty and Students presented their work at this conference. Students from our department who presented work included: **John Vu**, **Jean Lim**, **Mariola Sadowska** and **Tracy Ruckwardt**.

Dr. Martin Flajnik was invited for seminars at Iowa State University (30 September), The National Institute of Environmental Health Sciences in North Carolina (8 October), and at Duke University (9 October).

GRANTS AWARDED

The Center for Vaccine Development was awarded the largest grant in the history of the University of Maryland, Baltimore. The 4½-year, \$42 million dollar grant from the National Institute of Allergy and Infectious Diseases (NIAID) establishes UMB as the lead institution of the Middle Atlantic Regional Center of Excellence (RCE) for **Biodefense and Emerging Infectious** Diseases Research. UMB will head a consortium of 16 biomedical research institutions to carry out the NIAID's strategic plan for biodefense research. The cooperative projects involve developing new and improved vaccines, diagnostic tools and treatments for bioterror agents and naturally occurring emerging infections, and training the next generation of biodefense investigators.

The NIAID has also awarded a cooperative agreement, "Live vector vaccines against agents of bioterror, "to Dr. James Nataro and colleagues. This 41/2-year project will combine the vast experience of the CVD and the Chemical and Biological Defence Center, Porton Down (UK) in the development of live attenuated enteric bacterial vaccines against anthrax, plague, and botulism. The vaccines will be very safe and will be designed to elicit both mucosal and systemic responses, with protection being elicited from a single dose of the vaccine within one week of immunization. A prime-boost strategy will also be investigated to protect those exposed to very high doses of a bioweapon. It is anticipated that the products developed will be tested in animals, with the aim of generating a series of vaccine candidates for immediate Phase 1 human trials.

Dr. Patrik Bavoil's lab is one of two subcontracted academic partners on a grant to TIGR to sequence six Chlamydia genomes. The project termed "Chlamydia Taxogenomics" has its own website at

http://www.tigr.org/tdb/chlamydia/main.html.

The Center for Vaccine Development's Tenth Annual Frontiers in Vaccinology Lecture was held on November 14, 2003. Stanley A. Plotkin, M.D., Emeritus Professor of Pediatrics, University of Pennsylvania, Emeritus Professor of the Wistar Institute, and Medical and Scientific Consultant, Aventis Pasteur, presented "The past, present and future of vaccination." Several Microbiology and Immunology

faculty/joint-faculty members, including **Drs. James Kaper, James Nataro, Christopher Plowe, and Marcelo Sztein**, also presented summaries of their vaccinology-related research during the two-day meeting leading up to Dr. Plotkins's lecture. Many other department members attended the meeting and lecture.

SPOTLIGHT ON: Dr. Farber



Dr. Donna Farber is originally from Philadelphia. She did her undergraduate studies at the University of Michigan and earned her PhD in Biochemistry at the University of California Santa Barbara. She worked as a postdoctoral fellow in Kim Bottomly's lab at Yale University and later in with Oreste Acuto at the Pasteur Institute in Paris.

She enjoyed the experience of learning French while in Paris. In 1996 she started her first faculty position at University of Maryland College Park, where she taught undergraduate and graduate courses in immunology.

In 2000, Dr. Farber was recruited to UMB and brought four graduate students with her. The major focus of the research in her lab is the memory immune responses mediated by T-helper or CD4 T cells. She is particularly interested in how memory cells are generated and maintained. Her current Lab consists of her lab manager, Wendy Lai, a postdoctoral fellow, Deepa Patke, two students, Vaishali Mane and Francesca Okoye, a technician, Anju Kadavil, and a surgeon, Dr. David Leeser. Dr. Adam Bingaman, a surgeon fellow, is also affiliated with her lab, and she is currently looking to hire another postdoctoral fellow. fellow. Dr. Farber gives lectures to the medical students and gives the lectures on memory T cells in the Immunology course in our department.

She lives near Roland Park north of Baltimore with her husband, David, who teaches French history at Johns Hopkins University, and their two children, Elana, 8, and Joseph, 5.

In her free time, Dr. Farber enjoys playing the piano, jogging, and reading novels. Her favorite authors include Tracy Chevalier, Jonathan Franzen, W. Somerset Maugham, and Daphne Du Maurier. She also enjoys reading non-fiction books on the history of science and on science and society.

PUBLICATIONS

Aug. 16 – Nov. 15, 2003.

Publications having department students as authors/co-authors are designated with a ♦.

Bold-face is used to identify department members.

(Do you not see your work here? - Don't forget to submit new publications to The Micro-Scoop in time for the next issue!)

Allen A, Obaro S, Bojang K, **Awomoyi A**, Greenwood BM, Whittle H, Sirugo G, Newport M. Variation in TLR4 and susceptibility to group A meningococcal meningitis in Gambian children. The Pediatric Infectious Disease Journal. Nov 2003. 22: 11: 1018-1019.

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GSA COMPUTER LOAN PROGRAM

Are you in the process of writing but don't have a computer outside of lab? Wish you could do some work from home?

