

Newsletter of the Department of Microbiology & Immunology and Graduate Program in Molecular Microbiology & Immunology, University of Maryland School of Medicine

SPOTLIGHT ON FACULTY: Dr. Diana Oram



Dr. Diana Oram began her first faculty position as Assistant Professor at UMB approximately one year ago. Her primary appointment is in the Dental School, with secondary appointments in the Department of

Microbiology and Immunology and the Department of Molecular Medicine, within the School of Medicine. She earned her PhD in Microbiology and Molecular Genetics at Emory in 1999, studying conjugative transposition in Dr. June Scott's laboratory. During this time, she met her future husband, Dr. Mark Oram, at a conference. Prior to coming to Maryland, she spent five years with Dr. Randall Holmes as a post-doctoral fellow at the University of Colorado School of Medicine.

Her research focuses on genetic and biochemical analyses of Gram-positive bacterial physiology and their application to elucidating mechanisms by which bacterial pathogens cause disease. The primary focus is the toxin-producing bacterial species *Corynebacterium diphtheriae*. As well as being a toxigenic human pathogen, *C. diphtheriae* serves as a model organism for the study of iron-dependent gene regulation in Grampositive and acid-fast bacterial species.

The diphtheria toxin repressor DtxR is the primary iron-responsive transcriptional regulator in *C. diphtheriae*, and regulators homologous to DtxR are found in many

bacterial species. Interestingly, a protein similar to the ferric uptake regulator Fur is also found in *C. diphtheriae*. The metabolism of iron and protection from the deleterious effects of reactive oxygen species are irretrievably linked. Iron is an essential cofactor for many enzymatic reactions. However, under oxidizing conditions, iron is available to participate in the Fenton reaction, resulting in highly reactive species capable of causing damage to cellular components.

Dr. Oram's lab is investigating the role(s) of DtxR and the Fur-like regulator in controlling oxidative stress protection systems. Illuminating the mechanisms that protect *C. diphtheriae* from reactive oxygen species will likely provide information on possible mechanisms by which *C. diphtheriae* evades those host defenses that rely on causing oxidative damage and may reveal new targets for the development of antimicrobial agents.

In addition to her work with *C. diphtheriae*, Dr. Oram has expanded her focus to include

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iron- and oxidative stress-dependent gene regulation in the Gram-positive nosocomial pathogen *Enterococcus faecalis*. One of the goals is to characterize the role of proteins with homology both to DtxR and Fur in pathogenesis of and gene regulation in *E. faecalis* and thereby to provide new targets for the development of antimicrobials.

Her lab staff includes one postdoctoral fellow, **Dr. Semhi Apak**, graduate student **Kelsy Smith**, and research assistant **Joelle Woolston**. The lab is getting ready to move to the new Dental School building. Her hobbies away from the lab include gardening, soccer and cycling with Mark. However, much of that is on temporary hold now, as she and Mark are expecting in mid-November. While the new baby's name is still undecided, she did say that it is a boy. Congratulations and Good Health!

SCIENCE IN THE PUBLIC INTEREST: DESIGNING A BETTER ANTIBODY, WITH THE SHARK'S HELP

Dr. Helen Dooley, a post-doctoral fellow in Dr. Martin Flajnik's lab, spoke with **Khandra Sears** about the modern-day applications of studying evolutionary immunology.

KS: Tell me a little about what you do in the Flajnik lab.

HD: My current research is to detail aspects of humoral immunity in the nurse shark, *Ginglymostoma cirratum*. We've been able to show that our sharks can generate a good, antigen-specific response with different immunoglobulin (Ig) isotypes and memory, in the absence of class switching or germinal centers.

KS: So what makes shark antibodies (Abs) so special?

HD: Well, back in 1995 a new antigen receptor termed Ig New Antigen Receptor (NAR) was identified by the Flajnik lab in nurse sharks. IgNAR is a heavy chain homodimer, with a binding region about half the size of human or

mouse Igs, and in this respect is similar to a non-conventional Ig found in camels. Further analysis showed IgNAR has a huge CDR3 diversity, and the binding region contains more disulfide bonds than conventional Igs.

