



Inside MBC

"...molecular medicine through biotechnology"

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Chancellor visits UMBI

USM's new chancellor, Dr. William E. Kirwan, visited the UMBI Board of Visitors at its fall meeting. It was the first time Dr. Kirwan had visited UMBI since becoming chancellor. However, he is very familiar with UMBI, having been President of University of Maryland College Park at UMBI's inception. Past President of Ohio State University in Columbus, Ohio, and UMCP, Dr. Kirwan is familiar with the issues facing the sciences in academic institutions. He is an advocate of UMBI in principle and in practice and is behind the CARBII project, due to be discussed in the upcoming legislative session.

Many members of the UMBI community may not be familiar with the Board of Visitors. Headed by Dr. Martin Apple, President of the Council of Scientific Society Presidents, the board includes many of Maryland's most influential biotechnology industry leaders. While the names may not be familiar to all of our scientists, the companies they lead are — EntreMed, Inc., Guilford Pharmaceuticals, Inc., MdBio, Inc., MedImmune, Inc. among others. The efforts and good will of our Board of Visitors helps UMBI maintain a high profile within the state.

Swimming with Sharks

While many members of the MBC faculty use animals for research, these tend to be the usual lab rats, mice, and rabbits. Dr. Les Baillie, a microbiologist who specializes in anthrax, has begun to use something decidedly *un-usual*—sharks! In collaboration with Drs. Helen Dooley and Martin Flajnik of the Department of Microbiology and Immunology, University of Maryland Baltimore, Dr. Baillie is exploring the possibility of using nurse sharks to produce antiserum against anthrax.

Antibody-based assays, used to detect biological substances, are both specific and rapid. However, they are temperature sensitive

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*Nurse sharks, *Ginglymostoma cirratum*, grow from 2-13 ft.*

Dr. Fang Settles In



Our newest faculty member, Dr. Shengyun Fang, is settling in to his new office and laboratory on the third floor of the Medical Research Facility. In order to accommodate him and utilize our laboratory space more efficiently, several faculty members rearranged their space, coordinated by Tim Hughes. Drs. John Collins, Gerald

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Grant Routing Now Online

Grants are the primary source of funds for basic research and the process by which they are funded is a mixture of science and bureaucracy. After a grant is reviewed by the MBC administration, the next step is to “route” the grant through UMBI’s Office of Sponsored Programs run by Mr. Dean Drake. He is responsible for seeing that the grants follow the guidelines setup by each funding agency. UMBI is obliged by law to sign off on each grant. This is because the grant, although written by a faculty member to fund his/her research, is actually awarded to the institution. It is also the institution which guarantees the accuracy of the accounting and that ensures the funds have been appropriately spent.

In addition to its legal role, UMBI collects information about the size and type of grants being submitted for many state mandated and administrative reasons. Previously, routing was started after a form was completed by hand. The information would then be entered into a data base by Mr. Drake’s office. In order to streamline this process and reduce the number of errors inherent in copying information, an online entry form has been developed. Although the online form is currently experimental, it is hoped that this system will give both the Centers and UMBI Central greater access to information and make the entire process more efficient.

At the MBC the faculty will not be using the online system, though other Centers may have faculty members do the actual data entry. Authorized users for MBC are limited to Tim Hughes, Assistant Director and Pamela Wright, Research Coordinator. Faculty members, however, will notice a new look to the routing sheet that they must sign before the grant is sent to UMBI Central.

Name Change

The Center for Agricultural Biotechnology (CAB) has changed its name to Center for Biosystems Research (CBR) to better reflect its broad scope of research.

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Sharks continued.

and easily rendered useless under extreme conditions. However, unlike antibodies produced in mammalian species, shark antibodies, which are structurally quite different from human antibodies, are extremely temperature stable. Shark antibodies retain activity even after boiling and can be stored for long periods of time. This makes them ideal for developing environmental tests for the presence of anthrax, where field conditions can make traditional antibody assays impossible.

