

newsletter

Case Western Reserve University MSTP mstp.cwru.edu

From the Director

2002-2003

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Medical Scientist Training Program Case Western Reserve University School of Medicine Room T401 10900 Euclid Avenue Cleveland, OH 44106-4965 216.368.3404

This has been a busy year for the CWRU MSTP. We had many program events and activities for our current students, plus the effort applied to the application and admissions process for incoming students. I would like to recognize the strong and spirited efforts of our students that made these efforts so fruitful. The summer and winter retreats were highly successful, as were our other program events (evening seminar series, visiting scientist, etc). Thanks to the MSTP Council and Jodi Thomson, we also had some fun social activities to promote our sense of community. In addition, this year we completed the competitive renewal of our NIH training grant, a process that occurs once each five years. The application and renewal process entailed a lot of work, especially from Deidre Gruning and Donna McIlwain, who slaved over tables of data on our students and faculty. The students all submitted reports, and many participated in the site visit, which occurred in March. While administrative implementation and issuing of an award notice have not yet occurred, at this point the scientific review is complete with a recommendation for 31 slots, our present size. This will keep our MSTP on a stable course over the next five years and allow us to build on the momentum that we have already achieved. Many thanks to all of the students, faculty and staff who contributed to this successful application process!

One change in the program this year is the departure of our Associate Director, Sandy Lemmon, who will be leaving this summer for University of Miami (Florida). We are very sad to see Sandy leave, and we will miss her vigorous efforts on behalf of the students and the program. Sandy has been particularly important in counseling students in the first two years of the program. Fortunately, we have an outstanding replacement for the Associate Director position, as George Dubyak is now assuming that role. Other changes in program administration include the addition of Keith Armitage as MSTP Advisor for Clinical Curriculum and Residency Application and the addition of Gary Landreth to the Steering Committee (replacing Bob Miller as the representative for Neurosciences).

This year we had some wonderful student accomplishments. Perhaps most important, our students continued to publish very strong scientific articles and presented their work at national and international meetings. I would also like to note awards received by our students this year. Lepow Medical Student Research Day awards went to Zongqi Xia (Dean's First Prize for an M.D./Ph.D. Student), Tehnaz Parakh (Alpha Omega Alpha Honor Society Prize), Tarek El Sawy (Alpha Omega Alpha Honor Society Prize), Jim Bayrer (Dean's Honorable Mention Prize) and Darrell Rubin (Dean's Honorable Mention Prize). We had two students, Brian Lestini and Steve Potter, who completed the program this year, and both received awards at graduation. Brian Lestini was

program this year, and both received awards at graduation. Brian Lestini was elected to the Alpha Omega Alpha Honor Medical Society and received both the *(continued on page 5)*

Transitioning Students-2002

е	S	Atheir Abbas, Munster, IN. <i>undergraduate institution:</i> Case Western Reserve University. <i>scien-tific interests:</i> Undecided. Vijay Bhoj, <i>undergraduate institution:</i> College of New Jersey.
		David Chang, Grand Blanc, MI. undergraduate institution: University of Michigan. scientific interests: Biomedical Engineering and Neuroscience
n	t	Elizabeth Chiang , Beachwood, OH. undergraduate institution: California Institute of Technology. scientific interests: Neuroscience.
+		Thomas Cowan , Yukon, OK. undergraduate institution: University of Southern California. scientific interests: Biomedical Engineering and Neuroscience
		Jamal Derakhshan, Charleston, WV. undergraduate institution: West Virginia University, Physics, scientific interests; Biomedical Engineering.
e	C	Michael Drage, Beachwood, OH. undergraduate institution: Boston College, Biology. scientific interests: Immunology, Infectious Disease, and Neuroscience.
		Coby Larsen, Chandler, AZ. undergraduate institution: Brigham Young University, Chemical
r	e	Lenette Lu, San Francisco, CA. undergraduate institution: Swarthmore College, Biology. scien- tific interests: Genetics, Cell Cycle, Infectious Diseases, and Cancer.
	n	Fatima McKindra, Little Rock, AR. undergraduate institution: Spelman College, Biology. scien- tific interests: Molecular Biology and Cancer Biology.
		Shibani Mukerji, Phoenix, AZ. undergraduate institution: Yale, Neurobiology. scientific interests: Neuroscience.
n	t	Obinna Ndubuizu , New Carrollton, MD. u <i>ndergraduate institution:</i> University of Maryland Baltimore County. scientific interests: Neuroscience.
	_	Nicole Pecora Undergraduate Institution: Case Western Reserve University.
		Bridgette Roth, Medina, OH. undergraduate institution: Hiram College, Chemistry. scientific interests: Physiology and Cell Biology
9		Austin Schenk, East Hartford, CT. undergraduate institution: Dartmouth College, Biophysical Chemistry, scientific interests: Bioinorganic Chemistry, Immunology, and Infectious Disease