KS: And what properties do these atypical characteristics confer on this Ig class?

HD: The IgNAR binding region is amazingly stable! Even after I boiled it for three hours, it was still able to bind antigen; we know now it is able to unfold and then refold back to its original shape! If we do this with human or mouse Abs, they just fall apart. It also remains stable for long periods at ambient temperature and exhibits very high affinity and specificity. For twenty years, people have tried to make stable Abs that retained the affinity and specificity of mammalian Abs; they were part of the shark response the whole time!

KS: So, for those of us who have nightmares when we hear the letters Ig, what significance does this unusual Ig have for Ab design and the public interest?

HD: For one, IgNAR binding regions can be easily expressed in *E. coli*, so we have an inexpensive source of these amazing little Abs. All this can be translated into better, cheaper diagnostic technology. Think inexpensive diagnostic kits that don't have to be shipped via cold chain or can sit on a shelf for months without losing effectivity. We're currently working on IgNAR-based reagents for the detection of anthrax, which would allow easy shipping and storage in the field.

KS: Very interesting. So what other possibilities do you see for this technology? HD: The possibilities are endless! IgNAR-based kits could be used to diagnose diseases quickly and cheaply, particularly in areas where it's difficult to find highly trained staff or to keep reagents cold. Imagine something like a pregnancy test, but used instead for disease diagnosis. This technology could also be applied to other biodefense or disease targets, drug testing, even environmental pollutants —basically any situation where you need a "quick and easy" answer.

KS: How difficult is it to isolate Ag-specific IgNAR Abs from the nurse shark?

HD: Well, the immune response in sharks is much slower than that of mammals, so we typically have to immunize monthly before getting a good response in the fourth or fifth month. We then take a blood sample and use PCR to clone out the IgNAR repertoire. In the future we hope to immunize with antigen "cocktails," to speed this process up a little.

KS: What role do you think IgNAR plays in the shark humoral response?

HD: Well, Abs make up about fifty percent of the shark's blood protein. Most of that is IgM, but IgNAR accounts for maybe ten percent. Currently, we think IgNAR is responsible for binding to viruses and possibly clearing chronic infections that require a highly specific response.

KS: Cool! Well, Helen, thanks for your time.

GRANTS AND AWARDS

Dr. Mike Criscitiello (Flajnik lab) gave an invited talk in September at the College of William and Mary in Virginia.

Dr. Martin Flajnik was invited to give seminars at: the University of Montana in April; a protein engineering symposium in Boston (a talk shared with Dr. Helen Dooley) in April; and the FASEB Meeting on Transplantation near Aspen, CO, in June. Dr. Flajnik also taught a course on Evolution of the Immune System in Sao Paolo, Brazil, in September.

Dr. James Kaper received approval for the competitive renewal of his cholera grant for five more years of funding.

Dr. Diana Oram was awarded a K22 Research Scholar Development Award (NIH/NIAID AI60882-01) entitled, "Control of Oxidative Stress Defenses in *Corynebacterium diphtheriae.*"

Dr. Sudhakar Kalakonda (Kalvakolanu lab) was awarded the Milstein Young

Investigator Award for cytokine research by the International Society for Interferon and Cytokine Research in Vienna, Austria.

MEETINGS AND POSTERS

Nicole Ammerman and **Khandra Sears** (Azad lab) presented a poster at the American Society for Rickettsiology meeting in Pacific Grove, CA, in September. They both won travel awards from the Society to attend the meeting.

Charlotte Andreasen, Roger Plaut, and Zoë Worthington (Carbonetti lab) each presented posters at the 106th General Meeting of the American Society for Microbiology, Orlando, FL, in May. Charlotte won a travel award to attend the meeting.