One of the continuing problems, on which Dr. Baillie is focusing his research, is the lack of a real time, specific test for the presence of anthrax. Culture techniques are time consuming and, while molecular techniques such as PCR are available, they are complicated by the cross reactivity of *Bacillus anthracis* (anthrax) with its evolutionary kin. PCR, while it can be very specific, is not easily done in the field, is subject to contamination, and requires expensive hardware.

Dr. Baillie and his colleagues showed that immunization with recombinant protective antigen from *B. anthracis* could produce a highly specific and thermal stable antiserum. Their work is just preliminary, having started with two sharks. Early indications suggest that this approach should work. Anthrax is just one of many microorganisms and biological substances for which there are no good environmental assays.

Dr. Baillie envisions developing a test similar to the familiar pregnancy home test (an antibody based test for hCG, a pregnancy induced hormone). The new anthrax detection test should be easily and unequivocally done by untrained individuals, although a more complicated test requiring some training would still be a great leap forward. A quantitative version of the “quick” field test would also be of great value.

The first step is still finding a good source of antibodies and it looks like Dr. Baillie has reeled in a keeper!



Dr. Martin Flajnik of the University of Maryland Baltimore injects a nurse shark.

Distinguished Lecturer



On October 23, 2003, Dr. David Eisner, British Heart Foundation Professor and Chair of Cardiac Physiology, University of Manchester, spoke on “Control and Uncontrol of Calcium in Heart.” This was somewhat of a homecoming for Dr. Eisner, as he has worked in Dr. W. J. Lederer’s laboratory off and on for over 20

years.

Focusing on both contraction and relaxation, Dr. Eisner pinpointed the “control points” of the heartbeat which were calcium dependent. During contraction the calcium concentration of the sarcoplasmic reticulum increases to initiate contraction. Trigger calcium enters the cell through “calcium channels” and that triggers release from intracellular stores (sarcoplasmic reticulum, SR) through the ryanodine receptors. The contraction follows.

For a heart cell to relax and prepare for another contraction, the process must be reversed and the calcium concentration in the cytosol must decrease to resting levels. The decrease is due to a “Ca²⁺ pump”, the SR Ca²⁺ ATPase. It pumps Ca²⁺ back into the SR. The amount of calcium coming into the cell must equal the amount of calcium going out of the cell the system to work properly. Also the amount of Ca²⁺ released from the SR through the ryanodine receptors must equal the amount of Ca²⁺ pumped back into the SR by the SR Ca²⁺ ATPase. The precision, with which these processes must be done, not to mention the coordination between all heart cells, continues to be major focus of Dr. Eisner’s work.

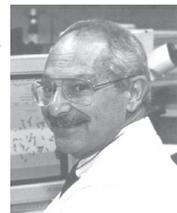
Dr. Eisner has spent his entire career elucidating the fundamental pathways of calcium signaling in heart. He received his D.Phil. from Oxford University, where, as a student, he worked with Dr. Lederer, who was a post-doctoral fellow there. He was the youngest lecturer ever appointed at University College London. His work continues to be recognized throughout the world and it was a pleasure having him back “home.”

MBC/UMBI Perspectives

By Tim Hughes

1988...a five year plan and more faculty appointments...

In May of 1988 Dr. Maimon Cohen, Dr. Mike Levine and Tim Hughes co-authored the first MBC 5-year plan. It was the faculty hiring plan and the original basis for what would come later - a research facility program document. The facility program document provided justification for the purchase of the old Hutzler’s warehouse and its development into the building where the MBC lives today.



