Research by Fox Chase medical oncologist Elizabeth R. Plimack, MD, and colleagues is helping find appropriate treatments for patients with muscle-invasive bladder cancer (MIBC) by identifying different subtypes of the cancer and determining which patients are likely to respond to chemotherapy prior to surgical bladder removal.

Although radical cystectomy is the most common treatment for MIBC, cisplatin-based chemotherapy before surgery improves the prognosis for many patients by helping reduce the risk of relapse and shrinking tumor size. While 30 to 50 percent of patients benefit from such neoadjuvant chemotherapy (NAC), the rest do not. Plimack and colleagues are investigating ways to predict whether a patient will respond to NAC, so that patients are not unnecessarily exposed to chemotherapy or delays in surgical treatment.

One way to minimize time to surgery is to condense chemotherapy. The researchers conducted a trial with an accelerated neoadjuvant regimen of methotrexate, vinblastine, doxorubicin, and cisplatin (AMVAC) to examine its effectiveness and tolerability. They found that providing three cycles of the therapy in half the standard time (six vs. 12 weeks) yielded a significant patient response—15 of the 44 patients showed no sign of remaining cancer at the conclusion of the trial, and had few serious side effects. This finding, published in the Journal of Clinical Oncology, suggests that AMVAC works and can expedite patients’ time to surgery.

continued on page 4

**THE TOPLINE**

- An accelerated neoadjuvant chemotherapy regimen is tolerable and effective for patients with muscle-invasive bladder cancer (MIBC)
- Three genes can predict which MIBC patients are likely to respond to cisplatin-based chemotherapy
- There are three distinct varieties of MIBC, which have biomarkers analogous to similar subtypes in basal and luminal breast cancers

Experimental structure of the retinoblastoma-associated protein, Rb, with three positions marked that, when mutated, are associated with response to the AMVAC treatment. Each domain of the protein is shown in a different color.
A Time for Translation

With our laboratories located a short walk down the hall from our clinics, Fox Chase researchers and clinicians cross paths every day—both literally and in their work. Long a focus at Fox Chase, our bench-to-bedside science will take another leap forward with the arrival of Wafik S. El-Deiry, MD, PhD, FACP, our new deputy cancer center director for translational research.

Throughout a remarkable career, Dr. El-Deiry’s insights have led to important scientific discoveries—starting with his identification of p21 (WAF1) more than 20 years ago—many of which he has successfully moved into clinical application. In his new role, he is working to strengthen our processes for harnessing scientific findings, from our own labs and worldwide, that enable us to make the greatest contributions to cancer care.

Our labs—where researchers look in-depth at the pathways and processes that lead to cell proliferation and drug resistance—are where these contributions germinate. In this issue, you’ll read about exciting studies underway at Fox Chase, all of which hold promise for patients:

• Transporter membrane proteins are the focus for a team of researchers from Fox Chase and Temple, who have shifted the field’s attention from the widely studied P-glycoprotein to a seemingly more viable target called ABCC10 (page 5).

• In clinical trials, an antibody-drug conjugate being tested for relapsed metastatic colorectal cancer appears to be safe and tolerable (page 8).

• Boasted by recently acquired grant funding, five Fox Chase researchers are hard at work on projects with potential clinical impact for ovarian, colorectal, and kidney cancer, lymphoma, and EGFR-dependent cancers (pages 6-7).

• Patients with muscle-invasive bladder cancer will benefit from the work of Fox Chase researchers who have identified three genes that predict which patients are most likely to benefit from neoadjuvant chemotherapy before surgery (cover).

As our researchers examine the molecular elements that trigger or advance cancer, it is our patients—being treated a few steps away—that drive their quest for discovery. I hope you will enjoy following along as we chart their progress in moving translation at Fox Chase forward.

Richard I. Fisher, MD
President and CEO
SPOTLIGHT ON TRANSLATIONAL RESEARCH

Wafik S. El-Deiry, an international leader in translational research and one of 40 active American Cancer Society research professors, joined Fox Chase in October as deputy cancer center director for translational research. He serves as co-leader of the molecular therapeutics research program and treats patients with colorectal cancer.

Together with his lab, El-Deiry came to Fox Chase from Penn State University’s Milton S. Hershey Medical Center and the Penn State College of Medicine. His team is focused on developing new and personalized therapies to treat resistant cancers. He received his MD and PhD in biochemistry from the University of Miami School of Medicine before completing a medical residency and oncology fellowship at The Johns Hopkins Hospital and Oncology Center. Prior to serving as Penn State chief of hematology/oncology, El-Deiry held leadership roles at the University of Pennsylvania Abramson Cancer Center.

