Differences in the immune tumor microenvironment in association with individual self-reported race in multiple myeloma

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Multiple myeloma (MM) is an incurable cancer of plasma cells, a type of differentiated B-cell, and represents the most common blood cancer in African American (AA) individuals. The age-adjusted prevalence and incidence of MGUS (the pre-malignant condition prior to the onset of MM) and MM is ~2-3-fold higher among AA individuals compared to non-Hispanic White (NHW) individuals. Emerging evidence implicates a central role for the immune tumor microenvironment (iTME) in MM immune surveillance and disease pathogenesis. However, no studies to date have examined the iTME composition in AA patients with MM. Given the increased risk of MM among AA individuals, we evaluated the composition of the iTME in AA patients with MGUS/SMM and MM.

The iTME was characterized in 94 viably frozen whole bone marrow (BM) aspirates obtained from 39 AA and 55 NHW individuals. Of the 39 BM samples from AA individuals, 23 had MM, 2 had SMM, 6 had MGUS and 8 did not have a PC malignancy. Of the 55 BM samples from NHW individuals, 32 had MM, 3 had SMM, 6 had MGUS and 14 did not have a PC malignancy. The frozen specimens were stained using the Maxper Direct Immune Profiling Assay Kit (Fluidigm) acquired with a Helios mass cytometer. A total of 22 immune cell populations were analyzed by the Cytobank software. An unpaired Student's t-test/Mann-Whitney U test was used to compare two independent groups. All tests were two-tailed and $p<0.05$ was considered significant.

In relation to the $CD45^{+}CD66b^{-}$ lymphocyte population, we observed a similar distribution of the 22 immune populations between healthy AA and NHW individuals and also between AA and NHW individuals with MGUS suggesting significant differences of the BM were not evident prior to MM disease. In contrast, significant increases in total T cell populations (AA 52.3% vs. NHW 37.9%, $p<0.001$) including increases in CD8+ (AA 9.6% vs. NHW 5.2%, $p<0.05$) and CD4+ terminal effector T cells (AA 5.9% vs. NHW 2.5%, $p<0.05$) and senescent like CD28-CD57+ terminal effector T cells were identified in AA patients with MM. After adjusting for patient age and sex, AA patients with MM retained an overall increase in total T cells (OR 1.59 (95%CI 1.2-2.01, $p=0.00023$). This was accompanied by a reduction in total monocytes (OR 0.88 (95%CI 0.78-1, $p=0.045$). Future studies will coorelate these results to scRNA seq data and determine whether the increased senescent T cell populations in AA patients with MM contribute to reduced tumor surveillance contributing to increased risk of MM.