Race-related *LMO7* exon skipping enhances prostate tumor invasion

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Background, Methods, Results, Conclusions:
Prostate cancer (PCa) affects disproportionally African American (AA) men in comparison with white or Asian men. According to the Surveillance, Epidemiology, and End Results Program (SEER), the mortality from PCa in black men is 2-5 times higher than in white or Asian men. In addition to differences in social determinants of health, differences in biological mechanisms contribute to the PCa disparity. We reported previously results from a comparative analysis of the transcriptomes of PCa specimens from 20 AA and 15 white patients, identifying 1,188 differentially expressed genes. In addition to the race-related aggregate gene expression differences, we also identified 2,520 differential RNA splicing events between these tumor specimens from AA and white patients. Among the 2,520 events, we prioritized 25 events, which had also been reported by Tsai et. al., 2015 to be differentially expressed between tumor and normal breast, lung and liver samples in The Cancer Genome Atlas (TCGA). To elucidate the function of these 25 events, we used Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR)-CRISPR associated protein 9 (Cas9) methodology to generate PCa cells expressing each of the race-related alternative RNA splice variants. To date, we have generated DU145 PCa cells that express the following exon skipping events: *LIM Domain 7 (LMO7) exon 12*, *Integrin Subunit Alpha 6 (ITGA6) exon 27* and *Actin Binding LIM Protein Family Member 3 (ABLIM3) exon 14*. The genotype of these cells was confirmed by PCR. Preliminary proliferation analysis demonstrated that skipping of *ITGA6 exon 27* slowed doubling time of the cells compared with the parental cells. Interestingly, the cells expressing the *LMO7 exon 12* skip appear more mesenchymal-like. Preliminary invasion analysis suggests that *LMO7 exon 12* skipping increases (~ 4 times) the ability of the cells to pass through a Matrigel matrix, suggesting an increased invasive and metastatic potential of these cells. In conclusion, we have identified race-related RNA splicing events in PCa that function in processes relevant to oncogenesis. Further analysis of the biological significance of these race-related RNA splicing events *in vitro* and *in vivo* is underway. Our approach to analyze RNA splicing in the context of PCa disparity has the potential to uncover novel biological mechanisms underlying this disparity and to discover novel therapeutic targets.

Conflict of Interest: NONE

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