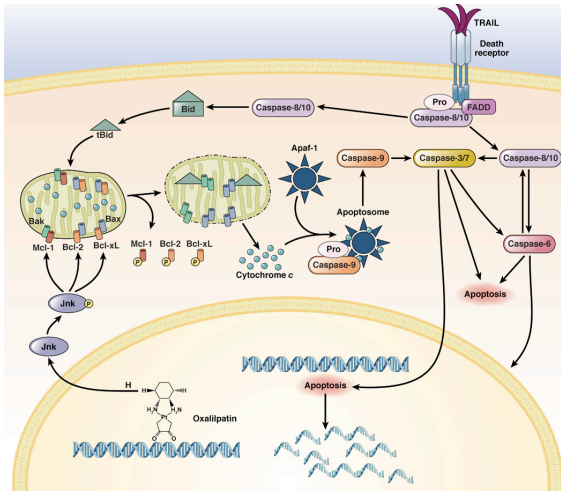
Dean Paz visit to El-Deiry Lab 6-29-11

Laboratory of Translational Oncology and Experimental Cancer Therapeutics

Agenda for 10:00 – 10:30 AM



1- Meet Lab Personnel in Lab Facilities

2- Tour Lab Facilities including:

Small Animal Optical Imaging Core

CTC Isolation and Analysis Core

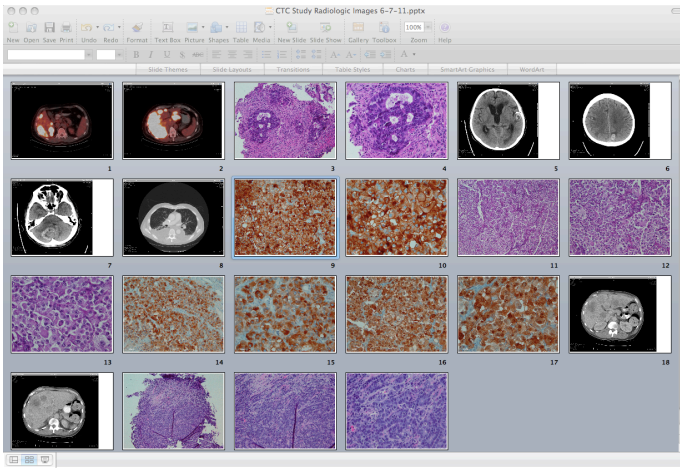
3- Briefly discuss some ongoing research including:

Multidisciplinary research involving circulating tumor cells (Penn State CTC-TME Research Program; CTC-Interest Group)

Discuss work just published in Science Translational Medicine

Learn about translational research efforts (TIC10, quinacrine, mutant p53)





Summary of Lab Interests:

The El-Deiry Lab was established in 1994 and moved to Penn State University to the new Penn State Hershey Cancer Institute facility in **March of 2010**. The lab is focused on unraveling cell death signaling pathways in cancer and in developing new drugs that can be brought to the clinic. Thus the lab uses molecular biology, cell biology, genetics, pharmacology and imaging techniques for a variety of in vitro and in vivo techniques. The drug discovery and development capability involves identification of new agents for further development as well as identification of new uses of approved drugs. There are exciting examples of both of these strategies. Since the move to Penn State the Lab has led an institution-wide effort to develop circulating tumor cell technology for both clinical care and research. The Lab is supported by a small animal imaging core facility and a CTC isolation and analysis core that has been CLIA certified since April of 2011. The lab is involved in a number of collaborative basic and translational projects with investigators throughout the cancer institute and Hershey Medical Center. The lab is committed to supporting the development of novel personalized therapy approaches for cancer.

Current Lab Members:

Wafik El-Deiry, M.D., Ph.D.	Principal Investigator, Professor
Niklas Finnberg, Ph.D.	Assistant Professor
Nathan Dolloff, Ph.D.	Assistant Professor (July 1, 2011)
Kristi Peters, Ph.D.	Senior Scientist
Arunasalam Navaraj, Ph.D.	Senior Scientist
Shengliang Zhang, Ph.D.	Senior Scientist
Junaid Abdulghani, M.D. Ph.D.	Staff Scientist
Elizabeth Matthew, Ph.D.	Staff Scientist
Kimberly Scata, Ph.D.	Staff Scientist
Avi Das, M.D.	Staff Scientist
Bo Hong, Ph.D.	Post-doctoral Scientist
Lanlan Zhou, Ph.D.	Post-doctoral Scientist
Roslyn Crowder, Ph.D.	Post-doctoral Scientist
Jean-Nicolas Gallant	Technical Specialist
Joshua Allen	Visiting Graduate Student (U. Penn)
Hairong Cheng	Visiting Graduate Student (China)
Varun Vijay Prabhu	Graduate Student (Molecular Medicine Program)
Olivier Noel	Rotating Student (M.D. Ph.D. Program)
David Dicker	Senior Research Specialist, Lab manager
Yvette Liu, M.D.	Technical Specialist

