

CONCEPT-TO-CLINIC

Center for Targeted Therapy

THE DEPARTMENT OF EXPERIMENTAL THERAPEUTICS

VOLUME II – ISSUE 1 – MARCH 2007

Center for Targeted Therapy Offers RNAi Screening Service

The summer of 2007 will bring new opportunities to investigators at M. D. Anderson as the Center for Targeted Therapy introduces its newest service – high throughput screening (HTS) of the human genome RNAi library.

The **RNAi Screening Service** allows researchers the chance to further develop potential targets by utilizing this HTS – which contains siRNAs targeting ~21,000 known human genes. This hypothesis-driven technology enables investigators to identify previously unknown modulators of genes of interest.

Prior to running a screen, there are several critical steps that must take place in order for the screen to be successful.

The first step is **assay development** and in order to benefit from the siRNA screen, an optimum assay is a necessity.

- All interested investigators will provide a brief summary of his/her proposed study in order that the screening service can advise the investigator on best practices for developing the assay – which can include selection of controls and readouts.
- Once development is underway, the investigator will perform preliminary studies to optimize the assay. Under guidance from the screening service, investigators work through parameters outlined in the standard operating procedures to ensure that the most favorable conditions for the assay are realized and an acceptable Z-factor is achieved.
- **Timeframe for assay development: three to six months.**

Assay validation is the second fundamental step that must occur

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Experimental Therapeutics Lecture Series • Wednesdays • 9 a.m. • SBC Auditorium B2.4750

April 25, 2007.....**Ira Pastan, M.D.**, Center for Cancer Research, National Cancer Institute

May 9, 2007.....**Anna Mapp, Ph.D.**, University of Michigan

June 6, 2007.....**David Cheresch, Ph.D.**, Moores Cancer Center at University of California, San Diego

First ET Research Staff Forum Shows Promise

The Department of Experimental Therapeutics held its first **Research Staff Forum** on Friday, Feb. 2, 2007.

The forum began with Garth Powis, D.Phil., professor and chair of the Department of Experimental Therapeutics and director of the Center for Targeted Therapy, presenting an overview of the Center for Targeted Therapy.

His presentation detailed how experimental therapeutics will be the anchor department for the CTT and included a brief report from Elizabeth Grimm, Ph.D., professor and deputy chair of the Department of Experimental



Pictured from left to right: front row-Michael Sun, Pijus Mandal and Bill Marks; back row-Tao Lu, Edd Felix, Nathan Ihle and Mary Ayres

Therapeutics, on the CTT building and estimated completion dates.

Powis also outlined his vision for personalized medicine and the development process of new anti-cancer compounds and demonstrated how the department and the programs comprising the CTT will utilize this process to support the mission of M. D. Anderson.

Next, each member of the steering committee presented a brief outline of their respective laboratory's research activities, staffing and goals.

- **Pijus Mandal**, a research scientist in Dr. John McMurray's lab, spoke about the chemistry core and described in detail their work in designing and developing STAT3 inhibitor compounds and construction of peptidomimetic compounds to enhance efficacy of action of these inhibitors.
- **Mary Ayres**, a research investigator and laboratory manager for Dr. Varsha Gandhi's lab, spoke about their research in developing DNA-directed therapeutics against hematological malignancies.
- **Tao Lu**, a research scientist working in Dr. Walter Hittelman's lab, discussed their work in studying the cellular oncology of a broad variety of cancers. Lu captured the audience's attention by showing two short videos of cellular invasion and cell cycle processes that were prepared using the live cell-imaging microscope.
- **Bill Marks**, a senior research assistant working with Dr. Michael Rosenblum, explained the activities of their group in the design, construction and production of novel fusion proteins linked to toxic molecules and specifically targeted to unique tumor antigens.

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Ruoning Wang is pictured (second from left) with the other Presidents' Research Scholarship recipients and George M. Stancel, Ph.D., dean of GSBS Houston (far left), and John Mendelsohn, M.D., president of M. D. Anderson (far right).

Ruoning Wang, a graduate research assistant in Dr. Jian Kuang's lab, is one of four recipients of the **Presidents' Research Scholarship** at The University of Texas Graduate School of Biomedical Sciences at Houston.

Wang receives a one-year, \$5,000 scholarship awarded through funding from the presidents of the UT Health Science Center at Houston and M. D. Anderson for demonstrating distinction and excellence in research.

Wang's research project, "**Erk-Map Kinase Mediated Cdc25 Activation During G2/M Transition**," also earned him the Genes and Development (G&D) Graduate Program annual **Senior Research Award** this year as a post-candidacy student.

Criteria for this award focuses on the progress a student has made in his or her project and publication of said work in high-quality journals. As the recipient of this award, Wang will present the Grady Saunders Student Lecture at the annual G&D retreat in March 2007.

