



October 2010

From the director

About a day and a half of travel time from Indianapolis is the city of Eldoret, Kenya. That's a trip many people from the IU School of Medicine and Moi University School of Medicine have been making for the past two decades when a

partnership began between the two schools. That partnership began with a few handshakes and a lot of faith and has developed into a program so successful that it has been nominated more than once Nobel Peace Prize. (The IU-Moi story is well chronicled in "Walking Together, Walking Far" by Fran Quigley.)



Loehrer

What this partnership has accomplished is nothing less than outstanding. Based on a model of care, more than 100,000 Africans are under treatment for HIV and part of a program that not only provides medicines but also nutrition and self-esteem through a jobs program.

The progress in one area opens the doors to others. Six years ago, that door cracked open for me during a dinner with Bob Einterz, one of the founders of the IU-Kenya Partnership and now associate dean of global health for the IU School of Medicine. He showed me a picture that he carries with him. It was of a young boy with a huge mass protruding from his right jaw. It was the classic picture of Burkitt's lymphoma. Though Burkitt's lymphoma is eminently treatment, this picture was a reminder to Bob of a missed opportunity. For me, it was a call to service.

In 2010, cancer has become the number one cause of premature death in Kenya and sub-Saharan Africa. This occurs with the knowledge that most cancers are associated with infections (HPV, HIV, EBC, hepatitis B and C, H.pylori) and not yet tainted with the Western curse of tobacco-related cancer. Lymphoma and sarcomas are common among children, but the lack of drugs, radiation and trained oncologists provide the backdrop of despair.

In the last few years, we have secured funding from the Levinson Foundation and some corporate sponsors -- notably Lilly, then Pfizer -- who have provided the support for the building of infrastructure for cancer care, research and education. When I first visited Moi five years ago, we were seeing about 350 patient visits a year. This past month when I returned, we were on target to nearly 4,000 visits.

Most patients with curable cancer have access to drugs. The program has leapfrogged because of the commitment of dedicated staff and facilities at Moi, but much credit also has to go to Matt Strother, MD, assistant professor in the Division of Hematology/Oncology at the IU School of Medicine. Matt moved to Eldoret with his family immediately upon completion of his fellowship in hematology/oncology and clinical pharmacology. It is his passion and dedication that has created the infrastructure of hope. It is his wife, Justyn, and his three children who have created an inspiration to Matt.

In my quarter century as a medical oncologist, I have witnessed many medical marvels -- the invention of CT scans, MRI, the cure of germ cell tumors, the birth of biologics and the acceptance of clinical trials as the standard of care for cancer patients. I also have seen the growth of the business of medicine, where revenue drives care delivery and where discussion of global health coverage is a divisive issue.

A visit to Eldoret reminds me in a quiet way that we have the opportunity to do it a bit better. To create a health care environment based on prevention and screening; providing care to those who can truly benefit from treatment and palliative care to those who cannot. That difference is being made halfway around the world. A difference felt by young children, parents and grandparents who feel the pain of disease and the loss of loved ones no differently than us. When you get tired or frustrated with life's journey here, pause for a bit and remember those less fortunate.

Sincerely,

Patrick Loehrer, MD
Director, IU Simon Cancer Center



October 2010

Physical symptoms prevalent no matter what stage of cancer, including remission

Twenty-two physical symptoms associated with cancer -- symptoms often unrecognized and undertreated -- are prevalent in all types of cancers regardless of whether the

patient is newly diagnosed, undergoing treatment, or is a cancer survivor, according to researchers from the Indiana University schools of medicine and nursing and the Regenstrief Institute.

Common symptoms include fatigue, pain, weakness, appetite loss, dry mouth, constipation, insomnia, and nausea. These physical symptoms are associated with substantial functional impairment, disability, and diminished quality of life.



Kroenke

The study of 405 patients was reported in the Oct. 11 issue of the *Archives of Internal Medicine*. Numerous physical symptoms, rather than just a few, were prevalent in patients with cancer and this prevalence did not diminish after completion of therapy.

"We found that regardless of where they are in the course of their diseases, many individuals with cancer have a high symptom burden," Kurt Kroenke, MD, the study's principal investigator and first author, said. Dr. Kroenke is a researcher at the IU Simon Cancer Center, an investigator at the Regenstrief Institute, and a Chancellor's Professor of Medicine in the IU School of Medicine.

"These symptoms impact them at home and at work throughout their lives," he said.

Study participants -- all of whom had pain, depression, or both -- experienced substantial disability, reporting on average 17 of the past 28 days as either bed days or days in which they had to cut down on activities by at least 50 percent. Almost all patients reported feeling tired (97.5%) and most (78.8%) were bothered "a lot" by this symptom. Of the 22 symptoms studied, 15 were reported by more than half of the study participants.

