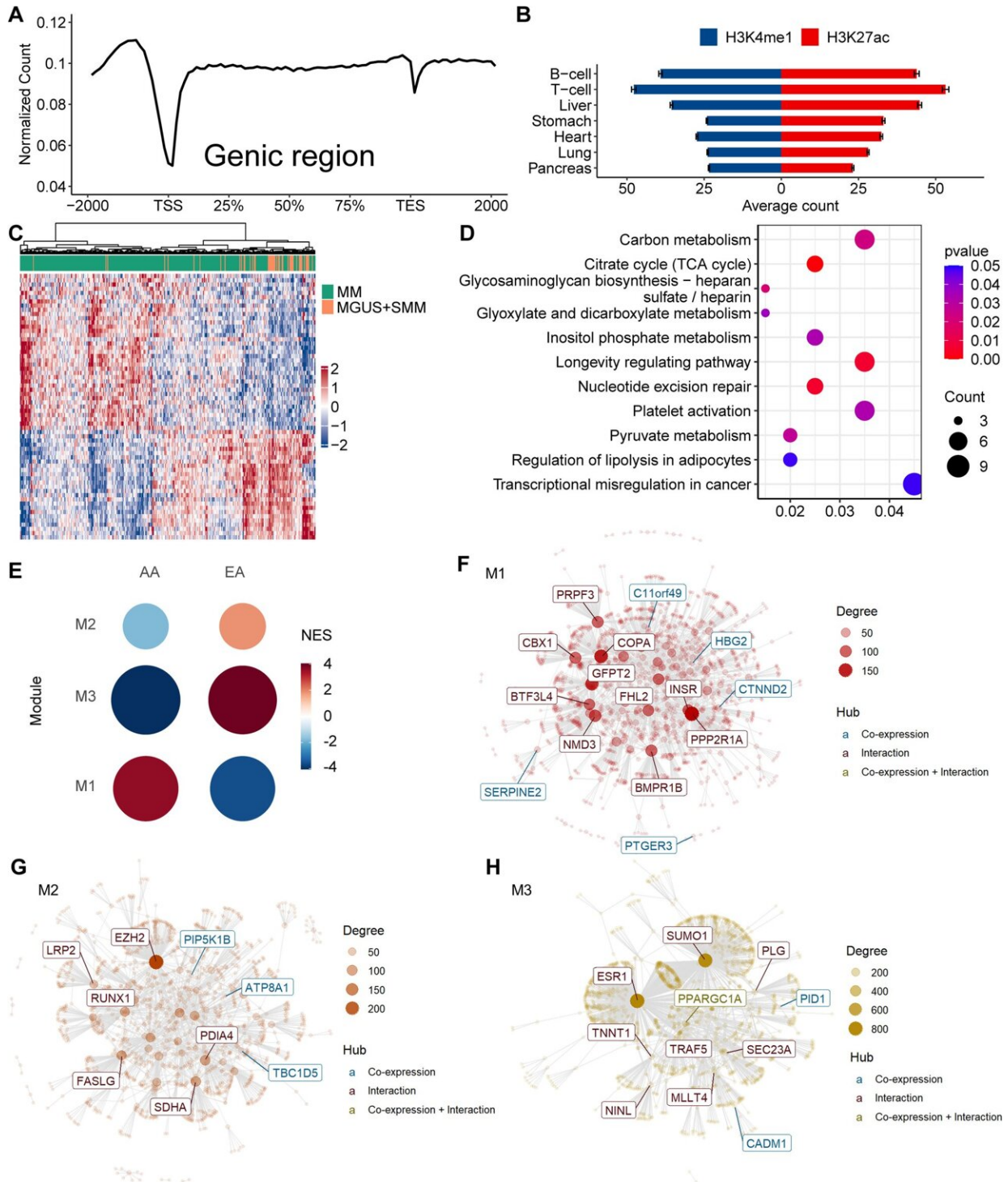


Investigating racial differences in multiple myeloma

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Genome-wide profiling of 5hmC from cfDNA derived from EA and AA patients with MM and its precursors. Genome-wide 5hmC was profiled in patient-derived plasma cfDNA samples using the 5hmC-Seal and the next-generation sequencing. The 5hmC-Seal data summarized for gene bodies were

