#### **News and Notes**

# Raymond J. Hohl, M.D., Ph.D., appointed director of Penn State Hershey Cancer Institute

Raymond J. Hohl, M.D., Ph.D., recently accepted an appointment as director of Penn State Hershey Cancer Institute, effective March 1, 2014. Dr. Hohl holds the Holden Family Chair and is associate chair of the Department of Internal Medicine, University of Iowa Carver College of Medicine, as well as associate director for clinical and translational research, Holden Comprehensive Cancer Center, University of Iowa. At Penn State, he will hold academic appointments as professor in the departments of Medicine and Pharmacology.

of hematology and medical oncology as well as clinical pharmacology.

Dr. Hohl received his M.D. from Rush Medical College, Rush University, and a Ph.D. in pharmacology from Rush University. After completing a residency in internal medicine and a fellowship in hematology/oncology at the University of Chicago, he joined the faculty of the University of Iowa College of Medicine in 1991 as an assistant professor of internal medicine. He was promoted to associate professor of internal medicine and pharmacology in 1997 and to full professor in 2002. At Iowa, Dr. Hohl has held numerous leadership and administrative roles including serving as director of the division of hematology, oncology, and blood and marrow transplantation, and director of the fellowship program in hematology and oncology. His research leadership roles have been in both the Holden Comprehensive Cancer Center and the University of Iowa's

Institute for Clinical and Translational Science. His patient care has spanned the full breadth

Dr. Hohl's research focuses on discovery and development of novel anti-cancer therapies, particularly those related to the interactions between cholesterol biosynthesis pathways and the malignant phenotype. His work ranges from novel chemistry to basic laboratory studies to innovative human clinical trials. His research has been well-supported by grants from the NIH, Roy J. Carver Charitable Trust, Department of Defense, Leukemia and Lymphoma Society, American Institute for Cancer Research, and other sources; in addition, he has been a principal investigator for many investigator-initiated clinical trials.

He has published more than 100 peer-reviewed articles and reviews and 12 book chapters, and served as associate editor for the text Pharmacology and Therapeutics: Principles to Practice. A reviewer for numerous journals, he currently serves as associate editor for the Nature journal Clinical Pharmacology and Therapeutics and is on the editorial advisory board of Lipids. Dr. Hohl is an inventor for two key patents related to his research and is cofounder of a biotechnology company that is advancing these discoveries to human therapies. He has served in prominent leadership roles in professional groups including the American Society for Clinical Pharmacology and Therapeutics (board of directors, 2003-2006; president, 2010-2011) and the Iowa Oncology Society (vice president, 2004-2006; president, 2006-2008). Dr. Hohl has also served on review panels and committees for the NIH and other organizations.

In addition to his research, clinical and administrative accomplishments, Dr. Hohl has extensive experience teaching graduate, medical, and other health sciences students in both classroom and clinical settings. He has mentored junior faculty and supervised numerous

pharmacology and molecular biology PhD students, as well as post-doctoral researchers and clinical fellows and more than 20 undergraduate students participating in summer research programs.



### Craig Meyers, Ph.D., Appointed Program Leader

Craig Meyers, Ph.D., was recently appointed program leader for the Cancer Virology and Immunology Program at Penn State Hershey Cancer Institute. Dr. Meyers joined Penn State College of Medicine as an assistant professor in the Department of Microbiology and Immunology in 1993 and rose through the ranks to full professor in 2002. As a result of his achievements in 2012, Dr. Meyers was awarded the rank of distinguished professor. In 2013, Dr. Meyers was awarded one the highest honors awarded to alumni by his Alma Mater, Brigham Young University, the Alumni Achievement Award.

