

Inside MBC

"...molecular medicine through biotechnology"

Volume 6, Number 1

January-February, 2003

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Governor-Elect Visits UMBI for BOV Meeting

The winter meeting of UMBI's Board of Visitors, a distinguished group of outside advisors, was particularly memorable with the attendance of Governor-Elect Robert L. Ehrlich. He came at the invitation of President Jennie Hunter-Cevera, a member of his transition team. Along with the Board, all of the center directors had a chance to hear the Governor-Elect discuss his interest in biotechnology and higher education. MBC's director, W. J. Lederer commented "I'm really excited to meet our chief executive and share with him discoveries in molecular medicine."

The Board of Visitors, headed by Dr. Martin Apple, includes many of Maryland's most influential biotechnology industry leaders. Through their efforts and good will, UMBI maintains a high profile within the state.

UMBI Annual Report

The 2002 version of UMBI's Annual Report is out. This year highlights MBC faculty members, Drs. Shenyung Fang, Chris Geddes and Les Bailie. In addition, three students, Leann Massey from Dr. Mervyn Monteiro's laboratory, Andrew Ziman from Dr. W. J. Lederer's laboratory and David Freilich from Dr. Joseph Kao's laboratory, were profiled. Great pictures!

New Cause of Heart Disease Discovered

Rarely does MBC research excite anyone outside scientific circles, but a paper in Nature has done just that. Dr. W. Jonathan Lederer, Director of the MBC and head of its Institute of Molecular Cardiology, has discovered a new mechanism for a form of sudden cardiac death (SCD), called "Long QT Syndrome, Type 4" (LQT4). Cardiovascular disease, of which cardiac arrhythmia and SCD are major symptoms, and stroke are the leading causes of death world-wide. Dr. Lederer led the investigation into the cellular cause of this inherited arrhythmic disturbance.

Using state-of-the-art instrumentation and a novel animal model, the research team examined why members of a family in France died suddenly and unexpectedly in the prime of life. Lederer and his team collaborated with other primary investigators from Duke University headed by Drs. Vann Bennett and Peter Mohler and with investigators at INSERM in Nantes, France, headed by Dr. Denis Escande. Key local investigators included Drs. S. Guatimosim, L-S. Song and K. Dilly from MBC and T. B. Rogers and W. duBell from the School of Medicine at University of Maryland, Baltimore.

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Spotlight on Central

The first in a series about UMBI Central administrative staff.

Taken for Granted

Both the boon and bane of any faculty member's existence is the submission of grants. And while they are the ones who must write and perform, no grant gets submitted without the help and authorization of UMBI's Office of Sponsored Programs (OSP), headed by Dean Drake. While his name appears on the front sheet of every grant submitted, most faculty members would not recognize the face.

Dean came to UMBI in 2001, first as Manager of OSP and now as Director. He had been with the Department of International Health, Johns Hopkins School of Public Health since 1994 and in the private sector before that. He says he enjoys working here, that everyone works together and that there is a high level of trust that is very satisfying.

Besides checking over and signing off on grants and contracts, OSP is responsible for the management of awards, including allowable costs; tracking funding opportunities, training personnel in research administration and generally knowing everything there is to know about

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Drake continued.



Dean Drake

outside funding sources. Dean is particularly interested in making as many resources easily available as possible to the faculty of all the centers. This is demonstrated by the greatly expanded web site for OSP. As he put it: "I would rather communicate how to get there rather than answer the question directly." He is a big supporter of COS, the

Community of Science, an institutional web resource to which UMBI contributes. This is a great resource for funding sources, contacting colleagues and maintaining CV's (See *Inside MBC*, Vol. 4, No. 5).

One of his most ambitious projects in online routing of grant proposals (See *Inside MBC*, Vol. 5, No. 5). This is still in beta testing. At MBC, only Pamela Wright and Tim Hughes are authorized to use the online system. The system is designed to speed up processing, as well as create a database for administrators to use when looking at funding levels and productivity, among other things.

In the future, Dean would like to have more face-to-face contact with the faculty. He is interested in having "brown-bag" lunches at each center to answer questions about resources available to researchers and other questions about funding processes. Not one to stand still, he is also working on a marketing degree and wants to increase OSP's input to the strategic objectives of UMBI.

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Back issues of *Inside MBC* are available on the web at:
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Posters Made Easy

As every graduate student knows, one of the first ways they communicate with the greater scientific community is the presentation of a poster at a national meeting. While quintessential scientific communication tools, they are generally approached with loathing and trepidation; the "artistic" nature of the presentation seeming somehow foreign. Yet slide presentations, also requiring illustrations, are handled more confidently. MBC students and faculty members can now merge the two mediums with the purchase of a 42 inch, high end, Hewlett Packard large format printer.

