

Potential biological factor contributing to racial disparities in prostate cancer

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Researchers have uncovered a potential biological factor that may contribute to disparities in prostate cancer incidence and mortality between African-American and non-Hispanic white men in the United States, according to results presented here at the Sixth AACR Conference on the Science of Cancer Health Disparities in Racial/Ethnic Minorities and the Medically Underserved, held Dec. 6-9.

In the United States, African-American men are 1.5 times more likely to develop [prostate cancer](#) and more than twice as likely to die from the disease compared with non-Hispanic white men.

"The causes of prostate cancer disparities are numerous, complex, often interrelated, and only partially understood," said David P. Turner, Ph.D., assistant professor in the Department of Pathology and Laboratory Medicine at the Medical University of South Carolina in Charleston.

"We have identified a potential relationship between sugar-derived metabolites and cancer that may provide a biological link with socioeconomic and environmental factors known to contribute to prostate cancer disparities.

"As our bodies use the sugars that we consume for energy they generate waste products, or metabolites, including molecules called advanced glycation end products, or AGEs," Turner explained. "AGEs naturally accumulate in our tissue as we grow older, and they have been implicated in diseases associated with aging such as diabetes, heart disease, and Alzheimer's disease. They can also cause increased

inflammation and the generation of potentially harmful chemicals known as reaction oxygen species, which both promote cancer.

"Critically, a common source of the AGEs that accumulate in our bodies is the foods we eat, which has significant implications for cancer health disparities and our overall health.

"We found that AGE levels were highest in African-American men with prostate cancer," said Turner. "Because obesity, poor eating habits, and an inactive lifestyle all promote AGE accumulation, and these factors are often more evident in African-Americans, we hypothesize that there is a link between these factors that could help explain why African-American men are more likely to develop prostate cancer and die from the disease."

Turner and colleagues examined circulating and intratumoral AGE levels in 16 African-American and 16 non-Hispanic white men with prostate cancer. They found that AGE levels were higher in serum from cancer patients compared with individuals without cancer. When analyzing AGE levels in prostate tumor samples, levels were highest in tumor samples from African-American patients. In addition, AGE levels in [prostate tumors](#) correlated with levels of a molecule to which AGEs bind to mediate their effects, called receptor for AGE (RAGE).

"We think that the AGE-RAGE signaling pathway promotes prostate cancer and that increased AGE accumulation may represent a biological mechanism promoting prostate cancer disparity," said Turner.

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Presenter: David P. Turner, Ph.D.

Title: Advanced glycation end-products are increased in prostate cancer

and may promote racial disparity

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African American cancer patients are more likely to die of their disease than their European counterparts. Our research has identified a potential mechanistic link between carbohydrate derived metabolites and cancer associated pathways which may provide a biological consequence of the socioeconomic and environmental factors that are known to drive cancer health disparity.

Glycation is the non-enzymatic glycosylation of sugar moieties to biological macromolecules such as protein and DNA which produces reactive metabolites known as advanced glycation end products (AGE's). AGE's accumulate in our tissues as we grow older and drive many of the complications associated with diseases displaying health disparity including diabetes, metabolic syndrome, Alzheimer's and heart disease. Low income, obesity and an inactive/sedentary lifestyle are established factors driving cancer health disparity. Apart from their production during normal metabolism, AGE's are also formed through the ingestion of food and by external environmental factors such as lack of exercise. AGE content in the Western Diet has consistently increased over the last 50 years due to increased consumption of sugar laden and cheap processed/manufactured foods which are high in reactive AGE metabolites and can promote obesity.

We therefore examined circulating and intra-tumoral AGE metabolite levels in clinical specimens and identified a race specific, tumor dependent pattern of accumulation in prostate cancer serum and tumor. In mouse xenograft models, AGE accumulation was highest in the more aggressive tumors. One way AGE's mediate their deleterious effects is by functioning as ligand for the trans-membrane receptor for AGE (RAGE). In diabetes and other diseases, the AGE-RAGE signaling axis

is a pro-inflammatory pathway leading to the upregulation of pro-inflammatory cytokines through increased NFκB activation. Higher AGE levels in prostate tumors corresponded with higher RAGE expression and increased NFκB transcriptional activity. In immortalized prostate cancer cell lines AGE treatment increased cancer associated processes and RAGE expression levels. Loss of function studies show that AGE mediated increases in cancer associated processes was dependent upon RAGE expression.

These data implicate the AGE-RAGE signaling axis as a potential biological mechanism promoting prostate cancer and indicate that increased AGE accumulation may represent a biological mechanism promoting prostate cancer disparity.

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