HLA and disease: Missing clinical data on laboratory request forms – a missed opportunity

To the Editor: HLA typing is one of the most vital tools in the pre-transplantation work-up process.[1] However, not only is HLA typing vital in identifying suitable donors, but it may also assist in disease association studies. One of the major pitfalls of HLA disease association studies is that many HLA-associated disease studies remain unconfirmed and based on diminutive case-control studies, open to selection bias and spurious positive associations. Furthermore, to firmly establish specific HLA-disease associations, it is necessary to perform large case-control studies in diverse ethnic groups.[2] In recent years, there has been increased awareness of the value of HLA typing in disease association studies and effective donor enrolment in South Africa (SA).[3] In our laboratory we performed 1 151 HLA typings between 2005 and 2019, equating to ~77 typings per year. Individuals included possible donors, patients with end-stage renal failure, patients with haematological malignancies, and numerous patients with other less common disorders. We therefore believe that these relatively large numbers have adequate statistical power to make reliable inferences regarding HLA and specific disorders in our population.

Unfortunately, one finding was that nearly a third of all patient HLA typing request forms did not state the underlying clinical reason for requesting the specific test. In the majority of these cases (25.4%), no clinical details were supplied to the laboratory. 'Recipient for transplant' or 'work-up for transplant' were other common nonspecific phrases used on the request forms. Consequently, we missed the opportunity to comprehensively study HLA and disease association in these cases. According to the College of American Pathologists Laboratory General Checklist,[4] clinical information should be included on a test requisition when appropriate. We consider HLA typing an appropriate setting where clinical information is required, and that the addition of clinical details greatly enhances the capacity to perform HLA-associated disease studies. We believe that sharing clinical details with the laboratory may significantly contribute to our understanding of the underlying mechanisms of HLA-associated disease susceptibility, and ultimately contribute to improved clinical management of patients. One SA study reported that clinical information is commonly lacking on laboratory request forms. Additionally, it was found that a single physician education session on completion of laboratory request forms did not change this practice (apparently owing to the unsuitable design of the laboratory request form).[5] A contributing factor may also be that clinicians are not aware of the possible long-term contribution that specific clinical information may have on the clinical utility of specific HLA disease associations, as this information would not necessarily have an immediate impact on the clinical management of their patients.

Taken together with our findings, there is therefore a need for both an increase in clinician awareness regarding the possible impact of clinical information on HLA disease association studies and future patient management, and a revision of our HLA-specific laboratory test request forms to afford clinicians more opportunity to share clinical information with the laboratory. In this way, by working together, we can attempt to prevent another missed opportunity.

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