

Cancer Lines

The newsletter for UNC Lineberger Comprehensive Cancer Center and the N. C. Cancer Hospital

Fall 2008



the inside line up

Prostate Cancer Project: Beating the Odds Against Cancer . . . and Mother Nature

In 2005, Hurricane Katrina slammed into the Gulf Coast, triggering the largest engineering failure in our nation and causing catastrophic flooding in New Orleans. The impact on the Crescent City community - including its health care system - has been well-documented. But many people don't know that an historic prostate cancer study was almost washed out by the rising waters.

But let's start at the beginning.

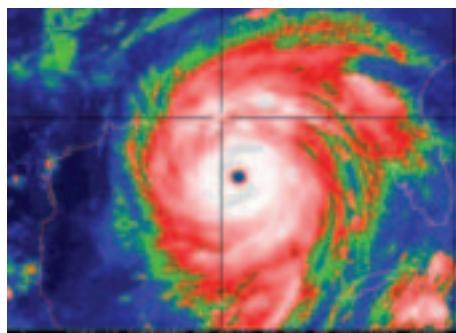
In 2003, James Mohler, MD, associate professor of surgery (urology), pathology and laboratory medicine and UNC Lineberger member, partnered with investigators at Louisiana State University Health Sciences Center and colleagues at nine other institutions to propose a study. Its goal: to uncover the factors responsible for the extremely high prostate cancer mortality rate of African-American men in North Carolina, one of the highest in the nation. Louisiana was chosen as a comparison site because African-American men there have one of the lowest prostate cancer mortality rates in the country. Mortality rates for Caucasian-American men in both states are similar and much lower than for their African-American counterparts.

After a one-year application process, a consortium received a Department of Defense Prostate Cancer Research Program (DoD PCR) Awards program grant of \$9,913,157 for a multidisciplinary population-based study of 2,000 men with newly diagnosed prostate cancer. The Prostate Cancer Project or PCaP was on its way.

"There is no biological reason we know of for the difference in mortality rates in the two races," explains Mohler, now chair of the department of urologic oncology, leader of the prostate cancer program and professor of oncology at Roswell Park Cancer Institute and professor of urology at the University of New York at Buffalo. He also still serves on the UNC faculty and maintains a lab at Lineberger.

"What was needed was a study that could look at the whole picture, not just nutrition, or just access to care, etc., and to do so with a large sample of both African-American men and Caucasian-American men," explains Elizabeth Fontham, DrPH, MPH, dean and professor at the LSU School of Public Health and LSU PCaP director.

PCaP should determine the relative contributions of racial differences in interaction with the health care system, the biology of the man who gets prostate cancer and the cancer itself in these profound racial differences in prostate cancer mortality. The study is evaluating differences in factors such as attitudes about prostate cancer early detection, use of PSA, access to health care, diet, genetics and tumor biology.



The eye of Hurricane Katrina approaches New Orleans.

A Broader Perspective

The broad view will help researchers understand what factors contribute to the increased risk in development of and death from prostate cancer among African Americans. "This in turn will help us know which factors can be modified, and thus

continued on page 3

Study Looks at Genetics' Role in Treatment Outcomes

A new research study endeavors to discover whether a change in dosage of the popular breast cancer drug tamoxifen, can help improve results in women who don't break down the drug as effectively as others.

Tamoxifen is a selective estrogen receptor modulator (SERM) used to treat pre-menopausal women with hormone-receptor-positive breast cancer. It is approved by the Food & Drug Administration in 20mg and 40mg daily doses.

Studies suggest its effectiveness may be rooted in how the body metabolizes the drug. Women who break down the drug more efficiently produce higher amounts of endoxifen, a byproduct of metabolizing tamoxifen. It is hypothesized that these women typically respond better to the treatment.

