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Letter to the Editor

High-Resolution HLA Typing for Sensitized Patients: Advances in Medicine and Science Require Us to Challenge Existing Paradigms

To the Editor:

In the March 17 issue of *AJT*, an editorial by Cecka, Reed and Zachary (1) commented on our personal viewpoint article wherein we proposed that HLA mismatch acceptability for sensitized transplant candidates should be determined at high-resolution levels (2). This editorial seems to express the view that HLA antigen-based testing be maintained as is despite its inherent deficiencies. We are perplexed by conflicting comments that more HLA complexity ''should be pretty low on the list of priorities'' while simultaneously mentioning a need for HLA-DQA and DP typing and ''better'' resolution of HLA-DRB3/4/5 types.

Furthermore, the statement that ''a whole bunch of antibodies, each recognizing a single HLA antigen or allele'' places little emphasis on the concept that those antibodies are epitope specific. The editorial states that epitopes are theoretically based on ''nucleotide sequence similarities between HLA alleles'' and ''only a few have been documented with antibodies.'' During the past 2 decades, many investigators, notably Paul Terasaki's group, have confirmed unique HLA epitopes defined by antibodies and three recent publications list 97 HLA-ABC, 50 HLA-DR, -DQ, -DP and 21 MICA antibody-verified epitopes recorded so far in the International Registry of HLA Epitopes at http://www.epregistry.com.br (3–5).

The editorial expresses the opinion that ''more information is almost always better than less when making clinical decisions, except when it is not directly applicable to the problem at hand.'' Clearly, it does not consider the limitations of antigen-based matching as problematic and that ''it is likely that one or two patients on a waiting list might benefit from knowing which HLA alleles are expressed by the donor.'' How these numbers were determined is itself an interesting question. An informal survey among viewpoint article authors revealed that the number of highly sensitized patients with specific allele-reactive antibodies was >10%. Accordingly, hundreds of such patients on the US national waiting list would benefit from high-resolution typing. Most transplant programs are government funded and fairness and equity in the organ allocation process is of considerable importance even if it only impacts a small percentage of transplant candidates.

We acknowledge that ''it is difficult to tease out the precise impact of allele-level typing and identifying epitopes on the chance of a transplant for a sensitized patient.'' This editorial has a calculation for a single allele with a 0.5% frequency and for a 10% admixture population concluding that only 1 in 2000 donors would have this allele. However, this calculation fails to acknowledge that (1) a given population may have multiple alleles corresponding to a given antigen, (2) many alleles have frequencies well above the cut-off point of 0.5% and (3) admixtures may have multiple population and ethnic groups each with their own distinct alleles. These factors all contribute to the allelic diversities of donors and recipients especially when worldwide transplant programs are considered.

Rather than clutching to old paradigms, we must apply the newest scientific concepts and the most precise technologies to define humoral barriers to successful transplantation. Let's move forward.

Disclosure

The authors of this manuscript have no conflicts of interest to disclose as described by the *American Journal of Transplantation*.

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