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“Our finding is exciting because it raises the possibility that methods to modulate ubiquitin expression in humans may provide a novel therapeutic opportunity to treat Huntington’s disease and other related polyglutamine disorders.”

Dr. Mervyn Monteiro

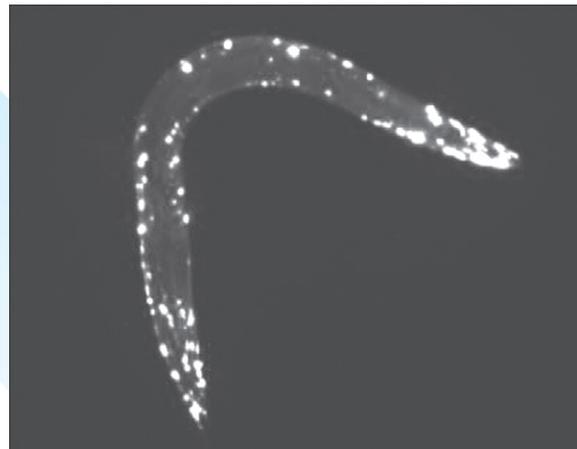
Hope for Huntington’s

Huntington’s disease (HD) is a devastating age-related neurological illness, affecting approximately, 1 in every 10,000 people, and whose symptoms include severe behavioral and emotional disturbances and severe cognitive impairment. HD is a familial disease that is passed from parent to child through a mutation in the normal gene. Each child of an HD parent has a 50-50 chance of inheriting the HD gene. The duration of the disease usually lasts for ~15-20 years, ultimately resulting in death. Currently, there is no effective way to prevent or cure HD. Recently, MBC researchers, headed by Dr. Mervyn Monteiro, discovered a new approach to understanding Huntington’s disease, which may lead to new therapies for this disease.

HD is caused by an abnormal expansion of a trinucleotide sequence (CAG) in the gene encoding the huntingtin (htt) protein. Since CAG encodes the amino acid glutamine, the resulting protein has too many glutamine repeats (polyglutamine). The exact mechanism by which expanded polyglutamine tracts cause disease is not understood. Interestingly, however, proteins with longer polyglutamine repeats are more prone to aggregate, and it is believed that these aggregates may be toxic.

Dr. Monteiro, an investigator at the MBC, became interested in the possibility that ubiquitin, a protein his group had identified as an interactor of presenilins, mutations in which cause

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Animal model of Huntington’s disease. The round worm Caenorhabditis elegans overexpresses htt (the white lumps), the protein which causes Huntington’s disease when it is abnormally expressed and accumulated. These worms also exhibit erratic movement similar to human sufferers.

Annual Report
for 2005

Legislative
Testimony

UMBI Nominations
For Biotech Awards

Each year UMBI looks back over the previous twelve months. The highlights and activities are published in the annual report. It is always interesting to see what the other centers have been doing. This year's annual report again reflects the broad range of research at UMBI, as well as its excellence.



Each year, UMBI's President Dr. Jennie Hunter-Cevera gives testimony to the legislative committees responsible for overseeing UMBI's state budget. The written testimony is always available on the UMBI web site.

UMBI prepared four nominations in three categories for the First Annual Greater Baltimore Region Bioscience Awards, including MBC's **Dr. Chris Geddes** for Best New Product or Progress Award, for his development of microwave enhanced fluorescence assays. Other nominees were COMB and the Blue Crab Advanced Research Consortium and IHV/Profectus Biosciences, Inc. in the Best Academic/Industry Collaboration category and Dr. Claude Nash, UMBI's Vice President of Research and Development, in the Leadership in Bioscience category. The winners, alas not from UMBI, were announced on February 21,

A Sun-ny Day and More

Dr. Chris Geddes was in the news again this January, when one of the lead articles in the Health & Science section of the *Baltimore Sun* for Friday, January 20, 2006 highlighted his work on microwave enhanced fluorescence. *Sun* reporter Dennis O'Brien had interviewed Dr. Geddes in December, but the article did not make it into print immediately. The *Sun* article led to a TV spot on WBAL on January 23 (Watch the clip on the MBC web site). These were in addition to his research being highlighted by the National Cancer Institute as part of their online Nanotech News on January 17 and in the February 2006 issue of *Biophotonics*. If this was not enough, he joined MBC Assistant Professor Bruce Vogel for a live discussion on a Voice of America radio show (the tape is also on the MBC web site) on February 2.

In a UMBI press release, Dr. Geddes said that he believes that "This is amongst one of the most fundamental discoveries for immunoassays since the Nobel Prize was awarded to Yalow, Schally and Guillemin for their pioneering work in immunoassays in 1977". Time will tell if this is true, but for now his research has caught a lot of people's attention which is great for Dr. Geddes and good for the MBC.



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Congratulations!

Rushi Talati, a high school student mentored by Dr. (Inside MBC, Vol. 8 No. 3), received The Award of Distinguished Projects category of the Howard County Math, Science, held on February 25, 2006 for his project entitled "Detecting cells in culture."

