Reply to Ashktorab et al.: Mutational landscape of colon cancers in African Americans

We are pleased to read the letter by Ashktorab et al. (1). We agree with Ashktorab et al. on the need for additional whole-exome sequencing of colon cancers arising in African Americans and on the value of continuing to add more cases to the numbers of African American colon cancers that have been characterized. The additional 11 African American colon cancers reported by Ashktorab et al. will be a helpful addition in this regard (2). We agree with Ashktorab et al. that the absence of mutations in EPH receptor A6 (*EPHA6*) and Folliculin (*FLCN*) from the 11 microsatellite-stable (MSS) samples they studied is not surprising, given that less than one mutation in either of these genes would be expected. In the interest of clarity, we point out that neither *APC* nor Kirsten rat sarcoma viral oncogene homolog (*KRAS*) were included in the list of new genes our study identified as significantly mutated in African American colon cancers (3). However, both our study (ref. 3, table S14) and studies by others (4) all detected a higher rate of *KRAS* mutations in colon cancers from African Americans compared with Caucasians. We also agree with Ashktorab et al. that WD repeat domain 87 (*WDR87*) is significantly mutated in colon cancers arising in African Americans, although our study found that *WDR87* is also a target for mutations in colon cancers arising among Caucasians, and thus it is not in the top 15 genes whose mutations we found are highly associated with colon cancers arising in African Americans (3). We join Ashktorab et al. in hoping that the initial findings reported in PNAS will spur larger efforts in studies of ethnicity-associated differences in the mutational landscapes of colon and other cancers, as well as studies aimed at elucidating the underlying biological mechanisms by which these differences arise.

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1 Ashktorab H, et al. (2015) Next-generation sequencing in African Americans with colorectal cancer. *Proc Natl Acad Sci USA* 112:E2852.

2 Ashktorab H, et al. (2015) Identification of novel mutations by exome sequencing in African American colorectal cancer patients. *Cancer* 121(1):34–42.

3 Guda K, et al. (2015) Novel recurrently mutated genes in African American colon cancers. *Proc Natl Acad Sci USA* 112(4):1149–1154.

4 Sylvester BE, et al. (2012) Molecular analysis of colorectal tumors within a diverse patient cohort at a single institution. *Clin Cancer Res* 18(2):350–359.

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The authors declare no conflict of interest.

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