In spite of high symptom prevalence, the researchers did not uncover greater use of the health care system. There may be

several explanations for this, including patients' inclinations to focus on cancer treatment while with their physicians or to accept the symptoms as an inevitable result of the disease or its treatment. Alternatively, the explanation may lie with the fact that those in the study, as cancer patients or former patients, were already frequently interacting with many parts of the health care system.

"Patients and their families should be encouraged to bring up symptoms like pain or insomnia with physicians. But because oncologists are necessarily focused on treatment of the cancer itself, they often have insufficient time to optimally evaluate and manage symptoms and other factors impacting quality of life. We have shown in an earlier study that one effective solution might be a partnership between a telephone-based symptom management team and community-based oncology practices," Dr. Kroenke said.

The previous study, published earlier in 2010 in the *Journal of the American Medical Association*, reported that an economical, centralized approach is feasible to conduct and significantly improved symptoms of pain and depression in patients in any phase of cancer. That approach gave patients, many of whom lived in underserved rural areas, one-stop assistance they probably wouldn't have had access to unless they went to a major cancer center, Kroenke said.

Recognizing and managing physical symptoms such as fatigue, pain, nausea, and insomnia may make a significant difference regardless of type or phase of cancer. The researchers plan to investigate medical and behavioral strategies and combinations of both approaches to control these symptoms.

In addition to Dr. Kroenke, co-authors of "Somatic Symptoms in Patients with Cancer Experiencing Pain or Depression" are Xin Zhong, RN, and Janet Carpenter, PhD, RN, of the IU School of Nursing; Dale Theobald, MD, PhD, of Community Home Health Hospice and Symptom Management Group; Jingwei Wu, MS, of the IU School of Medicine; and Wanzhu Tu, PhD, of the Regenstrief Institute and the IU School of Medicine.

The study was supported by a grant from the National Cancer Institute.



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Core spotlight

Clinical Pharmacology Analytical Core

The [Clinical Pharmacology Analytical Core](#) (CPAC) is available to assist IU Simon Cancer Center investigators as well as external partners with preclinical and clinical pharmacokinetic data in support of their research projects and scientific goals.

The CPAC quantifies drugs and small molecules, determines protein binding of these compounds, and provides pharmacokinetic data to principal investigators. The core, which has been in existence since September 2004, primarily works with clinical investigators to provide pharmacokinetic information on drug interactions. More recently, the CPAC has assisted preclinical investigators by providing pharmacokinetic information on small molecules.

The process of rational drug design is based upon a strong foundation of biology, chemistry, *in vivo* pharmacology, and pharmacokinetics. Relevant pharmacokinetic studies should be conducted in small animal models or *in vitro* systems before the first drug administration in humans. Results from these preclinical studies allow the principal investigator to implement structural changes in a drug molecule to optimize the activity of the drug or alter its pharmacokinetic properties prior to the move to a more regulated and expensive clinical phase of drug development.

As a result of the identified need for preclinical pharmacokinetic information early in the drug discovery process (via ITRAC experimental design mapping), CPAC interacts closely with other IUSCC-shared resources, the [In Vivo Therapeutics \(IVT\) Core](#), [Chemical Synthesis Core](#), and the new [Therapeutic Validation Core](#). Over the past few years, the CPAC and IVT Core have worked together to generate data that allow principal investigators to better evaluate molecules that are being developed within the IUSCC that show promise as novel cancer drugs.

In response to the increase in pharmacokinetic studies, the CPAC has expanded its capacity, in equipment and personnel. The CPAC currently has three state-of-the-art HPLC-MS/MS instruments for quantification of drugs and metabolites. Two of these instruments (API 4000, Thermo Quantum Ultra) allow quantification of pg/mL concentrations in as little as 5 μ L of plasma, circumventing the need to obtain large volumes of blood from small animals.

In addition to the three HPLC-MS/MS's, the core facilities have additional HPLC systems (equipped with UV, fluorescent, or other detectors) that may be used for routine analyses or purification procedures, and all the necessary equipment for storage and preparation of samples.

The Clinical Pharmacology Analytical Core is located in the Division of Clinical Pharmacology on the seventh floor of the Myers Building in Wishard Memorial Hospital.

For more information, please contact David Jones, CPAC director, at 630-8726 or drjones1@iupui.edu. You can access the process and consultation form [here](#).



October 2010

News briefs

Membership criteria changes

IU Simon Cancer Center membership criteria, benefits, and responsibilities have been updated. Membership in the IU Simon Cancer Center is open to full-time faculty of Indiana University or IUPUI who contribute on some level to the overall mission of the cancer center in areas of research, education, patient care, or community outreach. [Learn more.](#)

Miss a Combined Seminar Series?

Did you miss a Combined Seminar Series? You can now watch it online. A full listing of past Seminar Series events is [here](#). Also, speakers for the 2010-11 academic year have been announced. You can find the schedule [here](#).