During the last 20 years, Dr. Meyers has achieved national and international renown for his visionary work on human papillomaviruses (HPV), a known cause of cervical cancer and other malignancies. Since its discovery in the 1930's until 1992 there was no known technique for culturing papillomavirus. Many careers had been spent on trying to discover techniques for growing HPV in culture but had all ended in failure. In the early 1990's using an innovated three-dimensional organotypic culture system to grow fully differentiated human epithelium in vitro, Dr. Meyers was able to demonstrate for the first time the ability to grow infectious papillomavirus in culture. His studies resulted in the publication of a seminal manuscript in Science in 1992. This is still the only method for the growth of HPV in the laboratory. Being the first to grow HPV, Dr. Meyers also developed techniques to titer, measure infectivity, test neutralizing antibodies, measure natural neutralizing titers of the host, and measure the efficacy of microbicides and disinfectants. Dr. Meyers has also developed technologies allowing for the genetic analysis of HPV replication, virion morphogenesis, maturation, structure, and infectivity.

These innovations have allowed Dr. Meyers to publish studies covering a wide range of areas including: understanding the basic molecular biology of papillomavirus replication and oncogenesis, defining the role of cofactors such as tobacco in the carcinogenic process, describing the nature of the viral structure, elucidating infectivity pathways and how to block them, monitoring immune protection, and describing the role of HIV and anti-HIV drugs on HPV-associated cancers. With twelve manuscripts published in 2011 his research productivity continues to be impressive. Dr. Meyers has also distinguished himself through his efforts to establish collaborations with other investigators, both at Penn State and at other institutions around the world, that maximize the impact of his research not just on basic science but on clinical practice and clinical health.

In addition to his groundbreaking work on HPV, Meyers' laboratory has recently reported on the discovery that a non-disease-causing human virus, adeno-associated virus type 2 (AAV2), has the ability to kill human breast, cervical, prostate, mesothelioma, and melanoma cancer cells in the laboratory. AAV2 belongs to the parvovirus genus dependovirus and is called dependovirus because it has been historically characterized as requiring co-infection of an unrelated helper virus to replicate. Although the helper virus requirement is not absolute, it appears to induce the appropriate cellular environment needed for AAV replication. This suggests that AAV replication is possible in the absence of a helper virus once appropriate cellular conditions are established. A variety of genotoxic

agents have induced transformed or tumor cell lines semi-permissive for AAV replication. Dr. Meyers has demonstrated that AAV2 could replicate autonomously in vitro in fully differentiated epithelium.

Dr. Meyers reported that in HPV/AAV2-coinfected cultures, wild-type AAV2 targeted the p21WAF1 cyclin-dependent kinase inhibitor (CDKI) for accelerated proteosome-mediated degradation, a potential mechanism of AAV2 suppression of HPV oncogenesis. He demonstrated a specific interaction between AAV2 and HPV unmasking a previously undocumented capacity of the wild-type AAV2 virus to induce apoptosis in HPV-infected cells but not in normal keratinocytes. Induction of apoptotic cell death was not dependent on the state of the HPV DNA (episomal or integrated), the stage of the cancer, the HPV type (HPV16, 18 or 31), or on whether the cell line was derived from human biopsy tissue or infected in vitro. However, AAV2 was unable to induce apoptosis or induce any observable deleterious effects following infection of primary keratinocytes.

Dr. Meyers next investigated whether this affect was specific to cervical cancer cell lines or had a broader potential. His recent publication demonstrated that wild-type AAV2 was also able to induce apoptotic pathways in breast cancer cell lines derived from low-grade and high-grade cancers. Again AAV2 infection had no effect on normal breast epithelial cells. In unpublished preliminary studies Dr. Meyers has shown that AAV2 can kill the triple-negative breast cancer cells, MDA-MB-435, both in vitro and in vivo in a mouse breast cancer model.

Dr. Meyers has also tested human cancer cell lines derived from prostate cancer, squamous cell carcinoma of the skin, melanoma, and mesothelioma and in each case AAV2 infection was able to induce cell death. Finally, Dr. Meyers has identified a potential common trigger protein for the induction of the cell death pathways induced by AAV2.