Returning to the Lab

Mursalin Anis, Pathology. advisor: H. Boom.

Ramani Balu, Neuroscience. advisor: Ben Strobridge. area: Electrophysiology and ion channels.

Lindsey Burrage, Genetics. *advisor:* Joe Nadeau.

Christy Butler, Neuroscience. advisor: Alfred Malouf.

Mike Davis, Pharmacology. *advisor:* Clark Distelhorst. *area:* Role of inositol triphosphate in glucocorticoid-induced apoptosis. **Molly Fuller**, Neuroscience. *advisor:* Robert Miller. *area:* Cytokines' effects (especially BMP's) on proliferation and differentiation of neural precursor cells, and possibly how the ability to decrease proliferation and increase differentiation could be useful in altering brain tumor behavior.

Roger Lin, Biomedical Engineering. *advisor:* David Huang. *area:* Optical coherence tomography and the evaluation of retinal pathologies.

Jared Miller, Neuroscience. *advisor:* Jerry Silver. *area:* The lab studies the role scarring, at both the cellular and extracellular matrix levels, plays in inhibiting central nervous system regeneration. I am going to be looking at the behavior of motor neurons and cortical neurons in a tissue culture model of the CNS scar and hopefully learn what sort of treatments and/or environment favors cellular regeneration.

Jonathan Mosley, Pharmacology. *advisor:* Ruth Keri. *area:* Normal and abnormal processes in mammary gland development. **Steve Ostrowski**, Neuroscience. *advisor:* Gary Landreth. *area:* Alzheimer's disease.

Dolly Padovani-Claudio, Neuroscience *advisor:* Robert Miller. *area:* Nervous system development and regeneration after injury. **Brenda River-Reyes**, Pathology. *advisor:* Alan Levine.

Catherine Rottkamp Neuroscience. advisor: Stephen O'Gorman.

Mark Ruszczycky, Biochemistry. advisor: Vernon Anderson. area: Enzyme chemistry and mechanism.

Davis Ryman, Genetics. advisor: Bruce Lamb. area: Alzheimer's disease and mapping genetic loci involved in amyloid production and processing.

Dave Shultz, Pathology advisor: George Stark area: Cytokine signaling pathways.

Transitioning Students-2002

The New Ph.D.'s

Last Spring these students successfully defended their theses, and they have now reentered medical shool to complete medical degrees.

Michael Altose Paul Carey, Biochemistry

Jeff Bailey Evan Eichler, Genetics Robin Jump Alan Levine, Pathology

Dan Leventhal Dominique Durand, Biomedical Engineering

Kalonji Collins Zahra Toossi and Eric Arts, Molecular Virology Gabe Owens John Nilson, Pharmacology

Anne Deucher Richard Eckert, Physiology and Biophysics Jullia Rosdahl Susann Brady-Kalnay, Molecular and Microbiology

Alex Garber Rolf Renne, Molecular Virology Dana Schwarz Terry Magnuson, Genetics

Dr. Kristin Kaelber (Long) Internal Medicine/Pediatrics

MetroHealth Medical Center

Dr. Erika Noss Internal Medicine Brigham and Women's Hospital

Dr. Shannon Morris

Internal Medicine University of North Carolina Hospital

Dr. William Stacey

Internal Medicine Transitional University Hospitals of Cleveland **Dr. Jason Yustein** *Pediatrics* Johns Hopkins University



Retreats

Winter Retreat 2002 by Phil Verhoeff

On February 7, 2002, the MSTP community gathered for the 3rd annual Winter Scientific Retreat at the College Club in Cleveland Heights. This retreat provides an opportunity for students in the Ph.D. phase of the program to present their research to their peers. Students early in their Ph.D. training may also present a poster outlining the research they've proposed, although personal experience suggests that this proposed research will not likely represent what the student will accomplish. MSTP students currently in the first two years of medical school are encouraged to attend largely because it allows them the opportunity to see the research that older students are doing, and because it acquaints them with potential mentors.