Dr. Cohen

The first 5-year plan described how, over the next five years, we would hire people, mostly faculty, and into which scientific foci they would be hired. Based on the recommendations of the MBC Scientific Advisory Committee, four programmatic foci were included in this plan – Boimaging/Biosensing/ Bioprocessing; Molecular Neurology; Molecular Genetics; and Vaccine Development/AIDS/Immunology. Additionally, a number of core facilities were identified and included in the plan for development. These included Protein & Peptide Synthesis; Biopolymer Facility; Peptide & Oligonucleotide Synthesis; NMR Mass Spectroscopy Facility; Flow Cytometry; and Fermentation and Bioprocessing. Amazingly, that plan was realized nearly intact.

Dr. Govind Rao was hired as our second primary faculty member in July of 1988, in affiliation with University of Maryland Baltimore County (UMBC), Department of Biochemical Engineering. His appointment was matched with Dr. Steve Coppella, who held his primary appointment at UMBC and now a secondary one in the MBC. As discussed previously, this matching gave MBC faculty members space when MBC did not yet have a home of its own. These appointments were quickly followed by the appointment of Dr. Roger Schultz as the third primary faculty member in MBC. He was hired in cooperation with the University of Maryland School of Medicine. Department of Obstetrics and Gynecology and the Division of Human Genetics, of which Dr. Maimon Cohen, our co-director was chair.

Additional secondary faculty members – Dr. Dana Hilt (Department of Neurology, School of Medicine) and Dr. William Randall (Department of Pharmacology and Experimental Therapeutics) – were also hired in 1988. Thus, including the two Co-directors, the MBC now had 9 faculty members, one assistant director, one administrative assistant, four post-doctoral fellows, 2 research technicians and four graduate students. It was growing according to plan.

Next...1989, a time of upheaval and continued growth...

MBC Happenings

Comings and Goings

Dr. Russell DiGate was appointed Associate Dean for Research and Graduate Education in the School of Pharmacy, September 1, 2002.

Dr. Shengyun Fang, Assistant Professor, started September 1, 2002.

Grants and Contracts

W. J. Lederer, NHLBI, NIH, "Subcellular organization and Ca²⁺ signaling in heart failure" a subcontract of a Program Project Grant with **Dr. Terry Rogers**, UMB, 9/1/02, \$328,571, year 1 of 5.

W. J. Lederer, NHLBI, NIH, "Slip Mode Conductance in Heart," 9/1/02, \$371,250, year 3 of 5.

Publications

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Fang continued.

Rosen and Marian Jackson graciously moved laboratories or vacated space to accommodate Dr. Fang. The changes did not affect any on-going research but reflect the natural evolution of careers and space needs. For example, Dr. Jackson is now Associate Vice President for Academic Affairs at UMBI Central. Dr. Fang occupies her old laboratory. Packing and clearing laboratories is never easy but everyone's good will has contributed to make this a relatively painless process.

Dr. Fang comes to us from NIH and brings his expertise on apoptosis and ubiquitination of proteins. His approach and methods bring important new approaches to the MBC. Additionally, collaborations are rapidly developing between Dr. Fang and other investigators within the MBC and UMBI. Dr. Fang already has experience in applying basic research via the patent process and is at home in the UMBI environment.

Herman P, Maliwal BP, **Lakowicz JR**. Real-time background suppression during frequency domain lifetime measurements. ANAL BIOCHEM 309 (1): 19-26 OCT 1 2002

DiCesare N, **Lakowicz JR**. Charge transfer fluorescent probes using boronic acids for monosaccharide signaling. J BIOMED OPTICS 7 (4): 538-545 OCT 2002

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Talks and Travels

Shengyun Fang, Invited Speaker, "RINGing for ubiquitination," Department of Microbiology and Cell Biology, West Virginia University, October 8, 2002.

W. J. Lederer, d'Agrosa Lecture, "When Sparks Fly--Calcium Signaling in Heart," St. Louis University, St. Louis, MO, September 10, 2002.

W. J. Lederer, Invited Speaker, Shanghai Institutes for Biological Science, Chinese Academy of Sciences, Shanghai, P.R. China, "Calcium Signaling in Heart," October 7, 2002.