Recent Publications (since March 2010):

Dolloff, N.G., Mayes, P.A., Hart, L.S., Dicker, D.T., Humphreys, R., and El-Deiry, W.S. Off-target Lapatinib activity derives from TRAIL death receptor up-regulation. **Science Translational Medicine**, in press (online June 8), 2011.

Mayes, P.A., Dolloff, N.G., Daniel, C.J., Liu, J.J., Hart, L.S., Kuribayashi, K., Allen, J.E., Jee, D.I.H., Dorsey, J.F., Liu, Y.Y., Dicker, D.T., Brown, J.M., Furth, E.E., Klein, P.S., Sears, R.C., and El-Deiry, W.S. Overcoming hypoxia-induced apoptotic resistance through combinatorial inhibition of GSK-3beta and CDK1. **Cancer Research**, in press (August 1 issue), 2011.

Faltas, B., Zeidan, A., Peters, K., Das, A., Joudeh, J., Navaraj, A., Dolloff, N.G., Harvey, H.A., Jiang, Y., Allen, J.E., Dicker, D.T., and El-Deiry, W.S. Identifying circulating tumor stem cells that matter: the key to prognostication and therapeutic targeting. **J. Clin. Oncol.**, in press (online June 20), 2011.

Allen, J.E., and El-Deiry, W.S. Oxaliplatin uses JNK to restore TRAIL sensitivity in cancer cells through Bcl-XL inactivation. **Gastroenterology**, in press (online June 20), 2011.

Kuribayashi, K., Finnberg, N., Jeffers, J.R., Zambetti, G.P., and El-Deiry, W.S. The relative contribution of pro-apoptotic p53-target genes in the triggering of apoptosis following DNA damage in vitro and in vivo. **Cell Cycle**, in press (July 15 issue), 2011.

Hart, L.S., Dolloff, N.G., Dicker, D.T., Koumenis, C., Christensen, J.G., Grimberg, A., and El-Deiry, W.S. Human colon cancer stem cells are enriched by insulin-like growth factor-1 and are sensitive to figitumumab. **Cell Cycle**, in press (July 15 issue), 2011.

Wang, W., Gallant, J-N., Katz, S.I., Dolloff, N.G., Smith, C.D., Abdulghani, J., Allen, J.E., Dicker, D.T., Hong, B., Navaraj, A., and El-Deiry, W.S. Quinacrine sensitizes hepatocellular carcinoma cells to TRAIL and chemotherapeutic agents. **Cancer Biol. Ther.**, in press, 2011.

Gallant, J-N., Allen, J.E., Smith, C.D., Dicker, D.T., Wang, W., Dolloff, N.G., Navaraj, A., and El-Deiry, W.S. Quinacrine synergizes with 5-fluorouracil and other therapies in colorectal cancer. **Cancer Biol. Ther.**, in press, 2011.

Katz, S.I., Zhou, L., Ferrara, T., Wang, W., Mayes, P.A., Smith, C., and El-Deiry, W.S. FLT-PET may not be a reliable indicator of therapeutic response in p53-null malignancy. **Int. J. Oncol.**, 39:91-100, 2011.

Zhang, H., Qiao, H., Bakken, A., Gao, F., Huang, B., Liu, Y.Y., El-Deiry, W., Ferrari, V.A., and Zhou, R. Utility of dual-modality bioluminescence and MRI in monitoring stem cell survival and impact on post myocardial infarct remodeling. **Acad. Radiol.**, 18:3-12, 2011.

Dews, M., Fox, J.L., Hultine, S., Sundaram, P., Wang, W., Liu, Y.Y., Furth, E., Enders, G.H., El-Deiry, W., Schelter, J.M., Cleary, M.A., and Thomas-Tikhonenko, A. The myc-miR-17-92 axis blunts TGB-beta signaling and production of multiple TGF-beta-dependent antiangiogenic factors. **Cancer Research**, 70:8233-8246, 2010.

