Spring 2005

THE MICRO-SCOOP

Newsletter of the University of Maryland School of Medicine
Department of Microbiology & Immunology

SCIENCE IN THE PUBLIC INTEREST

Green Tea: Drink Your Way to Healthy Joints

By Dr. Kamal Moudgil

A variety of synthetic and natural products are regularly being investigated for their therapeutic potential in the quest for finding a cure for rheumatoid arthritis (RA). Although there is some evidence for the anti-arthritic activity of certain herbal products (used in Chinese, Indian, and Nigerian medicine, etc.) and other nutraceuticals, the mechanisms of action of such agents are largely unexplored. Green tea, a product of dried leaves of *Camellia sinensis*, is the most widely consumed beverage in the world. There is anecdotal evidence for the beneficial effect of green tea in the treatment of rheumatoid arthritis from practitioners of complementary and alternative medicine. In our laboratory, we recently confirmed the anti-arthritic activity of green tea using an animal model of RA.

In our study*, we tested the polyphenolic compounds extracted from green tea (PGT). The main polyphenols in green tea include epicatechin, epigallocatechin, epicatechin-3-gallate, and epigallocatechin-3-gallate, which is the major constituent of PGT both by weight and by antioxidant activity. These polyphenols are rich in anti-oxidants that have been shown to possess anti-inflammatory and anti-cancer properties. We examined PGT for its anti-arthritic activity using the rat adjuvant arthritis model of human RA. Arthritis can be induced in Lewis rats by injection of heat-killed *M. tuberculosis* (Mtb), and the Mtb-triggered T cell response directed against heat-shock protein 65 (Hsp65) is believed to mediate the disease process. Interestingly, RA patients also develop T cell response to Hsp65.

We investigated whether PGT can downmodulate the severity of adjuvant arthritis, and examined the effect of PGT on antigen-specific immune mechanisms involved in this disease. Our results demonstrate that PGT has significant anti-arthritic activity. Lewis rats fed PGT in drinking water before Mtb injection were significantly protected from development of arthritis compared to control rats given regular water. Furthermore, PGT had an immune-stimulating effect on antigen (Hsp65)-specific T cells, and it also altered (immune deviation) the cytokine response of these T cells from T helper 1 (Th1) to T helper 2 (Th2) type.

Human autoimmune diseases such as RA, diabetes mellitus, and multiple sclerosis are associated with predominantly Th1-type (damaging) responses against the disease-related antigens. On the basis of the evidence from animal models of these diseases that a Th2-type (protective) response can prevent or suppress disease activity, various approaches for inducing deviation of the cytokine response from Th1 to Th2 type are being exploited for therapeutic purposes. In our study, the anti-arthritic activity of green tea was also associated with immune deviation. Similar results have been obtained in another study on green tea by Dr. Haqqi and colleagues (at Cleveland) using a different animal model of arthritis. In addition, other components of tea (e.g., Cofpropamine (Cofa), a caffeine derivative) besides PGT have also been found to possess anti-arthritic activity.

We hope this interesting lead from animal models will be further exploited for therapeutic purposes in RA patients through systematic clinical trials. Botanical products like green tea could serve as useful adjuncts to conventional anti-arthritic drugs, whose use may be associated with significant adverse effects.

* The experiments were performed by postdoctoral fellow Hong R. Kim and were supported through an NIH grant to the Center for Integrative Medicine (directed by Dr. Brian Berman).

IN THIS ISSUE:

MEETINGS AND TRAVEL

Charlotte Andreasen, Roger Plaut, and Dr. Zoë Worthington (Carbonetti lab) presented at the Mid-Atlantic Microbial Pathogenesis Meeting in Wintergreen, Virginia, February 6-8, 2005. All three presented posters, and Dr. Worthingon also gave a talk entitled "Investigating the Translocation of Pertussis Toxin from the ER to the Cytosol - Evidence for Exploitation of the ERAD Pathway."

Dr. Shane M. Ceraul, **Dr. Sayeedur M. Rahman**, **Dr. Albert Mulenga**, **Magada Beier**, **Sheila Dreiher,** and **Uzma Alam** (Azad lab) all completed the Mid-Atlantic Centers of Excellence BSL-3 training course, February 14-16, 2005.

