Making the Right Matches: *Exploring Intersections among genetic ancestry, self-reported race and origin, and HLA haplotypes of prospective transplant donors*

Aliya Saperstein, Stanford University
Jill Hollenbach, Children's Hospital of Oakland Research Institute

This project is an attempt to unite expertise in population genetics and the social demography of race and ethnicity to solve the practical problem of how to match potential donors and recipients through the National Marrow Donor Program (NMDP).
It draws on unique data from a pilot study of more than 1,700 individuals currently represented in the U.S. donor registry who completed a questionnaire about their racial, ethnic and perceived ancestral origins, and also submitted a buccal swab for genetic analysis. We compare the information provided by several different methods of measuring and conceptualizing racial ancestry to one another, and then ask which measures (alone or in combination) are most closely associated with the markers used to make transplants matches from members of the registry. The gold---standard of bone marrow transplant matching aims for matches on at least six loci of the human leukocyte antigen (HLA) genes. Finding such matches requires high-resolution typing of potential donors, but the current cost is prohibitive for typing all 11 million members of the U.S. registry. Instead, NMDP relies on an algorithm to predict which low---resolution HLA types are likely to make the best matches for a given recipient. This algorithm, in turn, relies on information based on the donors' self---reported race/ethnicity from their recruitment form. Social scientists have repeatedly expressed concerns about claims that self---reported race is a good predictor of genetic difference, but some research and clinical practice continues to assume that self---identified race has medical relevance as a proxy for biological processes or genetic markers. Rather than debate the appropriateness of this decision in the abstract, we take the practices already in place at NMDP as our starting point and aim to examine the degree to which one's self---reported race/ethnicity, using categories approved by the Office of Management and Budget for federal data collection, is associated with the presence of "mixed" or otherwise rare HLA types (as they are represented in the current registry), and whether it performs better as a predictor of such types than other possible measures of origin or ancestry, both self---reported and assessed through genetic typing using ancestry---informative markers (AIMs). These question forces social science researchers to confront a life---threatening circumstance in which it is already widely believed that one's racial or ancestral origin affect one's ability to find a transplant match. Indeed, the push to prioritize matching by race/ethnicity – at least in the case of bone marrow transplants – is promoted by many patients and their families. Mixed race groups have organized recruitment campaigns and attempt to raise awareness about how people of non---European ancestries are underrepresented in the registry. Although non---racialized approaches to making matches might be ideal, they are currently cost prohibitive, and arguments at the level of social science theory about the "social construction" of race/ethnicity, are unlikely to resonate either with the medical researchers seeking to optimize registry searches or the people who are in desperate need of its services. At the same time, urgent medical necessity should not prohibit more measured evaluation of the assumptions that justify current clinical practice. Making better matches should be the goal of everyone involved in the transplant process. We illustrate

the potential of this data and our approach by appending a short paper currently under review.

We plan to complete additional analyses in advance of the October conference that explore the intersections of self---reported and genetic ancestry markers for donors with particularly rare HLA types. In future analyses, we also intend to utilize the estimated probability of having a given "racial" HLA type rather than simply the ultimate classification that assigns every donor either an "African," a "European," an "Asian" or an "Amerindian" haplotype. This will help to avoid some of the tautological reasoning involved in clustering the AIMs using a count consistent with broad continental groups, or otherwise relying on prior distributions that assume current typologies used to describe racial/ethnic diversity in the U.S. are also accurate for the purposes of optimizing bone marrow transplant matches. We hope both our results and our analytical approach will help to move discussion of the role of race in medical practice and genetic research forward from its current stand---off to a more interdisciplinary and collaborative stage.