Dr. Patrik Bavoil gave a talk at the Pfizer Trachoma Scientific Exchange Meeting in Phoenix, AZ, in January. He also presented at the 4th Workshop of the European Cooperation in the field of Scientific and Technical Research (COST) Action 855 on Zoonotic Aspects of Animal Chlamydioses, Edinburgh, UK, in September, and was chair of the Genomics and Pathogenicity session.

Rebecca Brady and **Sandy Jacobsen** (Shirtliff lab) each presented posters at the 106th General Meeting of the American Society for Microbiology, Orlando, FL, in May. They also presented posters at the 11th International Symposium on Microbial Ecology, in Vienna, Austria, in August. Rebecca won a travel award to attend the meeting.

Andrew Hebbeler (Pauza lab) attended the 2nd Conference on Gammadelta T cells in San Diego, CA, in March. He has also been invited to speak at the 10th Annual Conference on Malignancies in AIDS and Other Opportunistic Infections in Bethesda, MD, in October.

Quan M. Nhu received a travel award from the Society for Leukocyte Biology to present work at the 2006 Joint Meeting of the Society for Leukocyte Biology and the International Endotoxin and Innate Immunity Society in San Antonio, TX, this November.

- **Dr. Jan Peters** and **Dr. Laurel Burall** (Bavoil lab) each presented posters at the 106th General Meeting of the American Society for Microbiology, Orlando, FL, in May.
- **Dr. Diana Oram** and Dr. Mark Oram presented a poster at the 106th General Meeting of the American Society for Microbiology, Orlando, FL, in May.
- **Dr. Suzana Radulovic** attended the 20th Meeting of the American Society for Rickettsiology and the 5th International Conferences on Bartonella as Emerging Pathogens in Asilomar, CA, in September. She gave an oral presentation, was senior author on a poster, and was also a member of the Scientific Planning Committee.

Chun Tan (Bavoil lab) gave a talk at the Eleventh International Symposium on Human Chlamydial Infection, in Niagara-on-the-Lake, Ontario, Canada, this summer. Dr. Zhi Liu (Bavoil lab) also presented at this conference.

PUBLICATIONS

Publications having department students as authors/co-authors are designated with a ◆. Bold face is used to identify department members.

- **Brady RA**, Leid JG, Costerton JW, and **Shirtliff ME**. Identification of *Staphylococcus aureus* proteins recognized by the antibody-mediated immune response to a biofilm infection. *Infect*. *Immun*. 2006. 74:3415-3426.
- ♦ **Brady RA**, Leid JG, Costerton JW, and **Shirtliff ME.** Osteomyelitis. *Clin. Micro. News.* 2006. <u>28</u>: 65-72.
- **Brady R**, Leid JG, Calhoun JH, and **Shirtliff ME**. Osteomyelitis. *FEMS Immun. Med. Micro*. 2006. In press.

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- Calhoun J, Christensen G, **Brady RA**, **Shirtliff ME**. Osteomyelitis. In "Expert Guide to Infectious Diseases," JS Tan (ed), American College of Physicians-American Society of Internal Medicine, Philadelphia, PA. 2006. In press.

Crane DD, Carlson JH, **Bavoil PM**, Hsia R-c, Tan C, Kuo C-c, and Caldwell HD. *Chlamydia trachomatis* polymorphic membrane protein D is a species-common pan-neutralizing antigen, *Proc. Natl. Acad. Sci.* 2006. <u>103</u>:1894-1899.

- Criscitiello MF, Saltis M, and Flajnik MF. An evolutionarily mobile antigen receptor variable region gene: doubly rearranging NAR-TCR genes in sharks. *Proc. Natl. Acad. Sci.* 2006. 103:5036-5041.
- ♦ Deetz CO, **Hebbeler AM**, Propp N, Cairo C, Tikhonov I, and **Pauza CD**. Interferon-gamma secretion by human Vgamma2Vdelta2 T cells after stimulation with antibody against the T cell receptor plus the Toll-like Receptor 2 agonist, Pam3Cys. *Infect. Immun.* 2006. <u>74</u>: 4505-4511.