Varsha Gandhi, Ph.D., professor in the Department of Experimental Therapeutics, was selected to serve a five-year term, beginning January 2007, as a member on the editorial board of the journal *Blood*.

Members are selected by the editor and are "called upon to provide concise highlights of specific articles for the Inside Blood section and are depended on to review several manuscripts per year."

Blood is a publication of the American Society of Hematology.

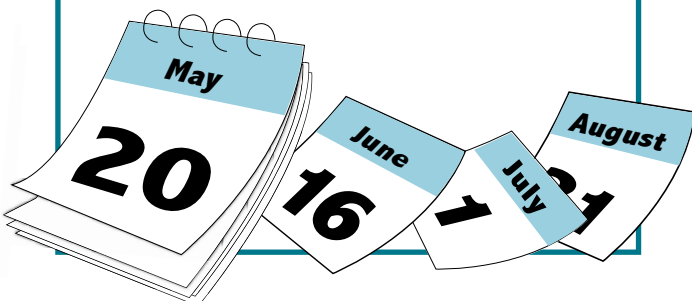
SAVE THE DATE...

ET Research Staff Forum

Friday, May 4, 2007

11:30 a.m. to 12:30 p.m.

R11.1100, Rooms 5 through 8



Deepa Sampath, Ph.D., an instructor in Dr. Bill Plunkett's lab in the Department of Experimental Therapeutics, received a grant from the **CLL Global Research Foundation**.

Sampath's proposal, "Transcriptional Activation to Target CLL," earned funding in the amount of \$100,000 until Aug. 31, 2007.

The CLL Global Research Foundation is a nonprofit organization committed to accelerating progress toward the control and cure of chronic lymphocytic leukemia and related leukemias and lymphomas.

Sampath was one of 12 grant recipients from the foundation in 2006.

Bill Plunkett, Ph.D., professor in the Department of Experimental Therapeutics, was recognized with the **Potu N. Rao Award for Excellence in Basic Science** at the First Annual

Division of Cancer Medicine Faculty Recognition and Award Program in December 2006.



Bill Plunkett, Ph.D., pictured on right, receives the Potu N. Rao Award for Excellence in Basic Science from Waun Ki Hong, M.D.

Requirements of the nominees included: conducting impeccable laboratory-based research; publishing important scientific findings in high profile, high impact journals; providing outstanding collaboration and/or support to colleagues; serving as a role model for students and trainees wishing to pursue a career as a

basic scientist; carrying out work that has gained international recognition; and obtaining significant external funding for his/her research efforts.

Plunkett was one of four faculty nominated for the award.

Bharat Aggarwal, Ph.D., professor in the Department of Experimental Therapeutics, had a recent article titled "Embelin, an Inhibitor of XIAP, Blocks Nuclear Factor-B (NF-B) Signaling Pathway Leading to Suppression of NF-B-regulated Anti-apoptotic and Metastatic Gene Products" that was one of the top 10 articles viewed by the online readership of *Molecular Pharmacology* in October 2006.

Published in the January 2007 issue, and Oct. 6, 2006 online ahead of print, in *Molecular Pharmacology*, a publication of the American Society for Pharmacology and Experimental Therapeutics, the article can be viewed by visiting the following Web site <http://molpharm.aspetjournals.org/>.

PROMOTIONS

Congratulations on a job well done! **Lidia Vogelsang** was promoted to Program Coordinator of ET Educational Programs. She is responsible for coordinating the new GSBS Program in Experimental Therapeutics and assisting Dr. Varsha Gandhi in her role as director of education and faculty development for the department.

The Department of Experimental Therapeutics continues to grow by leaps and bounds. Please welcome the newest members of our staff.

Shuxing Zhang, Ph.D., has joined the department as an assistant professor specializing in computational drug modeling. Dr. Zhang's office is Y6.6083, his lab is located in Y6.6086 and he can be reached by phone at (713) 745-2958.

Fredika Robertson, Ph.D., has joined the department as a professor and she will work closely with Dr. Ferrari in the nanobiotechnology lab. Dr. Robertson's office and phone number may be accessed through Lotus Notes.

Yanjie Zhao joined Dr. Razelle Kurzrock's lab as a research assistant I and can be reached at (713) 792-3523 and found in room Y7.5306.

Dr. Walter Hittelman's lab has two newcomers – **Dr. Chang Lee**, a visiting scientist, and **Shangfeng Liu**, a postdoctoral fellow. Both are located in Y1.5609 and can be reached at (713) 792-2961.

Amit Rai joined Dr. Bharat Aggarwal's lab as a postdoctoral fellow and can be reached at (713) 792-6460 and located at Introgen (INT2.204).