Dr. Meyers now proposes to challenge an accepted dogma of our time—that breast cancer therapy needs to be formulated on an individual patient basis guided by the molecular heterogeneity of the cancer, the stage of the cancer, and the invasiveness and metastatic state of the cancer. His central hypothesis is that wild-type AAV2 is able to infect and specifically trigger death pathways using a common molecular target in breast cancer cells regardless of type or stage leaving normal cells unharmed. He proposes studies to exploit AAV2 and/or the common molecular target it induces to treat and cure human breast cancer. The impact in the number of lives saved, improved quality of life, alleviation of human suffering, and medical cost savings would be inestimable.



# Goldenberg Appointed Chief of the Division of Otolaryngology-Head and Neck Surgery

<u>David Goldenberg, M.D.</u>, was recently appointed chief of the Division of Otolaryngology–Head and Neck and Surgery in the Department of Surgery. An accomplished researcher, clinician and educator, Dr. Goldenberg is nationally recognized as a leader in head and neck cancer and thyroid surgery.

After obtaining his M.D. degree from Ben Gurian University of the Negev in Israel, Dr. Goldenberg trained in Surgery and Otolaryngology–Head and Neck Surgery at Ram bam Medical Center in Haifa, Israel. He then pursued a fellowship in Head and Neck

Oncologic Surgery at Johns Hopkins after which he joined the faculty at Penn State Hershey

in the Division of Otolaryngology–Head and Neck Surgery. In 2010, he was promoted to professor of surgery. In addition to his role as division chief, Dr. Goldenberg serves as director of the Head and Neck Surgery Program as well as Associate Director of Surgical Services, Penn State Hershey Cancer Institute.

An accomplished academic surgeon, Dr. Goldenberg has authored over 150 manuscripts and book chapters as well as 154 presentations at regional, national, and international meetings. His research interests include thyroid and other head and neck cancers for which he has received both institutional and NIH funding.

#### **New Providers**

- <u>Colette Pameijer, M.D.</u> (surgical oncology)
- <u>Joyce Wong, M.D.</u> (surgical oncology)

# Harriet C. Isom, Ph.D. Retires Following 37 Years at Penn State Hershey

Congratulations to Harriet C. Isom, Ph.D., on her retirement from Penn State College of Medicine. Dr. Isom joined Penn State College of Medicine in 1976. She was promoted to professor in 1987 and was named distinguished professor in Microbiology and Immunology in 2000. Dr. Isom served on many departmental, Penn State Hershey Cancer Institute, and College of Medicine committees. She maintained continuous NIH funding since her first R01 award in 1978. In addition, she served as the principal investigator on the Cancer Institute/Pennsylvania Department of Health contract from 1998 to 2013.

The Cancer Institute is much stronger today because of her leadership, research, compassion and drive. Between 2000 and 2003, Dr. Isom served as chair of the Cancer Center Support Grant Planning Committee, and during 2001-2003, she was named interim research director for the Cancer Institute. In 2003, she accepted the responsibility of chairing the search committee for the director of the Cancer Institute. One of her most important contributions was her leadership of the Cancer Institute's Viral Oncogenesis and Host Defense (now known as Cancer Virology and Immunology) Program. Dr. Isom was an outstanding program leader; she was a champion for her members and facilitated much collaboration within her program as well as across the entire Cancer Institute.

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Dr. Isom and Chandra P. Belani, M.D., Miriam Beckner Distinguished Professor of Medicine, Penn State Hershey Medical Center and Deputy Director, Cancer Institute



Left to right: Colleen Kelley, Chandra Belani, Karen Basehore, Harriet Isom, Rita Lahr, Denise Andrisani, Erica Benning

On December 16, 2013, the Cancer Institute and the Department of Microbiology and Immunology co-sponsored a symposium entitled "Virology and Cell Biology—The Liver and Beyond" in honor of Dr. Isom's retirement. Many of her past graduate students and post-doctoral scholars returned to participate in the all-day symposium. A farewell reception was held in the Cancer Institute following the symposium. Many thanks to Jianming Hu for helping to organize this event.