Dr. Shane M. Ceraul, **Dr. Sayeedur M. Rahman**, **Sheila Dreiher**, and **Uzma Alam** also completed the Middle Atlantic Regional Center of Excellence for Biodefense and Emerging Infectious Diseases bioinformatics training course on February 16, 2005.

Dr. Martin Flajnik gave talks at the Veterinary Immunology Meeting in Orlando, FL in November, The University of Rochester (NY) in December, and at Albert Einstein College of Medicine in New York, NY in February.

Dr. Johanna Porter-Kelley attended the Minority Trainee Research Forum on September 22-26, 2004.

Dr. Johanna Porter-Kelley & **Uzma Alam** attended the 4th Annual Malaria Research Meeting on February 7, 2005.

Dr. Sayeedur M. Rahman presented a talk entitled "Molecular and Functional Domain Analysis of *secA* homolog from *Rickettsia*" at the Mid - Atlantic Microbial Pathogenesis Meeting, February 6-8, 2005.

Zachary Roberts presented a poster at the Society of Leukocyte Biology meeting in Toronto, Canada in October.

Dr. Mark Shirtliff was an invited speaker at the Center for Biofilm Engineering at Montana State University on March 3, 2005. He was also an invited speaker at Winthrop University Hospital in Mineola, NY on February 3, 2005.

Dr. Maria Salvato presented a one hour seminar on Lassa Fever virus on the internet for the Regional Centers of Excellence in Biodefense on March 30, 2005.

SPOTLIGHT ON: DR. RICARDO FELDMAN

Dr. Feldman was born and raised in Argentina. He obtained his Masters degree in Biochemistry at the University of Buenos Aires. After coming to the U.S., he earned a PhD in Cell Biology at New York University in 1979. Dr. Feldman's post-doctoral work included research on retroviruses and oncogenes with Dr. Hidesaburo Hanafusa at Rockefeller University, followed by work at the National Cancer Institute on signal transduction and oncogenesis.

Dr. Feldman came to the Department in 1990. He has had a long-term interest in the role of tyrosine kinases in myeloid cell development and leukemogenesis. Recent work in his lab is focused on developing ways to target genes to different cell types in vivo in a mouse model. In one track of his research, he hopes to use viral vectors to target genes to hematopoietic stem cells that would lead to recapitulation of the chromosomal translocations that occur in leukemias, with the goal of developing agents to kill these cells. In another track, Dr. Feldman would like to target genes to Type 2 pneumocytes in the lung as models for carcinogenesis and other lung pathology.

Currently, Dr. Feldman's lab includes students Minjun Yu and Justin Sausville. He teaches students in the Department's Virology course (for which he has been course master for many years) and in the Medical Microbiology and Problem-Based Learning courses for medical students.

His family consists of his wife, Susannah, who teaches Biology at Towson University, and two grown children, Naomi and Benjamin. In his spare time, Dr. Feldman enjoys reading literature, listening to classical music, and attending opera and ballet performances.

GRANTS

Dr. Abdu Azad's lab members are proud to announce his achievements. Dr. Azad has recently been awarded an additional RO1 grant from the NIH, for a total of four simultaneous active RO1 grants. This is unprecedented in the Department. Three grants involve investigating Rickettsial-host interactions and one grant involves investigating the Plasmodium liver stage.

PUBLICATIONS

PUBLICATIONS HAVING DEPARTMENT STUDENTS AS AUTHORS/CO-AUTHORS ARE DESIGNATED WITH A ♦. BOLD FACE IS USED TO IDENTIFY DEPARTMENT MEMBERS.

♦ **Carbonetti, N.H.**, Mays, R.M., **Artamonova, G.V**., **Plaut, R.D.**, and **Worthington, Z.E.V.** Proteolytic cleavage of pertussis toxin S1 subunit is not essential for its activity in mammalian cells. BMC Microbiology 2005. 5:7.

♦ **Dinglasan, R.R.**, **Porter-Kelley, J.M.**, **Alam, U.**, and **Azad, A.F.** Peptide mimics as surrogate immunogens of mosquito midgut carbohydrate malaria transmission blocking targets. Vaccine. 2005. 23:2717-24.

Dinglasan, R.R., Valenzuela, J.G., and **Azad, A.F.** Sugar epitopes as potential universal disease transmission blocking targets. Insect Biochemistry and Molecular Biology. 2005. 35:1-10.