The administrative team gained three new members – **Audrey Gentry**, accounting specialist; **Mayra Gonzalez**, senior secretary; and **Myisha Pennington**, administrative assistant. Audrey is located at FC6.3056 and can be reached at (713) 792-3525 and Mayra can be found at FC6.3036 and be reached by calling (713) 794-1141. Myisha is assisting Drs. Varsha Gandhi and Bill Plunkett and is located in office T6.3928 and can be reached at (713) 792-3336.

Zhehui Feng joined Dr. Jian Kuang's lab as a research scientist and can be reached at (713) 792-3694 and found in room Y1.5609.

William Mansfield is now part of Dr. Waldemar Priebe's lab as a research assistant II. He can be reached by calling (713) 563-9895 and is located in Y6.6071.

Dr. Robert Bast's lab gained **Ly K Le** as a research assistant I. She is located in Y7.5821 and can be reached at (713) 792-3791.

On a related note... **Sukhen Ghosh**, in Dr. David Farquhar's lab, and **Xiaojun Liu**, in Dr. Bill Plunkett's lab, each made the switch to research scientist from postdoctoral fellow. Sukhen can be found in Y7.5729 and his phone is (713) 792-3783 and Xiaojun is located in T6.3932 and can be reached by phone at (713) 792-3336.

Center for Targeted Therapy Offers RNAi Screening Service *(continued from page 1)*

to ensure a successful screen. At this stage, a member of the investigator's laboratory should be selected to work with the screening service from this point forward. This step is necessary to ensure that the individual most knowledgeable about the area of interest being screened is able to gauge the condition of cells undergoing early testing.

- Assays selected for HTS are subjected to a preliminary screen using the kinome sub-library.
- Together, service staff and a technician from the investigator's laboratory will work through the systems put in place to determine if the assay can be reproduced accurately under conditions required for the screen.
- Assays that pass the sub-library pre-screen will undergo HTS of the entire human genomic library. All conditions determined by the assay development will be screened in duplicate for the ~21,000 known human genes.
- **Timeframe for assay validation: one to two months.**

The third step is the **HTS** itself – with the capability to monitor two types of readouts.

- **Absorbance** – A readout to determine cell viability. A reliable approach, siRNA can be used in combination with a drug to determine other sensitizing genes to that drug.
- **Luminescence** – Use of reporter assays to study upstream regulators of transcription factors.
- **Timeframe for HTS: five to seven weeks.**

The entire process, from assay development to high throughput screen, can be lengthy – taking a minimum of six months and possibly as long as a year. While there is no fee for maintenance, labor or even the screen itself, investigators do incur charges. Investigators are responsible for the cost of cell lines; reagents (e.g., transfection, viability); and disposable materials (e.g., test plates, tips)

used in the screen. Ultimately, the cost is dependent upon the type of assay and, **as an estimate only**, can conservatively begin at \$10,000 and increase from there. The screening service staff will provide an estimate specific to your study.

High throughput screening of siRNA libraries has resulted in an increase in the amount of information available on the regulation of signaling pathways and drug targets (*please see references below*), thereby creating an opportunity for academicians at M. D. Anderson to further their research by generating data developed through these screens for novel targets and ideas – bringing them one step closer to the goal of personalized medicine.

For more information on the **Center for Targeted Therapy's RNAi Screening Service**, please contact **Geoffrey Bartholomeusz, Ph.D.**, assistant professor in the Department of Experimental Therapeutics and director of the RNAi Screening Service, through Lotus Notes.

References:

1. Berns, K., Hijmans, E.M., Mullenders, J., et al. A large scale RNAi screen in human cells identifies new components of the p53 pathway. (2004) *Nature*, 428:431-437.
2. Mackeigan, J.P., Murphy, L.O. and Blenis, J. Sensitized RNAi screens of human kinases and phosphatases identifies new regulators of apoptosis chemoresistance. (2005) *Nature cell Biol.* 7:591-600
3. Pelkmans, L., et al. Genome-wide analysis of human kinases in clathrin-and caveolae/raft-mediated endocytosis. *Nature*, 436:78-86



Pictured in Krakow, Poland at the First Polish-American Symposium are left to right: Waldemar Priebe, Ph.D., Gabriel Lopez-Berestein, M.D., Sonia Lopez, Charles Conrad, M.D. and Mary Johansen, Pharm.D.

Waldemar Priebe, Ph.D., professor in the Department of Experimental Therapeutics, worked with a group of Polish scientists to organize the **First Polish-American Symposium on Strategic Approaches to Drug Discovery and Development in Academia** held Nov. 12 to 14, 2006 in Krakow, Poland.

M. D. Anderson and, specifically, the Department of Experimental Therapeutics were well represented at the symposium with Priebe offering both introductory and closing remarks.

