

momentum

Spring 2004

A newsletter from the DAMON RUNYON CANCER RESEARCH FOUNDATION

smoke screen

[FOCUS ON: LUNG CANCER]

As part of our continuing series on specific cancers, this issue of 'momentum' focuses on efforts to beat lung cancer through early detection.

Beating cancer will require advances on many fronts. The likelihood of curing virtually any type of cancer is dramatically higher when caught at an early stage, making improvements in early detection very critical to relieving the devastation of cancer. In this Q&A, we highlight the research of Damon Runyon-Lilly Clinical Investigator* Pierre Massion, MD, Assistant Professor at Vanderbilt University, who is developing innovative screening tests for lung cancer, the leading cause of cancer-related deaths in this country.

What is the magnitude of the lung cancer challenge?

PM: About 170,000 people will be diagnosed with lung cancer in 2004 and only about 14% of those newly diagnosed will survive beyond 5 years. In fact, more patients die of lung cancer than breast, prostate and colon cancer combined. It is obviously frustrating that eighty-five percent of these deaths are attributable to smoking and preventable. So while we race to find better diagnostics and treatments, important work must also focus on tobacco addiction (see related story).

Why is the death rate so high?

PM: Patients typically do not experience any symptoms until the tumor is large and has spread. In those cases, surgery, the most effective treatment, is usually not an option.

How can we find lung cancer earlier?

PM: What we need is a way to screen people at high risk on a regular basis, like the Pap smear for cervical cancer. Past studies found that regular chest X-rays and analysis of sputum for those at highest risk of

developing lung cancer could pick up more cases but, unfortunately, did not affect people's outcomes. Current studies are trying spiral computed tomography (CT scans) to see if they might be more effective, but ideally you would want to catch the tumors before they are visible by either method.

What kind of screening tools are you developing?

PM: My laboratory is studying lung cancer cells to see if there are specific genes and proteins that indicate that the cell is cancerous or likely to become cancerous. These molecular "signatures" may be more sensitive than visual techniques and would allow us to detect tumors much earlier—before they can be seen on an X-ray or CT scan. There is also the potential to use these molecular techniques to assess the risk of developing lung cancer in the future. For example, we know that cigarette smoking is the single biggest risk factor, but only about 10 percent of lifetime smokers develop lung cancer. What makes these people different is one question we would like to answer with these molecular tests.

What would be the ideal screening test?

PM: The most alluring possibility is to test for markers of lung cancer in the blood. I am currently directing a study to develop a basic diagnostic blood test for lung cancer. Right now we are detecting about 60% of stage I lung cancers with excellent specificity and are working hard to improve this percentage. Our next step would be to develop a test that assesses the risk of developing cancer, which is even more challenging. I believe that we will get there and that there will be a blood test for lung cancer screening of high risk individuals.



Pierre Massion, PhD

What if your tests reveal that someone is likely to develop lung cancer?

PM: The goal will be to offer what is known as a chemopreventive agent—a drug that could decrease their risk of getting lung cancer. Right now, we do not have such a drug, but chemoprevention is a very active area of research. For the time being, we would follow them very closely so a tumor would be caught and removed at the earliest stage possible. In addition, we could offer them the opportunity to join a clinical trial of the newest investigative chemopreventive agents. If they were smokers, this would obviously be their strongest warning to stop.

What drives you to do cancer research?

PM: I see the devastation of cancer up close as a physician treating patients battling the disease. I lost my grandfather to lung cancer, so I know what my patients and their families are up against. Devoting the majority of my time to lung cancer research means that I may someday have the opportunity to provide better answers for them. The award from the Damon Runyon Foundation is allowing me the protected time I need to do research. It is also such a renowned award that people look at me differently when they know that I am a Damon Runyon-Lilly Clinical Investigator. It is a tremendous honor, and it is inspiring to know that the Damon Runyon community is behind me every step of the way.

* The Damon Runyon Cancer Research Foundation has a partnership with Eli Lilly and Company to fund the Clinical Investigator Award.

turning the tables on addiction



Tamara Darsow, PhD

Everyone knows by now about the dangers of cigarette smoking and the challenge of nicotine addiction. Imagine the possibilities if we could prevent addiction in the first place. That is the goal of Damon Runyon Fellow Tamara Darsow, PhD.

Tamara's research at the Salk Institute of Biological Sciences in La Jolla, California goes right to the site of action of nicotine—the human brain. She is examining what happens when nicotine reaches the brain and is following the precise sequence of events put in motion by that first inhale. Previous work

has shown that regular exposure to nicotine increases the number of nicotine receptors on the cell surface. Having more receptors available through which nicotine can activate the brain cells is thought to be a critical step that underlies addiction.