♦ **Djavani, M**., Topisirovic, I., **Zapata, J.C**., **Sadowska, M.**, **Yang, Y.**, **Rodas, J.**, **Lukashevich, I.S.**, Bogue, C.W., **Pauza, C.D.**, Borden, K.L.B., and **Salvato, M.S.** The Proline-Rich Homeodomain (PRH/HEX) Protein Is Down-Regulated in Liver during Infection with Lymphocytic Choriomeningitis Virus. Journal of Virology. 2005. 79:2461–2473.

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♦ **El-Asady, R.**, Yuan, R., **Liu, K.**, Wang, D., Gress, R.E., Lucas, P.J., Drachenberg, C.I., and **Hadley, G.A.** TGF-b-dependent CD103 expression by CD8+ T cells promotes selective destruction of the host intestinal epithelium during graft-vs-host disease. Journal of Experimental Medicine, in press.

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Jordan, D.M., Cornick, N., Torres, A.G., Dean-Nystrom, E.A., **Kaper, J.B.**, and Moon, H.W. Long polar fimbriae contribute to colonization by *Escherichia coli* O157:H7 in vivo. Infection and Immunity. 2004. 72(10):6168-71.

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♦ **Kanack, K.J.**, Crawford, J.A., **Tatsuno, I.**, Karmali, M.A., and **Kaper, J.B**. SepZ/EspZ is secreted and translocated into HeLa cells by the Type-III Secretion System of Enteropathogenic *Escherichia coli*. Infection and Immunity, in press.

Leverton, L.Q., and **Kaper, J.B**. Temporal expression of enteropathogenic *Escherichia coli* virulence genes in an in vitro model of infection. Infection and Immunity. 2005. 73(2):1034-43.

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Rahman, M.S., Simser, J.A., Macaluso, K.R., and **Azad, A.F.** Functional analysis of *secA* homologues from rickettsiae. Microbiology. 2005. 151(Pt 2):589-96.

♦ **Sacci, J.B.**, Ribeiro, J.M.C., Huang, F., **Alam, U.**, Russell, J.A., Blair, P.L., Witney, A., Carucci, D.J., **Azad, A.F.**, and Aguiar, J.C. Transcriptional Analysis of In Vivo *Plasmodium yoelii* Liver Stage Gene Expression. Molecular and Biochemical Parasitology, in press.

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♦ Tomson, F.L., Viswanathan, V.K., **Kanack, K.J**., Kanteti, R.P., Straub, K.V., Menet, M., **Kaper, J.B**., and Hecht, G. EPEC EspG disrupts microtubules and in conjunction with Orf3 enhances perturbation of tight junction barrier. Molecular Microbiology 2005, online early access.

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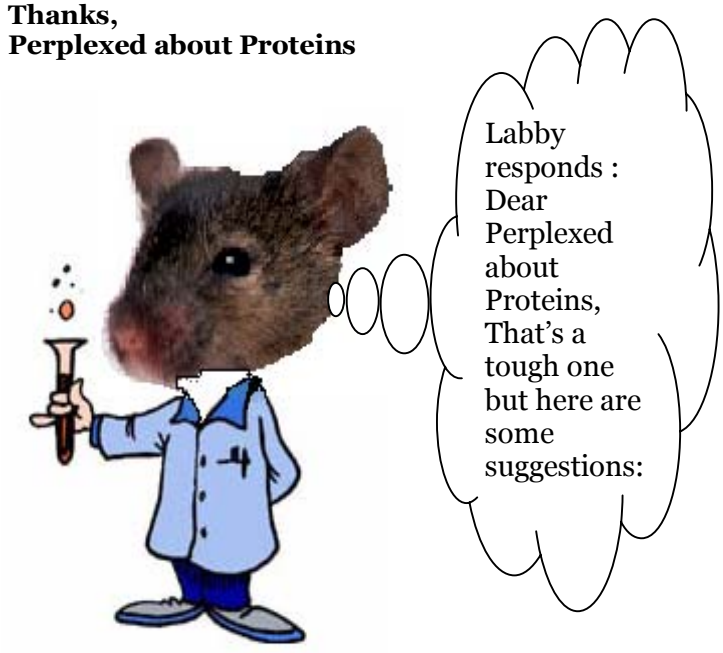
DEAR LABBY: YOUR SOURCE FOR LAB HELP

Dear Labby,
Please help me. For months, I have been having problems expressing membrane and cell wall proteins in an *E. coli* expression system. Any advice would be greatly appreciated.