During the session titled “Drug Discovery and Development in Academia in the USA,” several members of ET presented: Priebe – “Novel Agents Targeting Brain Tumors: An Integrated Interdisciplinary Approach to Drug Discovery;” **Gabriel Lopez-Berestein, M.D.**, professor, – “Nanoparticle Delivery of Nucleotides: The Drug Development Program at M. D. Anderson Cancer Center;” and **Timothy Madden, Pharm.D.**, associate professor, – “Drug Development in an Academic Environment: One Approach.” Also, **Charles Conrad, M.D.**, associate professor in the Department of Neuro-Oncology, presented “Drug Design and Development in Academia: The Clinician’s Perspective.”

Additionally, Priebe and Lopez moderated a roundtable discussion titled “Discovery and Translational Research in Academia.”

Other sessions included “Drug Discovery in Academia in Poland” and “Polish Biotechnology Industry: Can Academia Help? Attracting American Investors” with topics focusing on the comparison of logistics and financial systems in Poland and the U.S. that are necessary to support this type of research.

Supported by the Polish Ministry of Science and Higher Education, conference organizers intended the symposium to encourage the involvement of academia in Poland in the process of novel drug discovery and development and new methods for the treatment of disease. Organizers also hoped to identify areas of collaboration between the two country’s researchers and institutions while providing guidance on best practices to stimulate drug discovery and the commercialization process.

Varsha Gandhi, Ph.D., professor in the Department of Experimental Therapeutics, presented “Forodesine – Preclinical Studies” at the “**It’s Time to Take Care of T-Cell Lymphomas**” congress hosted by the Institute of Hematology and Oncology “L. e A. Seràgnoli” in Bologna, Italy on Oct. 22 to 24, 2006.

Additionally, Gandhi participated in a ‘meet the expert session’ with a presentation titled “Nucleoside Analogs in Leukemia” at the **48th Annual Meeting of the American Society of Hematology** in Orlando, Fla. on Dec. 10, 2006.

Kapil Mehta, Ph.D., and **Bharat Aggarwal, Ph.D.**, professors in the Department of Experimental Therapeutics, were each invited to speak at the **26th Annual Convention of Indian Association for Cancer Research and International Symposium on Translational Research in Cancer** held Jan. 17 to 19, 2007 in Bhubaneswar, India.

Mehta’s presentation was titled “Development of Drug Resistance and Metastatic Phenotypes by Cancer Cells: A New Perspective” and Aggarwal presented “Targeting Inflammation for Prevention and Therapy of Cancer.”

Also, Aggarwal presented “Targeting NF- κ B by Dietary Agents for the Prevention and Therapy of Cancer: Add Spice to Your Life” at the **CNIO (Spanish National Cancer Research Centre) Symposium on Molecular Markers in Cancer Therapy** held Nov. 27 to 29, 2006 In Madrid, Spain.

Peiyang Yang, Ph.D., assistant professor in the Department of Experimental Therapeutics, made an oral presentation titled “Antitumor Activity of Fish Oils Against Human Lung Cancer is Associated with Altered Formation of PGE₂ and PGE₃ and Regulation of AKT Phosphorylation” at the **3rd International Conference of the Society of Integrative Oncology** that took place Nov. 9 to 11, 2006, in Boston.

Several ET faculty participated in “**Chemistry in Cancer Research: A Vital Partnership**” – a joint conference of the American Association for Cancer Research and the American Chemical Society that took place Feb. 4 to 7, 2007 in San Diego.

An abstract titled “Markers of Intracellular Nitrosative and Oxidative Stress in Melanoma Tumor Cells Identify the Subset of Melanoma Patients with Shortest Survival” from **Elizabeth Grimm, Ph.D.**, professor and deputy chair, was selected for an oral presentation.

In addition to chairing a session on drug discovery, **Waldemar Priebe, Ph.D.**, professor, had a poster presentation titled “Modular Design of DNA Binding Agents Capable of Penetrating Blood-Brain Barrier and Targeting Brain Tumors.”

Other poster presentations were “Structural Basis for Interactions between Phosphopeptide-based Inhibitors and Stat3” by **John McMurray, Ph.D.**, associate professor, and “Anticancer Alkaloids: Optimized Total Synthesis of Tetrahydrosecamine” by **William Bornmann, Ph.D.**, professor in the Department of Experimental Diagnostic Imaging.



Working hard or hardly working? Bryant Darnay, Ph.D., and Mei Koh, Ph.D., pictured on the slopes in Big Sky, Mont. while attending a Keystone Symposium.

Bryant Darnay, Ph.D., assistant professor, and **Mei Koh, Ph.D.**, research scientist, both in the Department of Experimental Therapeutics, attended the **Keystone Symposium on Ubiquitin and Signaling (B4)** in Big Sky, Mont. on Feb. 4 to 9, 2007.

Darnay’s poster was titled “Mechanistic Insight into the TRAF Family of RING-dependent E3 Ubiquitin Ligases.”