Large format printers use a roll of paper so that any length can be printed. This means that a poster can be printed out on one sheet instead of numerous sections mounted separately. Commercial printers have been doing this for years, but at \$250 or more per poster the cost is generally too high for most laboratories and one major error means another \$250. Even with the most expensive photo glossy paper, the MBC printer brings the cost/poster down to approximately \$25.

There is a learning curve involved, however. Posters can be created by several applications, but generally MBC people are most comfortable with Microsoft PowerPoint®. Moving slides, which are generally the configuration of a sheet of paper, to something that is 42"x56" (Some versions of PowerPoint limit the size to this) has its downside. Things which looked great projected do not necessarily print well. Fonts and graphics need to be enlarged and written explanations are needed.

Pamela Wright, Assistant to the Director, has created some instructions and helpful hints that can be found in the Staff Section of the MBC web site. She is also in charge of supplies. The printer is on the MBC network and Mike Kelly, MBC's IT person, takes care of that connection.

The printer arrived in November and was put to immediate use for the UMBI Research Day in December. It got its first real workout for the Biophysics meeting in San Antonio, Texas which began March 1st (see the next issue of *Inside MBC* for an article on this important meeting). Presenting original data is exciting and necessary for everyone at MBC. Now it can be artistic as



Posters decorate the hallways outside laboratories.

Heart continued.

The genetic defect in humans and in the mouse model was an inadequate amount of an important “adaptor” protein, ankyrin-B. This protein links one protein to another, permitting other proteins to be properly located within the structure of a cell. In the reduction or absence of ankyrin-B, proteins involved in cellular calcium regulation are placed improperly. This leads to an abnormal increase in the amount of calcium within the heart cell. This change in calcium causes the heart to beat improperly and, in the case of LQT4, chaotically. Interestingly, this does not happen all of the time and rarely in young individuals. The rare occurrence of the development of calcium-dependent electrical chaos in the heart accounts for the fairly normal behavior of the heart for most people who are afflicted with LQT4. The fatal event appears to be triggered by unexpected stress and possibly an increase in adrenaline - as would happen when individuals are startled. Even then, the death-causing electrical chaos is rare. Humans and animals are afflicted with LQT4 when only one of the two genes for ankyrin-B is defective or absent. When both are absent, the condition is lethal.

This research caused an immediate response in the scientific community, with two commentaries being published almost immediately. One was in same volume of *Nature* as the article; the other in *Nature Medicine* in March, 2003. The public became aware of this groundbreaking research when Dr. Terry Rogers, one of the collaborators, was interviewed by Donna Hamilton of WBAL-TV on the day the paper was published. The segment was aired on WBAL's 5:00 p.m. news program. Numerous other secondary sources have picked up on the research around the world.

By discovering the molecular and cellular causes of LQT4, Lederer and his colleagues open the door to possible therapies for this and related heart diseases. Furthermore, the work provides a clue to how important, specific proteins are organized within the cell and this too may lead to new diagnostics and therapies for heart disease.

Mohler, P.J., Schott, J.-J., Gramolini, A.O., Dilly, K.W., Guatimosim, S., duBell, W.H., Song, L.-S., Haurogné, K., Kyndt, F., Ali, M.E., Rogers, T.B., Lederer, W. J., Escande, D., Le Marec, H., Bennett, V. (2003) *Ankyrin-B mutation causes type 4 long-QT cardiac arrhythmia and sudden cardiac death.* *Nature* 421(February 6):634-9.

Nattel, S. (2003) *Lost anchors cost lives.* *Nature* 421(February 6):587-590

Marks, A.R. (2003) *Arrhythmias of the heart: beyond ion channels.* *Nature Medicine* 9 (3):263-4

New Faculty Members

MBC welcomes Dr. Timothy Read as Adjunct Assistant Professor from The Institute for Genomic Research and Dr. William duBell as Affiliate Assistant Professor from the Department of Biochemistry and Molecular Biology, UMB.

That Time of Year

January signals the start of the legislative session for the State of Maryland and this year's session is looking unusually discouraging. With a new Republican governor but the usual Democrat-dominated legislature, conflicts are inevitable. Couple that with continued economic woes and the future of higher education in Maryland does not look rosy.

Each year, USM institution presidents and other representatives testify before various committees in both houses of the state legislature. However, under the current fiscal crisis, this year's testimony takes on greater significance.

Higher education is one area where budget cuts can be made without incurring constitutional or entitlement problems. By the end of February, it was clear that USM, as a whole, had already lost 12% of its funding and deeper cuts were being discussed. The final budget will depend upon whether the legislature goes along with Governor Erhlich's plan to legalize slot machines at race tracks. The outcome will not be known until the end of the legislative session in April.