Thanks,
Perplexed about Proteins



Dear PAP,
Do you have the proteins cloned into an inducible promoter system? Sometimes if your proteins are in too high of a concentration it messes things up in the cell. A system like pBAD can help solve this.
Jenn Smart

Dear PAP,
I feel your pain. Does the protein contain a signal sequence? There are signal sequence prediction programs (such as signalP) available on the internet at **www.expasy.org**. If so, you might try to clone your gene so that the encoded protein lacks this signal sequence. Create a forward primer for your gene so that it starts just after the putative signal sequence region. You may have to include a methionine start codon in this primer. Amplify your gene by PCR and clone it into your expression

vector. Since the signal sequence will be missing from your "new" recombinant protein, it won't be directed to the membrane and should (hopefully) remain soluble. Of course, if you want the protein directed to the membrane this won't help much. Other alternatives include expression from a low copy vector (something with a p15A origin of replication) or expression from a tightly regulated promoter, such as pBAD, present in the pBADmycHis cloning vectors (Invitrogen). Membrane proteins are notoriously hard to express. For reference, you can read the sordid details ad nauseum throughout the early papers by Silhavy describing the cloning of the *sec* genes from *E. coli*.
Good Luck!
Chris Coker

Labby says:
Any other suggestions for this problem can be e-mailed to the Microscoop. If you need expert advice on a particular problem or are willing to lend your expertise to help solve problems, please let us know at the Microscoop.

SPOTLIGHT ON STUDENTS: FIFTH YEARS

Jenn Smart (Kaper lab) originates from the heart of the great Midwest, Omaha, Nebraska. She earned a BS in Biology with honors from Truman State University in Kirksville Missouri. Her previous work experience prior to her arrival at the University of Maryland includes working for Dr. Cynthia Cooper at Truman State University on tumor biogenesis in rat cells as well as working with Dr. Neal Chamberlain of A.T. Still University (formerly Kirksville College of Osteopathic medicine) on quorum sensing in *Staphylococcus epidermidis* and *S. aureus*. Her summers involved working for Dr. Phillippe Arnaud of the Medical School of South Carolina on molecular biology and working for Dr. Charles Cox of the University of Iowa on a study of iron regulation in *Pseudomonas aeruginosa*. Currently, Jenn works with in Dr. James Kaper's lab on two projects: the identification of the role of Orf4 in type III secretion of EPEC and the identification of genes regulated by the Lee encoded regulator (Ler) of EHEC using microarray analysis. When her busy lab schedule will allow, she loves to travel. She also enjoys reading and attending cultural activities including art museums, center stage playhouse, and the Baltimore Symphony Orchestra. After graduating, Jenn plans to look for a post-doctoral position.

Andrew Hebbeler (Pauza lab) was born in Cincinnati, OH and raised across the Ohio River in the Northern Kentucky suburb of Park Hills. He attended Thomas More College, a small liberal arts school in Northern Kentucky, and received a Bachelor's degree in Biology and Philosophy. Prior to coming to UMB, he worked at the Northern Kentucky Independent District Health Department doing HIV/STD outreach education, and he interned at the University of Alabama, Birmingham in the lab of Dale Benos, studying the etiology of AIDS dementia. His dissertation work involves characterizing the mechanism of tumor recognition by Vγ2Vδ2 T cells and understanding effects of their selective depletion following HIV-1 infection. After completing his thesis work, he plans to extend his understanding of HIV pathogenesis by creating a postdoctoral project that merges his interests in basic science research and international public health. In his free time he loves reading and exercising, spending time outside and competing in running races and triathlons.

Kamalesh Bala (Moudgil lab) is from Tamil Nadu, India. He earned his Bachelor of Medicine and Bachelor of Surgery degree from Madras Medical College, India in 2000. During his years in medical School, Kamalesh became interested in Immunology and decided to pursue his PhD in basic immunology research. Kamalesh's research interests include immunologic tolerance to self antigens as well as pathogenesis of adjuvant arthritis. After graduation, Kamalesh wants to continue working on the novel clinical aspects in the field of autoimmunity. In his leisure time Kamalesh enjoys working out in the gym and closely follows professional tennis as well as current affairs. He has a taste for exploring newer and exotic foods from all over the world.