the primary targets for differential analysis between MM and its precursors (MGUS + SMM, i.e., MGUS and SMM combined) in all samples, using multivariable logistic regression models, controlling for age, sex, and self-reported race/population. In addition, we performed differential analysis between EA and AA patients with MM only. A The captured 5hmC-Seal reads in cfDNA are more abundant in gene bodies relative to the flanking regions and depleted at the promoter regions, based on the GENCODE annotations (hg19). TSS: transcription start site; TES: transcription end site. B The captured 5hmC-Seal reads are enriched in histone modifications marking enhancers (H3K4me1 and H3K27ac) derived from B-cells and T-cells compared with other tissue types. The annotations for H3K4me1 and H3K27ac were obtained from the Roadmap Epigenomics Project. The standard error is shown as the error bar. C The heat map shows the top 63 differential gene bodies between MM and its precursors in the combined EA and AA patients. D Shown are the enriched KEGG pathways among the top 500 differential gene bodies between MM and its precursors in the combined EA and AA samples. The X-axis represents the ratio between the number of differential genes and the total genes in a given pathway. E The Co-expression Network Enrichment Analysis was performed for differential gene bodies between EA and AA to provide further biological insights. Specifically, three modules (Module 1: 254 genes; Module 2: 156 genes; and Module 3: 75 genes) are shown from the modular gene co-expression analysis using the top 500 differential gene bodies between AA and EA patients with MM as the input. NES: normalized enrichment score. F–H Shown are the protein–protein interaction networks constructed for the co-expression and/or interaction modules identified from differential gene bodies between EA and AA patients with MM. Credit: *Journal of Hematology & Oncology* (2022). DOI: 10.1186/s13045-022-01327-y

Investigators have identified distinct epigenetic pathways in African American and European American patients diagnosed with multiple myeloma, according to a Northwestern Medicine study published in the *Journal of Hematology & Oncology*.

The findings improve the understanding of epigenetic mechanisms

underlying disparities in disease diagnosis and reveal potential therapeutic targets.

"We could utilize these population-specific epigenetic modifications to better diagnose in those patients or prevent multiple [myeloma](#) in a population-specific way," said Wei Zhang, Ph.D., professor of preventive medicine in the Division of Cancer Epidemiology and Prevention and senior author of the study.

Multiple myeloma (MM) occurs when cancerous white blood [cells](#), specifically plasma cells, accumulate in bone marrow. Plasma cells are key for proper immune response, but in MM, cancerous [plasma cells](#) overtake normal blood-forming cells, leading to low blood counts.

Diagnosis of MM is rare, however previous work has found that the disease is two to three times more likely to be diagnosed in African Americans than in European Americans. While risk factors such as socioeconomic factors and obesity can contribute to the different rates of diagnoses in this patient population, they don't fully explain the increased risk, according to Zhang.

"Multiple myeloma is very different, because so far, clinically or epidemiologically and based on known [risk factors](#), we really don't have the ability to distinguish patients with a higher or lower risk in our [general population](#)," Zhang said.

The team aimed to identify modifications in 5-hydroxymethylcytosines (5hmC), a known epigenetic biomarker of cancers that had yet to be investigated in the context of MM.

In the study, the investigators used 5hmC-Seal, a chemical-labeling based technique which captures epigenetic modifications in fragments of DNA, and next-generation genome sequencing to profile DNA samples

from 342 patients with MM and high-risk conditions—227 European American and 115 African American patients.

Of the identified top-ranking 500 genes with different 5hmC levels, the investigators found that 95 percent contained population-specific cellular pathways. Specifically, amino acid metabolism pathways were more prevalent in African American patients and cancer-related signaling pathways were more prevalent in European American patients.

"We identified population-specific 5hmC related pathways between multiple myeloma patients and those with high-risk conditions, meaning there appears to be some population-specific biological [pathway](#) that leads to this disease in these patients," Zhang said.

According to Zhang, next steps include determining whether these population-specific [epigenetic modifications](#) contribute to different patient survival rates.

"If we observe that population-specific 5hmC is related to differential patient survival, then we could actually utilize 5hmC as a novel biomarker that can help us monitor treatment response and detect patients with minimal residual disease in a population-specific way," Zhang said.

More information: Brian C.-H. Chiu et al, Genome-wide profiling of 5-hydroxymethylcytosines in circulating cell-free DNA reveals population-specific pathways in the development of multiple myeloma, *Journal of Hematology & Oncology* (2022). [DOI: 10.1186/s13045-022-01327-y](https://doi.org/10.1186/s13045-022-01327-y)

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