For this particular retreat, 11 students presented talks (15 minutes each) while 25 students presented posters at one of two poster sessions. Of note, more than 50% of this year's speakers have subsequently returned to medical school as third year medical students, suggesting that giving a talk at the Winter Retreat bodes well for a future as an MD-PhD. Your's truly does continue to languish in the lab, however, in spite of giving a talk.... but I digress. The talks this year were on such topics as TGF-b-induced alterations in gene expression, ovulatory surges of hCG and the formation of granulosal cell tumors, sorting nexins in mice, and serotonin receptor targeting. The engineers told us about the Flat Interface Nerve Electrode and volume registration during 3D MRI and CT. Whatever all that means. Finally, we also heard about a KSHV latency factor, DNA polymerase missense insertion mechanisms, calcium-dependent involucrin expression regulation, Peyer's patch mononuclear cell function in IL-10 knockout mice, and lastly (and most importantly), membrane blebbing and cytokine release in macrophages in response to activation of the P2X7 receptor by ATP. Please contact this humble reporter for more information about this topic.

The poster presentations were on a variety of topics from many different labs, including a poster on Raman spectroscopy, which I thought I would never hear of again after my second semester of Physical Chemistry in college. We heard about nuclear receptor coactivators, the human genome, fruit fly gender determination, round worm anesthetic responses, and virology. A healthy dose of immunology was present as well, in the form of antigen presentation, autoimmune myocarditis, inflammatory bowel disease, neutrophil activity in cardiac allografts, and lipid rafts in T cells. Overall, the poster session was interesting and informative for all who participated and gave an opportunity for less-structured conversations while munching tasty appetizers.

Our invited speaker for this retreat was Sean Morrison, from the University of Michigan. I was considering whom to invite in the weeks after 9/11 and opted to invite someone within a short drive to speak about a socially and politically important topic: hence, I invited Dr. Morrison to discuss his work with stem cells. Dr. Morrison is a rising star in the stem cell field, having completed his graduate training at Stanford on hematopoietic stem cells in the laboratory of Irv Weissman and his post-doctoral training with David Anderson at Cal Tech on neural stem cells. Given the recent reports on the possibility of shifting bone-marrow-derived cells into a nervous system phenotype, and the controversy surrounding embryonic versus adult stem cells for therapeutic modalities, this was a great choice for a speaker. Of note, he is also an Assistant Investigator for the Howard Hughes Medical Institute, as well as carrying Assistant Professor appointments in Cell and Developmental Biology and in the Department of Internal Medicine at Michigan. Dr. Morrison presented us his recent work in studying the molecular factors regulating neural development into either neurons, glial cells, or myofibroblasts. Dr. Morrison's talk was excellent and certainly brought many of us up to speed on the real science behind much of the publicity we hear about in the news.

Overall, this was a marvelously successful Winter Retreat and I enjoyed putting it together. With any luck, this year's will be great too, and it will hopefully be the last one I attend!

Retreats

Summer Retreat 2002

by Mike Lobritz

The annual MSTP summer retreat was held July 31 – August 1 at Maumee Bay State Park near Toledo, OH. The summer retreat is a chance for the MSTP community to come together to hear lectures, discuss programmatic development, and further, it provides an opportunity for the new first years to get acquainted with the students and administration. This year's keynote speaker was Dr. Paul Ewald, Professor of Biology at the University of Louisville. He studies the evolutionary biology of parasitism, and in two lectures he spoke on several controversial topics. His first lecture, derived from his most recent book, *Plague Time*, discussed the role of infectious causation in the etiology of diseases normally ascribed to non-infectious sources, and engaged the audience in a debate on the possible infectious causation of schizophrenia. In a later lecture, based on his book *Evolution of Infectious Disease*, Ewald discussed his own research on the evolution of virulence in *Vibrio cholera*.

