Inside MBC "...molecular medicine through biotechnology"

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UMBI Policies and Procedures Under Review

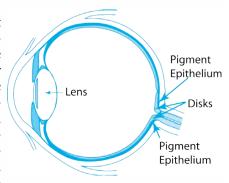
A major effort is under way at UMBI to review all the policies and procedures currently in place at the institution and rewrite or create those that are either outdated or missing. Everything from hiring practices to IT policy to firing practices must be looked at. At the center of this effort is the Policy and Procedures Committee, chaired by MBC's Assistant Director Tim Hughes. Representatives from all the centers and UMBI central are on the main committee, which is charged with overseeing this effort. Specific or specialized subcommittees are created as needed to deal with particular issues or already existing advisory groups, such as the Information Systems Advisory Board (ISAB), are asked to draft policies.

The draft policies are available on the staff/senate web site (http://www.umbi.umd.edu/senate/index.htm). Everyone is encouraged to comment upon these policies before they go into effect. MBC Senate representatives, Dr. Bruce Vogel, Dr. Hali Hartmann or Tim Hughes, will be happy to pass on your comments. You can view current policies in effect at http://www.umbi.umd.edu/pandp/index.html. This page also includes USM policies to which UMBI must adhere as well.

Seminars Go International

May and June brought three different yet scientifically intertwined speakers to the MBC. On May 2, Dr. Dennis Schultze from the Casey Eye Institute, Oregon Heath and Science University visited the MBC, hosted by Dr. Bruce Vogel. Dr. Schultz studies age-related macular degeneration. This disease is characterized a slow progressive loss of sight in older people and is one of the major causes of blindness in persons over the age of 65. He has identified a gene associated with one form of the disease using the published human genome and a family with a history of the disease. The gene encodes fibulin 6, one member of a family of proteins found in the extra-cellular matrix, the "glue" that

holds cells together to form tissues. In the eye (see the figure right), it is found in the layer of cells (pigment epithelium) that covers the photoreceptors (disks). This layer recycles the material coming off the photoreceptors as they are regenerated over time. When this material is not recycled properly, it accumulates and blindness ensues. Recognizing where the repair mechanism is failing is the first step in developing treatment strategies.



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Graduation Time Again



Dr. Stacy Stabler, M.D., Ph.D.

May is an exciting time at academic institutions. Young men and women who have been mentored by faculty members for several years are sent forth for the next step in their careers. Dr. Stacy Stabler is one such individual from Dr. Mervyn Monteiro's laboratory. She was an M.D.-Ph.D. student who had finished her Ph.D. in April of 2001. This May she received her M.D. Her work on presinilin and its role in Alzheimer's Disease started with her rotation through Dr. Monteiro's laboratory and continued even after she began clinical studies for the M.D. degree. M.D.-Ph.D. students

continued on page 2

Graduation continued.

typically take two years of classes, two years of research ending with the Ph.D. and then finish with two years of clinical studies. She has been accepted into a residency program in General Medicine at the University of Wisconsin in Madison. Dr. Stabler is the first person in her family to go into medicine. She is the second student of Dr. Monteiro's to complete the dual degree. Dr. Alex Mah finished last year (*Inside MBC*, Vol. 5, No. 3).

It is not only the younger generation that pursues advanced degrees. Mrs. Tongo Best, long-time Admin-

istrative Assistant at the MBC, put USM's tuition remission benefit to good use and finished her Bachelor of Science degree in Social Science at Coppin State University. She remains with the MBC, however, and expects to continue taking classes. It took Mrs. Best over 20 years, off and on, to finish her degree. Being the mother of two sons, one of who has already graduated from college



Mrs. Tongo Best, B.S.

and the other who is in high school, limited the number of classes she could take at one time. However, her perseverance has paid off.

Congratulations to both our graduates!

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MBC/UMBI Perspectives

By Tim Hughes

The 1990's begin...

The 1990's began with a charge from President Rita Colwell to Dr. Stephen Max (then Associate Vice President for Research at University of Maryland Baltimore [UMB]) to chair a search committee for MBC's first permanent director. The committee, including representatives from UMB Schools of Medicine (Dr. Max, Dr. Phyllis Wise), Dentistry (Dr. Van Thompson), and Pharmacy (Dr. Marilyn Speedie) and University of Maryland Baltimore County (Dr. Richard Wolf), began their quest immediately.

