June 2012

IU research leads to risk factor test for rare chest cancers

Research conducted by physicians and scientists at the Indiana University School of Medicine has resulted in a genetic test to predict the risk of recurrence of thymoma, a rare tumor of the upper chest. The study results were presented June 2 in a poster presentation at the 2012 American Society of Clinical Oncology Annual Meeting in Chicago.

Sunil Badve, MBBS, MD, **Patrick Loehrer** Sr., MD, and colleagues have pinpointed 19 genes that appear to forecast the chance that thymoma patients will develop a second tumor after the first is removed via surgery. These biomarkers were initially identified based upon genomic analysis of 36 frozen thymoma samples from patients at the Indiana University Melvin and Bren Simon Cancer Center. Additional tests confirming the results were later performed on 75 other thymoma biopsies provided by other institutions.


Badve

“Obtaining objective molecular data to support traditional histological assessment will lead to improved diagnostic accuracy for thymomas and thymic cancers,” Dr. Badve said. “The test, which recently completed validation, is called DecisionDx-Thymoma and provides an objective, accurate assessment of an individual’s risk of metastasis.”

The ability to predict this risk of recurrence -- also known as metastasis -- will help physicians create individualized treatment plans that avoid side effects caused by adjuvant treatments that may be unnecessary in some patients. Adjuvant treatments, such as radiation and chemotherapy, are given in addition to the primary treatment, such as surgical removal of the tumor.

All development and validation work on the test was performed by Castle Biosciences Inc., a rare cancer molecular diagnostics company whose mission is to serve individuals afflicted with rare or orphan cancers. The test also will be exclusively marketed by the company.

Thymomas are rare but also one of the most common types of cancers found in the upper chest. Tumors are often discovered on a chest X-ray when a patient suffers from chest pain, cough or difficulty swallowing – or a previously associated autoimmune disorder – and can spread throughout the chest and body. Treatment consists of surgical removal followed by radiation or chemotherapy in patients believed to be at high risk for metastasis. Under the traditional disease classification process used to identify the likelihood of metastasis – the Masaoka staging system – a significant number of patients staged as “low risk” still experienced recurrence.

The more accurate assessment of recurrence risk provided by DecisionDx-Thymoma could reduce or eliminate the need for these painful additional treatments after removal in patients who test at a low risk for thymoma recurrence.

“The ability to accurately assess metastatic risk based upon the thymoma’s molecular signature will enable personalizing therapeutic options,” Dr. Loehrer, director of the IU Simon Cancer Center and an international expert on thymomas and thymic carcinomas, said. “This will assist in deciding which patients should receive post-operative therapy.”

IU is uniquely positioned to collect and analyze thymomas and thymic tumors because of researchers such as Dr. Loehrer, who have been sought by patients for expert care over the past 30 years.

The partnership between Castle Biosciences and the IU investigators was brokered by the Indiana University Research and Technology Corp. in fall 2011 after the group worked with the IU investigators to file disclosure on the genes used in their research before their poster presentation at the American Society of Clinical Oncology in 2011. The partnership with Castle Biosciences provides access to state-of-the-art facilities capable of technical validation of the thymoma test in laboratories accredited by the College of American Pathologists and certified by the Clinical Laboratory Improvement Amendment of the U.S. Food and Drug Administration.

Support for early research was also provided by the Indiana Clinical and Translational Science Institute and IU Simon Cancer Center.

“It is well recognized that rare cancers typically do not have accurate staging systems as it relates to predicting recurrence or metastasis,” Derek Maetzold, CEO of Castle Biosciences, said. “We created our company with the focus on working with academic centers such as Indiana University for the purpose of providing objective laboratory reports that would improve staging accuracy and thus improve risk benefit decisions as it relates to individual treatment plans. The DecisionDx-Thymoma test meets this objective.”

The test became available for routine clinical ordering this month.

June 2012

Olanzapine controls breakthrough chemotherapy-induced nausea and vomiting

Cancer patients who suffer chemotherapy-induced nausea and vomiting are experiencing effective relief as a result of new Indiana University research indicating the usefulness of the anti-psychotic olanzapine to control these potentially debilitating side effects.