The retreat's evening lecture was presented by Dr. Henry Kreuzman, Chair of the Department of Philosophy at Wooster College. He gave an interactive session on the history of epidemiology and infectious disease, and a brief talk on medical ethics. Three seminars were presented this year, the first by Dr. Patrick Leahy, Manager of the Gene Expression Array Core Facility. Dr. Leahy discussed the technology surrounding the Affymetrix GeneChip, including preparation and processing of samples, data acquisition, and analytical services available through this CWRU facility to the research community. Other workshops were delivered by Jennifer Heron, a real estate agent from Smythe Cramer realty, who discussed real estate options for MSTP students in the greater Cleveland area, and by Dr. Matt Warman, Professor of Genetics at CWRU, who discussed the perils of the scientific publication process.

The retreat was marked by the usual conviviality including the annual MSTP softball game, early morning tennis with Cliff, and of course, the Japanese art of karaoke, which included for the first time ever a song and dance routine between the Director and Director Emeritus of the program. We all hope that it won't be the last.

(continued from page1)

Noether Memorial Fund Award for excellence in the area of Therapeutics and the Department of Pediatrics Award to a fourth year student who displays compassion and excellence in the care of children and their families. Steve Potter received the Martin Wahl Memorial Fund Award to an M.D./Ph.D. student who demonstrates both independence and excellence in research and clinical skills, and the Department of Neurology Award to a fourth-year student with the most outstanding performance in Neurology at University Hospitals of Cleveland/ VA Medical Center. Brian will be doing his residency in Pediatrics at Children's Hospital, Los Angeles, and Steve will be doing his residency in Neurology at the Cleveland Clinic. Both students received their first choice residency.

While our MSTP has a very successful structure, we continue to strive to improve it. Over the last year we have incorporated three new programs into the MSTP: Biomedical Engineering/Physician Engineer Training Program (PETP), the Chemistry Graduate Program and the Graduate Program in Genetic and Molecular Epidemiology. These additions to the MSTP expand the scope of research topics and activities that is available to our students. As we go into the future we will continue to improve the program by enhancing mentorship and training, and to promote high academic and scientific accomplishment by our MSTP students. We will continue to develop and implement program activities, including our retreats, evening seminars, etc. MSTP Council is planning a new CWRU Clinical Scholars Program, which may integrate research presentations by our students and clinical fellows with research interests and activities. We are looking forward to another exciting and successful year in the CWRU MSTP!

Student Activities

MSTP Council 2001-2002 by Lewis Rosenberg, president emeritus

The MSTP Council had another productive season in the 2001-2002 school year. Dedicated officers and chairpersons had not only good ideas but also the determination and desire to see them through. As usual, the council met monthly over dinner to discuss MSTP issues and events. Attendance among the council members was excellent but among non-members was scarce, save for the periodic hungry student seeking brief refuge from the lab. Our new director, Cliff Harding, easily found his place in the council and led with light-hearted confidence. All in all, this past year's council was an unqualified success.

The council had several novel accomplishments. Of greatest note is the completion of the revised web page, a project which was begun several years ago. Current Web Page Committee chairperson Brent Weinberg built on the vision of Roee Lazebnik and Jim Bayrer to create a page that must be among the best MD/PhD pages in the country. It has become an excellent resource for prospective and current students alike. Also of note is the creation of the Service Committee. This committee was the brainchild of Lindsay Burrage who is also the chairperson. It will help fulfill a common desire of students to improve the Cleveland community.

The MSTP council also fulfilled its duties in its usual annual roles. The Monthly Meeting Committee, chaired by Mark Ruszczycky, more than succeeded in the difficult task of finding speakers that appealed to the entire community, and also organized a menu each month that was beyond the call of duty. Ram Balu, who always seemed to have a dozen ideas for speakers for MSTP functions, was appropriately the chairperson of the Guest Speakers Committee and succeeded well in finding and recruiting fascinating guests. The formidable task of organizing the summer retreat was completed by first year student Mike Lobritz, who organized a retreat that will be hard to top. Molly Gallogly was the chairperson of the Intro to MSTP Committee, a job made both fun and difficult by the flexibility afforded the chairperson, and commendably found useful and interesting activities for the first year students. Dave Shultz was the chairperson of the Social Committee whose success in that position is best exemplified by the fact that he made our illustrious director rethink his career as a professional bowler. Mark Ruszczycky, as chairperson of the Newsletter Committee, spent much of his valuable time politely but sternly reminding authors to submit articles so that this newsletter might be a success.