In February 1990 Dr. Joseph Kao was recruited from the University of California, Berkeley (from the Laboratory of Dr. Roger Tsien) as an MBC Assistant Professor, with a secondary appointment at UMB School of Medicine, Department of Physiology. Dr. Kao's research interests included the design, chemical synthesis and application of fluorescent probes and photosensitive "caged" compounds in cell physiology. As with previous MBC hires, his appointment was "matched" with a complementary UMB faculty member – in this case Dr. W. Jonathan Lederer from the Department of Physiology. In April of 1990 Dr. Marian Jackson joined the MBC Faculty as an Assistant Professor. Dr. Jackson, who came to the MBC from the Baylor College of Medicine Institute for Molecular Genetics in Houston Texas, was jointly appointed in the UMB Department of Neurology with additional links to the Division of Human Genetics and the Graduate Program in Molecular and Cell Biol-

July 1990 marked an important milestone in progress

toward establishing a permanent home for the MBC. The new fiscal year brought \$2.6M from the Maryland state capital budget to purchase the Hutzlers warehouse from the City of Baltimore. This major funding decision instilled tremendous confidence that the 200,000 gross square foot building on Lombard Street would one day be occupied by existing and future MBC fac-



Courtesy of the Peale Museum

ulty and staff. The City of Baltimore was pleased to sell the facility to the University. Based on MBC's approved program plan, their enthusiasm was high with the promise, and the economic advantage, of over 350 employees working in the city all aligned with the city's theme at that time: "Baltimore: Where Science Comes to Life".

Next...Finding the right leader...



Seminars continued.

Beginning in June, many visitors from Europe and elsewhere are in the United States for various scientific meetings. Often they give talks and visit colleagues here in addition to the meetings. Dr. Marcel Egger was one of these. He is from Dr. Ernst Niggli's well-known cardiology laboratory at the Institute of Physiology, University of Bern, Switzerland and had been in MBC Director Dr. W. J. Lederer's laboratory in the 1990's. Dr. Egger spoke June 16, 2003 on "Refractoriness of sarcoplasmic reticulum calcium release and remodeling of the sodiumcalcium exchange function during cardiac hypertrophy." Hypertrophy, or enlargement, of the heart is one of the common symptoms of cardiac disease. It is believed that the heart gets larger to compensate for the decrease in efficiency as the underlying cause of the disease affects function. Dr. Egger discussed his work that shows that the heart becomes less responsive over time to calcium induced calcium release when it is hypertrophic. He also showed that this is a global phenomenon in the heart. As our understanding of the underlying causes of heart disease grows, it may be his work that allows the disease to be controlled when the cause cannot be cured.

Scientific meetings also brought another visitor to the MBC, this one from the opposite side of the globe, New Zealand. Dr. Mark Cannell is Chair of the Department of Physiology, University of Auckland, New Zealand. Dr. Cannell was one of Dr. Lederer's first postdoctoral fellows in the 1980's. On June 25, he spoke on "Making light work in the lens and cardiac muscle – From molecular biology to function and back." He really had two talks in one. The first part about his work on the lens of the eye was particularly fascinating. (The location of the lens is noted on the figure on page 1.) The cells in the center of the lens are clear but not dead. Using a variety of imaging techniques, he showed that the cells are nearly emptied of most organelles through incomplete apoptosis, making the cells clear. Apoptosis, also called programmed cell death, is the process by which cells die naturally. The biochemical events involved in this process are becoming very well understood because disruption of apoptosis can cause cancer. That this process is arrested naturally has some intriguing implications in the study of aging.

Dr. Cannell also spoke about his studies on spontaneous hypertensive rats. He showed that there is a disruption in the contractile force generated by cardiac myocytes in these animals. The expected explanation for this decreased contractile force would usually focus on decreases in calcium cycling. However, Dr. Cannell showed that calcium cycling was only slightly aberrant and not decreased. Imaging studies showed that the collagen in these spontaneous hypertensive rats was crosslinked to a high degree and that this was physically disrupting contractions. Further work on this novel and surprising finding will include using molecular biological techniques to look at genetic changes.

Tricks of the Trade

By Pamela Wright

Mastering Masters: Creating your own PowerPoint template

One of the most powerful features of PowerPoint, is its ability to apply a global design or "design template" to a presentation. It comes with a large selection but these tend to be business oriented. Thus, you may wish to create your own. They appear easy to create; just add the elements you want and "Save As" a template. However, while this saves design elements, it does not format text or control other useful features of the preset templates. What is missing are changes to the Masters.