Kim Raines, who received her PhD in the fall of 2000 at Rosen's laboratory, was featured in the UMBI Research report. Dr. Rosen is a secondary faculty member but has been at MBC. Since Kim did her thesis work in the building, she has many MBC staffers.

History on Display

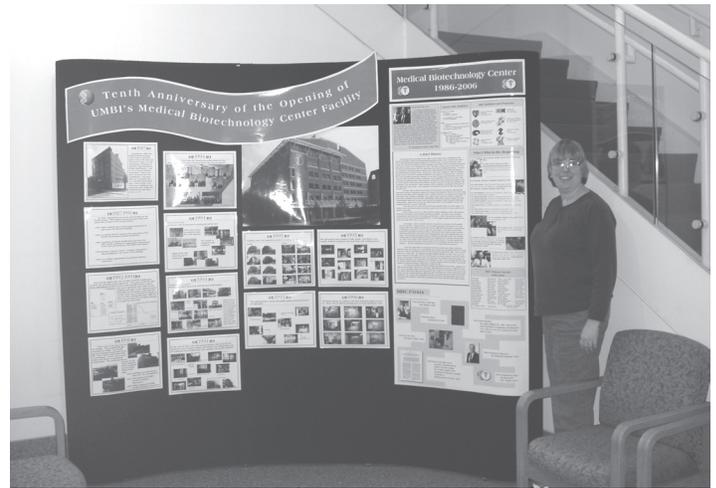
By Kyleen Graham

In the fall of 2005, UMBI began a year-long celebration of its 20th anniversary. As a part of UMBI, the MBC is proud to help them celebrate this momentous occasion. But 2006 also commemorates two other anniversaries within UMBI: the 10th anniversary of the opening of the Medical Research Facility (MRF) and the 20th anniversary of the founding of the Medical Biotechnology Center.

Inspired by UMBI's ongoing efforts, Mrs. Pamela Wright, Assistant to the Director and PR Liaison, has assembled a display located prominently in the lobby of the MRF which depicts the development of the building, originally called the Medical Biotechnology Center Facility. Over the past month or so, Mrs. Wright has been collecting and editing photos of the MRF and MBC. Spending the better part of a day, Mrs. Wright assembled the display to chronicle both the history of the facility and how far the MBC has come in its 20 years of existence from a center with no real home to one located in a large, historic building.

"Seeing the transformation the building underwent is astonishing. Just by looking through the pictures taken during construction, you can see how many changes were made to make this facility what it is today. It's been very interesting and a lot of fun looking through the various faces of those that passed through here and reading about the founding of the Center," said Mrs. Wright.

The first two panels of the towering display show the transformation from an empty warehouse to a state-of-the-art research building. Included on the display is a large picture of the Hutzler warehouse circa



Pamela Wright in front of the finished display.

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Huntington's continued

Alzheimer's disease, might be involved in regulating HD pathogenesis because ubiquilin proteins were reported to bind to expanded polyglutamine proteins. In a recently published paper, Dr. Monteiro and his colleagues showed that when ubiquilin was overexpressed in an animal model of HD, the animals no longer showed the motility defects associated with HD. They also showed that ubiquilin could reduce polyglutamine protein aggregation and cell death, in a HeLa cell line expressing htt, in a dose dependent manner.

Dr. Monteiro says, "Our finding is exciting because it raises the possibility that methods to modulate ubiquilin expression in humans may provide a novel therapeutic opportunity to treat Huntington's disease and other related polyglutamine disorders."

To date, at least eight other neurological disorders are associated with an expansion of polyglutamine tracts; these disorders include dentatorubral-palidolusian atrophy, spinal and bulbar muscular atrophy, and spinocerebella ataxias 1, 2, 3, 6, 7 and 17. Thus polyglutamine expansion causes several human neurological disorders, all of which may benefit from Dr. Monteiro's research.

The work was very quickly picked up by the news media. Baltimore's *The Daily Record* featured it on February 15, 2006 and the HD Lighthouse, a Huntington's Disease support group's web page, discussed it on February 16.

Hongmin Wang, Precious J. Lim, Chaobo Yin, Matthias Rieckher, Bruce E. Vogel, and Mervyn J. Monteiro. Suppression of Polyglutamine-Induced Toxicity in Cell and Animal Models of Huntington's Disease by Ubiquilin. Human Molecular Genetics Advance Access published on February 6, 2006. doi:10.1093/hmg/ddl017 [Abstract] [Accepted Manuscript]

W. Jonathan Lederer
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MBC Happenings

Comings and Goings

Theresa Gallagher has joined Dr. Les Baillie's laboratory as a Research Assistant. Research Associates **Drs. Qiangming Sun** (Fang Laboratory) and **Qingyuan Yang** (Baskakov Laboratory) have left. Assistant Professor **Jeanine Ursitti** has resigned.