McGovern, P.E., Christofidou-Solomidou, M., Wang, W., Dukes, F., Davidson, T., and El-Deiry, W.S. Anticancer activity of botanical compounds in ancient fermented beverages. **Int. J. Oncol.**, 37:5-14, 2010.

Allen, J.E., and El-Deiry, W.S. Targeting oncoproteins for molecular cancer therapy. **The Molecular Basis of Human Cancer**, Second Edition, Coleman, W.B., Editor, in press.

Allen, J.E., and El-Deiry, W.S. Circulating tumor cells and colorectal cancer. **Curr. Colorectal Cancer Rep.**, 6:212-220, 2010.

Abdulghani, J., and El-Deiry, W.S. TRAIL receptor signaling and therapeutics. **Expert Opin. Ther. Targets**, 14:1091-1108, 2010.

Chen, F., Wang, W., and El-Deiry, W.S. Current strategies to target p53 in cancer. **Biochemical Pharmacology**, 80:724-730, 2010.

El-Deiry, W.S. Funding the marathon: Investigators need more than basic experiments and clinical trials to advance the war on cancer. **Cancer Biol. Ther**. 9:749-751, 2010.

Abstracts:

Natsuizaka, M., Kalman, R., Ohashi, S., Takaoka, M., Klein-Szanto, A., El-Deiry, W.S., Diehl, J.A., Herlyn, M., and Nakagawa, H. IGF-independent regulation of EMT by insulin-like growth factor binding protein-3 in transformed human esophageal cells. 101st Annual AACR meeting, Washington, D.C., April 2010.

Finnberg, N.K., Arunasalam, N., Lang, K., Cerniglia, G., Motoyama, N., Zhou, B-B., and El-Deiry, W. Targeting of DR5/TRAIL-R2 in combination with irinotecan triggers p53- and chk2-dependent gastrointestinal toxicity in mice in vivo and synergistic cell death in human gastrointestinal epithelial cells in vitro. 101st Annual AACR meeting, Washington, D.C., April 2010.

Dolloff, N.G., Hart, L.S., Mayes, P.A., and El-Deiry, W.S. Dual GSK-3b/CDK inhibitors induce multiple myeloma cell death and eliminate putative cancer stem cell populations. 101st Annual AACR meeting, Washington, D.C., April 2010.

Dolloff, N.G., Hart, L.S., Mayes, P.A., Dicker, D.T., Humphreys, R.C., Gilmer, T.M., and El-Deiry, W.S. Novel anti-tumor activity of lapatinib derives from off-target up-regulation of TRAIL death receptors. 101st Annual AACR meeting, Washington, D.C., April 2010.

Wang, W., Katz, S.I., Abdulghani, J., Dicker, D., and El-Deiry, W.S. Quinacrine sensitizes hepatocellular carcinoma cells to TRAIL via up-regulating DR5 and eradicating MCL-1. 101st Annual AACR meeting, Washington, D.C., April 2010.

Hart, L.S., Finnberg, N., Dolloff, N.G., Rodgers, Z.B., Dicker, D.T., Thomas-Tikhonenko, A., and El-Deiry, W.S. High-resolution imaging and anti-tumor effects of GFP(+) bone marrow-derived cells homing to syngeneic mouse colon tumors. 101st Annual AACR meeting, Washington, D.C., April 2010.

Hart, L.S., Dicker, D.T., Grimberg, A., Christensen, J., and El-Deiry, W.S. The fully human IGF-1 receptor antibody, CP-751,871, targets putative colon cancer stem cell populations. 101st Annual AACR meeting, Washington, D.C., April 2010.

Allen, J.E., Patel, L., Krigsfeld, G., Mayes, P.A., Wu, G.S., and El-Deiry, W.S. Breflate upregulates TRAIL gene transcription in Bax-null cells and induces TRAIL-mediated apoptosis independently of p53 in TRAIL-sensitive tumor lines. 101st Annual AACR meeting, Washington, D.C., April 2010.

Crowder, R.N., Dicker, D.T., and El-Deiry, W.S. Diminished caspase 8 and c-Myc protein expression in human fibroblasts provides insight into normal cell resistance to TRAIL-mediated apoptosis. 101st Annual AACR meeting, Washington, D.C., April 2010.

Scata, K.A., and El-Deiry, W.S. The DNp73 isoform provides novel insights into the regulation of p53 by BRCA1 to favor cell survival over cell death. 101st Annual AACR meeting, Washington, D.C., April 2010.