Eugene Kim (Moudgil lab) is originally from Seoul, South Korea and grew up in southern California. He earned his BS in Biology from UCLA and pursued a master's degree in Immunology at New York Medical College.
While at UCLA, Eugene was working in a pediatric AIDS clinic lab as a lab assistant when he became curious about immunology. In his attempt to explore immunology more, he joined the lab of Dr. Eli Sercarz and worked directly under Dr. Kamal Moudgil in the field of adjuvant arthritis.
After finishing his MS, Eugene decided to join Dr. Moudgil's new lab at UMB and subsequently was accepted as a PhD student in the Department. As a graduate student, Eugene received an NIH institutional training grant. His thesis project is focused on the role of a regulatory epitope of self (rat) heat shock protein 65 in the pathogenesis of adjuvant arthritis. In the future, Eugene hopes to diversify his research focus to the use of stem cell transplantation for autoimmune diseases.
Eugene is married to Catherine Tsai, MD who is a fellow in gastroenterology at Naval Medical Hospital, Bethesda, MD. Eugene spends his free time playing with his five-month old daughter, Kaitlyn. He also likes reading and enjoys a sci-fi novel just as much as a book on financial investments. He plays tennis and practices classical fencing and swordsmanship to keep in shape.

GRADUATES

Jennifer Snyder, Fall 2004. Dr. Snyder grew up in Buffalo, NY and earned her Bachelor's degree at the University of Rochester, NY. She came to UMB in the fall of 2000 and joined Dr. Harry Mobley's laboratory. Here she worked on the transcriptome of UPEC and the significance of type I and P fimbria in urinary tract infection. After graduating in the fall of 2004, she received a call from Dr. Mike Levine, who is the Center Leader for the Center for Vaccine Development. Dr. Levine offered her a job as Research Coordinator for the Middle Atlantic Regional Center of Excellence for Biodefense and Emerging Infectious Disease Research (MARCE). Her job, which did not previously exist, entails site visits, meetings, and some lab work. She keeps track of about thirty different research projects at sixteen different institutions in Maryland, Washington DC, Pennsylvania, Virginia, and West Virginia. The CVD oversees these institutions and is in charge of distributing $46 million among them. Dr. Snyder ensures that the funds are spent according to the grant applications, that results are produced, and that the labs have adequate funding and resources. Dr. Snyder has been married to her husband, Matt, for four years. She enjoys playing volleyball, and her team made it to the Regionals in Germantown this year. She enjoys spending her free time with her husband at their house in Ellicott City.

ALUMNI – WHERE ARE THEY NOW?

Rhoel Dinglasan, Spring 2004. After graduating from Dr. Abdu Azad's lab, Rhoel made a big move all the way across town, joining the laboratory of Dr. Marcelo Jacobs-Lorena at the Johns Hopkins Bloomberg School of Public Health as part of the Malaria Research Institute. Dr. Jacobs-Lorena let Rhoel develop a wholly new research approach within the limits of his program. This research plan involves the biochemical characterization of carbohydrate-binding ligands of the *Plasmodium* parasite and their cognate receptors in the mosquito and mammalian hosts. Rhoel is retraining himself as a Glycobiologist/Biochemist by attending Glycobio/Glycoproteomics seminars (at JHU, JHMI and NIH) as well as enrolling in a course on Complex Carbohydrate Analysis conducted at the University of Georgia. On the home front, his wife has finally joined him here in Baltimore, having defended her PhD thesis at Yale last November. She is currently a post-doc at COMB/UMBI in Dr. Gerardo Vasta's laboratory. Unlike Rhoel, she gets to do SCUBA diving in Cozumel as part of her research work.

NEW ARRIVALS

Two new post-docs from Glen Barber's lab at the University of Miami School of Medicine have joined the department:
Heather Ezelle has joined Bret Hassel's lab to work on the ubiquitin-like protein, ISG15. Heather got her BS and PhD from the University of Miami where she worked on the immune response to VSV-expressed Hepatitis-C virus proteins in mice. While Baltimore's weather may not compare to the balmy climes of Miami, Heather is looking forward to being closer to her family in the mid-atlantic region, and to exploring the local spots of interest.