The Graduate Student Association has both Mac and PC laptops available for students to borrow. Borrowing a laptop from the GSA is free and easy. Simply fill out the Computer Loan Policy and Request form and have either Chelsea Lane or Andrew Hebbeler sign it. Forms are submitted to Michele Vitolo and laptops can be checked out for up to one week.

For more information, contact Michele Vitolo: Bressler Research Building, Room 7-018 Phone: 8-5482

E-mail: mailto:mvitolo@umaryland.edu

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DID YOU KNOW??

Are you in the process of writing and looking to see how others have written up their theses? Or just graduated and curious to see your "masterpiece?" Luckily there is a database of dissertations for you to search and download in PDF format (for those dissertations published after 1997). UMI specializes in archiving dissertations for university libraries all over the world.

In order to access the UMI database, you must first configure your browser proxy. For instructions, check out:

http://www.umaryland.edu/helpdesk/help/docs/proxy.html). Following configuration, you can access the searchable Proquest Digital Dissertations at http://wwwlib.umi.com/dissertations/search) using your Umnet username and password.

Rang C, Galen JE, **Kaper JB**, Chao L. Fitness cost of the green fluorescent protein in gastrointestinal bacteria. Can J Microbiol. 2003 Sep;49(9):531-7.

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GRADUATES



Tracy J. Ruckwardt, Fall 2003. Tracy was born the third of six children of Robert and Gayle Ruckwardt in Pittsville, Wisconsin, 27 years ago. She attended University of Wisconsin, Eau Claire as an undergraduate and then started her graduate

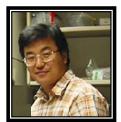
studies in the laboratory of Dr. C. David Pauza at University of Wisconsin, Madison. Two years after joining the lab, she made the trip to the East Coast when her advisor moved to the University of Maryland to join the Institute of Human Virology. She did her dissertation work on the Tat protein of HIV-1 in Dr. Pauza's lab. She spent much of her spare time rowing with the Baltimore Rowing Club and hanging out with friends and her boyfriend, Tim, and his dog, Rigger. She dreams of a productive career, traveling the world, getting a pilot's license, and rowing in the Olympics, among other things, but would be happy in the short term with getting a car that is less than 10 years old. Tracy will be doing a short post-doctoral term in Dr. Pauza's lab and then pursuing another post-doctoral position in viral immunology.



Angela Janson, Fall 2003. Angela did her dissertation work in the lab of Dr. Harry Mobley where she studied urinary tract infections caused by the bacterium *Proteus mirabilis*. Angela was born in Michigan and has lived in Maryland since

the age of 5. She did her undergraduate work at UMBC and got her Master's degree at Johns Hopkins School of Public Health where she worked on bacterial vaginosis. She enjoys walking her dog, Lola, trail running, riding her bike, and having drinks with friends.

ALUMNI — WHERE ARE THEY NOW?



Jynho Kim graduated from UMB in 2001. He did his dissertation work in Dr. Ricardo Feldman's laboratory where he studied the role of Fes tyrosine kinase in myeloid cell differentiation and function. Following a year of work

as a postdoctoral fellow in Dr. Feldman's lab, he moved to Johns Hopkins where he is a Research Associate in Dr. Philip Beachy's lab at the Howard Hughes Medical Institute, Department of Molecular Biology and Genetics. His studies focus on mechanisms of Hedgehog signaling in development and cancer. Jynho was born in Korea, married Jiyun Choi in 1991, and currently resides in Baltimore County with his wife and their son Youngju, who is 2 ½ years old. In his spare time, Jynho enjoys hiking.



Pinaki Rana Dutta successfully defended his thesis in December, 2002. The majority of his thesis work was published in the Journal of Biological Chemistry in October 2003. His work focused on structure function analysis of the plasmid-encoded

toxin of enteroaggregative *E. coli* in Dr. James Nataro's lab in the Center for Vaccine Development. He is currently finishing up his last year in medical school and is in the process of applying for residency. In his spare time he studies classical Odissi dance and teaches cooking classes at "A Cook's Table" in Federal Hill.

CONGRATULATIONS!!!

Sandy Jacobsen's (Mobley) daughter, Alex, and her U-11 soccer team, the Maryland City Mustangs, won first place in their division with a final record of 7-1. The girls were coached by Sandy and by Kim Reading.



Ashley Haines (Flajnik) and her husband, Jimmy, are expecting their first child, a boy, in March 2004.

Calvin Williams (Azad) and his wife, Stacey, are expecting their first child, a daughter that they plan to name Cailyn Simone Williams, this December. Calvin is currently in his first year of medical school and will return to the graduate school this summer.

Vaishali Mane's (Farber) boyfriend, Eric, and his band, The Aidenn Trilogy, recently released



their CD
"Amalgam." The other two members of the band are John Kadavil (the husband of Anju Kadavil, who is a new technician in Dr. Farber's lab)

and Michael Sapko. "The Aideen Trilogy" is a hard rock/metal band with a total of 3 members, all of whom are former or current graduate students at UMB. You can read more about them on their website.