Allen, J.E., Krigsfield, G., Mayes, P.A., Patel, L., Dicker, D.T., Wu, G.S., and El-Deiry, W.S. The small molecule TIC10 has potent anti-cancer efficacy mediated by induction of TRAIL production in normal and tumor cells. 102nd Annual AACR meeting, Orlando, FL, April, 2011.

Scata, K.A., and El-Deiry, W.S. BRCA1 regulates p53 target expression via DNp73. 102nd Annual AACR meeting, Orlando, FL, April, 2011.

Hong, B., Chen, F., Dicker, D.T., and El-Deiry, W.S. Restoration of p53 pathway signaling and apoptotic induction by prodigiosin and its structurally-related compound (NSC247562) in p53-deficient human colon carcinoma cells. 102nd Annual AACR meeting, Orlando, FL, April, 2011.

Abdulghani, J., Allen, J.E., Dicker, D.T., Smith, C.D., Humphreys, R.C., and El-Deiry, W.S. Sorafenib sensitizes solid tumors to TRAIL or TRAIL receptor agonist antibodies. 102nd Annual AACR meeting, Orlando, FL, April, 2011.

Peters, K.L., Allen, J.E., Dicker, D.T., Das, A., Joudeh, J., and El-Deiry, W.S. CTC profiling: Integration of biomarker analysis with current Veridex CellSearch technology. 102nd Annual AACR meeting, Orlando, FL, April, 2011.

Finnberg, N.K., Arunasalam, N., Lang, K., Cerniglia, G., Motoyama, N., Zhou, B-B., and El-Deiry, W.S. Chk2-inhibition promotes increased killing of human colorectal cancer cells and protects from gastrointestinal toxicity following irinotecan/TRAIL death receptor agonists (TDRA). 102nd Annual AACR meeting, Orlando, FL, April, 2011.

Dolloff, N.G., Mayes, P., Dicker, D., and El-Deiry, W. Sangivamycin-like molecules (SLMs) suppress the expression of oncogenic gene translocation products and induce apoptosis of multiple myeloma cells. 102nd Annual AACR meeting, Orlando, FL, April, 2011.

Das, A., Allen, J.E., Dicker, D.T., Peters, K.L., Joudeh, J., and El-Deiry, W.S. Quantum Dot multiplexing of prognostic marker and stem cell marker expression in colorectal cancer circulating tumor cells. 102nd Annual AACR meeting, Orlando, FL, April, 2011.

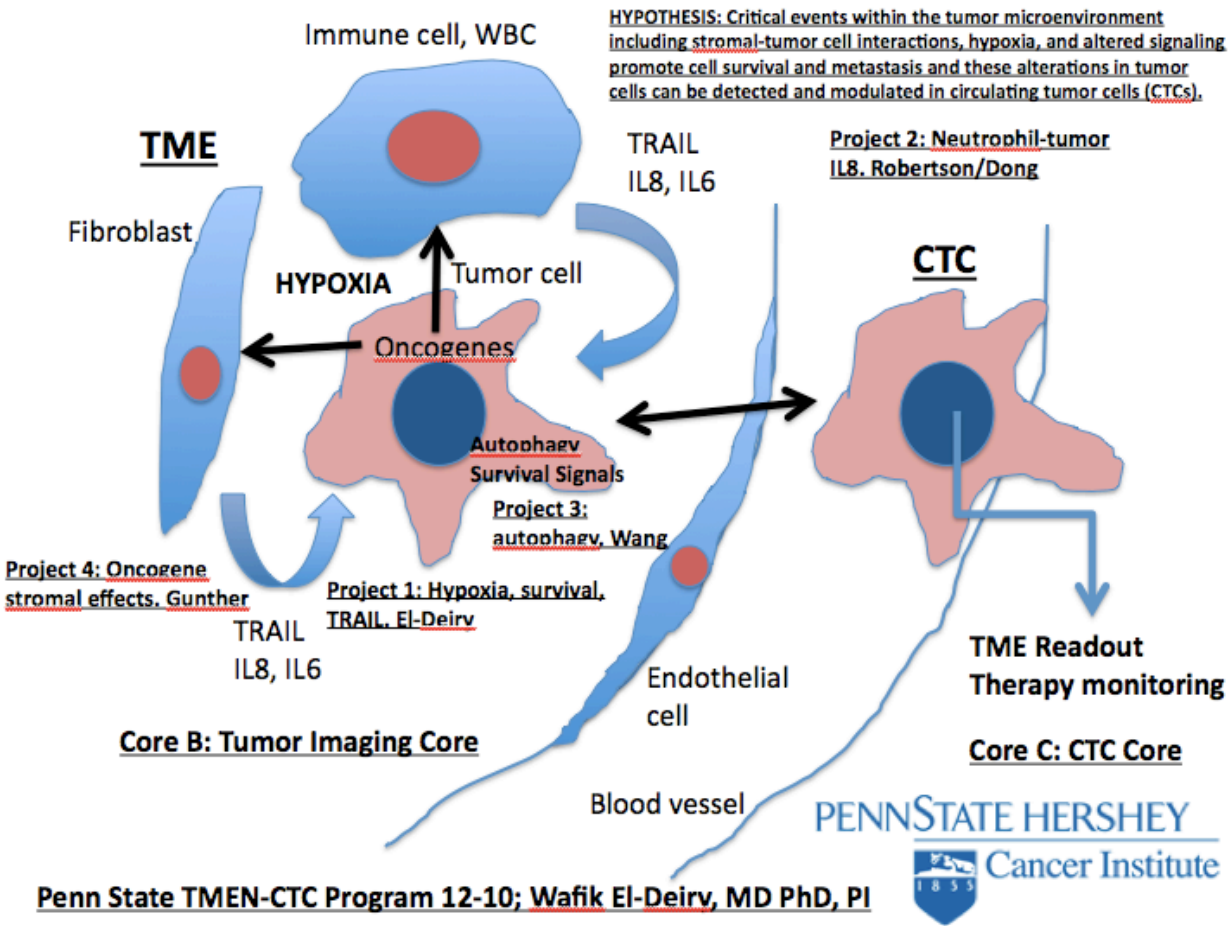
Crowder, R.N., Dicker, D.T., and El-Deiry, W.S. Decreased caspase 8 protein expression and incomplete caspase 3 activation in TRAIL-resistant normal human fibroblasts and epithelial cells. 102nd Annual AACR meeting, Orlando, FL, April, 2011.