Q&A:
Wafik S. El-Deiry, MD, PhD, FACP

Q: How did you decide on a career in colorectal cancer research and treatment?
A: I went into medical oncology because I enjoy taking care of patients, dealing with multiple organ systems, and I find the science fascinating. I was privileged to work with Bert Vogelstein at Johns Hopkins as he was unraveling the molecular genetics of colorectal cancer, which was career-shaping for me. Much of my research and clinical effort is focused on this disease, which is becoming increasingly complex. We have more drugs, we’re targeting therapies in a more individualized way, and patients are living longer.

Q: Why did you decide to come to Fox Chase, and what do you hope to accomplish here?
A: Fox Chase has a national reputation as a leading cancer center—a place where fundamental discoveries in science are made and where clinical trials bring this new knowledge to patients. The continuing challenge is to accelerate that process and make it more efficient. The Center is already distinguished by active collaboration between scientists and clinicians—something I hope to nurture and expand. Fox Chase also has a very impressive clinical trials program, which includes sought-after national trials from industry and cooperative groups as well as innovative investigator-initiated trials.

Q: Why is translational research an important field in the current era of cancer medicine?
A: Translation brings together the best that a cancer center has to offer—its discoveries and outstanding clinical service—in order to positively impact patients. As we get better at translation, one of the goals is to be able to predict which patients will respond to therapy. Then clinical trials are smaller, less expensive, and the path to getting new treatments approved is faster and more efficient.

From the Philadelphia chromosome to current efforts targeting genetic and epigenetic pathways, Fox Chase has a great history of translation. Maintaining this legacy into the future will involve ongoing innovation, technological advances to help patients, and collaborations spanning disciplines and institutions—all with the aim of impacting scientific and clinical progress regionally and globally.

Q: What has been your career highlight to date?
A: One highlight was the discovery of p21, or WAF1, a universal cell cycle regulator that controls cell division after chemotherapy or radiation, on which a class of drugs called CDK inhibitors is based. More recently, my lab developed a first-in-class compound that is now in clinical trials to target the pathway of a “death receptor”—a molecule my lab discovered in the 90s, which controls tumor cell death by the immune system. As a physician-scientist, it is exciting to have a basic science discovery move from your lab into clinical testing with the potential of eventually helping patients.
Using Genetics to Improve Treatment Selection for Muscle-Invasive Bladder Cancers

MIBC patients in the AMVAC trial agreed to donate their stored tumor tissue for research. Using these samples, Plimack and her colleagues sequenced the tumor DNA and found that patients who responded to AMVAC had a mutation in one of three genes associated with a tumor’s ability to repair its DNA. Responders also had higher numbers of mutations overall, suggesting that the cancer’s inability to repair its DNA leads to both accumulation of gene mutations and sensitivity to chemotherapy.

“If this test is confirmed to be predictive, we can test patients when they are diagnosed, identify patients who won’t benefit from NAC, and send those patients directly to surgery to save time,” says Plimack. “But if they carry at least one of these mutations, we can treat them with NAC knowing they are likely to respond.”

For another study that examined gene expression in MIBC, Plimack and her team shared samples of tumors from their AMVAC study with David McConkey, PhD, and his team of researchers at MD Anderson. Using RNA expression profiling, they identified three distinct varieties of MIBC: luminal, basal and “p53-like.” Like basal breast cancers, the basal MIBC subtype was characterized by p63 gene activation, squamous differentiation, and more aggressive disease at presentation. The luminal subtype showed active peroxisome proliferator-activated receptor gamma (PPARγ) and estrogen receptor transcription, and these tumors were enriched with activating fibroblast growth factor receptor 3 (FGFR3) mutations, suggesting they might be susceptible to FGFR inhibitors.

The p53-like subtype had biomarkers usually associated with the wild-type version of the p53 tumor suppressor protein—even though these tumors did not always express wild-type p53—and were highly resistant to cisplatin-based chemotherapy. Tumors of though these tumors did not always express wild-type p53—and the wild-type version of the p53 tumor suppressor protein—even

Co-authors on the study include Roland Dunbrack, PhD, Tim Brennan, MS, Yan Zhou, MISE, PhD, Mark Andrade, PhD, Roman Yelensky, PhD, Ilya Serebriiskii, PhD, Jean Hoffman-Censits, MD, Alexander Kutikov, MD, FACS, Katherine Alpaugh, PhD, Essel Dulaimi Al-Saleem, MD, Rosalia Viterbo, MD, FACS, Richard E. Greenberg, MD, FACS, Costas D. Lallas, MD, Yu-Ning Wong, MD, MSCME, Eduard J. Trojalski, MD, Norma Palma, PhD, Vincent A. Miller, MD, Erica Golemis, PhD, and Eric Ross, PhD.

