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International Conference on
Prostate Cancer

June 22-24, 2015   Florida, USA

Somatic MLL3 mutations associated with aggressive prostate cancer in African Americans

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Incidence of Prostate Cancer (PCa) is higher in African Americans than any other race. African-American men are more frequently diagnosed with high grade tumors resulting in greater mortality than other races. The contribution of genetic factors to the aggressiveness of PCa in African Americans is largely unknown. We hypothesize that exome sequencing of African-American prostate tumors and matched blood samples may reveal unique mutations that contribute to the aggressiveness of PCa in African Americans. In this study, we performed exome sequencing on nine aggressive-phenotype prostate tumors as well as the blood samples from the corresponding African-American patients in order to identify somatic mutations associated with aggressive PCa. Bioinformatics analysis was then performed to identify novel putative somatic mutations. Mutation frequency in the nine samples was compared to the reported mutation frequency in Caucasians in order to select those mutations unique to African Americans. A total of seventy-four genes containing recurrent, novel somatic mutations were identified. MLL3 somatic mutations identified in African-American PCa samples have a higher frequency (2/9) than in Caucasian PCa (2/112). As a result, the mutations within the MLL3 gene were selected for validation through Sanger sequencing, confirming the presence of these mutations in the original samples. While large sample set validation of these results is still required, exome sequencing technology has the potential to identify somatic mutations unique to aggressive AA PCa which may provide the basis for improved prognostic tests and personalized treatment options, ultimately reducing the disparity.

Biography

Brian J Burkett is currently an MD/MPH student at Tulane University with an MPH concentration in epidemiology. Prior to Medical School, he completed a MS in neuroscience at Tulane and a BM in flute performance at Baldwin-Wallace Conservatory. He is a DeBakey Research Scholar at Tulane and was awarded First Place Overall in the Stanley S Scott Cancer Center Short-Term Research Experiences in Cancer 2014 poster competition.

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Notes:

J Cancer Sci Ther
ISSN: 1948-5956 JCST, an open access journal

Prostate Cancer-2015
June 22-24, 2015

Volume 7, Issue 5

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