Considering Ancestry: Biomaterial Model Systems of Health Disparity

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Statement of Purpose: Biomaterial platforms, intended to be used in the investigation of human health and disease, often incorporate cells of unknown ancestry or that lack diversity. To develop tools and platforms that benefit the entire human population, we must consider the ancestry of cells and intentionally diversify the cells we use in our designs. First, we conducted a review of the literature to understand how ancestry of cells is considered in biomaterial model systems. We surveyed articles published during a six-month period between July 1st through December 31, 2019. We investigated the following journals: ACS Biomaterials Science and Engineering, Advanced Healthcare Materials, Frontiers of Bioengineering Biotechnology, Journal of Biomedical Materials, Journal of Translational Medicine, Lab on Chip, Nature Biotechnology, Nature Biomedical Engineering, Science Translational Medicine, and Scientific Reports. This timeframe provides a glimpse of current practices without the risk of confounding effects from the disruptions in research practice caused by the COVID-19 pandemic.

Second, using biomaterials, my group investigates the contribution of ancestry to cellular function in disease pathology. We work to assess ancestral contribution to systemic lupus erythematosus (SLE). SLE is an autoimmune disease that causes chronic inflammation, tissue damage and often cardiovascular diseases (CVD) in the form of vasculitis. SLE is a health disparity; women and women of color are the dominate population suffering from SLE. A recent data review stating that among prevalent cases in the two Georgia counties studied, 89.9% of patients were female and 76.7% were of African ancestry [1]. Women of African ancestry with SLE also experience higher mortality rates than women of European ancestry with SLE [2]. The source of susceptibility to SLE based on ancestry is less well understood. To identify the distribution and activity of monocyte immune cells in propagating vasculitis in SLE, we have designed a biomaterial model system to interrogate the interactions between monocytes and microvessels to mimic small vessel vasculitis that occurs in SLE.

Methods: *Cell Sources:* Under UF IRB approval, we characterize peripheral monocytes from four distinct groups of female donors: women of African ancestry with SLE (AA SLE), women of African ancestry healthy controls (AA HC), women of European ancestry with SLE (AE SLE) and women of European ancestry healthy controls (AE HC). *3D Culture:* Cells were encapsulated inside of the 3D PEG hydrogel and cultured for 7 days in 3D before analysis. Human dermal microvascular cells are co-cultured with each patients' monocytes. *Enzyme-Linked Immunosorbent Assay (ELISA):* ELISA was be used to quantify common inflammatory soluble factors in the system *Gene Expression:* To assess EC inflammation, we conducted NanoString gene expression analysis for genetic pathways associated with cytokine signaling, endothelial cell function, and nitric oxide synthase.

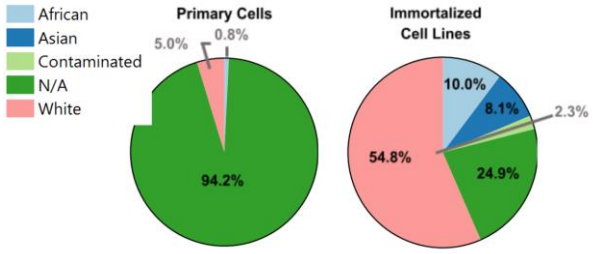

Figure 1: Ancestral background reporting in primary or immortalized cells in Biomaterial journals from 7/1/19-12/31/20.

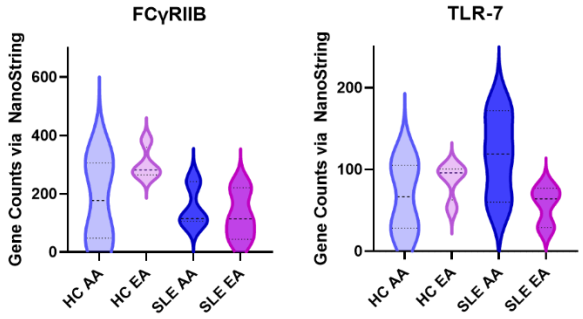

Figure 2: Ancestry influences gene expression of FCγRIIB and TLR7 in PBMCs isolated from Healthy Controls (HCs) African and European ancestry. SLE, an autoimmune disease, also influences gene expression by ancestry. AA= African Ancestry; EA= European Ancestry.

Results: Following our analysis, we found that under 6% of primary cells used in the articles had information on race or ancestry, while about 78% of the cell lines investigated had a known race (**Fig. 1**). Among both primary cells and cell lines, the vast majority of cells with reported race were from white donors. This initial work highlights the major limitations in the field of biomaterials in considering alternative ancestries in our model systems. To represent the entire spectrum of human health, we believe the ancestry of cells should be carefully considered during the design stage of the work. The genetic and epigenetic differences between cells of different ancestral backgrounds should be recognized as instrumental players in the cells' responses to stimuli, and so should no longer be casually ignored.

From our work profiling differences in ancestry for SLE, we assessed the contribution of self-identified ancestry to PMBCs in systemic lupus erythematosus (SLE) and found differences with respect to ancestry and disease pathology (**Fig. 2**). Specifically, we found alterations in Fc receptor RIIB and toll-like receptor 7 (TLR7) gene expression in an ancestry-dependent manner.

Conclusions: Diseases disproportionately impact certain populations of our world. We must use biomaterials to address health disparities.

References: [1] Lim, S. S. Morb. Mortal. Wkly. Rep. 68, 419–422 (2019). [2] Pons-Estel, G. J. Seminars in Arthritis and Rheumatism 39, 257–268 (2010).