Asbestos Exposure May Be Required to Cause Mesothelioma—Even in Patients with Risk-Increasing Mutation

While mutations in the BAP1 gene are known to increase risk for mesothelioma, new findings by Fox Chase researcher Joseph R. Testa, PhD, and colleagues indicate that asbestos exposure is also generally necessary to develop the disease.

In a study published in the August 15 issue of Cancer Research, the team exposed mice with and without BAP1 mutations to asbestos, and they also followed a group of unexposed mutated mice to see if they developed any cancers.

By the end of the study, 73 percent of mutated mice exposed to asbestos had developed mesothelioma, compared to only 32 percent of mice without a BAP1 mutation. However, none of the unexposed mice with BAP1 mutations showed signs of mesothelioma after 110 weeks of follow-up. “To get mesothelioma, having a BAP1 mutation doesn’t appear to be enough,” says Testa, co-leader of Fox Chase’s cancer biology program and lead author on the study. “Our studies suggest that you generally need to be exposed to asbestos as well.”

Mesotheliomas in BAP1-mutated mice appeared sooner and were more aggressive than those in non-mutant mice. The tumors from mutant mice typically lost the second copy of BAP1, leading to complete inactivation of BAP1, and the resulting tumors became more invasive and showed increased growth properties. They also showed less activity in a protein encoded by Rb, a gene commonly mutated or deleted in cancer, suggesting that it had been blocked as a result of the inactivation of BAP1.

The level of asbestos exposure used in the study was sufficient to induce mesothelioma or other asbestos-related deaths in all mutated mice, whereas 20 percent of mice without BAP1 mutations were still alive at the conclusion of the study. This suggests that mutation carriers may be susceptible to tumor development at exposure levels that may not always be sufficient to cause cancer when a BAP1 mutation is not present.

Although mutated mice that were not exposed to asbestos did not develop mesothelioma during the study, Testa says, “we can’t say definitively yet that genetics alone can’t cause some cases of mesothelioma.”

Co-authors on the study include: Jinfei Xu, PhD, Yuvaraj Kadariga, MD, PhD, Mitchell Cheung, PhD, Jianming Pei, MD, Jacqueline Tu, PhD, Student, PhD, Hongzhuang Peng, PhD, Jayashree Karar, PhD, and Frank J. Rauscher, PhD.
Fox Chase-Temple Team Pursues a New Avenue in Transporter Membrane Proteins

**THE TOPLINE**

- Researchers identified transporter membrane protein ABCC10 as a viable target in mammary tumors; next, they will test its potential as a target in lung tumors
- A collaborative search for an optimized ABCC10 inhibitor is underway using molecular models

Because of their ability to carry drugs out of cells, affecting biological processes such as metastasis, migration, and proliferation, transporter membrane proteins have long been a focus in cancer research. For the last 30 years, much of the research in this area has focused on P-glycoprotein, or Pgp, but after many failed studies and clinical trials, research on Pgp has fallen out of favor. However, preliminary studies by researchers at Fox Chase have revealed another transporter membrane protein, ATP-binding cassette, subfamily C, member 10 (ABCC10), as a potentially more successful target for anti-cancer drugs.

A major limitation of inhibiting Pgp is that it causes other transporter membrane proteins to be induced, leading to increased toxicity and lethality. But Fox Chase researcher Elizabeth Hopper-Borge, PhD, found that inhibiting ABCC10, also known as MRP7, has the opposite effect—in some cases it downregulates other transporters and other proteins important to cell signaling pathways, leading to reduced drug resistance and a better response in tumors.

A study by Hopper-Borge and colleagues, published in the *British Journal of Cancer* in June 2014, examined whether inhibiting ABCC10 would make mice with mammary gland tumors more responsive to docetaxel, a taxane commonly used to treat breast cancer. The team bred ABCC10-negative and -positive mice to the common mammary tumor virus-polymavirus middle T (MMTV-PyVmT) model, whose tumors are highly analogous to human breast tumors. They found that the loss of ABCC10 affected multiple biological parameters in the mice’s tumors, and increased their survival.

Studies of human lung cell lines in xenograft models showed similar biological effects to those seen with mouse mammary tumors. Hopper-Borge believes ABCC10 will prove to be an even better target in treating lung tumors, and her team is currently breeding mice to explore this theory.

“Our ultimate goal is to move this research into a clinical trial once we find an optimized compound,” Hopper-Borge says.

In pursuit of this compound, Hopper-Borge began working with Temple University organic chemist Rodrigo Andrade, PhD, who tested existing novel inhibitors against ABCC10 and found that the results were effective—further confirming ABCC10’s viability.

Next, they teamed up with Fox Chase researcher Roland Dunbrack, PhD, who specializes in protein structure prediction. Using experimental data Hopper-Borge gathered while testing a preliminary compound that Andrade created, Dunbrack will develop models to predict whether and how a compound will bind to ABCC10—yielding information about how to strengthen the compound.