Koh presented a poster titled “A Novel E3-ubiquitin Ligase, SART1, Ubiquitinates HIF-1 α Under Hypoxic Conditions and

Inhibits Tumor Growth.”

Experimental Therapeutics Develops Model for Mentor Program

The Department of Experimental Therapeutics is paving the way for junior faculty to advance their professional development goals by developing a mentor program that is structured to include tenured, tenure-track and non tenure-track faculty members.

The Mentorship Committee, led by **Varsha Gandhi, Ph.D.**, professor and director of education and faculty development in the Department of Experimental Therapeutics, recognized the importance of establishing a mentor program and has paired each mentee with a tenured senior faculty member within the department who will provide general guidance and expertise in areas such as grant and patent writing; career options; and promotion and progress.

The committee identified three areas of concentration in which to categorize NTRA faculty to ensure that the unique mentoring needs of each group are met. The categories are as follows:

1. **Service oriented** – geared to providing service benefiting either departmental or institutional needs;
2. **Working for a primary investigator** – promoting and/or collaborating on PI's research;
3. **An academic track** – works in the lab of a PI while developing an independent academic career.

NTRA faculty will meet with his/her mentor – who is different than the PI in whose lab he/she currently works – at a minimum of once per year. The mentor also will participate in the mentee's evaluation with the PI.

To provide experience in all aspects of career development, NTRA faculty also have the opportunity to direct and take part in the departmental Research Seminar Series and to participate in didactic teaching and various departmental committees.

Tenured and tenure-track junior faculty will meet with his/her mentor at least twice a year and the mentor will participate in the mentee's annual evaluation with the department chair.

Going forward, the Mentorship Committee will review and modify the program as necessary.

If you have any questions regarding the ET Mentor Program, please contact Dr. Varsha Gandhi or **Dr. DahHsi Ho**, professor emerita and associate director of the mentor program in the Department of Experimental Therapeutics, through Lotus Notes.

TRAINEE NEWS

The Department of Experimental Therapeutics is proud to feature the work of its GSBS students selected to participate at the annual meeting of the American Association for Cancer Research taking place April 14 to 18, 2007 in Los Angeles. The following poster presentations include: section in which the poster appears; authors names; abstract number; title; and a brief summary.

Section: Experimental & Molecular Therapeutics 21

Authors

Jennifer A. Frey, Varsha Gandhi

Abstract #2413

Title

8-Amino-Adenosine inhibits RNA transcription by decreasing phosphorylation of the RNA Polymerase II C-terminal domain.

Summary

This study has demonstrated that 8-amino-adenosine treatment results in a decline in RNA synthesis as studied by uridine incorporation and quantitation of new RNA transcripts by real-time RT-PCR. Immunoblot analysis has indicated there is a decline in serine phosphorylation of the RNA polymerase II C-terminal domain in 8-amino-adenosine treated cells and further studies are underway to determine if the kinases responsible for this phosphorylation are affected by this nucleoside analog.

Section: Experimental & Molecular Therapeutics 24

Authors

Bahareh Tavana, Zai-Feng Huang, Abdul R. Khokhar, William G. Bornmann, Zahid H. Siddik.

Abstract #3194

Title

Downregulation of p21 induces cisplatin resistance in tumor cells harboring wild-type p53.

Summary

Our studies show that loss of p21 induces resistance and, conversely, reintroduction of p21 re-sensitizes refractory ovarian cancer cells to cisplatin. Our data also support combining SAHA and cisplatin therapy as a clinically effective solution for cisplatin resistance.

Authors

Cheng-Yu Tsai, William Plunkett

Abstract #3186

Title

Intracellular metabolism of GS-9219, a membrane permeable prodrug of 9-(2-phosphonylmethoxyethyl)guanine.

Summary

To study the cellular pharmacology and molecular pharmacodynamics of a novel nucleoside analogue in hematological malignancies.

Section: Cellular & Molecular Biology 33

Authors

Shaoyi Huang, Yinhuo Yu

Abstract #2834

Title

The ARHI tumor suppressor gene may prevent nuclear translocation of p-STAT3 by antagonizing the interaction of Ran with importin protein

Summary

Focused on the tumor suppressor gene ARHI bio-function and the mechanism. I am studying the interaction of ARHI with STAT3 and other proteins.

Section: Experimental & Molecular Therapeutics 32

Authors

Brett Ewald, Deepa Sampath, and William Plunkett

Abstract #4037

Title

Co-localization of the Mre11-Rad50-Nbs1 complex, phosphorylated ATM, and g-H2AX may identify sites of nucleoside analogue-induced stalled replication forks.

Summary

This investigation demonstrates nuclear co-localization of molecules after exposure to nucleoside analogue drugs. This occurs in the absence of detectable DNA double-strand breaks and may suggest that these molecules localize at sites of stalled DNA replication forks.