“This is the first time that breakthrough (chemotherapy-induced nausea and vomiting) has been studied in a systematic way,” **Rudolph Navari**, MD, PhD, lead author of the study, professor of medicine, associate dean of Indiana University School of Medicine-South Bend at the University of Notre Dame, and clinical director of the Harper Cancer Research Institute said. “This study suggests that olanzapine will be very useful in these patients who feel very sick and sometimes come to the clinic, hospital or emergency room. As a result, patients will feel better.”


Navari

Dr. Navari presented his findings earlier this month in Chicago at the American Society of Clinical Oncology annual conference.

Thirty to 50 percent of cancer patients who are receiving highly emetogenic treatments (causing nausea or vomiting) experience “breakthrough” side effects two to four days after chemotherapy. Besides affecting a patient’s quality of life, breakthrough chemotherapy-induced nausea and vomiting can necessitate reductions in their chemotherapy doses, possibly limiting the effectiveness of treatment.

Although there has been little research about breakthrough chemotherapy-induced nausea and vomiting, these symptoms often are treated with metoclopramide. The double-blind, randomized controlled trial compared olanzapine to metoclopramide. Patients who received olanzapine did significantly better than the patients who received metoclopramide.

The study monitored 80 patients from north central Indiana who experienced breakthrough chemotherapy-induced nausea and vomiting; half were given olanzapine, and half received metoclopramide. Olanzapine provided significantly more relief for both nausea and vomiting. Now available in generic form at a cost of 45 cents per dose, olanzapine has the additional advantage of being inexpensive. The study was supported by the Reich Family Endowment for the Care of the Whole Patient.

While olanzapine, approved by FDA for treatment of psychosis, is known to cause a variety of side effects when taken daily for six months or longer, it is administered to breakthrough chemotherapy-induced nausea and vomiting patients for no longer than three days. The short-term use in this study did not lead to any significant toxicities.

Dr. Navari has performed a number of studies that have identified olanzapine as an effective treatment for minimizing nausea and vomiting for various points during chemotherapy as well as

for reversing chemotherapy-induced anorexia.

“While we are far from preventing all cancers, I believe that we are close to eliminating much of the suffering associated with chemotherapeutics,” Dr. Navari said.

--Gail Hinchion Mancini

June 2012

Core spotlight

Transgenic and Knockout Mouse Core

The Transgenic and Knockout Mouse Core provides timely and cost-efficient services in the production of transgenic mice and knockout mice for use in basic science research.

Loren Field, PhD, the core's director, explained the differences between transgenic mice and knockout mice. A transgenic mouse is one "that you add a piece of DNA that wasn't there formerly," while a knockout mouse is one in which scientists have modified a gene that was already present, he said.

Genetically engineered mice are regarded to be essential tools in understanding human diseases.

Located in the Biotechnology Research and Training Center about one mile north of the Indianapolis medical school campus, the core offers:

- the production of transgenic mice (via pronuclear injection of recombinant DNA molecules)
- the production of knockout mice (via homologous recombination in ES cells)
- advice concerning construction of transgenic and gene targeting constructs, animal breeding, and maintenance of the resulting mouse colonies

For transgenic mouse production, investigators provide the DNA construct to the core. For knockout mouse production, the core provides three types of services: ES cell transfection, blastocysts injections, and rapid germ line breeding.

The core also offers embryo and sperm preservation and chimeric services.

For more information about the Transgenic and Knockout Mouse Core, contact William Carter at 278-0163.

June 2012

News briefs

24 Hours of Booty charity cycling event begins at 7 p.m. June 29

24 Hours of Booty, the official 24-hour cycling event of the Lance Armstrong Foundation and the premier national 24-hour road cycling charity event in the country, kicks off at 7 p.m. Friday, June 29. Funds raised from the event benefit the IU Simon Cancer Center.

24 hours of booty
ordinary riders
extraordinary cause

Edward F. Srour, PhD, is one of the organizers of the cancer center's team, Pedaling Cures, while survivor Michael Brunsman is one of the team's riders.
more

Mark your calendars: BCOG annual conference is Nov. 8-9

Mark your calendars for this year's BCOG Annual Fall Conference on "Team Science." Held Nov. 8-9 at the JW Marriott, the conference is sponsored by the Behavioral Cooperative Oncology Group (BCOG), a consortium of four universities: Indiana University, Michigan State, University of Michigan, and The Ohio State University. Co-sponsors are the Walther Cancer Foundation, IU Simon Cancer Center, Indiana Clinical and Translational Sciences Institute, and the Office of the Vice Chancellor for Research at IUPUI. Kara Hall, PhD, program director at the National Cancer Institute, will deliver the keynote address.