“We’re still learning a lot,” Hopper-Borge says, “but renewed interest in transporter membrane proteins is certainly starting to gain momentum.”

Hopper-Borge’s co-authors include Natalya Domanitskaya, PhD, Janet Wangari Talbot, PhD, Joely Jacobs, Elizabeth Peiffer, Chelsy Paulose, Ekaterina Malofeeva, PhD, Katherine Foster, Kathy Q. Cai, MD, PhD, Yan Zhou, MSE, PhD, and Brian L. Egleston, PhD.
New Funding Bolsters Promising Research Projects

**Why are many BRCA1-mutated ovarian cancer tumors resistant to chemotherapy?**
**How does cholesterol metabolism impact cells’ susceptibility to EGFR inhibitors?**

These are among the scientific questions that Fox Chase researchers, reinforced by new federal support, are probing, with implications for ovarian, colorectal, and kidney cancer, lymphoma, and more. *Fox Chase NOW* rounded up some of the most exciting projects underway in Fox Chase labs.

**Identifying Determinants of PARP-Inhibitor Sensitivity in Ovarian Cancer**
- **PI:** Neil Johnson, PhD, assistant professor, Molecular Therapeutics
- **Grant:** Department of Defense Ovarian Cancer Academy Award – Early-Career Investigator
- **Award:** $1.25 million over five years

Johnson works on cancers associated with BRCA1 and BRCA2 gene mutations. BRCA proteins are important for repairing DNA damage caused by some types of chemotherapy. The BRCA1 gene is commonly mutated in hereditary ovarian cancers, and these tumors typically respond well to chemotherapy or a newer class of agents called poly(ADP-ribose) polymerase (PARP) inhibitors. Despite substantial response rates, many patients with BRCA1 mutations appear resistant to PARP-inhibitor treatment, possibly because mutant forms of the BRCA1 protein can still repair DNA damage, resulting in chemotherapy resistance. Johnson’s research will identify mutant BRCA1 proteins that can repair DNA damage, investigate accompanying mutations that facilitate this process, and identify biomarkers for PARP-inhibitor sensitivity and treatment response.

**Synergistic Targeting of Cholesterol Metabolism and EGFR Signaling in Cancer**
- **PI:** Igor Astsaturov, MD, PhD, medical oncologist; assistant professor, Molecular Therapeutics
- **Grant:** R01 – National Institutes of Health
- **Award:** $2.2 million over five years

Astsaturov is studying a new pathway for limiting the function of EGFR (epidermal growth factor receptor), a protein on which many cancers depend for growth and which often proves resistant to targeting by inhibitor drugs. His team found that enzymes involved in cholesterol metabolism, specifically NAD(P) dependent steroid dehydrogenase-like (NSDHL) and sterol-C4-methyl oxidase-like (SC4MOL), also affect how cells handle EGFR. When these enzymes are inactivated in cancer cells, it makes them more susceptible to EGFR inhibitors. One plausible mechanism is that the metabolites normally processed by these enzymes are activating the liver X receptor protein (LXR), which signals the cell to get rid of cholesterol. Astsaturov and his team will use the five-year NIH grant to learn how this pathway works; examine the roles of NSDHL and SC4MOL in normal and cancerous cell growth; and determine whether targeting cholesterol metabolism and EGFR signaling using LXR will have a synergistic effect against EGFR-dependent cancers.

---

**BRCA1**

**Wild-type**

**Mutant**

Experimental analysis of BRCA1 protein localization after treatment with DNA-damaging chemotherapy. Green dots represent BRCA1 protein accumulation around double-stranded DNA breaks. In the BRCA1 mutant cell, the protein fails to accumulate at DNA breaks.

Blockade of SC4MOL or NSDHL (horizontal bar) increases meiosis activating sterols (MAS) levels and activates LXR. This causes perturbation of membrane cholesterol downstream of LXR via LDLR degradation and ABCA1 efflux, and antagonizes EGFR traffic and signaling and cancer cell growth.
Efficacy of Eldecalcitol (ED-71) in Colorectal Cancer Prevention in Apc\textsuperscript{Min} Mice

- PI: Margie L. Clapper, PhD, co-leader, Cancer Prevention & Control
- Grant: R21 – National Cancer Institute
- Award: $303,000 over one year

