Epidemiologic studies of SLE performed as early as the 1960s have noted that SLE is not only more common, but also more severe among ethnic minority populations. Subsequent studies have generated vigorous debate over the extent to which genetic, environmental or other factors account for these differences. However, most epidemiologic studies of ethnicity and SLE treat ethnic groups as homogeneous categories, thus obliterating the genetic, cultural, and socioeconomic diversity that exists within groups that could contribute to the observed differences. Using genetic ancestry rather than self-identified ethnicity provides some advantages when investigating ethnicity, genetics, and disease characteristics. This approach does not assume that racial or ethnic groups are homogeneous but rather capitalizes on genetic heterogeneity within groups to more effectively dissect the relationship between ethnicity, genetics, and disease risk. This project is designed to extend our genetic epidemiologic investigations of ancestry and SLE disease characteristics and takes advantage of a novel tool, the “ImmunoChip”. This unique genotyping array is comprised of ~200,000 genetic markers which were selected to provide detailed coverage of recently identified autoimmunity gene loci, and are also informative for comprehensive genetic ancestry. The project benefits from an extensive collaborative network, which has supported characterization of the UCSF Lupus Outcome Study (LOS) participants, and other SLE cohorts, for the ImmunoChip genetic marker set. The availability of SES and other covariate information on LOS participants allows us to control for these potentially important factors in our analyses. More specifically, we have the following aims: 1) characterize the relationship between genetic ancestry, including both continental and intra-continental ancestry, and SLE disease characteristics, including age at SLE diagnosis, renal disease, anti-dsDNA autoantibody production, and cumulative damage; and 2) determine whether recently identified genetic loci emerging from genome wide association and other genetic studies are risk factors for specific SLE manifestations. For gene variants associated with specific SLE manifestations, we are characterizing the extent to which these variants explain ancestry associations demonstrated in Aim 1. This project advances the field by elucidating more proximate factors that influence ethnic disparities in SLE, and our focus on health disparities synergizes well with the overall theme of our MCRC.