

Reply to "Contextualizing Racial Associations in Prostate Cancer to Expose Structural Causes"

Dev Karan, PhD^{1*}, Jo Wick, PhD², Seema Dubey, PhD¹, Chandan Kumar-Sinha, PhD³, Javed Siddiqui, MS³, Lakshmi P. Kunju, MD³, Kenneth A. Iczkowski, MD¹, Arul M. Chinnaiyan, MD, PhD³

¹Department of Pathology, MCW Cancer Center and Prostate Cancer Center of Excellence, Medical College of Wisconsin, 8701 Watertown Plank Road, Milwaukee, WI 53226, USA.

²Department of Biostatistics and Data Science, University of Kansas Medical Center, Kansas City, KS 66160, USA.

³Michigan Center for Translational Pathology, Department of Pathology, University of Michigan, Ann Arbor, Michigan 48109, USA.

*Correspondence to:

Dev Karan, Ph.D.

Department of Pathology

MCW Cancer Center

Medical College of Wisconsin

8701 Watertown Plank Road

Milwaukee, WI 53226

Tel: 414-955-5744

Email: dkaran@mcw.edu

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We thank Rollin et al. for their interest in our study and for highlighting the need for more nuance in describing implied genetic differences along racial lines that are arguably primarily a social construct. We also agree on using the term 'White' instead of 'Caucasian' as advocated by Rollin et al.

However, our study noted significant differences in the chemokines profile of CXCL2, CXCL5, and CCL23 across African American (AA) compared to White samples- with no direct or implied association with underlying drivers of this difference. As noted in our paper, the genetic and/or environmental associations of chemokine profiles in AA versus White prostate cancer patients have been described previously. As some of our notable observations track with previous reports, we have expressed our inferences along these lines as well.

We agree that numerous racial differences that have been described between AA and Whites concerning prostate cancer (and other cancers) may be highly influenced by socioeconomic factors and environmental exposures similar to the association of allostatic load with several other metrics of health and disease. However, a notable body of peer-reviewed literature also points to genetically based differences between self-identified racial groups underlying certain health and disease predispositions, including studies specifically in prostate cancer¹⁻³. Our findings, however, are descriptive in nature, and we do not provide mechanistic data as to whether these differences are due to genetic, racial, or socioeconomic aspects.

In order not to draw inferences beyond what our data affords, we discussed whether the increased levels of CXCL2 and CXCL5 in AA subjects is a consequence of genetics (genetics of race) or the environment, including diet and lifestyle (a part of structural racism), keeping in view that AAs are a heterogeneous group of people with varying life experiences and social and environmental exposures. We agree that a direct role of Duffy antigen receptor for chemokines (DARC) is not linked with prostate cancer; however, an increased level of CXCL2 and CXCL5 has been studied in cancer progression and metastasis. While the literature established the role of DARC, a protein that specifically binds to CXC chemokines, including CXCL5, an association of an increase in serum CXCL5 chemokine due to the loss of DARC could be viewed as a causative effect but not as a direct consequence of racial genetics. We acknowledge that a larger cohort of patients needs to be analyzed to establish if increased levels of CXCL2 and CXCL5 in AA subjects is a consequence of racial genetics (White vs AA) or structural barriers in AA men. Nonetheless, increased serum levels of CXCL2 and CXCL5 in AA subjects, irrespective of cancer, indicated the

association with race (could be racial genetics or associated with prostate cancer disparity based on structural racism). On the contrary, chemokine CCL23 could account for structural racism as we observed both race and cancer-specific differences. Overall, even as our study accurately reports noted “racial differences in serum chemokines in prostate cancer patients,” it does not purport to resolve the question of the underlying cause, whether genetic or environmental or perhaps a combination of these factors.

References

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