Abstract Title: Circulating class-switched antibody-secreting cells are enriched among MS patients self-reporting 'Black African', or 'Latin American/Hispanic' ethnicity relative to those reporting 'Caucasian' ethnicity

Main/Submitting author: Kiel M Telesford, PhD (Birth date: 01/03/1985)

Co-authors: Ulrike W. Kaunzner, MD, PhD ; Jai Perumal, MD; Susan A. Gauthier, DO MPH; Xian Wu, MPH; Ivan Diaz, PhD; Mason Kruse-Hoyer, MD; Casey Engel; Melanie Marcille ; Tim Vartanian, MD, PhD

Ethnicity-associated clinical disparity in MS is well documented. In the United States, MS patients self-reporting with 'Black African', or 'Latin American/Hispanic' ethnicities are more likely to experience a severe disease course relative to MS patients self-reporting 'Caucasian/European' ethnicity. Socioeconomic status influences but does not appear to completely account for this difference. Despite numerous reports corroborating these trends over the past 16 years, there are no published studies (to our knowledge) that directly investigate underlying immunobiology between these patient populations.

Retrospective chart review demonstrates heightened intrathecal IgG among African American MS patients relative to Caucasian patients. This observation, alongside the established role for B cells in MS pathogenesis, led us to quantify the relative burden of antibody-secreting cells (ASCs) in MS patients across different ethnic group cohorts. For this prospective, cross-sectional study we recruited 74 subjects with relapsing remitting MS, and 24 age-, and self-reported ethnicity-matched healthy donors to provide peripheral blood study samples. At the time of the study draw, MS subjects were either on Natalizumab infusion or off of disease modifying therapy. Using flow cytometry we analyzed blood samples for circulating ASC subsets.

Stratifying subjects according to self-reported ethnicity revealed a pronounced ASC differential. Our cohort comprising subjects identifying with 'Black African' or 'Latin American/Hispanic' ethnicity categories exhibited significantly elevated plasmablast levels relative to our cohort identifying with 'Caucasian/European' identity. These plasmablasts comprised both $CD138^{+}$ and $CD138^{-}$ populations. While the plasmablasts were predominantly class-switched, we also observed elevated frequencies of IgM^{+} populations. Notably, the ethnicity-associated differential was not observed among our healthy donor subjects, which lacked an MS diagnosis.

The enhanced plasmablast signature observed among MS patients of 'Black African' or 'Latin American/Hispanic' ethnicities suggest distinct underlying mechanisms implicated with MS immunopathogenesis. Such dysregulation may contribute to the severity disparity attributed to patient populations identifying with particular ethnic groups.