There are actually four Masters: Slide Master which controls the layout and style of all slides, Title Master which sets the style and layout for the title slide, Handout Master, and Notes Master. You can change these Masters by selecting View, Masters. When the Master comes up, you can click on the elements to change—text boxes, images, fonts, sizes or even add/delete elements. The changes are then applied to all the various layouts associated with a design template. These changes should be made before saving the template.

There is one quirk about using your own templates. When you save as a template, that template is NOT saved with the other presentation designs that come with PowerPoint. For Windows users this means when you start PowerPoint and choose "Create a new presentation using Design Template" you will not see your template there. This is because your template is saved in your user area not with the program templates. There are two ways to handle this. 1) You can create a blank presentation and retroactively apply your template ("Format, Apply Design Template"), which does come up as a choice in the list of other templates available or 2) You can start the "Save As" process, but change the directory to the program template folder. In Windows 2000 machines this is buried under C:/Program Files/Microsoft Office/ Templates/Presentation Designs. Placing your template here will make it show up when you choose "Create a new presentation using Design Template".

Macintosh users have an easier time of it. When you "Save As" a template it goes into a folder called My Templates. As long as you go into Project Gallery mode in Microsoft Office, that folder is clearly visible and you would just open your template stored in that folder. If you open PowerPoint directly, no design templates are shown and any of these would have to be found and applied retroactively.





MBC Happenings

In Memoriam

June 19, 2003: **Dr. Belding H. Scribner**, step father of Dr. W.J. Lederer, died at age 82. Dr. Scribner was a pioneer in kidney dialysis.

Comings and Goings

Dr. Kadir Aslan joined Dr. Chris Geddes laboratory as a Research Associate. Dr. Ilia Baskakov's laboratory now includes Research Associate **Dr. Leonid Breydo** and Research Assistant **Christopher Pabst. Dr. Jiahon Ni** is a new Research Associate in Dr. Joseph Kao's laboratory.

Dr. Les Baillie has left the MBC to join the U.S. Department of Navy's Medical Research Center. He retains an adjunct appointment at the MBC. **Mr. Steven Hibbs,** who worked with Dr. Baillie has resigned. **Ms. Tara Pierce**, receptionist, has left.

Grants and Contracts

Dr. Ilia Baskakov, NIH, NIA, "Reconstitution of Prion Transmission is Cells." 5/1/03, \$74,250, yr 1 of 1.

Dr. Mervyn Monteiro, NIH, NIGMS, "Functional Studies of Ubiquilin." 5/1/03, \$249,480, yr 1 of 4.

Publications

Williams RC, Rees ML, Jacobs MF, Pragai Z, Thwaite JE, **Baillie LWJ**, Emmerson PT, Harwood CR. Production of *Bacillus anthracis* protective antigen is dependent on the extracellular chaperone, PrsA. J BIOL CHEM 278 (20): 18056-18062 MAY 16 2003

Baillie L, Hebdon R, Flick-Smith H, Williamson D. Characterisation of the immune response to the UK human anthrax vaccine. FEMS IMMUNOL MED MICRO 36 (1-2): 83-86 MAY 15 2003

Read TD, Peterson SN, Tourasse N, **Baillie LW**, Paulsen IT, Nelson KE, Tettelin H, Fouts DE, Eisen JA, Gill SR, Holtzapple EK, Okstad OA, Helgason E, Rilstone J, Wu M, Kolonay JF, Beanan MJ, Dodson RJ, Brinkac LM, Gwinn M, DeBoy RT, Madpu R, Daugherty SC, Durkin AS, Haft DH, Nelson WC, Peterson JD, Pop M, Khouri HM, Radune D, Benton JL, Mahamoud Y, Jiang LX, Hance IR, Weidman JF, Berry KJ, Plaut RD, Wolf AM, Watkins KL, Nierman WC, Hazen A, Cline R, Redmond C, Thwaite JE, White O, Salzberg SL, Thomason B, Friedlander AM, Koehler TM, Hanna PC, Kolsto AB, Fraser CM. The genome sequence of *Bacillus anthracis* Ames and comparison to closely related bacteria. NATURE 423 (6935): 81-86 MAY 1 2003