Grants available to researchers

For the latest grant opportunities, visit the [Funding Opportunities](#) page on the IUSCC Web site.

Cancer center members in the news

- **Rafat Abonour, MD**, has been named a recipient of a Cancer Clinical Investigator Team Leadership Award, which is supported by the NCI. This administrative supplement award is designed to support, acknowledge, and recognize outstanding clinical investigators whose participation and activities promote successful clinical research programs and to promote retention of clinical investigators in an academic career in clinical research. Also, Dr. Abonour and about 20 other bicyclists crossed a finish line on the IUPUI campus Saturday, Oct. 9, ending the sixth Miles for Myeloma tour. Abonour and the others were greeted to the cheers of nearly 300 people -- mainly patients and their families -- who awaited their arrival. Thus far, Abonour's cycling event has raised \$220,000 this year. In the past six years, he has raised



more than \$1.5 million. [Learn more.](#)

- **Daniel Sliva**, PhD, and colleagues have published the dramatic effects of a natural formula against breast cancer. The results are found in the most recent publication of *Integrative Cancer Therapies*. Lead investigator Dr. Sliva said, "The formula we studied inhibits growth of highly metastatic human breast cancer cells, and suppresses metastatic potential of these cells." Despite significant advances in breast cancer treatment, available treatments for advanced stage breast cancer offer little hope. However, as the study shows, this potent integrative breast formula can be crucial in the fight against highly invasive breast cancer.
- **David Flockhart**, MD, PhD, Mayo Clinic researchers, and others have discovered genetic variants that lead to severe arthritis for a subset of women when taking aromatase inhibitors to treat their breast cancer. This serious side effect is so painful that many women halt their lifesaving medication. The findings appear in the online issue of *Journal of Clinical Oncology*.
- **Linda Malkas**, PhD, has been appointed to the Ovarian Cancer Integration Panel administered through the Office of Congressionally Directed Medical Research Programs.
- **David Ingram Jr.**, MD, will become the third Hugh McK. Landon Chair in Pediatrics, pending approval from the IU trustees.
- **Reuben Kapur**, PhD, will become the third Frieda and Albrecht Kipp Chair in Pediatrics, pending approval from the IU trustees. Dr. Kapur is currently the director of the hematologic malignancies and stem cell biology research group in the Wells Center.
- **Mark Kelley**, PhD, has been awarded a joint programmatic grant from the Purdue University Center for Cancer Research and the IU Simon Cancer Center for his pancreatic working group application. The award is made possible by the Jordan-Rieger Fund for Pancreatic Cancer.

The mission of the Pancreatic Working Group is to facilitate a consistent and productive exchange of ideas between clinicians and basic scientists for the understanding, prevention, and treatment of pancreatic cancer. The working group is a multi-functional research team, which includes both Purdue and IU researchers with the expertise to successfully study this currently incurable disease. Research collaboration is fostered through monthly working meetings accentuating their interconnectedness and highlighting areas of scientific synergy using bubble mapping and biologic schemes (invasion/metastasis, K-Ras signaling, Gemcitabine resistance). The working group includes 29 basic scientists and 17 clinicians from IU and PU. Dr. Kelley and **Thomas Howard**, MD, are co-project leaders.



As part of National Breast Cancer Awareness Month events, the Indianapolis Colts' Women's Organization presented a check to the IU Simon Cancer Center during the home football game on Oct. 10. Dr. Monet Bowling (second from right), assistant professor of surgery at the IU School of Medicine and a member of the breast cancer clinical team at the cancer center, accepted the check.

New members

[Jonathan Cherry](#), PhD
Department of Dermatology
 Associate member, Tumor
 Biology and
 Microenvironment

[Catherine Mosher](#), PhD
Department of Psychology
 Associate member, Cancer
 Prevention and Control

[Kathryn Coe](#), PhD
Department of Public Health
 Full member, Cancer
 Prevention and Control

[Samisubbu Naidu](#), PhD
Department of Dermatology
 Associate member, Tumor
 Biology and
 Microenvironment



[Hiremagular Jayram](#), PhD
*Department of Biochemistry
and Molecular Biology*
Full member, Experimental
and Developmental
Therapeutics

[Julie Otte](#), PhD
IU School of Nursing
Associate member, Cancer
Prevention and Control

[Travis Jerde](#), PhD
*Department of
Pharmacology and
Toxicology*
Associate member, Tumor
Biology and
Microenvironment

[Dan Spandau](#), PhD
Department of Dermatology
Associate member, Tumor
Biology and
Microenvironment

[Keith March](#), MD, PhD
*Department of Cellular and
Integrative Physiology*
Full member, Tumor Biology
and Microenvironment

[Bree Weaver](#), MD
Department of Medicine
Associate member, Cancer
Prevention and Control