Authors

Lei Guo, William Plunkett

Abstract #4030

Title

Induction of DNA double-strand breaks by NK314 via stabilization of topoisomerase II cleavage complexes, and inhibition of DNA-PK sensitizes cells to NK314

Summary

NK314 is a benzo[c]phenanthridine alkaloid that has shown promising antitumor activity in a diverse selection of tumor models, and is currently in phase I clinical trials. Our study demonstrated that NK314 induces DNA double-strand breaks by stabilization of topoisomerase II cleavage complexes, and inhibition of DNA-PK sensitizes cells to NK314.

American Journal of Physiology – Renal Physiology

Stanniocalcin-1 regulates endothelial gene expression and modulates transendothelial migration of leukocytes.

Chakraborty A, Brooks H, Zhang P, Smith W, McReynolds MR, Hoying JB, Bick R, Truong L, Poindexter B, Lan H, Elbejrami W, Sheikh-Hamad D.

Am J Physiol Renal Physiol. 2007 Feb;292(2):F895-904. Epub 2006 Oct 10.

Anticancer Research

Anticancer potential of silymarin: from bench to bed side.

Agarwal R, Agarwal C, Ichikawa H, Singh RP, Aggarwal BB.

Anticancer Res. 2006 Nov-Dec;26(6B):4457-98. Review.

Biochemical and Biophysical Research Communications

PTEN enhances TNF-induced apoptosis through modulation of nuclear factor-kappaB signaling pathway in human glioma cells.

Koul D, Takada Y, Shen R, Aggarwal BB, Yung WK.

Biochem Biophys Res Commun. 2006 Nov 17;350(2):463-71. Epub 2006 Sep 25.

Biochemical Journal

Phosphorylation of the proline-rich domain of Xp95 modulates Xp95 interaction with partner proteins.

Dejournett RE, Kobayashi R, Pan S, Wu C, Etkin LD, Clark RB, Bogler O, Kuang J.

Biochem J. 2007 Jan 15;401(2):521-31.

Biochemical Pharmacology

Inflammation and cancer: how hot is the link?

Aggarwal BB, Shishodia S, Sandur SK, Pandey MK, Sethi G

Biochem Pharmacol. 2006 Nov 30;72(11):1605-21. Epub 2006 Aug 4. Review.

Biology of Blood and Marrow Transplantation

Pharmacokinetics of once-daily IV busulfan as part of pretransplantation preparative regimens: a comparison with an every 6-hour dosing schedule.

Madden T, de Lima M, Thapar N, Nguyen J, Roberson S, Couriel D, Pierre B, Shpall EJ, Jones RB, Champlin RE, Andersson BS

Biol Blood Marrow Transplant. 2007 Jan;13(1):56-64.

Bioorganic & Medicinal Chemistry Letters

Solid-phase synthesis of Stat3 inhibitors incorporating O-carbamoylserine and O-carbamoylthreonine as glutamine mimics.

Mandal PK, Heard PA, Ren Z, Chen X, McMurray JS.

Bioorg Med Chem Lett. 2007 Feb 1;17(3):654-6. Epub 2006 Nov 6.

Blood

Fludarabine increases oxaliplatin cytotoxicity in normal and chronic lymphocytic leukemia lymphocytes by suppressing interstrand DNA crosslink removal.

Moufarij MA, Sampath D, Keating MJ, Plunkett W.

Blood. 2006 Dec 15;108(13):4187-93. Epub 2006 Sep 5.

British Journal of Cancer

Upregulation of p27 and its inhibition of CDK2/cyclin E activity following DNA damage by a novel platinum agent are dependent on the expression of p21.

He G, Kuang J, Huang Z, Koomen J, Kobayashi R, Khokhar AR, Siddik ZH.

Br J Cancer. 2006 Dec 4;95(11):1514-24. Epub 2006 Nov 7.

Cancer

Nuclear factor-kappaB (NF-kappaB) is frequently expressed in lung cancer and preneoplastic lesions.

Tang X, Liu D, Shishodia S, Ozburn N, Behrens C, Lee JJ, Hong WK, Aggarwal BB, Wistuba II.

Cancer. 2006 Dec 1;107(11):2637-46.

Cancer Research

A sequential blockade strategy for the design of combination therapies to overcome oncogene addiction in chronic myelogenous leukemia.

Chen R, Gandhi V, Plunkett W.

Cancer Res. 2006 Nov 15;66(22):10959-66.

Increased expression of tissue transglutaminase in pancreatic ductal adenocarcinoma and its implications in drug resistance and metastasis.

Verma A, Wang H, Manavathi B, Fok JY, Mann AP, Kumar R, Mehta K.

Cancer Res. 2006 Nov 1;66(21):10525-33.

Inhibition of prostate tumor growth and bone remodeling by the vascular targeting agent VEGF121/rGel.