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Haines AN, **Flajnik MF**, and Wourms JP. Histology and immunology of the placenta in the Atlantic Sharpnose Shark. *Placenta*. 2006. <u>27</u>:1114-1123.

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Hsu E, Pulham N, **Rumfelt LL**, and **Flajnik MF**. The plasticity of immunoglobulin gene systems in evolution. *Immunol. Rev.* 2006. 210:8-26.

◆ Li H, Deetz CO, Zapata JC, Cairo C, Hebbeler AM, Propp N, Salvato M, Shao Y, and Pauza CD. Vaccinia causes anergy to T cell receptor-dependent stimulation in human gd T cells. *J. Infec. Dis.* (in press).

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Liu Z, Hsia R-c, and **Bavoil PM**. Obligate intracellular parasitism 2. The Chlamydiaphages. In "*Chlamydia*: Genomics, Pathogenesis and Implications for Control," P.M. Bavoil and P.B. Wyrick (eds.), Horizon Press, London. In press.

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- Maroncle NM, Sivick, KE, Brady RA, Jones FE, and Mobley HLT. Protease activity, secretion, cell entry, cytotoxicity, and cellular targets of secreted autotransporter toxin (Sat) of uropathogenic *Escherichia coli*. *Infect. Immun*. 2006. In press.
- ♦ Ndejembi MP, Tang AL, and Farber DL. Reshaping the past: Strategies for modulating T cell memory immune responses. *Clin. Immun.* 2006. Aug 15; epub ahead of print.
- Ndejembi MP, Teijaro JR, Patke DS, Bingaman AW, Chandok M, Azimzadeh A, Nadler S, and **Farber DL**. Control of memory CD4 T cell recall by the CD28 costimulatory pathway. *J*. *Immun*. 2006. In press.

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Ohta Y, Goetz W, Hossain MZ, Nonaka M, and **Flajnik MF**. Ancestral organization of the MHC revealed in the amphibian Xenopus. *J. Immunol*. 2006. <u>176</u>:3674-3685.

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♦ Pauza CD, Hebbeler AM, and Wei H. AIDS and the rising risk for cancer: HIV infection attacks

gammadelta T cells and their role in tumor immunity. *Cell Sci.* Published online April 24, 2006:

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Tan C, Spitznagel JF, Hsia R-c, and **Bavoil PM**. The polymorphic membrane protein gene family of the *Chlamydiaceae*. In "*Chlamydia*: Genomics, Pathogenesis and Implications for Control," P.M. Bavoil and P.B. Wyrick (eds.), Horizon Press, London. In press.

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Wilson DP, Timms P, McElwain DLS, and **Bavoil PM**. Type Three Secretion, contact-dependent model for the intracellular development of *Chlamydia*. *Bull*. *Math*. *Biol*. 2006. <u>68</u>:1-18.



Dr. Abdu Azad and **Dr. James Kaper** (above) are both receiving occupational therapy, including electrostimulation. The treatment is helping Dr. Azad recuperate from a broken wrist, while Dr. Kaper is being treated for lateral epicondylitis (tennis elbow—although he doesn't play tennis!). The two men enjoy having a chance to chat during their treatments.

SPOTLIGHT ON: NEW STUDENTS



Steven Bowen is from Rochester, New York. He graduated from Syracuse University with a BS in Biology. For two years, Steven worked as a laboratory technician in the Department of Microbiology and

Immunology at the University of Rochester, studying T helper cell differentiation. He is interested in continuing to work in immunology but looks forward to gaining experience in other disciplines. Steven has a strong interest in music, both playing and listening—before moving to Baltimore, he played in a punk rock band.

