INSIDE MBC

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MEDICAL BIOTECHNOLOGY CENTER -UNIVERSITY OF MARYLAND BIOTECHNOLOGY INSTITUTE

Twenty Years of Research Excellence

Inside:

Mitochondrial Expert Joins MBC

The newest faculty member at the Medical Biotechnology Center, University of Maryland Biotechnology Institute, has nearly traveled around the world in pursuit of a career in science. Dr. Mariusz Karbowski grew up in Poland, getting a Master of Science degree at Adam Mickiewicz University in Poznan, Poland and majoring in Biochemistry and Molecular Biology. His next step was highly unusual in the scientific world. He traveled half way around the world to Nagoya University School of Medicine in Nagoya, Japan for his doctorate degree in cell biology and molecular pathology in 2001—an interesting and courageous choice considering he did not know any Japanese! Continuing his eastward passage, Dr. Karbowski has spent the last five years at the National Institute of Neurological Diseases and Stroke (NINDS).

Dr. Karbowski setting up his new laboratory.

Dr. Karbowski's research is focused on the mitochondria, cellular organelles that control much of the cell's energy production, among other essential functions. They are distinctly structured and are the only organelle outside the nucleus to have DNA. Dr. Karbowski is particularly interested in the protein synthesis pathways in the mitochondria and how this organelle maintains "quality control," that is how misfolded proteins are identified and

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In the Swing of Things

While MBC scientists work on finding cures for diseases, others are busy organizing foundations to raise both money and awareness. These two groups came together this fall at a golfing fund-raiser organized by the Maryland Chapter of the Huntington's Disease Society of America on September 18. MBC Professor Mervyn Monteiro, whose recent work has opened a new pathway to possible Huntington's therapeutics (*Inside MBC*, Vol. 9, No. 1), and his long-time golf partner, MBC Assistant Director Tim Hughes, took a day off to enjoy their favorite past time and support a worthy cause. The good weather and the excellent play at the Hillendale Country Club in Phoenix, Maryland made for a particularly good outing. Their foursome won first place and Tim Hughes also won longest drive.

Tim Hughes and Mervyn Monteiro also represented UMBI at the MDBio golf tournament on October 4. MDBio is a biotechnology umbrella organization which brings together institutions, industry, and government agencies to promote biotechnology in Maryland.

The winning foursome included (right to left): Russell Clark, president of Elluminis Consulting Group; Gabrielle Abiera, FOX45 TV Traffic Reporter; Tim Hughes; and Mervyn Monteiro.

UMBI News

CARB II Opens

Dignitaries were everywhere for the opening of UMBI's newest facility, CARB II. Located on the Shady Grove campus in Rockville, it is a 140,000 ft^2 building linked to the existing Center for Advanced Research in Biotechnology (CARB) facility. The complex is now called "UMBI, Shady Grove." The new building is a wonderful addition to UMBI.

MBC was represented by Dr. W. Jonathan Lederer, MBC Director; Timothy Hughes, MBC Assistant Director; and Pamela Wright, PR Liaison and Assistant to the Director. Senate Chair and MBC Professor Mervyn Monteiro and past Senate Chair and MBC Professor John Collins were also in attendance.

New Director of Communications

UMBI welcomes Dr. Gene Levinson as the new Director of Communications. Dr. Levinson has a strong science background and has written extensively for popular consumption.

Keeping Track

Beginning this summer, UMBI President Jennie Hunter-Cevera requested that each center and administrative office provide monthly reports of all activities to be shared between all units. With such a diverse, active, and growing institution, it had been increasingly difficult for centers to keep up to date with what was happening elsewhere in the organization. MBC decided to make its monthly reports available to everyone within the center as well. So beginning in September, monthly reports are available in the Staff Section of the MBC web site. You will need a UMBI login to access these reports. Check them out. The reports are particularly interesting and it is amazing how much happens in only one month!

Karbowski continued

degraded. Misfolded proteins have been implemented in numerous diseases including Alzheimer's, Huntington's and cystic fibrosis.

When asked why he chose the MBC and UMBI, Dr. Karbowski replied, "This is an easy question. The group of people I met during my interview. ... It was fun to discuss things, and hear good feedback from people I am to collaborate with. I thought that there is a chance to learn things from them, and also to provide my expertise in the research areas of other MBC members." He also noted that he especially liked the Bicycle Restaurant in downtown Baltimore when he came to interview.

Dr. W. Jonathan Lederer, Director of the MBC, commented, "Dr. Karbowski is just the kind of enthusiastic and energetic young scientist that makes the MBC and UMBI so successful."

Dr. Karbowski officially started as a tenure-track Assistant Professor in the MBC on September 1.