A therapeutic that would prevent nicotine-induced accumulation of these extra receptors could potentially keep addiction at bay. Tamara has identified the critical step that allows these receptors to accumulate and can now think about ways to interfere with this process.

Beating lung cancer will require researchers attacking the problem from many angles and the Damon Runyon Cancer Research Foundation is dedicated to supporting young scientists working on novel approaches to this important challenge.

a fitting tribute—enabling genius

When Laura Hartenbaum died from breast cancer after a valiant seven-year struggle, her friends and family took immediate action by establishing the Laura Hartenbaum Breast Cancer Foundation in her memory. They have chosen the Damon Runyon Cancer Research Foundation for their support and are funding a three-year Damon Runyon Fellowship Award. **Gopal Sapkota, PhD**, at Memorial Sloan-Kettering Cancer Center, has been selected as the Laura Hartenbaum Fellow. His work focuses on genetic defects in two signaling pathways within cells that are involved in the development of a wide range of cancers, including breast cancer. By understanding how these pathways interact, he hopes to identify more effective drug targets against cancer.

Gopal's incredible background is the story of true genius overcoming great challenges. He was born in the Himalayas and lived in a remote village without electricity or running water, two days walk from the nearest road. Because of his exceptional intelligence, he was invited to attend a prestigious school in



Left: Lorraine Egan, DRCRF Executive Director, accepts a check for \$30,000 from the founding members of Laura Hartenbaum Breast Cancer Foundation (from left) David Newberg, Ron Hartenbaum, Shelly Kassen, Michael Kassen and Beth Rand. DRCRF Scientific Director, Amy Francis, PhD (far right) was on hand to describe the exciting research their gift will support. Right: Gopal Sapkota, PhD



Kathmandu and then given a full scholarship to attend a university in England. Gopal is proof that great minds will find their way. Fortunately

for all of us, Gopal is focusing his impressive intellect on the ultimate challenge: understanding and beating cancer.

new board members



Elaine V. Fuchs, PhD: Damon Runyon helped launch Elaine's impressive career by awarding her a Damon Runyon Fellowship in 1977 at MIT. She is now the Rebecca C. Lancefield Professor of Mammalian Cell Biology and Development at The Rockefeller University and a Howard Hughes Medical Institute Investigator. Her research focuses on the molecular mechanisms of skin development and diseases, including cancer.



Alan M. Leventhal: Alan is Chairman and CEO of Beacon Capital Partners in Boston, Massachusetts. He is a recognized leader in real estate investment, as well as an active philanthropist. Given Damon Runyon's important role in funding outstanding young scientists in Massachusetts, we are thrilled to have a leading Bostonian on our Board.

STAR-POWER BREAKFAST CELEBRATING BRILLIANCE & BREAKTHROUGHS



Join us as we honor *Bob Wright, Vice Chairman of GE and Chairman of NBC*, at our annual breakfast benefit on May 19th at the Rainbow Room in New York City.

For more information, call Michael Stiver at 212.455.0501.

GO VERTICAL
THE ABSOLUTELY URBAN CLIMB FOR CANCER

by leaps and bounds

Last November, nearly 600 intrepid individuals met the 103-story challenge, racing to the top of the Sears Tower in Chicago to support Damon Runyon. Thanks to their extraordinary efforts, we raised \$68,000 and hope to break the \$100,000 mark at Go Vertical 2004, scheduled for November 14th. We also plan to take this event to the famous John Hancock Tower in Boston in the winter of 2005!

For more information, check out our website at www.drcrf.org.



new awardees

5 New Damon Runyon Scholars Chosen



Damon Runyon Scholar Award

The Damon Runyon Scholar Award, now in its ninth year, supports the development of outstanding scientists as they establish their own independent laboratories. In September, our distinguished Damon Runyon Scholar Review Panel, chaired by Inder Verma, PhD, from the Salk Institute in La Jolla, California, selected five outstanding investigators to receive the \$300,000 award.

