The Division of Surgical Research recently hosted its 5th Annual “Advances in Inflammation Research” Symposium on September 20 & 21, 2007.

Here are some highlights from the symposium.....

On Thursday afternoon, the program opened with a warm welcome and acknowledgements by Dr. Jorge Albina. He then introduced the first of three junior faculty speakers who presented their latest findings in the lab.

“Integrin regulation of human neutrophils in response to fungal beta-glucan”
Liz Lavigne, PhD

“Lymphocytes as an anti-apoptotic / anti-inflammatory regulator of extra-pulmonary acute lung injury”
Fabienne Venet, PhD

“IL-1 receptor determines fibrosis in sterile wounds”
Alan Thomay, MD
Dr. Cioffi extended his gratitude to the distinguished guest speakers for coming and offered acknowledgements to those who’ve continued to support the Department of Surgery and the Division of Surgical Research’s symposium efforts each year.

Dr. Cioffi introduced the Keynote Speaker, Ivona Aksentijevich, PhD, substituting for Dr. Daniel Kastner, who could not attend due to a family emergency.

Dr. Aksentijevich spoke on the topic “The expanding spectrum of systemic autoinflammatory diseases”.

Friday morning began with an informal “Meet-the-Professors” session.

This was followed by the afternoon session of speakers, held at the 70 Ship Street Conference Room on the Brown University campus.

Dr. Albina introduced the Friday afternoon speakers:

“Endoplasmic reticulum stress and inflammation in obesity and diabetes” by Gokhan Hotamisligil, MD, PhD

“Activation and counter-regulation in the innate immune System” by Christopher Karp, MD

“Mechanisms underlying the sterile inflammatory response to cell death” by Kenneth Rock, MD

“In vivo imaging of the immune response” by Ulrich von Andrian, MD

BE SURE TO ATTEND NEXT YEARS' RESEARCH SYMPOSIUM TO BE HELD ON SEPTEMBER 11 & 12, 2008
Brown Researchers Make Major Signal Transduction Discovery

How cells sense and respond to chemical messages – a process known as signal transduction – is a fundamental force in biology, controlling key processes such as cell growth and immune response. Now researchers from The Warren Alpert Medical School of Brown University and Rhode Island Hospital report a significant discovery in the field of signal transduction that could provide a new target for cancer, HIV and other drugs. Results are published in Cell.

As reported by Brown University Media Relations

PROVIDENCE, R.I. [Brown University/Rhode Island Hospital] — The chemical process known as acetylation plays a central role in cytokine receptor signal transduction – a fundamental biochemical cascade inside cells that controls the activity of antiviral and tumor-suppressing genes. A team of cell biologists led by Eugene Chin, M.D., a research professor in The Warren Alpert Medical School of Brown University and a staff researcher at Rhode Island Hospital in the Division of Surgical Research, report their findings in the journal Cell. Their results are surprising.

Scientists have long known that phosphorylation, an amino acid modifying process in proteins, is critical for switching receptors “on” and “off” on the surface of cells. Chin and his team studied how type 1 interferon binds to a receptor complex, known as the IFN-α receptor, on the cell surface to trigger an immune response. Chin and his team found that acetylation, another chemical process that modifies amino acids, plays a central role in activating interferon receptors. Interferons play a crucial role in the body’s defense against infection and uncontrolled cell growth. Type 1 interferon is widely used to treat, hepatitis B and C and cancers such as melanoma and leukemia.

“This is a major discovery in the field of signal transduction,” Chin said. “Tyrosine phosphorylation has been so far considered the major player in signal transduction. But what we discovered challenges this concept. We found another player – acetylation – in the process.” In their experiments, Chin and his team looked at how cells respond to type 1 interferon, a protein produced in response to a viral infection or other immune trigger. The researchers found that type 1 interferon receptors – which are found in every cell in the body – call up cytoplasmic CREB-binding protein, or CBP, to move up to the cell surface. CBP acetylates these receptors. That, in turn, sparks a biochemical cascade that attracts more proteins to create a complex called ISGF3. To activate this protein complex, Chin found, acetylation is required. Once that occurs, the complex travels to the cell nucleus to switch on anti-viral or tumor-suppressing genes.

The discovery of the acetylation of cytokine receptors marks a milestone in the study of signal transduction, the process of how cells receive and respond to chemical messages. Many diseases, such as diabetes, cancer and heart disease, occur when signal transduction goes awry. That’s why some drugs either inhibit or amplify signaling inside cells by targeting tyrosine phosphorylation. By showing that another chemical process is critical to signal transduction, Chin’s findings may explain why some anti-cancer or anti-viral drugs don’t work for everyone. And the findings provide an important new target for therapies that fight cancer and viral infectious diseases.

The Brown research team also included Xiaoli Tang, Jin-Song Gao, and Ying-jie Guan, all post-doctoral research associates in Chin’s Rhode Island Hospital laboratory. Bharat Ramratnam, an associate professor of medicine at Brown, also assisted with the research, along with Katya McLane, a scientist with Upstate/Chemicon International, Inc.

The National Cancer Institute funded the work.
Recognition

Alfred Ayala, PhD, received the Shock Society’s prestigious Scientific Achievement Award from Shock Society President, Daniel Brackets, PhD, at the 30th Annual Conference of Shock held in Baltimore, Maryland, June 9-12, 2007.