Geddes CD, Cao H, **Gryczynski I**, Gryczynski Z, Fang JY, **Lakowicz JR**. Metal-enhanced fluorescence (MEF) due to silver colloids on a planar surface: Potential applications of indocyanine green to in vivo imaging. J PHYS CHEM A 107 (18): 3443-3449 MAY 8 2003

Malicka J, **Gryczynski I**, Lakowicz JR. DNA hybridization assays using metal-enhanced fluorescence. BIOCHEM BIOPHYS RES COMM 306 (1): 213-218 JUN 20 2003

Malicka J, **Gryczynski I**, Fang JY, **Lakowicz JR**. Fluorescence spectral properties of cyanine dye-labeled DNA oligomers on surfaces coated with silver particles. ANAL BIOCHEM 317 (2): 136-146 JUN 15 2003

Khan N, Wilmot CM, **Rosen GM**, Demidenko E, Sun J, Joseph J, O'Hara J, Kalyanaraman B, Swartz HM. Spin traps: In vitro toxicity and stability of radical adducts.

Anthrax Genome Published

An important milestone was published in *Nature* this May, the complete genome sequence of *Bacillus anthracis*. This work was done at The Institute of Genomic Research (TIGR) as a coordinated effort by many researchers from many institutions throughout the world. Dr. Timothy Read, who is a secondary faculty member of the MBC and first author on the paper and Dr. Les Baillie, a secondary author who recently stepped down as a primary faculty member to become secondary, are both deeply involved in the MBC Biodefense Initiative, which focuses on the possible use of anthrax by terrorists. Dr. Baillie continues to head this initiative at the MBC. The genome sequence will allow researchers to understand the basic biology of B. anthracis and develop specific tests, more effective vaccines and targeted therapeutics to this deadly microorganism.

FREE RADICAL BIO MED 34 (11): 1473-1481 JUN 1 2003

Wei SK, **Ruknudin A**, Hanlon SU, McCurley JM, **Schulze DH**, Haigney MCP. Protein kinase A hyperphosphorylation increases basal current but decreases beta-adrenergic responsiveness of the sarcolemmal Na*-Ca²* exchanger in failing pig myocytes. CIRC RES 92 (8): 897-903 MAY 2 2003

Mansouri A, Ridgway LD, Korapati AL, Zhang QX, Tian L, **Wang YB**, Siddik ZH, Mills GB, Claret FX. Sustained activation of JNK/p38 MAPK pathways in response to cisplatin leads to Fas ligand induction and cell death in ovarian carcinoma cells. J BIOL CHEM 278 (21): 19245-19256 MAY 23 2003

Yoo D, Kim BY, Campo C, Nance L, King A, Maouyo D, **Welling PA**. Cell surface expression of the ROMK (Kir 1.1) channel is regulated by the aldosterone-induced kinase, SGK-1, and protein kinase A. J BIOL CHEM 278 (25): 23066-23075 JUN 20 2003

Wehrens XHT, Lehnart SE, Huang F, Vest JA, Reiken SR, Mohler PJ, Sun J, **Guatimosim S**, **Song LS**, Rosemblit N, D'Armiento JM, Napolitano C, Memmi M, Priori SG, **Lederer WJ**, Marks AR. FKBP12.6 deficiency and defective calcium release channel (ryanodine receptor) function linked to exercise-induced sudden cardiac death. CELL 113 (7): 829-840 JUN 27 2003

Geddes CD, Parfenov A, Roll D, **Gryczynski I**, Malicka J, **Lakowicz JR**. Silver fractal-like structures for metal-enhanced fluorescence: Enhanced fluorescence intensities and increased probe photostabilities. J FLUOR 13 (3): 267-276 MAY 2003

Geddes CD, Parfenov A, **Lakowicz JR**. Photodeposition of silver can result in metal-enhanced fluorescence. APPL SPECTROS-COPY 57 (5): 526-531 MAY 2003

Talks and Travels

Dr. W. J. Lederer, Invited Speaker, Third Symposium on Biochemical and Physiological Aspects of Muscle Research, Autonomous National University of Mexico. "Ca²⁺ Sparks in Heart Muscle". May 6-9, 2003.

Dr. Ilia Baskokov, 5/13/03, Department of Chemistry and Biochemistry, University of Maryland College Park, "Conformational Transition of the Prion Protein: Exception or Rule in Protein Folding?"

Dr. Ilia Baskakov, 6/30/03, Chiron Corporation, Emeryville, CA, "Refolding of Recombinant Prion Protein into Abnormal PrP^{Sc}-like Isoform."