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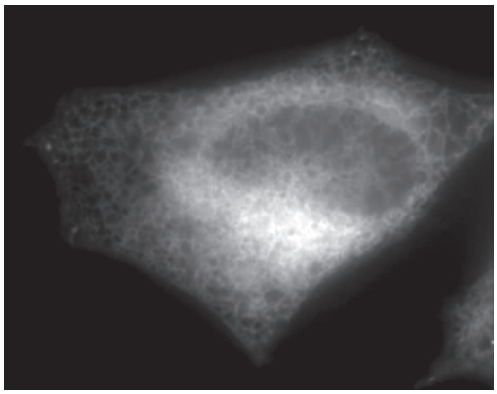
http://www.umbi.umd.edu/~mbc

Special Visitors

Dr. Shengyun Fang hosted a University, People's Republic o 11, 2006. The delegation, whi Anhui government officials, we American institutions looking a education and academic resear

Molecular Erasers

How do cells get rid of mistakes? UMBI scientists, led by Dr. Mervyn J. Monteiro at the Medical Biotechnology Center, University of Maryland Biotechnology Institute in Baltimore, Maryland, have discovered a new protein that is an integral part of the pathway used by cells to get rid of misfolded proteins before they cause major problems. These kinds of problems are believed to be responsible for many human diseases including, Alzheimer's disease, Huntington's disease, cystic fibrosis, α1-antitrypsin deficiency, congenital hypothyroidism, thyroglobin deficiency, osteogenesis imperfecta, albinism/tyrosinase deficiency, hypofibrinogenemia, and Pendred Syndrome to name a few.



Cell showing that erasin localizes to the endoplasmic reticulum.

As reported in an ePress article published in the Journal of Cell Science, Dr. Monteiro and associates discovered a novel human protein, which they have called "erasin," that functions like a molecular eraser, removing misfolded proteins from the endoplasmic reticulum (ER). The endoplasmic reticulum is the key cellular organelle where most functionally important proteins, such as receptors, are made. Failure to remove misfolded proteins from the ER, can clog up this chief protein synthesis apparatus, eventually leading to cell death. Earlier work had suggested that a molecular complex of many proteins exists in the ER to facilitate the removal and destruction of misfolded proteins by a process called ER-associated protein degradation (ERAD).

While many of the proteins involved in ERAD in yeast and other organisms have been characterized, little is known about this process in humans. The newly discovered erasin is a key component of the human ERAD complex. The UMBI scientists together with their collaborators at the Nathan Kline Institute in New York have found it is required to remove misfolded proteins from the ER and that erasin protein levels were preferentially increased in the brains of people afflicted with Alzheimer's disease. The scientists speculate that the increase in erasin expression in Alzheimer's disease may reflect a preemptive and perhaps a futile attempt of cells to get rid of toxic proteins from the brain. Thus, the identification of erasin could lead to a better understanding of Alzheimer's and new targets for intervention.

UMBI VP Visits MBC

David Bobbitt, UMBI Vice President for Institutional Affairs talked at September's faculty meeting, introducing both himself and the function of his office. The office's primary function is fund-raising and Mr. Bobbitt gave an excellent and well-received presentation of the intricacies of this work. While everyone is aware of the necessity of obtaining outside gifts, most faculty and staff tend to think of fund-raising as a mysterious and somewhat nebulous activity. Mr. Bobbitt quickly dispelled that myth by outlining the logical and highly organized process by which donors are identified and approached. His cogent and straightforward presentation, along with his outgoing personality, quickly won him support from the faculty.

Faculty members often resist cooperating with fund-raising, thinking that their time would be better spent in the lab. However, they now understand that whenever Mr. Bobbitt asks for their participation, it is because there is a real possibility of new funds, not just a shot in the dark.

a delegation from Anhui
f China, on September
ch included several
ere visiting a number of
t medical and graduate
rch.

MBC Happenings

Honors

Dr. Ilia Baskakov, Invited Review for the special issue on Prions: "Converting the prion protein: What makes the protein infectious." *Biochim Biophys Acta*. 2006 [Epub ahead of print] with L. Breydo.

Comings and Goings

Assistant Professor **Dr. Long-Sheng Song** has left for a tenure track position at the University of Iowa. Assistant Professor **Dr. Howard Doong** has left for a position as Associate Director for Technology Development at TrimGen Corporation, a biotechnology firm in Sparks, MD. Research Assistant **Chaobo Yin** has left Dr. Monteiro's Laboratory. **Dr. Didier Brochet** has joined the Institute of Molecular Cardiology as a Research Associate. **Dr. Joanna Paterson** is a Visiting Research Associate in Dr. Bruce Vogel's laboratory.

Grants and Contracts

Dr. W. Jonathan Lederer, UMB/NIH, "Subcellular Organization and Ca^{2+} Signalling in Heart Failure," 9/1/06, $359,039, yr 5 of 5.

Dr. Chris Geddes, UMB/NIH, "Metal-enhanced Fluorescence Sensing," 9/1/06, $59,486, yr 3 of 3.

Dr. Les Baillie, Imperial College of London/NIH, "T Cell Epitopes of Anthrax and Plague Vaccine Candidates," 9/30/2006, $ 81,000, yr 3 of 5.

Patents

Joseph R. Lakowicz, Zygmunt Gryczynski and **Chris D. Geddes** "Optical Structures for Metal-enhanced Sensing", US Patent NO: 7, 095, 502 B2, Issued August 22nd 2006.