Grants and Contracts

Mervyn Monteiro, NIH, "Functional Studies of Calmyrin," 2/1/06, \$297,291, yr 2 of 5.

Les Baillie, UMB Subcontract, "Rational Design of an Anthrax Toxin Neutralizing Vaccine," 2/1/06, \$491,804, yr 3 of 5

Publications

Bocharova OV, Makarava N, Breydo L, Anderson M, Salnikow VV, **Baskakov IV**. Annealing prion protein amyloid fibrils at high temperature results in extension of a proteinase K-resistant core. *J. OF BIOLOGICAL CHEMISTRY* 281 (4): 2373-2379 JAN 27 2006

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Sobie EA, **Guatimosim S**, Gomez-Viquez L, **Song LS**, **Hartmann H**, **Jafri MS**, **Lederer WJ**. The Ca^{2+} leak paradox and "rogue ryanodine receptors": SR Ca^{2+} efflux theory and practice. *PROGRESS IN BIOPHYSICS & MOLECULAR BIOLOGY* 90 (1-3): 172-185 JAN-APR 2006

Zhang J, **Lakowicz JR**. A model for DNA detection by metal-enhanced fluorescence from immobilized silver nanoparticles on solid substrate. *J. OF PHYSICAL CHEMISTRY B* 110 (5): 2387-2392 FEB 9 2006

Collins JH. Myoinformatics report: myosin regulatory light chain paralogs in the human genome. *JOURNAL OF MUSCLE RESEARCH AND CELL MOTILITY* 27 (1): 69-74 FEB 2006

Aslan K, **Geddes CD**. Microwave-accelerated metal-enhanced fluorescence (MAMEF): Application to ultra fast and sensitive clinical assays. *J. OF FLUORESCENCE* 16:3-8 JAN 2006

Talks and Travels

Dr. Long-Sheng Song, Invited speaker, "Local excitation-contraction coupling in normal and diseased hearts," Department of Cellular and Integrative Physiology, Indiana University School of Medicine, January 9, 2006.

Dr. W. Jonathan Lederer, Session Speaker, "Molecular Control of SR Release," 3rd Annual Larry and Horti Fairberg Cardiac Workshop: The Communicative Cardiac Cell, Sintra, Portugal, January 15-19, 2005.

Dr. Ilia Baskakov, Invited Speaker, "Synthetic Mammalian Prions: Assembly and Substructure," Department of Microbiology, New York University School of Medicine, New York, NY.

History continued

1930 as well as a collage of photos taken at the groundbreaking in 1994 with many notable public officials in attendance. It also details the extensive remodeling that went into recycling the neglected building.

The third and final panel showcases the early beginnings of the MBC and those individuals who helped get it started. Also on the panel is some current information about the center as well as a message from the current Director of the MBC, Dr. W. Jonathan Lederer and a brief but detailed history of the MBC. Some interesting MBC firsts and a list of the various institutes and centers that currently make up the MBC completes the commemoration of MBC's twenty years.

Faculty Candidates

January brought three more faculty candidates to the MBC. Mariusz Karbowski from the National Institutes of Health gave a seminar on January 5 entitled "Dynamics of mitochondrial membranes in cell life and death." He was followed on January 9 by Michael Lampson from Rockefeller University, whose seminar was entitled "Partitioning the genome: mechanisms that ensure accurate chromosome segregation in cell division." The last candidate, Mohan Viswanathan, arrived on January 12 from MIT and spoke on "Regulation of *C. elegans* lifespan by the silent information regulatory gene Sir-2.1." That brings the total number of candidates so far to five.

January 19, 2006.

Dr. Joseph Kao, speaker, "Controlling Biology with Light," Minisymposium on Nanobiotechnology, UMBI Shady Grove, Rockville, MD, January 24, 2006.

Dr. Ilia Baskakov, Opening Speaker, "Complexity of Prion Protein Polymerization Mechanism," Satellite Symposium on Protein Misfolding and Disease, University of Melbourne, Australia, February 3, 2006

Dr. Long-Sheng Song, Invited speaker, "Local and global Ca^{2+} signaling in cardiac myocytes," Department of Pharmacology, SUNY Upstate Medical University, February 3, 2006.

Dr. Ilia Baskakov, Invited Speaker, "Synthetic Mammalian Prions," 31st Lorne Conference on Protein Structure and Function, Australia, February 5-9, 2006

Dr. W. Jonathan Lederer, Symposium Speaker, " Ca^{2+} Regulation in Heart", 49th Annual Meeting of the Biophysical Society, February 13, 2005.

Dr. Long-Sheng Song, platform speaker, "Mechanisms of dysynchronous Ca^{2+} sparks in heart failure," 50th Annual Biophysical Society Meeting, Salt Lake City, February 19, 2006.

Special Activities

Dr. W. Jonathan Lederer, Co-organizer (with R. Kass), Keystone Meeting, "Cardiac Arrhythmias: Linking structural Biology to Gene Defects", Granlibakken Resort, Nevada, January 29-February 3, 2006