Baltimore native **Kristen Burdette** earned a BA in
Biology from La Salle
University in Philadelphia.
Kristen spent three
summers working at the
United States Army Medical
Research Institute of



Chemical Defense in Edgewood, Maryland, where she studied the apoptotic pathway following histone modifications in cells after exposure to sulfur mustard. She is interested in pursuing research in virology. In her spare time, besides catching up on sleep, Kristen enjoys cooking, dining out, reading, traveling, and spending money.



Preeta Dasgupta was raised in Calcutta and Bangalore, India. She earned a BS in Microbiology from St. Joseph's College at Bangalore University. Preeta's research experience includes work at the National

Institute of Immunology in New Delhi, where she studied the role of γ/δ T cells in combating Salmonella infections. She also worked at the Indian Institute of Science in Bangalore,

helping to clone the LIPL gene of *M*. *tuberculosis*. She is interested in continuing to study the mechanisms by which T and B lymphocytes combat pathogens. In her free time, Preeta enjoys reading fiction, particularly the works of P.G. Wodehouse.

Melissa Hayes was born and raised in Massachusetts and most recently lived in Worcester, MA. She earned a BS in Biotechnology with an emphasis in Biochemistry from Worcester Polytechnic Institute. Following



graduation, Melissa worked at Expressive Constructs, helping develop a fluorescent substrate-based assay for Salmonella. She later joined EXACT Sciences, working on optimization of an assay for colon cancer that involved purifying DNA from stool samples. Her parting gift from the company was a stuffed doll named Stoolie! Melissa is interested in studying virology. She loves shopping, trying new ethnic foods, and spending time at the beach.



Mark Marohn was born in Maine. As an Air Force brat, he was raised in several different places, the last being Colorado Springs, Colorado. Mark earned a BS in Molecular Biology from Lehigh University in

Bethlehem, Pennsylvania. After graduation, he worked for five years in the Department of Bacterial Diseases at Walter Reed Army Institute of Research in Silver Spring, MD. Mark is interested in studying the pathogenesis and virulence of microbial agents. He is an avid sports fan (Go Yankees!) and enjoys skiing, mountain biking, and rock climbing.

Brian Peters is from Altoona, Pennsylvania. He graduated with a BS in Microbiology from Penn State University. As an undergraduate, Brian worked at Fairway Labs



and M&M Mars. He also worked in the Biochemical Pharmacology department at the Walter Reed Army Institute of Research, where he studied the importance of cholinesterase in chemical warfare. At GlaxoSmithKline Pharmaceuticals, Brian worked on formulation chemistry. Most recently, he was employed by Biomol, performing biochemical assays, product development, and production work. He is interested in studying bacteriology. Brian enjoys playing acoustical guitar (self-taught), cooking, and watching college and professional football.



Kelsy Smith is from Monroe, Louisiana. She earned a BS in Microbiology from Louisiana State University. Following a year of work at an environmental testing lab, Kelsy started in the Microbiology PhD

program at State University of New York at Buffalo, joining a laboratory researching iron regulation and uptake in *Bordetella pertussis* and *bronchiseptica*. Having transferred to our program, she is now beginning her fourth year of graduate school. She is in **Dr. Diana Oram's** lab at the Dental School, where she studies iron regulation and oxidative stress response in *Corynebacterium diphtheriae*. In her spare time, Kelsy enjoys movies, TV, board games, and playing sports with friends (but only when it's not serious and you're not expected to be any good). She loves spending time with her Pomeranian, Jade, and her new kitten, Olivia.

Susan Steyert was born in Wisconsin and raised in northern Illinois. She obtained her BS in Chemistry from Andrews University in Berrien Springs, Michigan, and a PhD in Physical Chemistry



from the University of California, Berkeley. As an undergraduate, Susan worked in the Drug Identification Lab for the police department in Berrien County, Michigan, and at the Argonne National Laboratory in Argonne, Illinois. Her graduate work involved basic research on thermodynamic properties of transition metal alloys for high temperature applications. Susan spent a summer working with Silvia Pineiro in the Department of Medical and Research Technology here at UMB, studying *Bdellovibrio bacteriovorus*, after which she began our graduate program. She is interested in bacterial pathogenesis and gene regulation. Susan enjoys outdoor activities with her husband, David, and her two daughters, Vivian and Marilyn—that is, when they can actually coordinate their four busy schedules!