Standing, left to right: Tom Miller, Ed Cable, Bill Delaney, Rosa Serra, Jack Isom, Jason Starkey, Jianming Hu, John Bilello. Seated, left to right: Colleen Kelley, Dr. Isom, Annie Colberg-Poley

### **Upcoming Events**



## 2014 Pink Zone at Penn State: February 16

Mark your calendar for Sunday, February 16, 2014 at 1 p.m. for the 8th annual Pink Zone at Penn State when the Lady Lions welcome the Wisconsin Badgers to the Bryce Jordan Center. For more information about ticket sales, Pink Zone events and ways to give, visit pennsylvaniapinkzone.org. If you are a breast cancer survivor who would like to register for free bus transportation to

the Pink Zone game and a free t-shirt, <u>complete the registration form here</u>. Survivor registration deadline is January 31.

Official Pink Zone t-shirts are available for \$15 and can be purchased at Penn State Hershey Breast Center, 30 Hope Drive and Penn State Hershey Cancer Institute, 500 University Drive, Infusion Therapy Floor 1.

Watch the Pink Zone at Penn State video here!

#### Bladder Cancer Support Group Meeting: Saturday, March 15

The Penn State Hershey Cancer Institute's Bladder Cancer Support Group meeting on Saturday, March 15 will focus on cancer and nutrition, and will highlight various food safety and quality topics such as superfoods as a solution to health problems, organic produce, and household products to avoid. Speakers will include Holly Doan, GIANT Food Stores in-store dietitian, and Terry Lupia, bladder cancer survivor. The support group is open to all cancer patients, survivors and caregivers, and anyone else who is interested. The session will be held at Penn State Hershey's University Conference Center. Registration begins at 9:30 a.m.; meeting begins at 10 a.m. Light refreshments provided. For more information or to register in advance, call Theda Shaw, R.N., at 717-531-0003, ext. 285863.



#### **Fourth Annual Chocolate Tour**

Save the date for the Fourth Annual Chocolate Tour on Saturday, August 9, 2014 on the campus of the Milton Hershey School. With exciting run, walk and cycling events, there is something for everyone! The annual Chocolate Tour raises funds to support cancer research at Penn State Hershey. Click here for event details as they are posted.

#### **Education and Research**

### College of Medicine Named a Tobacco Center for Regulatory Science

#### Drs. Joshua Muscat and Jonathan Foulds to direct new center



Dr. Joshua Muscat

Penn State College of Medicine is one of 14 institutions nationwide named a Tobacco Center for Regulatory Science (TCORS). This \$20 million, five-year U.S. Food and Drug Administration/National Institutes of Health grant will fund research to help the FDA develop new and effective regulatory strategies for reducing the harm to health from tobacco products in the United States.

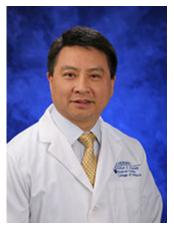
"Selection as one of the TCORS awardees is both a strong vote of confidence in the outstanding tobacco research being done at Penn State and an investment in research that promises to help reduce the enormous harm to health currently caused by tobacco smoking," said Dr. Daniel Notterman, vice dean for research and graduate studies, Penn State College of Medicine.

Drs. <u>Joshua Muscat</u> and <u>Jonathan Foulds</u> are the directors of the new center that will also train young scientists in the emerging field of tobacco regulatory science. Penn State TCORS will focus specifically on evaluating a wide range of health effects that may result from reducing the nicotine content in cigarettes including cravings to smoke, exposure to toxic tobacco substances, and smoking-associated stress and depression.

"The research at Penn State Hershey will provide critical new data in assessing the relative addictiveness and toxicity of reduced nicotine content cigarettes, particularly among individuals who may be most vulnerable," Muscat said.

Foulds added, "This research will really make a difference to public health in this country, and we will also train the next cohort of tobacco regulatory scientists." Click here to learn more.

# Bone Marrow Failure Research Video Interview with AA&MDSIF grantee Jeffrey Pu, M.D., Ph.D.



Jeffrey Pu, M.D., Ph.D., Penn State Hershey Cancer Institute and an Aplastic Anemia & MDS International Foundation grantee, was one of eight experts interviewed at the American Society of Hematology Annual Meeting in December. Dr. This meeting is the largest annual gathering of hematologists, oncologists, and allied health professionals who report and learn about significant new research findings from around the world. An AA&MDSIF grantee, Pu discussed his research about bone marrow failure disease and explained translational research.