Steven D. Bruner, PhD

“Mechanism and structure of natural product biosynthesis machinery,” Boston College, Boston, Massachusetts

Arshad B. Desai, PhD

Connie and Bob Lurie Scholar

“Molecular analysis of mitotic chromosome segregation,” Ludwig Institute for Cancer Research, La Jolla, California

Neil Hunter, PhD

“Molecular roles of Sgs1 and associated proteins during homologous recombination,” University of California, Davis, California

Eckhard Jankowsky, PhD

Lallage Feazel Wall Scholar

“Molecular mechanisms of tumor induced deregulation of eukaryotic translation initiation,” Case Western Reserve University, Cleveland, Ohio

Mohammad Movassaghi, PhD

Dale F. and Betty Ann Frey Scholar

“The chemical synthesis and study of biologically active complex molecules,” Massachusetts Institute of Technology, Cambridge, Massachusetts

34 New Damon Runyon Fellows Selected



Damon Runyon Fellowship Award

The Damon Runyon Fellowship Award supports the training of the brightest young postdoctoral scientists by established investigators in leading laboratories across the country. In November, the Foundation's Scientific Advisory Committee chose 17 new Fellows, and in February, 17 others were selected for the \$128,500 awards (\$174,500 for physician scientists*) designed to enlist the skills and creativity of the next generation in the fight against cancer.

NOVEMBER 2003

J. Christopher Anderson, PhD

“Synthetic biology of temporal pathways” with Adam P. Arkin, PhD, University of California, Berkeley, California

Zhirong Bao, PhD

“Automated cell lineage tracing in *Caenorhabditis elegans* and its applications” with Robert H. Waterston, MD, PhD, University of Washington, Seattle, Washington

Edward P. Browne, PhD

“The role of AOPEC3G in innate immunity to retroviruses” with Dan R. Littman, MD, PhD, New York University, New York, New York

Briana M. Burton, PhD

“Molecular mechanism of DNA translocation across membranes” with Tom A. Rapoport, PhD, Harvard Medical School, Boston, Massachusetts

Howard C. Hang, PhD

“A chemical approach towards MHC class II restricted antigen presentation” with Hidde L. Ploegh, PhD, Harvard Medical School, Boston, Massachusetts

David L. Hava, PhD

“Analysis of lipid and protein antigen presentation systems in dendritic cells following microbial infection” with Michael B. Brenner, MD, Brigham and Women's Hospital, Boston, Massachusetts

Valerie Horsley, PhD

“Regulatory mechanisms underlying skin development” with Elaine Fuchs, PhD, The Rockefeller University, New York, New York

Katrin Karbstein, PhD

“Molecular dissection of conformational switches in ribosome biogenesis” with Jennifer A. Doudna, PhD, University of California, Berkeley, California

Jess H. Leber, PhD

“SecA2-dependent secretion in *Listeria monocytogenes*” with Daniel A. Portnoy, PhD, University of California, Berkeley, California

Paul S. Maddox, PhD

“Molecular dissection of the kinetochore specification in *Caenorhabditis elegans*” with Arshad B. Desai, PhD, University of California, San Diego, California

Ayelet Maor-Shoshani, PhD

“The role of 3-methyladenine DNA glycosylase in the repair of cross-links in DNA” with Leona D. Samson, PhD, Massachusetts Institute of Technology, Cambridge, Massachusetts

Devin H. Parry, PhD

“Identification and characterization of genes involved in miRNA function in *Caenorhabditis elegans*” with Gary Ruvkun, PhD, Massachusetts General Hospital, Boston, Massachusetts

Scott T. Phillips, PhD

“Using organic synthesis to explore the mechanism of ritterazine B, a potent small molecule inhibitor of cell division” with Matthew D. Shair, PhD, Harvard University, Cambridge, Massachusetts

Gopal P. Sapkota, PhD

Laura Hartenbaum Fellow

“Regulation of Smad function by phosphorylation of the linker region” with Joan Massagué, PhD, Memorial Sloan-Kettering Cancer Center, New York, New York

Susan Ruth Schwab, PhD

“Visualizing regulatory T-cell migration and function” with Jason G. Cyster, PhD, University of California, San Francisco, California

Emmy W. Verschuren, PhD

“Emi1 regulation of the anaphase-promoting complex: defining a proteolytic switch controlling the proliferation differentiation decision” with Peter K. Jackson, PhD, Stanford University, Stanford, California

Joanna K. Wysocka, PhD

“Covalent histone modifications and epigenetic reprogramming during early mouse development” with C. David Allis, PhD, The Rockefeller University, New York, New York

FEBRUARY 2004

Daniel A. Colón-Ramos, PhD

“Directing behavior by altering synaptic specificity in *Caenorhabditis elegans*” with Kang Shen, MD, PhD, Stanford University, Stanford, California

Sandra E. Encalada, PhD

“Investigating signaling and transport connections revealed by prion proteins” with Lawrence S.B. Goldstein, PhD, University of California, San Diego, California

Sokol A. Haxhinasto, PhD

“Synergy between self-antigen and the oncogene c-MYC in lymphomagenesis” with Luk Van Parijs, PhD, Massachusetts Institute of Technology, Cambridge, Massachusetts