Clapper’s project examines the potential ability of an analogue of Vitamin D\textsubscript{3} (eldecalcitol, ED-71) to prevent colorectal cancer. Although several studies have demonstrated the protective effect of Vitamin D\textsubscript{3} against colorectal cancer, its use in humans has been hindered by its adverse effect on bone structure. Unlike Vitamin D\textsubscript{3}, ED-71 stimulates bone remodeling and suppresses bone resorption, leading to its approval in Japan for treatment of osteoporosis. Each year, approximately 112,000 new cases of colon cancer are diagnosed in the U.S., the majority of which are initiated by mutation of the “gatekeeping” Apc gene. Clapper and her colleagues have developed a unique strain of Min (Multiple Intestinal Neoplasia) mice (Apc\textsuperscript{Min+}FCCC) which, due to their extended lifespan and enhanced susceptibility to colorectal cancer, are ideal for testing chemopreventive agents and extrapolating the results to human disease. This study will use Apc\textsuperscript{Min+}-FCCC mice to assess the effectiveness of ED-71 in reducing colon cancer risk and modulating vitamin D receptor signaling. The researchers will also identify biomarkers of ED-71 effectiveness by comparing RNA and microRNA expression in colon tissues from treated and untreated mice using RNASeq and NanoString technology.

Interferon Activated Necrosis as a New Therapeutic Avenue for Kidney Cancer

- PI: Siddharth Balachandran, PhD, associate professor, Blood Cell Development and Function
- Grant: R01 – National Institutes of Health
- Award: $1,852,000 over five years

Balachandran is studying the cytokine interferon-gamma (IFN-\gamma), which in previous studies has shown the potential to provide lasting remission in metastatic renal cell carcinoma (RCC), but also produces severe toxic side-effects when employed at high doses as a monotherapy. Balachandran’s team is investigating how IFN-\gamma triggers necrotic death in tumor cells; how the tumor cell survival factor NF kappaB (NF-\kappaB) protects against IFN-\gamma; and how to exploit IFN-\gamma’s tumoricidal properties for treatment of RCC in vivo. The researchers will also identify biomarkers of IFN-\gamma effectiveness by comparing RNA and microRNA expression in colon tissues from treated and untreated mice using RNASeq and NanoString technology.

Dissecting the Role of ThPOK in Thymic Development and T Cell Differentiation

- PI: Dietmar J. Kappes, PhD, professor, Blood Cell Development and Function
- Grant: R01 – National Institutes of Health
- Award: $1,356,000 over four years

Kappes is studying the role of T helper inducing POZ-Kruppel Factor (ThPOK) in thymic development and T cell differentiation. ThPOK is a transcriptional regulator that encourages the differentiation of immature T cells into T helper (T\textsubscript{h}) cells and affects the further differentiation of T\textsubscript{h} cells; misregulated ThPOK expression can result in aggressive lymphomas. The goals of this project are three-fold: to elucidate the function of the ThPOK silencer, which regulates the expression of ThPOK during T cell development, and test the theory that nuclear factor of activated T cells (NFAT) and/or early growth response (EGR) transcription factors control the silencer; to analyze the role of the zinc finger protein Zfp281 in control of ThPOK transcription and in T cell development and function; and to define the influence of ThPOK on mature T cell function. Kappes and colleagues have developed a new mouse line for these studies in which ThPOK expression is selectively blocked in mature T cells via site-specific zinc finger proteins.

Mutation of the ThPOK silencer element dramatically alters representation of mature T cell subsets in mice. A site-specific Zn finger nuclease (ZFN) approach was used to introduce different mutations into the silencer of the endogenous ThPOK locus; proportions of mature T helper and killer cells in the blood of homozygous mutant mice were assessed by flow cytometric analysis of T cell receptor positive lymphocytes. Note that different mutations are neutral (PS17), promote (QC48), or antagonize (OB11) development/differentiation of T helper cells.
Fox Chase medical oncologist Efrat Dotan, MD, is spearheading a Phase I clinical trial of IMMU-130, an antibody-drug conjugate, studying its efficacy and safety for use against metastatic colorectal cancers (mCRC) that have relapsed.

“This is a novel treatment approach using an antibody-drug conjugate to deliver the treatment directly into the cancer cell and limit toxicity to healthy tissue,” says Dotan.

The main cancer-fighting component of the treatment is SN-38. Known as a topoisomerase inhibitor, SN-38 interferes with tumor cell replication, eventually leading to the death of those cells. Although long used in treating mCRC, the drug is normally delivered in the form of irinotecan, which requires processing by the patient’s liver to become metabolically active as SN-38. Despite this, the liver usually converts less than five percent of the drug to its active form. Conjugating SN-38 itself to another compound that binds specifically with cancer cells means that physicians can deliver a much more potent, targeted, and reduced dose of the drug, which they hope will be effective even for patients whose cancers relapsed after a chemotherapy regimen based on more traditional irinotecan treatment.

IMMU-130 is an immune conjugate in which SN-38 is attached to an anti-CEACAM5 antibody. CEACAM5, a carcinoembryonic antigen, is highly expressed on the surface of cancer cells in general and colorectal cancer cells in particular. Many colorectal tumors express high levels of CEACAM5, which makes it a prime candidate for targeting chemotherapy drugs to tumor cells without harming non-cancerous tissue.