Navaraj, A., Dicker, D.T., Dolloff, N., and El-Deiry, W.S. Multiplexed detection of phospho-ERK as a marker of H-Ras signaling, EGFR and cancer stem cell marker expression in breast cancer cells recovered from human blood. 102nd Annual AACR meeting, Orlando, FL, April, 2011.

Gallant, J-N., Wang, W., Dolloff, N.G., Allen, J.E., and El-Deiry, W.S. Novel combinatorial Quinacrine cancer therapies for advanced colon cancer. 102nd Annual AACR meeting, Orlando, FL, April, 2011.

Dolloff, N.G., Mayes, P., Hart, L., Dicker, D., and El-Deiry, W.S. Off-target lapatinib activity upregulates TRAIL death receptors in colon cancer cells. 102nd Annual AACR meeting, Orlando, FL, April, 2011.

Cazanave, S.C., Mott, J.L., Bronk, S.F., Werneburg, N.W., Masuoka, H., Guicciardi, M.E., Fingas, C.D., Charlton, M.R., El-Deiry, W.S., Kaufmann, S.H., and Gores, G.J. Death receptor 5 signaling promotes hepatocyte Lipoapoptosis. (ID# 1128410) 2011 AASLD Annual Meeting ('The Liver Meeting'), San Francisco, CA, November, 2011.



Clinical Trial Activity Involving Dr. El-Deiry as Principal Investigator and the El-Deiry Lab at Penn State Hershey Medical Center:

1. A Randomized, Multi-Center, Blinded, Placebo-Controlled Study of Mapatumumab ([HGS1012], A Fully-Human Monoclonal Antibody to Trail-R1) in Combination with Sorafenib as First-Line Therapy in Subjects with Advanced Hepatocellular Carcinoma (PSHCI 10-076). Sponsor: Human Genome Sciences.

2. Prevalence of Stem Cell and Prognostic Markers in Circulating Tumor Cells of Patients with Metastatic Colorectal Cancer Undergoing Chemotherapy (PSHCI 10-066). Investigator-initiated.
http://clinicaltrials.gov/ct2/show/NCT01286883?term=NCT01286883&rank=1

3. A Phase Ib, Open-Label, Dose-Escalation Study of the Safety and Pharmacokinetics of Multiple Doses of Dulanermin Administered Intravenously in Combination with Camptosar/Erbitux Chemotherapy or the Folfiri Regimen with or without Bevacizumab in Subjects with Previously Treated Metastatic Colorectal Cancer (PSHCI 10-042). Sponsor: Genentech.