Medical Xpress

New oncogene linked to prostate cancer in African Americans may lead to better diagnostic tools

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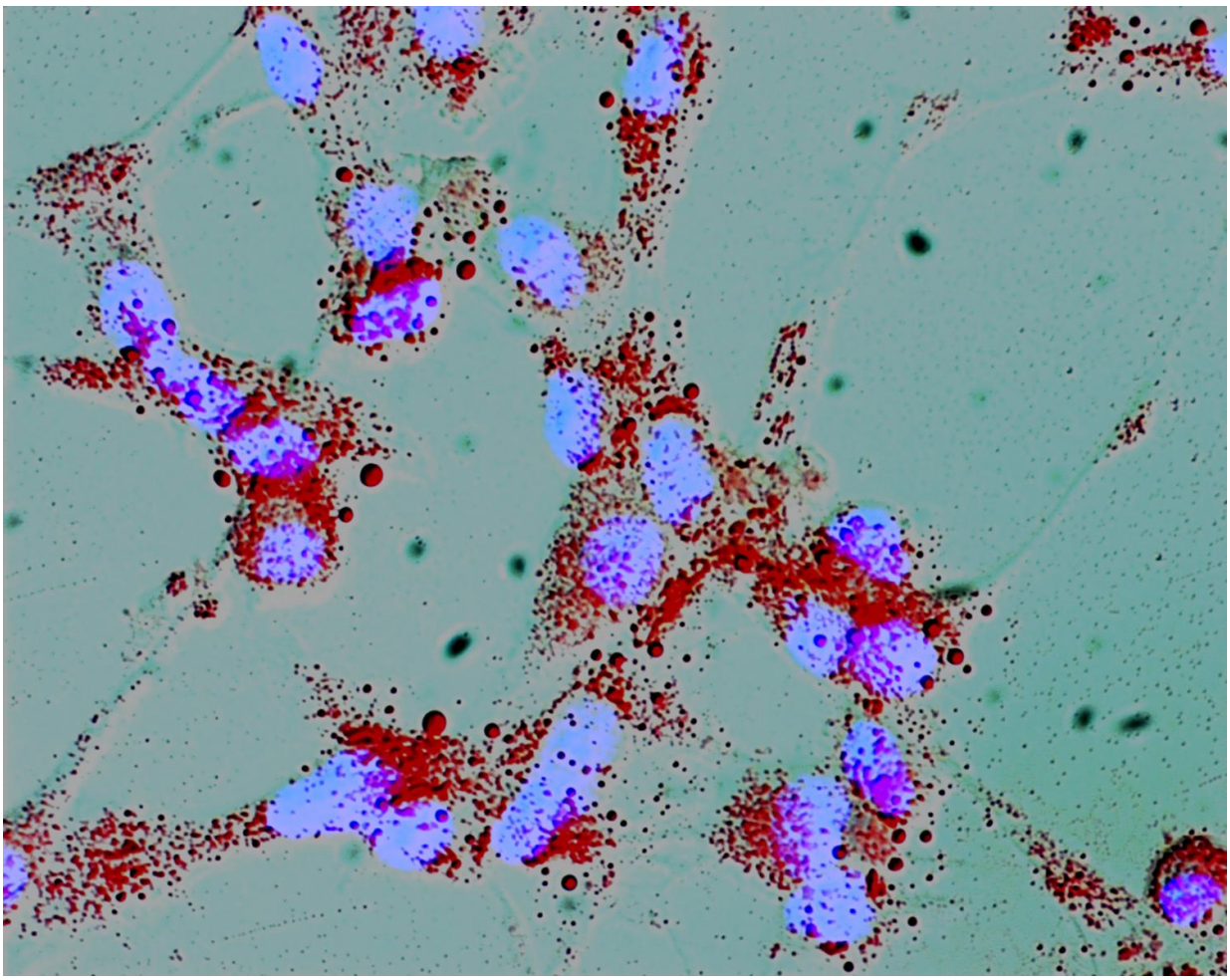

Increased lipogenesis (formation of fatty acids, in red) in prostate cancer cells. Lipids act as important energy storage during the spread of cancer. Therapies that disrupt lipogenesis or inhibit oncoproteins that enhance fatty acid

biosynthesis could potentially block tumor metastasis. Nucleus of the cell is stained blue. Credit: National Cancer Institute / Duncan Comprehensive Cancer Center at Baylor College of Medicine / Subhamoy Dasgupta.