The primary objective of the study is to evaluate the safety and tolerability of IMMU-130 and to determine the maximum tolerated dose among patients with mCRC who have been treated previously with at least one prior irinotecan-containing regimen. Accrual to the trial closed in December 2014, and so far Dotan and colleagues have observed good tolerability for the drug among study participants. Early signs of activity with this agent were seen with a few durable long-term responses.

“Our initial experience with this agent has been exciting, with manageable toxicity and some responses even in patients with irinotecan refractory disease,” says Dotan.

The researchers presented their preliminary results at the American Society of Clinical Oncology’s 2014 Annual Meeting.
SELECTED OPEN CLINICAL TRIALS

**BREAST CANCER**

*REP0210: A Single Arm, Preoperative, Pilot Study to Evaluate the Safety and Biological Effects of Orally Administered Reparixin in Early Breast Cancer Patients Who Are Candidates for Surgery*

Lori J. Goldstein, MD

**GASTROINTESTINAL CANCER (COLORECTAL)**

*A Phase Ib Study of Twice-Weekly IMMU-130 (hMN-14-SN38 Antibody—Drug Conjugate) in Patients with Colorectal Cancer*

Efrat Dotan, MD

**GASTROINTESTINAL CANCER (PANCREAS)**

*An International, Multi-Center, Double-Blind, Randomized, Phase III Trial of 90 Y-Cilavatuzumab Tetraxetan plus Low-Dose Gemcitabine versus Placebo plus Low-Dose Gemcitabine in Patients with Metastatic (Stage IV) Pancreatic Adenocarcinoma Who Received at Least Two Prior Treatments (PANCRIT-1)*

Steven J. Cohen, MD

**GENITOURINARY CANCER (RENAL)**

*AGS-003-007: An International Phase III Randomized Trial of Autologous Dendritic Cell Immunotherapy (AGS-003) Plus Standard Treatment of Advanced Renal Cell Carcinoma (ADAPT)*

David Y.T. Chen, MD, FACS

**HEMATOLOGIC CANCER (LYMPHOMA)**

*Belinostat plus Cyclophosphamide/Vincristine/Doxorubicin/Prednisone (BelCHOP) Regimen for Treatment of Patients with Peripheral T cell Lymphoma*

Stefan K. Barta, MD, MS, MRCP

**HYPERNATROCITOSIS**

*A Prospective Correlative Trial of Personalized Patient-Derived Xenograft (PDX or TumorGraft) Modeling in Patients with Metastatic or Recurrent Sarcoma*

Sujana Movva, MD

**THORACIC CANCER (NON-SMALL CELL LUNG)**

*CA209026: An Open-Label, Randomized, Phase III Trial of Nivolumab versus Investigator’s Choice Chemotherapy as First-Line Therapy for Stage IV or Recurrent PD-L1+ Non-Small Cell Lung Cancer*

Hossein Borghaei, DO

**FOR INQUIRIES, visit foxchase.org/ClinicalTrialsProgram or call 888-369-2427.**
Patients with HPV-Positive Throat Cancers More Likely to Make Complete Recovery without Surgery

At the ASTRO 2014 Annual Meeting, Fox Chase radiation oncologist Thomas Galloway, MD, presented a study showing that patients with human papillomavirus (HPV)-positive oropharyngeal cancer see significantly higher rates of complete response on a post-radiation neck dissection than those without HPV.

After radiation and chemotherapy, many head and neck cancer patients still have persistent lumps in their neck, albeit often smaller than when they were first diagnosed. Because surgery to remove these lumps can cause neck and shoulder problems and difficulty swallowing, Galloway’s team wanted to see if removing the lumps was necessary or if it was safe to let them dissolve on their own.

“Accurately defining which patients have achieved a complete response prior to surgery is of paramount importance,” says Galloway, director of clinical research and lead author on the study.

The team reviewed medical records from 396 patients whose oropharyngeal tumors had spread to at least one lymph node. Within 180 days after completing radiation therapy, 146 patients underwent neck surgery. For 99 patients, their records indicated whether or not their tumors had likely been triggered by HPV.

Galloway and his team found that HPV-positive patients’ cancers were less likely to recur, regardless of whether or not the tumors had completely disappeared following treatment. In fact, patients’ HPV status was the strongest predictor of survival to the end of the study.

Among the patients who underwent neck surgery, any lingering lumps were more likely to be benign in patients with HPV, either becoming permanent scars or eventually disappearing.

Currently, it is not routine to consider a patient’s HPV status when deciding whether to perform neck surgery. These findings suggest that perhaps it should be.

This study was supported by a Radiation Therapy Oncology Group and Community Clinical Oncology Program grant from the National Cancer Institute.