Darren Perkins has joined Stephanie Vogel's lab where he will study signal transduction in relation to TLR signaling. Darren received his PhD from the University of Miami where he studied the regulation of protein synthesis in response to VSV infection. In his spare time, Darren enjoys mountain biking, fishing, and (weather permitting) snorkeling.

The Center for Vaccine Development's Malaria Section has grown to include **Kirsten Lyke**, Assistant Professor of Medicine, who works on malaria immunology and vaccine trials, and **Miriam Laufer**, Assistant Professor of Pediatrics, who works on drug-resistant malaria and HIV in Malawi. Dr. Lyke recently had a paper published in Infection and Immunity entitled "Serum levels of the proinflammatory cytokines interleukin-1 beta (IL-1beta), IL-6, IL-8, IL-10, tumor necrosis factor alpha, and IL-12(p70) in Malian children with severe Plasmodium falciparum malaria and matched uncomplicated malaria or healthy controls", and Dr. Laufer had a paper published in Drug Resistance Updates entitled "Withdrawing antimalarial drugs: impact on parasite resistance and implications for malaria treatment policies."

CONGRATULATIONS!!!

Bryan Taylor (Reitz lab) and his wife, Christine, had their second daughter, Caroline Theresa, on February 21, 2005. She was 8lbs. 2oz. and 18 3/4 inches. She is here pictured with her big sister, Anna Elizabeth.

Eugene Kim and Catherine Tsai had their first child Kaitlyn Kim on October 29, 2004.

Dr. Albert Mulenga (Azad lab) has been appointed as assistant professor at Texas A& M.

Yellow Fever, the Microbiology and Immunology soccer team, won the UMB Championship finals against the team from the Dental School (2-1) on November 21, 2004.

The **"Say Cheese"** photo contest reception was held on March 14, 2005. **Charlotte Andreasen** (Carbonetti lab) received First Place in the "Best of Baltimore" category and Second Place in the "Home Sweet Home" category for students. **Shailesh Satpute**'s (Moudgil lab) photo of Camden Yards Station received Honorable Mention in the "Best of Baltimore" category**.** The photo contest was sponsored by the Athletic Center, Auxiliary Services, and the Office of Student Services. Photos were displayed in the HS/HSL Library and the Student Center.

This month **Dr. Chris Plowe** will be inducted into the American Society for Clinical Investigation (ASCI), established in 1908, one of the nation's oldest and most respected medical honor societies, at the group's annual meeting in Chicago. At present the Malaria Section does not have any students from our department, but with two large grants pending for clinical, molecular, and immunology studies in Mali and Malawi, now is an opportune time for students to express their interest by emailing **cplowe@medicine.umaryland.edu.**

NEWS – NEWS!!!

Dr. Nicholas Carbonetti has accepted the position as the new director of our graduate program in Microbiology and Immunology, effective effective July 1, 2005. Dr. Jan Cerny will continue as director of the NIH training program in Immunity and Infection.

FUN FACTS

Hurricane season: Mike Criscitiello, a University of Miami alum, overlapped with new post-docs Heather Ezelle and Darren Perkins in graduate school; he was helpful in their recruitment to UMB (for a reasonable fee). Additionally, Dr. Flajnik and Dr. Hassel are both University of Miami alumnai and Dr. Keegan's son attends UM now.

The hefty price of science:
In their catalog, VWR International offers a 'deluxe' tool set consisting of fourteen tools set at a *whopping* price of $195.33. Home Depot offers a 160 piece tool set containing nearly all the same tools $79.96.

Aldrich Science offers seven Pyrex brand drying trays for $170.34. You can purchase similar dishes included in a 19 piece Pyrex set (plus a pie dish) for $49.99 at Sears.

Where do you do *your* shopping?

Univ. of MD Graduate Student Association
&
Pigtowne Main Street Program

Invite You To A

Happy Hour Fundraiser

at

SLIDERS SPORTS BAR

504 Washington Blvd., Across from Camden Yards

Friday, April 22, 5pm

- **Half Price Appetizers**
- **Great Raffle Prizes**
- **O's v.Red Sox on T.V.**

Come Support Your Team and Your Community!

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We welcome your comments and suggestions.

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