Tony Tung Huang, PhD

“Characterization of the FANCD2 deubiquitinating enzyme activity in the Fanconi anemia pathway” with Alan D. D'Andrea, MD, Dana-Farber Cancer Institute, Boston, Massachusetts

Steven A. Jacobs, PhD

“Mechanism of protein/RNA interactions in telomerase” with Thomas R. Cech, PhD, University of Colorado, Boulder, Colorado

John Karanicolas, PhD

“Flexible backbone peptide design as a tool for mediating cellular processes” with David Baker, PhD, University of Washington, Seattle, Washington

Alain Laederach, PhD

“Elucidating the molecular mechanisms of RNA folding: a combined modeling and experimental study” with Russ B. Altman, MD, PhD, Stanford University, Stanford, California

Florence L. Marlow, PhD

“Animal-vegetal axis determination in the zebrafish” with Mary C. Mullins, PhD, University of Pennsylvania, Philadelphia, Pennsylvania

Olivier Nolan-Stevaux, PhD

“Function of receptor tyrosine kinases in multi-step carcinogenesis” with Douglas Hanahan, PhD, University of California, San Francisco, California

Siew Loon Ooi, PhD

“Chromatin structure and DNA double-strand break repair” with Steve Henikoff, PhD, Fred Hutchinson Cancer Research Center, Seattle, Washington

Eyleen J. O'Rourke, PhD

“Genetics of the feeding behavior in *Caenorhabditis elegans*” with Gary Ruvkun, PhD, Massachusetts General Hospital, Boston, Massachusetts

Pardis C. Sabeti, PhD

“Detecting rapidly evolving immunologic variants in the human genome from haplotype structure” with Eric S. Lander, DPhil, Massachusetts Institute of Technology, Cambridge, Massachusetts

Alice Tsang Shaw, MD, PhD *

“Ras signaling in embryogenesis and oncogenesis” with Tyler Jacks, PhD, Massachusetts Institute of Technology, Cambridge, Massachusetts

Georgios Skiniotis, PhD

“Molecular electron microscopy of silencing complexes” with Thomas Walz, PhD, Harvard Medical School, Boston, Massachusetts

Bosiljka Tasic, PhD

“Labeling single neurons with their synaptic partners: characterization of higher olfactory circuits in *Drosophila*” with Liqun Luo, PhD, Stanford University, Stanford, California

Meng-Fu Bryan Tsou, PhD

“Cell cycle control of centrosome duplication” with Tim Stearns, PhD, Stanford University, Stanford, California

Sarah M. Wignall, PhD

“Investigating meiotic chromosome segregation in *Caenorhabditis elegans*” with Anne M. Villeneuve, PhD, Stanford University, Stanford, California

congratulations to all!

did you know...



Damon Runyon is half owner of the land under Hollywood's famous Grauman's Chinese Theatre?

Yes, long-time donor John W. Malin bequeathed the land to us in 1967. On the site is the most famous movie theater in the world, home to celebrity-studded movie premieres and the legendary footprints of the stars. Interestingly, the theatre owners rent the property from us based upon a 1927 lease agreement that ties their payments to the gold standard. This means that 2004 will be a golden year for us with nearly \$10,000 per month going to support our scientists as a result of Mr. Malin's extraordinary gift!

If you would like to discuss creative giving options with us, please call 212.455.0500.

momentum PHOTO GALLERY



fund in the sun

In the Foundation's early days, founder Walter Winchell enlisted some unlikely allies to bring attention to the important work of the Damon Runyon Fund. He came up with contests of all kinds—raffles, tournaments, concerts, telethons—even going as far as naming a “Runyon Fund Girl” to help promote his mission.

Damon Runyon Cancer Research Foundation

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(For more information about our Broadway Tickets service, go to www.drcrf.org)

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✂️ Make a lasting impact on the fight against cancer!

There is only one way we will triumph over cancer—by funding brilliant and creative scientists. After providing for your loved ones, consider a bequest to the Damon Runyon Cancer Research Foundation. You will be helping to provide the steady stream of support needed to maintain the fast pace of groundbreaking research that will lead to new treatments and save lives. The following is sample language you can share with your attorney:

I give the sum of \$_____ to the Cancer Research Fund of the Damon Runyon-Walter Winchell Foundation, a charitable corporation located in New York, New York, for its general charitable purposes.

You can also leave a specific asset or a percentage of your estate to the Foundation. For more information, please call 212.455.0500.

Damon Runyon Cancer Research Foundation

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