Ma Named ASTRO Fellow

C.M. Charlie Ma, PhD, Fox Chase professor, vice chair of radiation oncology, and director of radiation physics, was named an ASTRO Fellow at the organization’s 56th Annual Meeting. The Fellows Program honors leaders in radiation oncology who have contributed at least 10 years of service to ASTRO and had a substantial impact on the field through their research, leadership, patient care, and education.

Fisher Presents on Diffuse Large B Cell Lymphoma Variant

Presenting at the 2014 Pan-Pacific Lymphoma Conference in Kohala, Hawaii, Fox Chase President and CEO Richard I. Fisher, MD, reviewed the biology, prognosis, and future therapies for double/triple hit, C-MYC alone diffuse large B cell lymphoma, a very aggressive variant that has poor response to standard therapy and poor overall survival. As more clinical research homes in on this disease, Fisher says, “the most provocative question is whether molecular abnormalities in these patients can be successfully targeted with new oral inhibitors.”

Nurses Discuss ICU Delirium Prevention

At the AACN Clinical Scene Investigator (CSI) Academy Innovation Conference in Philadelphia in September, four Fox Chase ICU nurses—Ashley Moyer, RN, BSN, Kaitlyn Gregory, RN, BSN, Allyson Lloret, RN, BSN, and Erin Longstreth-Papsun, RN, BSN, MSN, OCN—who developed a project they developed to facilitate the prevention and early detection of ICU delirium, Fox Chase was one of seven Philadelphia hospitals selected for the CSI Academy, a 16-month nursing leadership and innovation training program designed to empower hospital-based staff nurses to be clinician leaders and change agents whose initiatives measurably improve patient outcomes and hospital bottom lines.
FOX CHASE Welcomes

CLINICAL FACULTY

ANESTHESIOLOGY
Flore Macenat, MD, MS, a clinical anesthesiologist who specializes in interventional pain management, joins Fox Chase following a fellowship in pain medicine and a residency in anesthesiology at the Hospital of the University of Pennsylvania, as well as an internship in anesthesiology at Penn Presbyterian Medical Center. Macenat received her MD from the University of Medicine and Dentistry of New Jersey, as well as an MS in biology from Montclair State University.

Michelle McMaster, MD, joins Fox Chase as an anesthesiologist after completing her residency in anesthesiology at Thomas Jefferson University Hospital and a postgraduate year at Lankenau Hospital in Wynnewood, Pennsylvania. McMaster received her MD from Jefferson Medical College and a BS in nursing from the University of Pennsylvania.

DIAGNOSTIC IMAGING
Catherine Tuite, MD, joins the department of diagnostic imaging as a staff radiologist with expertise in women’s imaging and mammography. She comes to Fox Chase from the Hospital of the University of Pennsylvania, where she completed fellowships in vascular and interventional radiology in 1999 and more recently in women’s imaging. Tuite received her MD from the Mt. Sinai School of Medicine and was chief radiology resident at the Mt. Sinai Medical Center.

RADIATION ONCOLOGY
Mark A. Hallman, MD, PhD, has joined the department of radiation oncology as an assistant professor after completing his residency at Fox Chase. He is a member of the thoracic, genitourinary, and hematologic cancer programs. His research interests include improving the safety and efficacy of delivering stereotactic body radiation therapy as well as developing novel methods of radiation delivery to treat cancers that are currently untreatable with conventional therapies. Hallman received both his MD and a PhD in pharmacology and experimental therapeutics from the Medical University of South Carolina.

SURGICAL ONCOLOGY
Sanjay S. Reddy, MD, a surgeon trained in traditional as well as laparoscopic and robotic techniques, has joined Fox Chase’s department of surgical oncology after completing a two-year fellowship at the Center. Reddy completed his residency in general surgery at Beth Israel Medical Center in New York. His interests include incorporating minimally invasive surgical techniques to address and treat gastrointestinal cancers; treating patients with soft tissue malignancies, consisting of melanomas and sarcomas; and using hyperthermic intraperitoneal chemotherapy (HIPEC) following cytoreductive surgery for cancers of the peritoneum.

DEPARTMENT OF MEDICINE
Kyungsu Jung, MD, MPH, joins Fox Chase as a hospitalist in the department of medicine. He recently completed a residency in internal medicine at Saint Francis Hospital in Evanston, Illinois, after earning his MPH in biostatistics and epidemiology from Johns Hopkins University. Jung received his MD from Chung-An University College of Medicine in Seoul, South Korea.