As an institution, UMBI has become more visible. President Jennie Hunter-Cevera was part of the Governor's transition team. She and others spoke on UMBI's behalf this session. In particular, Admiral Charles R. Larson, USM regent, spoke glowingly of UMBI during his testimony, calling it “a real gem in our system” and “one of the smartest decisions this state ever made about investing in education and research.” He also mentioned Dr. Lederer's work on Long-QT syndrome (see page 1), noting that UMBI is not always thought of in terms of human health but that it is an important contributor in that area. In addition, the legislature was invited to “UMBI day,” held on January 28th. This annual exhibition, reception and entertainment, sponsored this year by MDBio, Inc., allows legislators to meet with the center directors and faculty in an informal atmosphere.

Dr. W. Jonathan Lederer, MBC Director, has kept faculty members and senior management apprised of developments. MBC will see some effects eventually. However, MBC is in very good shape, in part, because it is the leader in extramural funding on a per faculty basis among all the centers. That strength will minimize the worst of the budget woes.



MBC Happenings

Seminars

Dr. Ramanujan Hegde from the National Institute of Child Health and Human Development, NIH spoke on "Folding and Misfolding of the Prion Protein at the Endoplasmic Reticulum, February 21, 2003. Dr. Ilia Baskakov was the host.

Comings and Goings

Dr. Yuri Nagulaev from the Institute of Cytology, Russian Academy of Sciences, St. Petersburg, Russia arrived to begin a 2 month collaboration with Dr. Valeriy Lukyanenko.

Dannielle Watkins joined the business office, replacing Venus Windmiller. **Mr. Stephen Hibbs** joined Dr. Les Baillie's laboratory. **Dr. Xuehong Xu** is Dr. Shengyun Fang's new postdoctoral fellow. **Dr. Sunanda Deb** left Dr. Ila Baskakov's laboratory.

Grants and Contracts

Dr. Chris Geddes, Microcosm, "Metallic Nano-sensor Matrix with enhanced Fluorescence" 11/1/02, \$165,309, yr 1 of 2.

Dr. Chris Geddes, Cibavision, "Advanced Glucose Sensing for Diabetes." 1/1/03, \$300,000, yr 1 of 1.

Dr. Mervyn Monteiro, NIH, "Function of Alzheimer Disease Presenilin 2." 2/1/03, \$255,672, yr 4 of 5.

Dr. Joseph Kao, TEDCO, "Spatiotemporal Control of Gene Expression with Light." 2/3/03, \$50,000, yr 1 of 1.

Publications

Miroy G, **Monteiro MJ**. Expression and purification of a convenient Ca²⁺-calmodulin-dependent protein kinase II GST-fusion substrate. *Prot. Express. Purif.* 26 (3): 343-348 DEC 2002

Geddes CD. 1 and 2-photon fluorescence anisotropy decay to probe the kinetic and structural evolution of sol-gel glasses: A summary. *J. Fluor.* 12 (3-4): 343-367 DEC 2002

Lakowicz JR, Maliwal BP, Malicka J, Gryczynski Z, **Gryczynski I**. Effects of silver island films on the luminescent intensity and decay times of lanthanide chelates. *J. Fluor.* 12 (3-4): 431-437 DEC 2002

Campbell WH, Anderson WK, Burckart GJ, Clark AM, **DiGate RJ**, Lee VHL, Rogers ME, Miller KW. Institutional and faculty roles and responsibilities in the emerging environment of university-wide interdisciplinary research structures: Report of the 2001-2002 Research and Graduate Affairs Committee. *Am. J. Pharm. Edu.* 66: 28S-33S Suppl. S WIN 2002

Malicka J, **Gryczynski I**, Fang JY, Kusba J, **Lakowicz JR**. Photostability of Cy3 and Cy5-labeled DNA in the presence of metallic silver particles. *J. Fluor.* 12 (3-4): 439-447 DEC 2002

Polumuri SK, **Ruknudin A**, McCarthy MM, Perrot-Sinal TS, **Schulze DH**. Sodium-calcium exchanger NCX1, NCX2, and NCX3 transcripts in developing rat brain. *Cell. Mol. Physiol. Sodium-Calcium Exchange, Ann. NY Acad. Sci.* 976: 60-63 2002

Schulze DH, Pyrski M, **Ruknudin A**, Margolis JW, Polumuri SK, Margolis FL. Sodium-calcium exchangers in olfactory tissue. *Cell. Mol. Physiol. Sodium-Calcium Exchange, Ann. NY Acad. Sci.* 976: 67-72 2002