Henry Mullett, 7, patiently waits to dig into some cupcakes during Hooray Henry Day (June 6) at the IU Simon Cancer Center with one of his doctors, Jeffery Buchsbaum, MD, PhD. Andrea Pedregon of the Andrea Pedregon Foundation presented a $50,000 gift to the pediatric radiation oncology research program in honor of Henry, who is in kindergarten with her son. Andrea, wife of NHRA two-time Funny Car champion Tony Pedregon, raised funds through the sales of “The Real Families of the NHRA” calendars.

Vera Bradley Classic nets more than $1 million

Thank you, Vera Bradley! The 2012 Vera Bradley Classic Golf & Tennis Tournament raised $1,001,145. Funds support breast cancer research here at the IU Simon Cancer Center. To date, the Vera Bradley Foundation for Breast Cancer has donated nearly $16 million to the cancer center.

Cancer center members serve as mentors during summer programs

Two summer programs are currently underway in which students are working alongside IU Simon Cancer Center physicians and scientists.

The Future Scientist Program (FSP) -- a collaboration between Indianapolis Public Schools, the American Cancer Society, and the IU Simon Cancer Center -- began earlier this month and ends July 27. The program includes daily hours in a lab, weekly discussions, seminars and activities, campus field trips, and a final presentation to mentors, parents, and sponsoring organizations. The following cancer center members are serving as mentors: **Hiromi Tanaka**, PhD; **Elliot Androphy**, MD; **Qi-Huang Zheng**, PhD; **Ernestina Schipani**, MD, PhD; **Murray Korc**, MD; **Xiao-Ming Yin**, MD, PhD; and **Cong Yan**, PhD.

Th cancer center's Summer Research Program, now in its 10th year, aims to increase the number of high school and undergraduate students from underrepresented populations pursuing biomedical and behavioral science careers by providing positive and meaningful firsthand exposure to these fields. It ends July 31. The following cancer center members are mentors: **Clark Wells**, PhD; **Mark Mendonca**, PhD; **Eddy Srour**, PhD; **Christy Orschell**, PhD; **Attaya Suvannasankha**, MD; **Theresa Guise**, MD; **Tim Corson**, PhD; and **Julie Otte**, PhD.

Cancer center members in the news

- **Rafat Siddiqui**, PhD, has been named an editor of *Advances in Breast Cancer Research*. Also, Dr. Siddiqui presented “Docosahexaenoic Acid and Curcumin Induce Synergistic Cellular and Molecular Effects in Breast Cancer Cells” at the 10th Congress of the International Society for the Study of Fatty Acids and Lipids in Vancouver.

- The journal *Cancers* has published a study by a team led by **Tracy Vargo-Gogola**, PhD, related to her ongoing work on a family of genes active in mammary gland development and breast cancer. The study, "P190B Regulates Chromosome Segregation in Cancer Cells," describes a novel role for p190B as a regulator of chromosome partitioning during cancer cell division. The research suggests that p190B may affect the development of cancer by promoting aneuploidy (too few or too many chromosomes), which is a feature of nearly all solid tumors.

- **Kathy Miller**, MD, and colleagues concluded: “T-DM1 is well tolerated and has single-agent activity in patients with HER2-positive MBC who have previously received both approved HER2-directed therapies and multiple chemotherapy agents. T-DM1 may be an effective new treatment for this patient population.” The study appears in the *Journal of Clinical Oncology*.

New members

Heather Hundley, PhD
Department of Biochemistry and Molecular Biology
Associate member, Tumor Microenvironment and Metastases

Tim Masterson, MD
Department of Urology
Affiliate member

Rudolph Navari, MD, PhD
Department of Medicine
Affiliate member

Irina Petrache, MD
Department of Medicine
Full member, Hematopoiesis, Malignant Hematology, and Immunology Program

Milan Radovich, PhD
Department of Surgery
Associate member, Breast Cancer

William Wooden, MD
Department of Surgery
Associate member, Breast Cancer