RESEARCH FACULTY

CANCER PREVENTION AND CONTROL
Jennifer Barsky Reese, PhD, joins the Cancer Prevention and Control Program as an assistant professor with a research focus on cancer survivorship and quality of life issues. Reese completed postdoctoral fellowships in behavioral medicine at Duke University Medical Center and Johns Hopkins University School of Medicine before joining the faculty at Johns Hopkins. Her research centers on developing and evaluating interventions to improve the interpersonal relationships and quality of life of those with cancer. As a licensed psychologist, Reese’s clinical interests include working with individuals and couples to enhance their ability to cope with the unique emotional and relationship challenges brought on by cancer and its treatment.
Glusker Wins Procter Award

Jenny P. Glusker, PhD, DSc, Fox Chase professor emerita, has been awarded the William Procter Prize for Scientific Achievement by Sigma Xi, The Scientific Research Society. The annual award recognizes researchers who have made outstanding scientific contributions and have communicated their significance across disciplines. Glusker’s research interests include cancer-causing chemicals, enzyme mechanisms, and crystallography.

ASCO Names Knudson an Oncology Luminary

Fox Chase senior scientist Alfred G. Knudson Jr., MD, PhD, was honored as an Oncology Luminary by the American Society of Clinical Oncology during its 50th anniversary celebration. The honor recognizes exceptional individuals who have helped shape the field of oncology and have advanced progress against cancer. Knudson’s “two-hit” theory of cancer causation provided a unifying model for understanding cancer susceptibility in people with and without an inherited predisposition. Knudson also predicted the discovery of tumor suppressor genes.

Designation Confirms Expertise in Myelodysplastic Syndromes

Fox Chase has been recognized as a Center of Excellence by the Myelodysplastic Syndromes Foundation, one of four such centers in Pennsylvania. This designation honors institutions with an established research and academic program in myelodysplastic syndromes (MDS); recognized expertise; the ability to conduct and make available genetic research; a history of publications on MDS; and ongoing research into the syndrome, including Institutional Review Board-approved clinical trials.

“As an MDS Center of Excellence, we offer patients with MDS state-of-the-art care,” says medical oncologist Patricia Kropf, MD, director of the Fox Chase-Temple MDS program. “We have clinical trials designed specifically for patients with MDS. Our care team includes clinicians, researchers, hematopathologists, and other staff members with expertise in MDS who are dedicated to the care of these patients.”

American Association for Laboratory Animal Science Honors Klein

Hilton Klein, DVM, director of the Laboratory Animal Health Facility, has received the American Association for Laboratory Animal Science’s 2014 Joseph J. Garvey Management Award. The award recognizes an AALAS member for outstanding administration, management, or support of programs relating to the care, quality, or humane treatment of animals used in biomedical research. The work of Garvey Award recipients benefits both the scientific workplace and the care of animals, and they demonstrate active involvement in AALAS on a volunteer basis.

Glusker Wins Procter Award

Jenny P. Glusker, PhD, DSc, Fox Chase professor emerita, has been awarded the William Procter Prize for Scientific Achievement by Sigma Xi, The Scientific Research Society. The annual award recognizes researchers who have made outstanding scientific contributions and have communicated their significance across disciplines. Glusker’s research interests include cancer-causing chemicals, enzyme mechanisms, and crystallography.

ASCO Names Knudson an Oncology Luminary

Fox Chase senior scientist Alfred G. Knudson Jr., MD, PhD, was honored as an Oncology Luminary by the American Society of Clinical Oncology during its 50th anniversary celebration. The honor recognizes exceptional individuals who have helped shape the field of oncology and have advanced progress against cancer. Knudson’s “two-hit” theory of cancer causation provided a unifying model for understanding cancer susceptibility in people with and without an inherited predisposition. Knudson also predicted the discovery of tumor suppressor genes.

Designation Confirms Expertise in Myelodysplastic Syndromes

Fox Chase has been recognized as a Center of Excellence by the Myelodysplastic Syndromes Foundation, one of four such centers in Pennsylvania. This designation honors institutions with an established research and academic program in myelodysplastic syndromes (MDS); recognized expertise; the ability to conduct and make available genetic research; a history of publications on MDS; and ongoing research into the syndrome, including Institutional Review Board-approved clinical trials.

“As an MDS Center of Excellence, we offer patients with MDS state-of-the-art care,” says medical oncologist Patricia Kropf, MD, director of the Fox Chase-Temple MDS program. “We have clinical trials designed specifically for patients with MDS. Our care team includes clinicians, researchers, hematopathologists, and other staff members with expertise in MDS who are dedicated to the care of these patients.”

American Association for Laboratory Animal Science Honors Klein

Hilton Klein, DVM, director of the Laboratory Animal Health Facility, has received the American Association for Laboratory Animal Science’s 2014 Joseph J. Garvey Management Award. The award recognizes an AALAS member for outstanding administration, management, or support of programs relating to the care, quality, or humane treatment of animals used in biomedical research. The work of Garvey Award recipients benefits both the scientific workplace and the care of animals, and they demonstrate active involvement in AALAS on a volunteer basis.