Ruknudin A, **Schulze DH**. Proteomics approach to Na⁺/Ca²⁺ exchangers in prokaryotes. *Cell. Mol. Physiol. Sodium-Calcium Exchange, Ann. NY Acad. Sci.* 976: 103-108 2002

Schulze DH, Polumuri SK, Gille T, **Ruknudin A**. Functional regulation of alternatively spliced Na⁺/Ca²⁺ exchanger (NCX1)

isoforms. *Cell. Mol. Physiol. Sodium-Calcium Exchange, Ann. NY Acad. Sci.* 976: 187-196 2002

Ruknudin A, **Schulze DH**. Phosphorylation of the Na⁺/Ca²⁺ exchangers by PKA. *Cell. Mol. Physiol. Sodium-Calcium Exchange, Ann. NY Acad. Sci.* 976: 209-213 2002

Hale CC, Bossuyt J, Hill CK, Price EM, **Schulze DH**, **Lederer WJ**, Poljak R, Braden BC. Sodium-calcium exchange crystallization. *Cell. Mol. Physiol. Sodium-Calcium Exchange, Ann. NY Acad. Sci.* 976: 100-102 2002

Geddes CD. 1 and 2-photon fluorescence anisotropy decay to probe the kinetic and structural evolution of sol-gel glasses: A summary. *J. Fluor.* 12 (3-4): 343-367 DEC 2002.

Gryczynski Z, **Gryczynski I**, **Lakowicz JR**. Fluorescence-sensing methods. *Biophotonics, PT A Methods Enzym.* 360: 44-75 2003.

Reiken S, Gaburjakova M, **Guatimosim S**, Gomez AM., D'Armiento J, Burkhoff D, Wang J, Vassort G, **Lederer WJ**, and Marks AR. Protein Kinase A Phosphorylation of the Cardiac Calcium Release Channel (Ryanodine Receptor) in Normal and Failing Hearts. Role of Phosphatases and Response to Isoproterenol. *J. Biol. Chem.* 278:444-453 2003.

Malicka J, **Gryczynski I**, Maliwal BP, Fang JY, **Lakowicz JR**. Fluorescence spectral properties of cyanine dye labeled DNA near metallic silver particles. *Biopolymers* 72 (2): 96-104 2003.

Lakowicz JR, Malicka J, **Gryczynski I**. Silver particles enhance emission of fluorescent DNA oligomers. *Biotechniques* 34 (1): 62-+ JAN 2003.

Lakowicz JR, Kusba J, Shen YB, Malicka J, D'Auria S, Gryczynski Z, **Gryczynski I**. Effects of metallic silver particles on resonance energy transfer between fluorophores bound to DNA. *J. Fluor.* 13 (1): 69-77 JAN 2003

Mohler PJ, Schott JJ, Gramolini AO, Dilly KW, **Guatimosim S**, **duBell WH**, Haurogne K, Kyndt F, Ali ME, **Rogers TB**, **Lederer WJ**, Escande D, Le Marec H, Bennett V. Ankyrin-B mutation causes type 4 long-QT cardiac arrhythmia and sudden cardiac death. *Nature* 421 (6923): 634-639 FEB 6 2003

Kermis HR, **Rao G**, Barbari TA. Transport properties of pHEMA membranes for optical glucose affinity sensors. *J. Membrane Sci.* 212 (1-2): 75-86 FEB 15 2003.

Fang S, Lorick KL, Jensen JP, Weissman AM. RING finger ubiquitin protein ligases: implications for tumorigenesis, metastasis and for molecular targets in cancer. *Sem. Cancer Bio.* 13 (1): 5-14 FEB 2003

Rosen GM, Porasuphatana S, Tsai P, Ambulos NP, Galtsev VE, Ichikawa K, Halpern HJ. Dendrimeric-containing nitronyl nitroxides as spin traps for nitric oxide: Synthesis, kinetic, and stability studies. *Macromolecules* 36 (4): 1021-1027 FEB 25 2003.

Talks and Travels

Dr. Les Baillie, Invited Speaker, "Anthrax to Sharks, via Genomes" Department of Microbiology, University of Pennsylvania, February 5, 2003.

Dr. W.J. Lederer, Invited Speaker, Keystone Symposium on Molecular Pathology of Cardiac Arrhythmias, Santa Fe, New Mexico, "When Sparks Fly: Calcium signaling in heart". January 17, 2003.

Dr. W.J. Lederer, Invited Honorary Speaker, 2003 Biophysics Symposium, Dorothy M. Davis Heart & Lung Research Institute, Ohio State University. "When Sparks Fly: Calcium signaling in heart". February 6, 2003.