The executives this past year also worked to serve their MSTP community. The secretary was Jodi Thomson who diligently recorded all relevant discourse of the council meetings. Dave Shultz served as vice-president, filling in for the other executives' rare absences. Lewis Rosenberg was president; his job was made easy by the hard work and dedication of all the people already mentioned. This year's president is Ram Balu who has already confidently taken the reins and will undoubtedly lead the council through another successful year.

Monthly Dinner Meetings by Mark W. Ruszczycky

For some time the MSTP monthly dinner meetings have been a success in bringing together CWRU MSTP students in all phases of their training, and the 2001-2002 academic year was no exception. The dinner meetings this past year were coordinated by Ram Balu, Molly Gallogly, Davis Ryman, and Mark W. Ruszczycky, who were successful in acquiring a number of interesting and diverse speakers. Two speakers were from the Department of Biomedical Engineering: Hillel Chiel spoke on the modeling of *Aplysia* feeding behavior, and Hunter Peckham discussed neural prosthesis. Talks also included a history of electroconvulsive therapy delivered by Jonathan Sadowsky of the Department of History, while David Farrell from the CWRU Department of Physics described new progress in determining iron stores non-invasively using magnetic susceptibility measurements. We were also fortunate enough to have the director of the University of Rochester MSTP, Kerry O'Banion, who spoke on the various issues surrounding the process of drug development. A promising set of meetings is already being scheduled for the 2002-2003 year, which we are all very much looking forward to.

Student Activities

Selected Recent Publications

Bailey JA, Yavor AM, Viggiano L, Misceo D, Horvath JE, Archidiacono N, Schwartz S, Rocchi M, Eichler EE (2002) Human specific duplication and mosaic transcripts: the recent paralogous structure of chromosome 22. Am *J Hum Genet in press*

Collins K R, Quinones-Mateu ME, Wu M, Luzze H, Johnson J L, Hirsch C, Toossi Z, Arts E J. Human Immunodeficiency Virus Type 1 (HIV-1) Quasispecies at the Sites of *Mycobacterium tuberculosis* Infection Contribue to Systemic HIV-1 Heterogeneity. *Journal of Virology* 2002, *In press*.

Deucher A, Efimova T, Eckert RL. Calcium-dependent involucrin expression is inversely regulated by protein kinase C (PKC)alpha and PKCdelta. *J Biol Chem*. 2002 May 10;277(19):17032-40. Epub 2002 Feb 25.

Miura M, **EI-Sawy T**, Fairchild RL. Neutrophils Mediate Parenchymal Tissue Necrosis and Accelerate the Rejection of Complete Major Histocompatibility Complex-Disparate Cardiac Allografts in the Absence of Interferon-gamma. *Am J Path.* 2003 Feb; 162(2):509-519.

Brown CR, McCann JA, Hung GG, **Elco CP**, Chiang HL. Vid22p, a novel plasma membrane protein, is required for the fructose-1,6-bisphosphatase degradation pathway. *J Cell Sci* 2002 Feb 1;115(Pt 3):655-66 **Garber AC**, Hu J, Renne R. Latency-associated nuclear antigen (LANA) cooperatively binds to two sites within the terminal repeat, and both sites contribute to the ability of LANA to suppress transcription and to facilitate DNA replication. *J Biol Chem.* 2002 Jul 26;277(30):27401-11.

Gray JA, Bhatnagar A, Gurevich VV, and Roth BL (2003). The interaction of a constitutively active arrestin with the arrestin-insensitive 5-HT_{2A} receptor induces agonist-independent internalization. *Mol Pharmacol*, in press.

Jane-wit D, Yu M, Edling AE, Kataoka S, Johnson JM, Stull LB, Moravec CS, Tuohy VK. A novel class Ilbinding motif selects peptides that mediate organ-specific autoimmune disease in SWXJ, SJL/J, and SWR/J mice. *J Immunol*. 2002 Dec 1;169(11):6507-14.

