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## How Harold Freeman Navigated the System to take Patient Navigation from Concept to Standard of Care

BY ERIC T. ROSENTHAL

Patient navigation, conceived more than two decades ago to address disparities in access to health care among the poor and uninsured, will soon become a mainstream medical necessity with the American College of Surgeons Commission on Cancer mandate that cancer centers offer such services by 2015 as a condition for accreditation. Still, there are as yet no specific regulations regarding standardized training. This is part one of our look at the history and evolution of the concept to see how—and if—the cancer community is responding to guide patients through an increasingly complex health care system.

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## Higher BRCA1/2 Expression Associated with Exercise in Normal Prostate Tissue

BY RABIYA S. TUMA, PHD

egular vigorous exercise is associated with a reduction in the risk of prostate cancer progression and prostate cancer-specific mortality, according to previously published research. Now, investigators report that there are molecular differences in the prostate tissue in men who exercise regularly compared with those who don't. Specifically, three hours or more of brisk walking per week is associated with increased expression of the tumor suppressor genes BRCA1 and BRCA2 and increased expression of DNA-repair pathways in normal prostate samples from men with low-grade prostate cancer.



"There are many reasons to exercise. Here is another great reason to exercise: It may offer a prostate cancer benefit," said senior author June Chan, ScD, Associate Professor of Epidemiology and Biostatistics and Urology, and the Steven and Christine Burd-Safeway Distinguished Professor at the University of California, San Francisco, who presented the new results here at the Genitourinary Cancers Symposium (*Abstract 189*).

"Understanding the mechanisms by which lifestyle factors influence the



JUNE CHAN, SCD: "Here is another great reason to exercise: It may offer a prostate cancer benefit. Understanding the mechanisms by which lifestyle factors influence the prostate gland supports the development of novel strategies to predict, monitor, or prevent prostate cancer progression."

prostate gland supports the development of novel strategies to predict, monitor, or prevent prostate cancer progression."

"These data are important," said Jeffrey Meyerhardt, MD, MPH, Associate Professor of Medicine at Harvard Medical School and Dana-Farber Cancer Institute, who studies the effects of exercise in colon cancer patients. "We have consistent evidence that exercise can lower the risk of certain cancers, including colorectal, breast, and prostate cancers. This type of study helps to understand what is happening biologically to explain the association."

He said he is aware of very few similar studies in colon cancer, which is his focus. "There was a study by Ann *continued on page 20* 

#### →EXERCISE

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McTiernan's group [at Fred Hutchinson Cancer Center] looking for changes in prostaglandin levels in colon mucosa after exercise in [a randomized controlled trial], but no changes were seen."

#### Broad Approach

In the current study, Chan and colleagues took a broad approach and used microarray analysis to examine the effects of exercise on gene expression in

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The symposium is co-sponsored by the American Society of Clinical Oncology, the American Society for Radiation Oncology, and the Society of Urologic Oncology.

morphologically normal prostate tissue samples from men who had low-risk prostate cancer and were on an active surveillance. All of the men had previously participated in a nutritional supplement trial, during which 70 of them (out of 84 enrolled) had completed a baseline questionnaire that included information on exercise.

Of those, 23 men reported participating in three or more hours of vigorous physical activity per week, defined as walking at a pace of three or more miles per hour whereas 47 reported either less than three hours of activity per week or less vigorous activity. Microarray analysis showed that 184 genes were differentially expressed in the prostate tissue from these two groups.

"Of particular interest, the known tumor-suppressor genes BRCA1 and BRCA2 were upregulated in prostate tissue of men who exercised vigorously versus those who did not," she said in a news conference. "In a pathway analysis, cell cycle and DNA repair pathways were positively regulated in men who were involved in vigorous activity versus those who did less."

However, when the team split the study population a little differently, comparing the men who participated in any vigorous activity with those who reported no vigorous activity, no significant difference was found in gene expression. It appears, therefore, there may be some threshold or duration of vigorous activity that is important for benefit.

"These data are important. We have consistent evidence that exercise can lower the risk of certain cancers, including colorectal, breast, and prostate cancers. This type of study helps to understand what is happening biologically to explain the association." —Jeffrey Meyerhardt, MD, MPH

#### Mechanism?

When asked how exercise might affect gene expression in the prostate, Chan said that it was currently unclear. "It could be a larger systemic effect, or it could be a very localized effect in the normal [prostate] tissue and a field affect protecting the normal cells from adjacent tumor cells."

The team also looked for an association between body mass index (below 25 kg/ $m^2$  versus 25 kg/ $m^2$  or higher) with gene expression, but found no significant differences. Because of the small sample size, they were unable, however, to examine the impact of exercise and weight together on gene expression.

"This is a fascinating study," said the moderator of the news conference, Nicholas J. Vogelzang, MD, Chair and Medical Director of the Developmental Therapeutics Committee of US Oncology, who emphasized that these data are important for clinical practice.

He said that although the new results need to be confirmed in a larger study, he regularly recommends that his patients exercise regularly: "This is something we, as practicing physicians, bring to the clinic every day when we extol the virtues of exercise and cajole our patients to exercise more."