 $\underline{www.geocities.com/aidenntrilogy/home.html}.$



Vaishali Mane (Farber lab) was elected as President of UMB's International Student Organization(ISO). The ISO is affiliated with the USGA and represents international students on campus. It sponsors various subgroups including the

Indian Association, Chinese Association, and European Association. The ISO has many major events throughout the year, including the popular event, World Fest, in Spring. To learn more about the ISO visit the website www.umaryland.edu/iso.



Okoye (Farber) placed second in ational Ms. Figure competition. It November 15 at Reisterstown

Fall Picnic



This year's fall picnic was arranged by students of our department and sponsored by the faculty. The picnic was held on October 11th in a pavilion at the Centennial Park

in Columbia, Maryland, and was a great success.

This year's **Halloween Party** was a potluck lunch held in the seminar room on the 13th floor of BRB. There was a lot of great food and several people showed up in costumes. It was a great time for students, post-docs, faculty, and staff to come together.

Graduate School Open House was held on December 2nd and about 75 students attended. Jean Lim and Vaishali Mane manned our departmental table with June Green and did an excellent job. There was a prize drawing for Departmental hats and the winners were Stuart Blackwood from Morgan State University and Jasmine Daus from Parkville.

Holiday Party

This year's **Holiday party** was supported by contributions from the faculty and arranged by the administrative staff. It was held on Friday, December 12th on the fourth floor of HSFII and was a great success with door prizes, dessert contest, and games. The winners of the dessert contest were:

<u>Cake</u> - Barbara Wright (Administrative Staff)
<u>Cookies</u> - Barbara Wright (Administrative Staff)
<u>Pie</u> - Cannoli Pie - Karen Zaukus <u>Brownies</u> Charlotte <u>Cookies</u> - Barbara Wright <u>Other</u>
<u>Goodies</u> - Pumpkin Cream Cheese Roll - Michelle
Cooper <u>Best Chocolate Dessert</u> - David Silverman
<u>Best Decorated Dessert</u> - Jane Wilhelm <u>Best in</u>
Show - Michelle

Michelle Weber's Neiman Marcus Brownie Recipe:

1 box "Butter Recipe Yellow" cake mix 1 stick melted butter

1 egg

Combine and press into 13 X 9 pan.

Topping:

1 box confectionary sugar (1 lb)

1 stick melted butter

2 eggs

8 oz cream cheese

Combine, whip, and pour over mixture in pan. Sprinkle pecan pieces on top. Preheat oven to 350 and bake for 50-60 minutes. Let cool. For best results, cover and let sit overnight before cutting.

THE MICRO-SCOOP STAFF We welcome your comments and suggestions.

 $\begin{array}{c} Charlotte \ Andreasen - \ Graduates \,\&\, Alumni, \\ Congratulations \end{array}$

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Andrew Hebbeler - Publications, GSA,

MARK YOUR CALENDAR

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Angela Jansen - Science in the Public Interest

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Kristen Kanack - Meetings, Travel & Awards,

UPCOMING OPPORTUNITIES

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Roger Plaut - DEPARTURES & ARRIVALS,

SPOTLIGHT ON STUDENTS

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Submissions to THE MICRO-SCOOP:

Please send contributions (as email attachments) for the spring issue to a member of the THE MICRO-SCOOP staff by **MARCH 1**. Submissions may be edited to fit in the allotted space. Please identify department members in the text.

Announcements!!

- ◆ Faculty members from the Microbiology and Immunology Department are in need of computer-savvy students to help generate data figures. Students will be compensated for their time. Interested students can contact Gloria Smedley (BRB 13-011, gkruba@umaryland.edu) for more information.
- ♦ Prospective students will be visiting UMB in February of 2004. Please contact June Green for more information on how you can be involved!
- ♦ This year's Maryland Charities Campaign was a huge success! The Microbiology and Immunology Department increased their conributions by 43% over last year.

FROM THE GRADUATE STUDENT ASSOCATION...

Greetings! It's hard to believe that 2003 is almost gone. The GSA has spent the last few months planning and executing a variety of student activities. And with 2004 only days away, there are even more events just around the corner.

Planning has begun in full force for the 25th Annual Graduate Research Conference on April 23, 2004. The conference is jointly organized by graduate students from the UMB and UMBC campuses and will be hosted by the UMBC campus this year. The GRC is a fantastic way for graduate students to present their most recent data to members of the UM scientific community. To find out how you can be involved, please contact the GSA at gsa@umaryland.edu.

When traveling to conferences this Spring, remember that the Graduate Student Association provides Travel Fellowships. These travel awards were instituted in order to encourage student participation in professional societies and scientific meetings. Due to the limited supply of funds, only students who present papers or posters are eligible for reimbursement and only one award may be accepted per academic year. For application forms and award deadline information, please check http://www.graduate.umaryland.edu/gsa.

If you have questions, concerns or ideas on how the GSA can better represent our department, please feel free to contact Andrew Hebbeler (ahebb001@umaryland.edu) or Chelsea Lane (mlane002@umaryland.edu).

Happy Holidays! Andrew Hebbeler