Click here to watch the video interview and learn more about Dr. Pu's research.

#### Faculty Publications (October 2013 – January 2014)

 Allen, J.E., Saroya, B.S., Kunkel, M., Dicker, D.T., Das, A., Peters, K.L., Joudeh, J., Zhu, J., El-Deiry, W.S. (2013). <u>Apoptotic circulating tumor cells (CTCs) in the</u> <u>peripheral blood of metastatic colorectal cancer patients are associated with liver</u> <u>metastasis but not CTCs</u>. Oncotarget. Epub ahead of print.

- 2. Chen, Y. C., Prabhu, K. S., Das, A., and Mastro, A. M. (2013). Dietary selenium supplementation modifies breast tumor growth and metastasis. Int J Cancer 133, 20254-2064.
- 3. Clawson, G. A. (2013). Cancer. Fusion for moving. Science 342, 699-700.
- 4. Dovat, S. (2013). Ikaros: the enhancer makes the difference. Blood 122, 3091-3092.
- 5. Elcombe, C. R., Peffer, R. C., Wolf, D. C., Bailey, J., Bars, R., Bell, D., Cattley, R. C., Ferguson, S. S., Geter, D., Goetz, A. Goodman, J.I., Hester, S., Jacobs, A., Omiecinski, C.J., Schoeny, R., Xie, W., Lake, B.G. (2014). Mode of action and human relevance analysis for nuclear receptor-mediated liver toxicity: A case study with phenobarbital as a model constitutive androstane receptor (CAR) activator. Crit Rev Toxicol 44, 64-82.
- 6. Forester, S. C., and Lambert, J. D. (2013). Synergistic inhibition of lung cancer cell lines by (-)-epigallocatechin-3-gallate in combination with clinically used nitrocatechol inhibitors of catechol-O-methyltransferase. Carcinogenesis. Epub ahead of print.
- 7. Hong, B., Prabhu, V.V., Zhang, S., van den Heuvel, A.P., Dicker, D.T., Kopelovich, L., El-Deiry, W.S. (2013). <u>Prodigiosin rescues deficient p53 signaling and anti-tumor effects via up-regulating p73 and disrupting its interaction with mutant p53</u>. Cancer Res. Epub ahead of print.
- 8. Jones, S. A., Clark, D. N., Cao, F. Tavis, J.E., Hu, J. (2013). Comparative Analysis of Hepatitis B Virus Polymerase Sequences Required for Viral RNA Binding, RNA Packaging and Protein Priming. J Virol. Epub ahead of print.
- 9. Keller, P.W., Huang, R.K., England, M.R., Waki, K., Cheng, N., Heymann, J.B., Craven, R.C., Freed, E.O., Steven, A.C. (2013). <u>A two-pronged structural analysis of retroviral maturation indicates that core formation proceeds by a disassembly-reassembly pathway rather than a displacive transition</u>. Epub ahead of print.
- 10. Lambert, J. D. (2013). Does tea prevent cancer? Evidence from laboratory and human intervention studies. Am J Clin Nutr 98, 1667S-1675S.
- 11. Manni, A., Richie, J. P., Jr., Xu, H., Washington, S., Aliaga, C., Bruggeman, R., Cooper, T. K., Prokopczyk, B., Trushin, N., Calcagnotto, A., Das, A., Liao, J. and El-Bayoumy, K. (2013). Influence of omega-3 fatty acids on Tamoxifen-induced suppression of rat mammary carcinogenesis. Int J Cancer. Epub ahead of print.
- 12. McCormick, N. H., Hennigar, S. R., Kiselyov, K., and Kelleher, S. L. (2013). The Biology of Zinc Transport in Mammary Epithelial Cells: Implications for Mammary Gland Development, Lactation, and Involution. J Mammary Gland Biol Neoplasia. Epub ahead of print.
- 13. Savchenko, A.S., Borissoff, J.I., Martinod, K., DeMeyer, S.F., Gallant, M., Erpenbeck, L, Brill, A., Wang, Y., Wagner, D.D. (2013). Blood. Epub ahead of print.
- 14. Sweitzer, M.M., Geier, C.F., Joel, D.L., McGurrin, P., Denlinger, R.L., Forbes, E.E., Donny, E.C. (2013). Dissociated Effects of Anticipating Smoking versus Monetary Reward in the Caudate as a Function of Smoking Abstinence. Biol Psychiatry. Epub ahead of print.
- 15. Vyas, A. R., Hahm, E. R., Arlotti, J. A., Watkins, S., Stolz, D. B., Desai, D., Amin, S., and Singh, S. V. (2013). Chemoprevention of prostate cancer by d,l-sulforaphane is augmented by pharmacological inhibition of autophagy. Cancer Res 73, 5985-5995.
- 16. Warfel, N.A., Dolloff, N.G., Dicker, D.T., Malysz, J., El-Deiry, W.S. (2013). <a href="CDK1">CDK1</a> <a href="Stabilizes HIF-1a via direct phosphorylation of Ser668">Stabilizes HIF-1a via direct phosphorylation of Ser668</a> to promote tumor growth. Cell Cycle. Epub ahead of print.
- 17. Zhu, B., Ferry, C. H., Blazanin, N., Bility, M. T., Khozoie, C., Kang, B. H., Glick, A. B., Gonzalez, F. J., and Peters, J. M. (2013). PPARbeta/delta promotes HRAS-induced senescence and tumor suppression by potentiating p-ERK and repressing p-AKT signaling. Oncogene. Epub ahead of print.