A team of scientists has identified MNX1 as a new oncogene - a gene than can cause cancer - that is more active in African American prostate cancer than in European American prostate cancer. The finding suggests that genetic factors can contribute, at last in part, to the higher incidence of prostate cancer among African American men compared with men of other ethnic groups. The team includes scientists at Baylor College of Medicine, Third Military Medical University in China, the Michael E. DeBakey VA Medical Center, and Agilent Technologies India Pvt. Ltd. The study appeared Aug. 31 in *Cancer Research*.

"African Americans have about one-and-a-half times the incidence and twice the mortality associated with prostate cancer of European Americans, and the reasons for this are not clear," said senior author Dr. Michael Ittmann, professor of pathology & immunology at Baylor and the Michael E. DeBakey Department of VA Medical Center.

Most scientists think that some of the health disparities among ethnic groups can be explained by differences in biology. Socio-economic factors, such as unequal access to healthcare services that make African American men less likely to receive regular physical examinations and screening for prostate cancer, may also be involved.

To study the genetic differences between African American prostate cancer and European American prostate cancer, the scientists took advantage of the tremendously diverse resources available at the Dan L Duncan Comprehensive Cancer Center at Baylor, which include one of the most extensive African American prostate tissue banks.

"We determined the gene expression profiling of African American prostate cancers," said Ittmann, "and compared it with that of normal prostate tissue. Then, in collaboration with Dr. Chad Creighton, associate professor of medicine at Baylor and member of the Dan L Duncan Comprehensive Cancer Center Division of Biostatistics, we compared the gene expression profiling of African American prostate cancers with that of European American prostate cancers, which is available in published datasets."

"We found 24 genes that were different between the African American and the European American prostate cancer datasets," said Ittmann. "Some of the genes were less active in African American prostate cancer, but we concentrated on those that were more active as they could potentially be oncogenes. MNX1 was at the top of the list."

MNX1 had been previously described as an oncogene linked to infantile acute myeloid leukemia, a rare cancer of the bone marrow and lymph nodes.

"Our study so far suggested that MNX1 was likely an oncogene in prostate cancer. The protein the MNX1 gene produces is a transcription factor; it can turn on gene transcription in other genes, which results in those genes producing more of their proteins. So we went on and studied MNX1 more extensively," said Ittmann.

The scientists discovered that, compared with normal prostate tissues, both African American and European American prostate cancer have MNX1 genes that are more active and produce more of the MNX1 protein. However, MNX1 is significantly more active in African American prostate cancer than in European American prostate cancer.

Further research shed light on what can increase MNX1 activity in prostate cancer and strengthened MNX1's ties to the disease.

"Interestingly, we found that both androgens, such as testosterone, and AKT, a signaling pathway, increase MNX1 activity. It's been known for quite some time that androgens and the AKT pathway play a central role in prostate cancer," said Ittmann.

The scientists then determined whether increased MNX1 activity affected a metabolic pathway prostate cancer uses to grow. Dr. Arun Sreekumar, professor of molecular and cellular biology, who also is with the Alkek Center for Molecular Discovery and the Verna and Marrs McLean department of biochemistry and molecular biology at Baylor, performed lipid analysis in African American prostate cancer tissues and showed that products of lipid metabolism increased when compared with those of normal prostate tissues.

"I am excited that these data highlight the existence of a biological basis in health disparity in prostate cancer," said Sreekumar.

In summary, in African American prostate cancer androgen and the AKT signaling pathway can increase the activity of MNX1, which in turn increases lipid metabolism. Increased lipid metabolism is a hallmark of aggressive prostate cancer, which is more common on African American men.

These results can potentially lead to new approaches to treat and diagnose prostate cancer. For instance, currently, there are medications available to control lipid synthesis, which allows for exploring the effect of targeting lipid synthesis on prostate cancer growth. The scientists will also explore whether MNX1 can help predict cases of aggressive prostate cancer in the clinic.

"The better we can understand different subsets of prostate cancer, for instance, prostate cancer from African American men, the better we can treat them. A "one-size-fits-all" approach to treatment may not work for

all patients," said Creighton.

More information: L. Zhang et al, MNX1 Is Oncogenically Upregulated in African-American Prostate Cancer, *Cancer Research* (2016). DOI: 10.1158/0008-5472.CAN-16-0087

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