Jump, RL and Levine, AD 2003. Mechanisms of Natural Tolerance in the Intestine: Implications for IBD. IBD in press.

Lazebnik RS, Lancaster TL, Breen MS, Lewin JS, Wilson DL. Volume Registration Using Needle Paths and Point Landmarks for Evaluation of Interventional MRI Treatments. *IEEE Transactions on Medical Imaging*. 2003; *In Press*.

Lestini BJ, Sagnella SM, Xu Z, Shive MS, Richter NJ, Jayaseharan J, Case AJ, Kottke-Marchant K, Anderson JM, Marchant RE. Surface modification of liposomes for selective cell targeting in cardiovascular drug delivery. *J Control Release*. 2002 Jan 17;78(1-3):235-47.

Leventhal DK, Durand DM. Subfascicle stimulation selectivity with the flat interface nerve electrode. *Ann Biomed Eng.* 2003 Jun;31(6):643-52.

Silverman EK, **Mosley JD**, Palmer LJ, Barth M, Senter JM, Brown A, Drazen JM, Kwiatkowski DJ, Chapman HA, Campbell EJ, Province MA, Rao DC, Reilly JJ, Ginns LC, Speizer FE, Weiss ST. Genome-wide linkage analysis of severe, early-onset chronic obstructive pulmonary disease: airflow obstruction and chronic bronchitis phenotypes. *Hum Mol Genet.* (2002) 15;11(6):623-32.

Owens GE, Keri RA, Nilson JH. Ovulatory Surges of Human CG Prevent Hormone Induced Granulosa Cell Tumor Formation Leading to the Identification of Tumor-Associated Changes in the Transcriptome. *Mol Endocrinol.* 2002 Jun;16(6):1230-42.

Pai, R. K., D. Askew, et al. (2002). "Regulation of class II MHC expression in APCs: roles of types I, III, and IV class II transactivator." *J Immunol* 169(3): 1326-33.

(Selected Recent Publications from page 7)

Ramirez JJ, **Parakh T**, George MN, Freeman L, Thomas AA, White CC, Becton A. The effects of Neotrofin on septodentate sprouting after unilateral entorhinal cortex lesions in rats. *Restorative Neurology and Neuroscience* (2002), 20 (1-2): 51-9.

Thomenius MJ, Wang NS, **Reineks EZ**, Wang Z, Distelhorst CW.Bcl-2 on the endoplasmic reticulum regulates Bax activity by binding to BH3 only proteins. *J Biol Chem.* 2002 Dec 10.

Poirier M, Vincent G, **Reszko AE**, Bouchard B, Kelleher JK, Brunengraber H, Des Rosiers C. Probing the link between citrate and malonyl-CoA in perfused rat hearts. *Am J Physiol Heart Circ Physiol.* 2002 Oct;283(4):H1379-86

Rosdahl, J., Mourton, T., and Brady-Kalnay, S.M. The PKCd signaling pathway is required for PTPµ-dependent neurite outgrowth. *Molecular and Cellular Neuroscience*, 19, 292-306. 2002.

Murray K., Calaora V., **Rottkamp C.**, Guichert O. and Dubois-Dalcq M. (2002). Sonic hedgehog is a potent inducer of rat oligodendrocyte development from cortical precursors *in vitro*. *Mol. Cell. Neurosci.*, 19, 320-332.

Schade, A.E., Levine, A.D. Lipid raft heterogeneity in human peripheral blood T lymphoblasts as a mechanism for regulating the initiation of TCR signal transduction. *J. Immunology* 168:2233-2239 (2002).

Schwarz, D. G., Griffin, C. T., Schneider, E. A., Yee, D. & Magnuson, T. Genetic analysis of sorting nexins 1 and 2 reveals a redundant and essential function in mice. *Mol Biol Cell* 13, 3588-600 (2002).

Xia Z, Hufeisen S, **Gray J**, and Roth BL. (2003) The PDZ-binding Domain Is Essential for the Dendritic Targeting of 5-HT_{2A} Serotonin Receptors in Cortical Pyramidal Neurons *in vitro. J. Neurosci. In Press.*

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