# Faculty Awards (October 2013 – January 2014)

Investigator	Research	Sponsor
Chandra Belani	A Phase III, Double-Blind, Randomised, Placebo- controlled Study to Assess the Efficacy and Safety of Drug A (AZD6244: ARY- 142886) (Hyd-Sulfate) in Combination with Docetaxel	AstraZeneca
Chandra Belani	Phase I, Open-Label, Crossover, Randomized, Bioequivalence Study to Evaluate Two Formulations of Bendamustine (BDM) Hydrochloride (HCI) Administered to Cancer Patients	Eagle Pharmaceuticals, Inc.
Wafik El-Deiry	TIC10 anti-tumor effect through regulation of Foxo3a and TRAIL	National Cancer Institute
Jonathan Foulds	Pilot Randomized Trial of an Automated Smoking Cessation Intervention Via Mobile Phone Text Messages as an Adjunct to Varenicline in Primary Care: GRAND 2012	Pfizer Incorporated
Jonathan Foulds	Center for the Study of Tobacco Products	Virginia Commonwealth University
Barbara Miller	The Ion Channel TRPM2 Regulates Neuroblastoma Response to Chemotherapy Through Modulation of Oxidative Stress	Hyundai Hope on Wheels
George Moldovan	Dysregulation of the PARI Genomic Stability Pathway in Leukemia	The V Foundation for Cancer Research
Kathleen Mulder	Directional Motility and ERM Scaffolding in Pathfinder Pancreatic Carcinoma Cells	National Cancer Institute
Michael Reed	A Prospective, Randomized, Controlled Multicenter Clinical Study to Evaluate the Safety and Effectiveness of the Device A System for the Single-lobe Treatment of Severe Emphys	Spiration, Inc.
John Richie, Jr.	Dietary Methionine and Cysteine Restriction in Healthy Adults	Orentreich Foundation for the Advancement of Science
Cristina Truica	A Phase II Double-Blinded, Randomized, Placebo-controlled Study of Docetaxel in 1- methyl-D-tryptophan (indoximod) in Combination with Metastatic Breast Cancer	NewLink Genetics Corporation
Robin Wilson	Early Preparation and Inspiration for Careers in the Biomedical Sciences	National Institute of General Medical Sciences