But about 5 percent of breast cancer patients don't metabolize the drug well, and the FDA currently suggests they avoid

continued on page 3



4 Profile: Andy Olshan



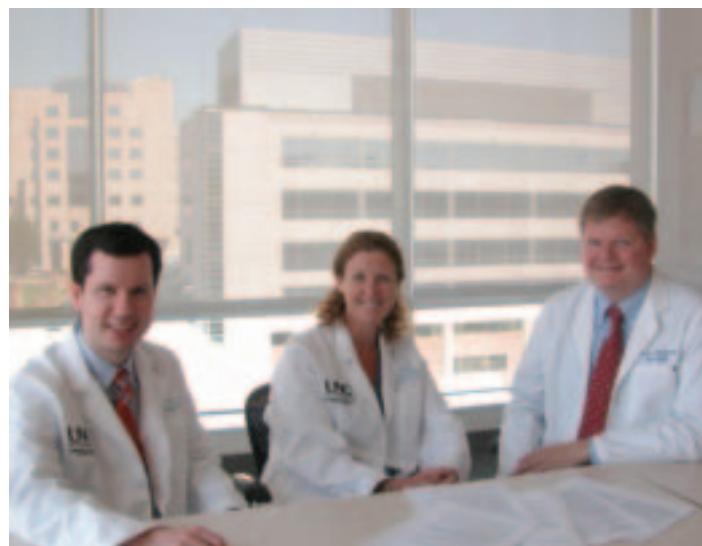
5 Colon Cancer Screening Program



6 Clinical Trial Recruitment



8 DeSimone Wins Lemelson-MIT Prize



Drs. William Irvin, Lisa Carey, and Howard McLeod discuss clinical trial data. The team is gathered in a conference room at the new Physicians' Office Building, overlooking the N. C. Cancer Hospital.

where public health resources should be focused in an effort to reduce risk and improve survival," explains PCaP Co-Director Jeannette Bensen, PhD, assistant professor of epidemiology at UNC Lineberger and UNC School of Public Health.

Two-thousand participants - 1,000 from each state - will populate the study. "It's critical that the population we end up with is representative of all the men in the study areas," explains Jane Schroeder, MPH, DVM, assistant professor of epidemiology at the UNC School of Public Health and a UNC PCaP member. "To be eligible, they have to be living in the study area at diagnosis - that's a 42-county area in North Carolina and 28 parishes in Louisiana. Subjects also have to be aged 40 to 79 and able to complete the study cognitively and physically."

The process could take a number of years. "We started recruiting and collecting in the Fall of 2004 in North Carolina and Louisiana," she recalls. "Then Hurricane Katrina hit."

When The Levee Breaks

By early August 2005, 211 New Orleans men had agreed to participate, biological samples and other data had been collected and the team had arranged to follow up with the subjects for future data-gathering.

Then the floodwaters came. "The New Orleans metropolitan area was decimated," Fonham recalls. "Our population was displaced, our hospitals were closed and many have not reopened, our staff lost their homes and had been living in FEMA trailers."

Amazingly, no research data was lost, and blood and tissue research samples were recovered from all but 28 research subjects. But PCaP wondered if the Louisiana part of the study could be continued given the challenges of living, working and conducting research in the shattered city.

"The study team was disappointed at first when there was a consideration that the Louisiana site might be dropped because of the devastation in the region," admits Joseph Su, PhD, MPH, associate professor at the LSU School of Public Health.

Tamoxifen

continued from page 1

tamoxifen. Another 40 to 50 percent of patients are intermediate metabolizers.

"Is their treatment being compromised by their genetics?" asks William Irvin, MD, a senior clinical research fellow and co-principal investigator with Lisa Carey, MD, Medical Director of the Breast Cancer Team at UNC.

The study aims to find out.

"We know that there are differences in the levels of the active form of tamoxifen between women who break tamoxifen down well, those who do it intermediately well, and those who don't break it down at all. What we don't know is if we can overcome these genetic differences simply by changing the dose of the drug," Irvin explains. Participants who are poor or intermediate metabolizers will have their dose increased from 20mg dose to 40mg, and researchers will see if endoxifen levels differ between the doses.