Fabienne Venet, PhD, received a Student/Postdoctoral Fellow Travel Award to the 40th Annual Society for Leukocyte Biology meeting held in Cambridge, MA October 11-13, 2007.

Congratulations are extended to Zhenglong Yuan, MD, and Joanne Lomas-Neira, PhD, who were both finalists in the Basic Science Category of the Young Investigator’s Award at the 15th Annual Research Celebration, held on November 13, 2007.

Academic Highlights

Papers, Posters & Publications

Papers

Zhenglong Yuan, Sandy Wong, Alexander Borrelli and Maureen A. Chung, Down-regulation of MUC1 in cancer cells inhibits cell migration by promoting E-cadherin/catenin complex formation Biochemical and Biophysical Research Communications, Volume 362, Issue 3, 26 October 2007, Pages 740-746

Abstracts
Dr. Christopher Muratore had 2 abstracts accepted for publication in SUS and AAS entitled “Pseudoglandular Lung Development is Altered by Tracheal Occlusion” and “Endotoxin Alters Branching Morphogenesis and Matrix Deposition of the Fetal Lung”

ABSTRACTS PRESENTED BY THE DEPARTMENT OF SURGERY AT THE 15TH ANNUAL HOSPITAL RESEARCH CELEBRATION

Neutrophil adhesion and migration is mediated by matrix rigidity. P. Oakes, D.P. Zitterbart, N.A. Morin, J. Tang, J.S. Reicher

Antigen presenting cells contribute to impaired T1 response through upregulating PD-1/B7-H1 expression. X. Huang, C.S. Chung, Y. Chen, A. Ayala.

Academic Highlights (continued)

ABSTRACTS PRESENTED BY THE DEPARTMENT OF SURGERY AT THE 15TH ANNUAL HOSPITAL RESEARCH CELEBRATION (continued)

Role of NKT cells in the immune dysfunction and injury in sepsis. C.S. Chung, B. Homer, Y. Chen, A. Ayala.


Rab5 Regulates MUC1 intracellular trafficking. X. Liu, Z. Yuan, M. Chung.


Pseudoglandular lung development is altered by tracheal occlusion. C. Muratore, F. Luks, Y. Zhou, M. Harty, J. Reichner, T. Tracy.

The effects of β1-Glucan pretreatment on TNF production in vivo. C. Newsome, B. Leblanc, J. Reichner


Mirizzi’s syndrome in a five month old boy. E. Osbourne, J. Greer, A.E. Martin, C.S. Muratore.


MUC1 associated cell proliferation in cancer cells is dependent on Presenilin/y-secretase cleavage. Z. Yuan, X. Liu, M. Chung.

“It is through science that we prove, but through intuition that we discover.”
~ Henri Poincare
**Research News**

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**Research Travel**

Dr. Alan Thomay gave an oral presentation at the 62nd Annual American College of Surgeons meeting in New Orleans in October, 2007. The title of his presentation was "**TLR4 determines macrophage polarization but not cellular infiltration in early sterile wounds**" by Alan A. Thomay, MD, Jean M. Daley, MD, Jonathan S. Reichner, PhD, and Jorge E. Albina, MD.

Dr. Thomay and Dr. Jean Daley presented posters at the 40th Annual Meeting for the Society for Leukocyte Biology in Cambridge, MA in October, 2007. The title of Dr. Thomay’s poster was "**Role of IL-1 receptor in wound healing**" and Dr. Daley’s was "**The Phenotype of Wound Macrophages**".

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**Save the Date**

The monthly **Seminar Series** lectures in the Division of Surgical Research covers topics on inflammation and injury in critical illness.

The schedule, updated regularly, can be found by [clicking here](#).

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**Upcoming Events**

**The Academic Surgical Congress**

Save the date for the 3rd Academic Surgical Congress, which will be held **February 13-15, 2008** in Huntington Beach, California.
Research Opportunities for Residents

Society of Surgical Oncology 2008 Clinical Investigator Awards

The Society of Surgical Oncology is pleased to announce it is accepting applications for the Society’s 2008-2010 Clinical Investigator Awards. Applicants must serve a central role in the conduct of a specific clinical research project. This could include a leadership role in a cancer trial, in cancer outcomes research, or a translational research project related to a prospective clinical trial.

Deadline for application submission is December 1, 2007. Additional information can be found at the SSO Oncology website.

Please visit our website for current information about the Division of Surgical Research’s Trauma and Inflammation Research Training Grant and the Versaci Surgical Scholarship. http://bms.brown.edu/surgery/research/index.html

Clinical Research Loan Repayment Program

The Clinical Research LRP is a vital component of our nation’s efforts to attract health professionals to careers in clinical research.

In exchange for a two-year commitment to your clinical research career, NIH will repay up to $35,000 per year of your qualified educational debt, pay an additional 39% of the repayments to cover your Federal taxes, and may reimburse state taxes that result from these payments.

To qualify, applicants must possess a doctoral-level degree, devote an average of 20 hours per week or more to research funded by a qualifying domestic non-profit organization, university or government entity (NIH grant support is not required). New applicants must also have outstanding educational loan debt equal to or at least 20% of their institutional base salary and be a US citizen or permanent resident. To access the online application and for a full list of eligibility requirements, visit the LRP website at www.lrp.nih.gov, or for assistance call the toll-free LRP helpline at 1-866-849-4047.