Mohamedali KA, Poblentz AT, Sikes CR, Navone NM, Thorpe PE, Darnay BG, Rosenblum MG.

Cancer Res. 2006 Nov 15;66(22):10919-28.

Cell Death & Differentiation

All pathways to cancer apoptosis meeting in Thiruvananthapuram (India).

Mehta K, Gandhi V, Aggarwal BB.

Cell Death Differ. 2006 Dec;13(12):2163-4. Epub 2006 Jun 2. No abstract available.

Cellscience

Carcinogenic Inflammation: Novel Tumor-enhancing Cytokines

Grimm EA, Poindexter NJ.

Cellscience Reviews. 2006 Oct 27;3(2):20. Commentary.

Chemistry & Biology

A new small-molecule Stat3 inhibitor.

McMurray JS.

Chem Biol. 2006 Nov;13(11):1123-4.

Clinical Cancer Research

Decreased expression of gene cluster at chromosome 1q21 defines molecular subgroups of chemoradiotherapy response in esophageal cancers.

Luthra MG, Ajani JA, Izzo J, Ensor J, Wu TT, Rashid A, Zhang L, Phan A, Fukami N, Luthra R.

Clin Cancer Res. 2007 Feb 1;13(3):912-9.

Expert Opinion on Investigational Drugs

Novel purine nucleoside analogues for T-cell-lineage acute lymphoblastic leukaemia and lymphoma.

Ravandi F, Gandhi V.

Expert Opin Investig Drugs. 2006 Dec;15(12):1601-13. Review.

Haematologica Reports

Forodesine – Preclinical Studies.

Gandhi V.

Haematologica Reports. 2006;2(13):35-37.

Journal of Biological Chemistry

Gamma-tocotrienol inhibits nuclear factor-kappaB signaling pathway through inhibition of receptor-interacting protein and TAK1 leading to suppression of antiapoptotic gene products and potentiation of apoptosis.

Ahn KS, Sethi G, Krishnan K, Aggarwal BB.

J Biol Chem. 2007 Jan 5;282(1):809-20. Epub 2006 Nov 17.

Site-specific Lys-63-linked tumor necrosis factor receptor-associated Factor 6 auto-ubiquitination is a critical determinant of I kappaB kinase activation.

Lamothe B, Besse A, Campos AD, Webster WK, Wu H, Darnay BG.

J Biol Chem. 2007 Feb 9;282(6):4102-12. Epub 2006 Nov 29.

TAK1-dependent signaling requires functional interaction with TAB2/TAB3.

Besse A, Lamothe B, Campos AD, Webster WK, Maddineni U, Lin SC, Wu H, Darnay BG.

J Biol Chem. 2007 Feb 9;282(6):3918-28. Epub 2006 Dec 8.

Journal of Biotechnology

Overexpression of biologically active VEGF(121) fusion proteins in Escherichia coli.

Kim S, Mohamedali KA, Cheung LH, Rosenblum MG.

J Biotechnol. 2007 Feb 20;128(3):638-47. Epub 2006 Dec 12.

Journal of Clinical Oncology

Cyclin D1 guanine/adenine 870 polymorphism with altered protein expression is associated with genomic instability and aggressive clinical biology of esophageal adenocarcinoma.

Izzo JG, Wu TT, Wu X, Ensor J, Luthra R, Pan J, Correa A, Swisher SG, Chao CK, Hittelman WN, Ajani JA.

J Clin Oncol. 2007 Feb 20;25(6):698-707.

Journal of Interferon & Cytokine Research

Soluble human MDA-7/IL-24: characterization of the molecular form(s) inhibiting tumor growth and stimulating monocytes.

Mumm JB, Ekmekcioglu S, Poindexter NJ, Chada S, Grimm EA.

J Interferon Cytokine Res. 2006 Dec;26(12):877-86.

Journal of Investigative Dermatology

Genetic variants of the vitamin D receptor gene alter risk of cutaneous melanoma.

Li C, Liu Z, Zhang Z, Strom SS, Gershenwald JE, Prieto VG, Lee JE, Ross MI, Mansfield PF, Cormier JN, Duvic M, Grimm EA, Wei Q.

J Invest Dermatol. 2007 Feb;127(2):276-80. Epub 2006 Sep 21.

Molecular Cancer Research

Programmed cell death-4 tumor suppressor protein contributes to retinoic acid-induced terminal granulocytic differentiation of human myeloid leukemia cells.

Ozpolat B, Akar U, Steiner M, Zorrilla-Calancha I, Tirado-Gomez M, Colburn N, Danilenko M, Kornblau S, Berenstein GL.

Mol Cancer Res. 2007 Jan;5(1):95-108.

Molecular Cancer Therapeutics

Glucocorticoid receptor transcriptional isoforms and resistance in multiple myeloma cells.