Elizabeth Urban (MD/PhD student) was raised in Montgomery County, Maryland. She earned her undergraduate degree from Catholic University in Washington, DC. After graduation,

Elizabeth worked for one year at the National Institute of Allergy and Infectious Diseases at NIH, where she studied the effect of structured treatment interruptions on the viral genome of HIV-positive patients undergoing highly active antiretroviral therapy. She is now in **Dr. David Pauza's** lab, where she studies the role of gamma delta T cells in HIV infection. Elizabeth enjoys spending time with family and friends, listening to music, surfing, snowboarding, and drinking a hot peppermint mocha while watching the snow fall.

RECENT GRADUATES

The following students have recently graduated from our program: **Kamalesh Bala**: "Differential suppression of epitopespecific T cells against self lysozyme by CD4+CD25+ regulatory T cells," *December 2005*; **M. Chelsea Lane**: "Role of Motility for Uropathogenic Escherichia coli during UTI and the Decision to Stick or Swim," *July 2006*; **Uzma Alam**: "Malaria: Integrin CD103 and the induction of protective immunity," *July 2006*; **Brian Taylor**: "Analysis of a Human Immunodeficiency Virus Type 1 R5 Strain that Exhibits an Expanded Tropism to CD4+ T-Cell Lines," *July 2006*.

NEW FACULTY

Svetlana Chapoval, MD, PhD, is an Interim Visiting Assistant Professor working with Dr. Achsah Keegan at the Center for Vascular and Inflammatory Diseases. Dr. Chapoval was born and raised in Ukraine. She received her medical degree at Pirogov Moscow Medical Institute and her PhD at Gamaleya Research Institute of Epidemiology and Microbiology, also in Moscow. She worked as a post-doctoral fellow in the Department of Immunology at the Mayo Clinic, where she studied the specificity of HLA Class II polymorphism in airborne allergen sensitivity. She later was an Associate Research Scientist in the Pulmonary and Critical Care Medicine Section at Yale University School of Medicine, where she worked on the effect of lung vascular endothelial growth factor expression on local dendritic cell activation and function. Her work with the Keegan group includes studying the role of STAT6 in resident pulmonary and nonpulmonary cells in allergic airway response, as well as the roles of IL-4 and IL-13 and their receptors in dendritic cell differentiation. She is married to Dr. Andrei Chapoval, an Assistant Professor in the Department of Otorhinolaryngology-Head and Neck Surgery here at UMB. They have two children, Dennis and Velina.

CONGRATULATIONS!



Dr. Laurel Burall (Bavoil lab) and her husband, Kyle, had their first son, Ian, on September 6. He was 9 lbs., 3 oz., and the family is doing well.

Victor Ayala (Carbonetti lab) and his wife Nelmarie are the proud parents of their second child, Victoria Marie, born March 8.



Maura Strauman (Nataro lab) got engaged to Jeff Finkelstein, who is currently a graduate student at University of Pennsylvania. They are planning a summer 2008 wedding.

Dr. Nathalie Maroncle (Kaper lab) and **Dr. Subhendu Basu** (Cross lab) were married this past summer in two ceremonies, one in France and one in India.

Cara Lang (Kaper lab) and Nick Morin (Nataro lab), both MD/PhD students, were married in Malta in September.

Also in the Kaper lab, Dr. Jang Won Yoon and his wife recently had their third child, a boy, while Dr. Mary Jane Lombardo recently gave birth to her first child, a boy.

Breaking news: two of our new students just got engaged! **Kristen Burdette** is engaged to Ted, and **Steven Bowen** is engaged to Corinne.

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