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UTMB

BMB Biochemistry & Molecular Biology

Chair's Message

Now starts the holiday season in full swing with an early Hanukkah starting December 1, on to Christmas and so on. This year was good for Galveston (no storms!), UTMB (we ended up in the black) and our Department, with new initiatives to bring outstanding graduate students on board, a new awareness of the need for career plans for our postdoctoral fellows, and a new Scientist career path that parallels the faculty track offering equivalent opportunities for advancement and salary equity. Our accomplishments reflect the hard work and commitment of our students, postdoctoral fellows, staff and faculty. The external review of the Sealy Center for Structural Biology was very positive, and one response will be a broader and much more extensive plan for faculty recruitment and infrastructure development. I am sure details will be forthcoming soon from the Dean and from Wayne. All in all, it speaks to a true growth period for a research area important to many of our faculty. In addition to our commitment for three new faculty recruitments in Structural Biology, now more feasible given the progress made in bringing Ike-damaged Cores back on line, we are also recruiting faculty in other areas this academic year.

While these are all good things, the new year will bring many challenges as uncertainty is now a major worry. Clearly, having multiple NIH grants or even being awarded one NIH grant will be more difficult. Already, the need for "clinical significance" has become a major determinant for even the most basic science-oriented proposals. The office of the Chair will do all it can to help faculty by offering the opportunity for "chalk talks" before experienced colleagues, presubmission grant reviews, editing help, etc. All of these require early planning and execution. Grants prepared in haste at the last minute will not only be likely to fail, but rob the faculty member of precious time that could be better spent in thorough preparation of a submission, publishing a paper that would help the chances for grant success, etc.

This past Thanksgiving weekend we had fairly good weather to enjoy our time with family and friends. Over the next holiday weeks, I wish all a safe, relaxing and fruitful experience -- a time to enjoy and also contemplate at leisure, I hope. The latter activity is always in short supply in our busy society. And don't forget to come to our party on December 10th and have a good time. On behalf of Karin and myself, I wish all a great Holiday Season and Happy New Year.

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Inside this issue:

Special Items of Interest

- Awards and Announcements
- SECC Fundraising Success

Awards and Announcements

Dr. Prem Joseph was awarded 3rd place Best Poster Award at the John S. Dunn, Sr. Gulf Coast Consortium for Magnetic Resonance, Conference on Magnetic Resonance in Cancer Research, July 22, 2010, at UT Health Science Center Houston. The title of his poster was "Probing the Role of CXC Motif in Chemokine CXCL8 for High Affinity Binding and Activation of CXCR1 and CXCR2 Receptors".

Graduate Program News

We are reaching the conclusion of 2010 and as often happens, we reflect upon the many challenges and accomplishments of the past year. We also have a great deal to be thankful for. No hurricanes reached our coastline, many students received awards recognizing their scientific achievements, others have graduated and are on the next step in their journey and new students have joined our Program.

The BMB/MBET Graduate Program Biological Chemistry Student Organization (BCSO) annual Toy Drive was an enormous success and through the generosity of our BMB family, we surpassed our goal of $100 per child. In coordination with the Child Protective Services of Galveston County, the BCSO sponsored four children, two girls ages 4 and 6 and two boys ages 7. The money collected over the $400 has been donated to the Galveston County Animal Shelter and will be used for food, vaccinations and medicine. We thank you for your contributions! To date, the students have raised $1,029!!

Thank you all for your incredible assistance making this holiday season so special for so many.

-Debora

Faculty on the Road

Dr. Sankar Mitra gave a talk at the annual Environmental Mutagenesis Society Meeting in Fort Worth, TX on October 26 in a session in which Steven Boldogh (Microbiology& Immunology) also presented his results.

Dr. Marc Morais was an invited speaker at Texas Tech University of Health Science Center, Lubbock, Texas, where he presented a seminar titled "The Molecular Machinery of Genome Packaging and Ejection in dsDNA Bacteriophages" on November 3, 2010.

Dr. Kay Choi gave a seminar at Texas Tech University of Health Science Center on November 4th titled "Self-regulation in the viral protease Npro"

State Employee Charitable Campaign (SECC)

BMB Gives Back

The State Employee Charitable Campaign (SECC) was created by legislation in 1993 and is a charitable giving campaign for the state government and higher education workplace. Each year, more than 55,000 state and higher education employees contribute and the campaign has grown to exceed $10.14 million donated to charitable organizations in 2009. These contributions help improve the quality of life for people in communities locally, across the country and around the world.

This year, there is increased need for contributions to almost all charitable organizations since many people have lost their jobs or are no longer able to contribute and the employees of the BMB Department rose to the challenge of giving back.

We would like to thank the incredible generosity of those in the BMB Department. Every member who donated had their name entered in a drawing for a $250 donation to the charity of their choice. The winners of this drawing were Dr. Venkateswarlu Gangavarapu, of the Prakash Laboratory. Dr. Gangavarapu selected the Children's Hunger Fund Charity. Mr. David Bowen, of the Schein Laboratory, selected the Big Brothers, Big Sisters Charity.

Below are the statistics for the past two years for our Department. Thank you for helping those in need.