Sanchez-Vega B, Krett N, Rosen ST, Gandhi V.

Mol Cancer Ther. 2006 Dec;5(12):3062-70.

Molecular Pharmacology

Embelin, an inhibitor of X chromosome-linked inhibitor-of-apoptosis protein, blocks nuclear factor-kappaB (NF-kappaB) signaling pathway leading to suppression of NF-kappaB-regulated antiapoptotic and metastatic gene products.

Ahn KS, Sethi G, Aggarwal BB.

Mol Pharmacol. 2007 Jan;71(1):209-19. Epub 2006 Oct 6.

Prostaglandins, Leukotrienes and Essential Fatty Acids

Determination of endogenous tissue inflammation profiles by LC/MS/MS: COX- and LOX-derived bioactive lipids.

Yang P, Chan D, Felix E, Madden T, Klein RD, Shureiqi I, Chen X, Dannenberg AJ, Newman RA.

Prostaglandins Leukot Essent Fatty Acids. 2006 Dec;75(6):385-95. Epub 2006 Sep 29.

Seminars in Oncology

Biomarkers of response to preoperative chemoradiation in esophageal cancers.

Luthra R, Luthra MG, Izzo J, Wu TT, Lopez-Alvarez E, Malhotra U, Choi IS, Zhang L, Ajani JA.

Semin Oncol. 2006 Dec;33 Suppl 11:2-5.

The Journal of Nuclear Medicine

PET of vascular endothelial growth factor receptor expression.

Cai W, Chen K, Mohamedali KA, Cao Q, Gambhir SS, Rosenblum MG, Chen X.

J Nucl Med. 2006 Dec;47(12):2048-56.

Toxicology

Curcumin down regulates smokeless tobacco-induced NF-kappaB activation and COX-2 expression in human oral premalignant and cancer cells.

Sharma C, Kaur J, Shishodia S, Aggarwal BB, Ralhan R.

Toxicology. 2006 Nov 10;228(1):1-15. Epub 2006 Aug 12.

INTRODUCING...



Name: Nargis Khalfe

Title: Administrative Assistant

Departmental Role: Support four faculty members (Drs. Ferrari, Priebe, Robertson and McMurray)

Birthplace: Nairobi, Kenya

The word that best describes me is: Caring

My proudest accomplishment is: Climbing to the top of Table

Mountain (elevation 3,566 feet) in Cape Town, South Africa

People who know me would say: "She is forever giving" (putting others before myself)

When not working for a living: I am either on the sidelines of a soccer field cheering on my kids, camping in the woods with the girl scouts or spending time with my family.

My heroes and/or heroines include: My Mother

Favorite or recent movies: "The Pursuit of Happyness"

Favorite or recent books: "The Heart of a Woman" by Maya Angelou

The most unique thing about me is: I can speak six languages including English, Swahili, Hindi, Urdu, Punjabi and Kokni.

Favorite quote(s): "A Smile is the Universal Welcome," Max Eastman

Favorite song(s): "I Just Called to Say I Love You" by Stevie Wonder

What I like most about Houston: I am surrounded by my family.

What I like least about Houston: Hurricane season and traffic

Something most people don't know about me: I love to cook, visit National Parks/Reserves and watch wildlife. Also, I am a volunteer for the American Red Cross.

First ET Research Staff Forum Shows Promise

(continued from page 1)

- **Nate Ihle**, a program coordinator for Dr. Garth Powis, described the broad range of activities in their laboratory regarding drug development. Ihle explained: how they use Drosophila genetics to screen for potential therapeutics targets; the siRNA screening program; imaging; and animal modeling.
- **Michael Sun**, a research scientist in Dr. Razelle Kurzrock's lab, remarked on their activities in translational research and the development of a potentially valuable micro-array DNA and RNA screening technology.
- **Edd Felix**, laboratory manager of the mass spectrometry lab for the Pharmaceutical Development Center and the M. D. Anderson analytical core, spoke about the formation of the PDC and its contribution to drug development within M. D. Anderson that assists both research and clinical faculty in the development of anti-cancer therapeutics and treatment modalities from concept to clinic. Felix also discussed the PDC's research in natural products and its nationally recognized research in bioactive lipids in cancer and inflammation.

In addition to sharing the research goals of their respective laboratories, each speaker presented a brief outline of equipment and laboratory techniques utilized by their group.

This forum was the first in a series of quarterly events and while the format of each forum may change, from speakers to posters to roundtable discussions, the objectives remain unchanged – to promote the career development of research staff as professional cancer researchers by enhancing their specialized skills and sharing useful laboratory techniques.

Concept-to-Clinic is a publication of the Department of Experimental Therapeutics at The University of Texas M. D. Anderson Cancer Center.

Published quarterly, we welcome submissions from members of the department and reserve the right to edit for length and style.

Please send submissions to:
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