Publications

Baillie LWJ. Past, imminent and future human medical countermeasures for anthrax. J APPLIED MICROBJIO 101 (3): 594-606 SEP 2006

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Miyake M, Shen JG, Liu SM, Shi HL, Liu WL, Yuan ZR, Pritchard A, **Kao JPY**, Liu KJ, **Rosen GM**. Acetoxymethoxycarbonyl nitroxides as electron paramagnetic resonance proimaging agents to measure O-2 levels in mouse brain: A pharmacokinetic and pharmacodynamic study. J PHARMACOL EXP THERAPEU318 (3): 1187-1193 SEP 2006

Fu Y, **Lakowicz JR**. Enhanced fluorescence of Cy5-labeled DNA tethered to silver island films: Fluorescence images and time-resolved studies using single-molecule spectroscopy. ANAL CHEM 78 (17): 6238-6245 SEP 1 2006

Aslan K, Malyn SN, **Geddes CD**. Fast and sensitive DNA hybridization assays using microwave-accelerated metal-enhanced fluorescence. BIOCHEM BIOPHYS RES COMM 348 (2): 612-617 SEP 22 2006

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Previte MJR, **Aslan K**, Malyn S, **Geddes CD**. Microwave-triggered metal-enhanced chemiluminescence (MT-MEC): Application to ultra-fast and ultra-sensitive clinical assays. J FLUOR 16 (5): 641-647 SEP 2006

Muriel JM, Xu XH, Kramer JM, **Vogel BE**. Selective assembly of fibulin-1 splice variants reveals distinct extracellular matrix networks and novel functions for perlecan/UNC-52 splice variants. DEV DYNAMICS 235 (10): 2632-2640 OCT 2006

Ray K, Badugu R, **Lakowicz JR**. Distance-dependent metal-enhanced fluorescence from Langmuir-Blodgett monolayers of alkyl-NBD derivatives on silver island films. LANGMUIR 22 (20): 8374-8378 SEP 26 2006

Liang J, Yin C, **Doong H**, **Fang S**, Peterhoff C, Nixon RA, **Monteiro MJ**. Characterization of erasin (UBXD2): a new ER protein that promotes ER-associated protein degradation. J CELL SCI 119 (19): 4011-4024 OCT 1 2006

Alewine C, Olsen O, Wade JB, **Welling PA**. TIP-1 has PDZ scaffold antagonist activity. MOL BIOL CELL 17 (10): 4200-4211 OCT 2006

Talks and Travels

Dr. Chris D. Geddes, Invited Speaker, Applied Physics Labs, Johns Hopkins University, "Ultra fast and sensitive DNA and protein detection using Microwave accelerated Metal-enhanced fluorescence", September 14, 2006.

Dr. W. Jonathan Lederer, Speaker, Workshop on Recognition and treatment of Rare Inherited Arrhythmias, NHLBI, "Local and Global Ca^{2+} Signaling Changes Link Rare to Common Arrhythmias," Bethesda, MD, September 14-15-2006.

Dr. Chris D. Geddes, Invited speaker, Johns Hopkins University for MARCE, "Metal-enhanced Fluorescence: Anthrax Detection in Clinical Samples in 30 Seconds," September 27, 2006.

Dr. W. Jonathan Lederer, Invited Speaker, Workshop on Cardiac Electrophysiology and Arrhythmia, Mathematical Biosciences Institute, Ohio State University, "Cardiac Calcium Dynamics," September 25, 2006.

Dr. Shengyun Fang, Invited Speaker, Anhui Medical University 80th Anniversary Celebration, "Targeting Ubiquitin Ligases for Drug Discovery," Anhui, PRC, October 2, 2006.

Dr. Ilia Baskakov, Selected Talk, PRION-2006 International conference "Probing the conformation of the prion protein within a single amyloid fibril using a novel immunoconformational assay," Torino, Italy, October 4, 2006.

Dr. Mervyn Monteiro, Seminar Speaker, Department of Physiology, University of Maryland Baltimore, "Taking Out the Garbage: The Role of Novel Ubiquitin-containing Proteins in the Disposal of Misfolded Proteins in Cells," October 5, 2006.

Dr. Bruce Vogel, Seminar Speaker, Center for Vascular and Inflammatory Diseases, University of Maryland School of Medicine, "Extracellular Matrix and Epithelial Morphogenesis in Worms and Mice," October 11, 2006.

Dr. W. Jonathan Lederer, Symposium Speaker, Consensus and Controversy in Cardiac Arrhythmias - 2006, The 8th International Dead Sea Symposium and 17th Rappaport Symposium Joint Meeting, "Calcium Handling in Health and Disease," Tel Aviv, Israel, October 15-18, 2006.

Dr. Ilia Baskakov, Plenary Lecture, IBC Conference on Structural and Biochemical Properties of Prions and Amyloids, "Prions: What makes the protein infectious?" Taipei, Taiwan, October 16, 2006.

Dr. Shengyun Fang, Seminar Speaker, Department of Neurology, Wayne State University "ER-associated Degradation and Neurodegenerative Diseases," October 20, 2006.

Dr. Ilia Baskakov, Seminar Speaker, Department of Physiology, University of Maryland Baltimore, "Prions: What Makes the Protein Infectious?" October 26, 2006.