-Debora Botting & Dr. Darrell Carney, BMB Gives Back coordinators

2010	Percent Participation
BMB Admin/Clerical	55%
BMB Post Doc Fellows	14%
BMB Research Staff	17%
BMB Students	30%
BMB Faculty	60%
ASG - 4	100%

2009	Percent Participation
BMB Admin/Clerical	0%
BMB Post Doc Fellows	5%
BMB Research Staff	0%
BMB Students	3%
BMB Faculty	12%

Publications

Hsieh C-C, Kuro-o M, Rosenblatt KP, Brobey R, **Papaconstantinou J.** (2010) The ASK1 -signalosome regulates p38MAPK activity in response to levels of endogenous oxidative stress in the Klotho mouse models of aging. AGING 2, 597-611.

Hsieh C-C, **Papaconstantinou J.** (2009) Dermal fibroblasts from long-lived Ames dwarf mice maintain their in vivo resistance to mitochondrial generated reactive oxygen species (ROS). AGING1, 784-802.

Papaconstantinou J, **Hsieh C-C.** (2010) Activation of senescence and aging characteristics by mitochondrially generated ROS: How are they linked? Cell Cycle 9, 1-3.

Szymanski, M.R., Jezewska, M.J., **Bujalowski, W.** The Escherichia coli PriA Helicase-Double-Stranded DNA Complex: Location of the Strong DNA-Binding Subsite on the Helicase Domain of the Protein and the Affinity Control by the Two Nucleotide-Binding Sites of the Enzyme. J. Mol. Biol. 2010 Sep 17;402 (2):344-62.

Pell LG, Gasmi-Seabrook GM, **Morais M**, Neudecker P, Kanelis V, Bona D, Donaldson LW, Edwards AM, Howell PL, Davidson AR, Maxwell KL. The solution structure of the C-terminal Ig-like domain of the bacteriophage λ tail tube protein. J Mol Biol. 2010 Oct 29;403(3):468-79. Epub 2010 Sep 6.PMID: 20826161.

Mukherjee A, Morales-Scheihing D, Gonzalez-Romero D, Green K, Taglialatela G, Soto C. Calcineurin inhibition at the clinical phase of prion disease reduces neurodegeneration, improves behavioral alterations and increases animal survival. PLoS Pathog. 2010 Oct 7;6(10). pii: e1001138.

Joseph P.R., Sarmiento, J.M., Mishra, A.K., Das, S.T., Navarro, J., Garofalo, R.P, and **Rajarathnam, K.** (2010) "Probing the Role of CXC Motif in Chemokine CXCL8 for High Affinity Binding and Activation of CXCR1 and CXCR2 Receptors." **J. Biol. Chem.** 285(38), 29262–29269.

Joseph, P.R, Yuan, Z, Kumar, E.A., Charvet, C.D., Lokesh, G.L., Kizhake, S., **Rajarathnam, K** and Natarajan, A. (2010) "Structural Characterization of BRCT-Tetrapeptide Binding Interactions." **Biochem. Biophys. Res. Commun.** 393(2), 207-210.

Featured Abstract by BMB Faculty

Probing the Role of CXC Motif in Chemokine CXCL8 for High Affinity Binding and Activation of CXCR1 and CXCR2 Receptors

Prem Raj B. Joseph[1], Jose M. Sarmiento[2], Anurag K. Mishra[1], Sandhya T. Das[1], Roberto P. Garofalo[3,4,] Javier Navarro[2,5], and Krishna Rajarathnam[1,4,5*]

[1]Department of Biochemistry and Molecular Biology, [2]Department of Neuroscience and Cell Biology, 3Department of Pediatrics, [4]Department of Microbiology and Immunology, [5]Sealy Center for Structural Biology and Molecular Biophysics, 301 University Boulevard, The University of Texas Medical Branch, Galveston, TX 77555, USA.

All chemokines share a common structural scaffold that mediate a remarkable variety of functions from immune surveillance to organogenesis. Chemokines are classified as CXC or CC on the basis of conserved cysteines, and the two subclasses bind distinct sets of GPCR class of receptors and also have markedly different quaternary structures, suggesting that the CXC/CC motif plays a prominent role in both structure and function. For both classes, receptor activation involves interactions between chemokine N-loop and receptor N-domain residues (Site-I), and between chemokine N-terminal and receptor extracellular/transmembrane residues (Site-II). We engineered a CC variant (labeled as CC-CXCL8) of the chemokine CXCL8 by deleting residue X (CXC ® CC), and found its structure is essentially similar to WT. In stark contrast, CC-CXCL8 bound poorly to its cognate receptors CXCR1 and CXCR2 (Ki > 1mM). Further, CC-CXCL8 failed to mobilize Ca2+ in CXCR2-expressing HL-60 cells or recruit neutrophils in a mouse lung model. However, most interestingly, CC-CXCL8 mobilizes Ca2+ in neutrophils and in CXCR1-expressing HL -60 cells. Compared to the WT, CC-CXCL8 binds CXCR1 N-domain with only ~ 5-fold lower affinity indicating that the weak binding to intact CXCR1 must be due to its weak binding at Site-II. Nevertheless, this level of binding is sufficient for receptor activation indicating that affinity and activity are separable functions. We propose that the CXC motif functions as a conformational switch that couples Site-I and Site-II interactions for both receptors, and that this coupling is critical for high affinity binding but differentially regulate activation.