But the team outlined a plan to restart in Louisiana and, in July 2006, DoD scientific reviewers agreed to allow PCaP to re-initiate enrollment, recruitment, field and laboratory activities. An additional \$1,717,430 was awarded in September 2006, with \$2,305,303 more awarded in July 2007 to recruit a new group of 1,000 participants in Louisiana.

As a result of the Herculean effort, the team re-contacted 176 of the 211 pre-Katrina participants. Because of the population displacement after Katrina, the recruiting area was expanded to include the Baton Rouge and Lafayette regions. Since resuming recruitment, the LSU PCaP team has interviewed 463 Caucasian-Americans and 250 African Americans as of July 30, 2008.

"It was difficult to focus on bringing back this study while fixing up personal property damaged by the flood," Su allows. "For example, Christine Brennan, our nurse coordinator and participant recruiter, spent months in her FEMA trailer making calls from her cell phone trying to recruit participants. The team was trying to prove to the DoD and ourselves that Louisianans are resilient and we can come back to what we were before."

The End Game

There's no doubt PCaP will have far-reaching implications. "The DoD PCRP believes that the



Drs. Jeannette Bensen, UNC Lineberger PCaP co-director, and Jane Schroeder, UNC PCaP faculty, review NC data from the PCaP study.

Pictured below (left to right): Dr. Joseph Su, LSU PCaP faculty; Dr. James Mohler, UNC PCaP director UNC Lineberger and Roswell Park Cancer Institute; Dr. Elizabeth Fonham, LSU PCaP director.



results from this study will break new ground and translate into preventing and treating the disease in those at greatest risk for death from prostate cancer," says Naval Captain Melissa Kaime, director of the Army's Congressionally Directed Medical Research Programs.

For PCaP researchers, though, the study has added importance. "Health care inequities shouldn't exist," Fonham asserts. "Regardless of race or ethnicity, income, education or any other societal factor, men with prostate cancer should have an equal likelihood of surviving the disease. Today that is not the case."

Until now, she continues, "No study has offered the opportunity to relate tumor aggressiveness to a comprehensive set of factors, some or all of which may play a role. Our ultimate goal is to understand those causes so that they can be reduced or eliminated." ●

Do You Know What It Means to Miss New Orleans?

Eight months after Hurricane Katrina's rampage scattered much of the New Orleans' population and most of PCaP's participants, an LSU team member received a phone call. It was one of the pre-Katrina study enrollees.

"He started out asking about how the staff weathered the hurricane to make sure we were all doing well," Su recounts. "He told us that he lived in the Lower 9th Ward when the flood water arrived. He broke the roof with an ax and stayed on the roof of his house for hours before he was air-lifted by rescue helicopter to the Superdome. He stayed there for several days before he was transported to Lafayette, Louisiana, and then to the Astrodome in Houston. He stayed at the Astrodome for weeks before he was moved to temporary housing in Houston."

When asked if he was calling in response to the re-contact letter that had been sent to all PCaP participants, his answer was surprising.

"He told us that he picked up the toenail clipper PCaP gave to him for clipping a toenail as a biological sample for the study and saw the 800 number on it," Su says. "He just wanted to talk to someone he could relate to." ●

The study is ground-breaking because until a few years ago, researchers and clinicians didn't know that metabolism made a difference. "We hope this trial leads us to more personalized doses for women," he says. "If they fall into a certain submetabolizing group, we may choose a different dose or a different drug."

The study is the first of many, according to Howard McLeod, PharmD, Fred N. Eshelman Distinguished Professor and director of the UNC Institute for Pharmacogenomics and Individualized Therapy. McLeod initiated the development of the study and will be part of the team interpreting and implementing the results.

DNA information to optimize therapy. "We appreciate the opportunity to help start this important change in medical practice and look forward to working with the patients of North Carolina to make sure that the best care is delivered to all," McLeod says. "With this study, our data will help each patient have a better chance of benefiting from this important therapy."

If you are interested in learning more about this study, please contact Donna Rowe, RN, at 919-966-4432 or Irvin at 919-966-0766. ●