ABSTRACT

Immunogenicity is a critical risk factor for long-term survival of both deceased and living donor kidney allografts. However, the currently accepted immunogenicity scale is constrained to integer values from 0 to 6 based on the six commonly typed HLA antigen groups. Moreover, due to short organ supply and difficulty of matching everyone perfectly, transplant programs do not attempt to match by HLA except for a few targeted programs thereby accommodating better HLA match for only 13% of transplanted patients. As a result, the majority of transplants are performed randomly with high HLA mismatch numbers as soon as any donor is available. Another reason for the lack of commitment to HLA matching is the ongoing debate about the real role and importance of HLA antigen mismatching in kidney allograft survival, which is considered dispensable by some as it is presumed that immunological risk is reversible with the use of immunosuppression.

We sought to redefine the concept of HLA immunogenicity. Instead of the current HLA antigen disparity system that is limited to 7 integers (0, 1, 2, 3, 4, 5 or 6), we tested a new concept based on HLA physiochemical properties resulting in a continuous scale (including both integers and fractions). In particular, we used a published Kosmoliaptsis algorithm to compute the immunogenicity scores based on the polymorphic donor amino acids and calculating their hydrophobic (HMS), electrostatic (EMS), and amino acid (AMS) mismatch scores. To this end, retrospective data on transplants and transplant follow-up were extracted from the Scientific Registry of Transplant Recipients

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DISSERTATION PRESENTATION

Dulat Bekbolsynov

May 14, 2018

"A New Concept of Immunogenicity to Calculate the Risk Stratification for Kidney Transplantation"

Ph.D. in

Biomedical Sciences

Abstract (cont.)

Statistically imputed high-resolution HLA types were used for immunogenicity calculation. The HMS/EMS/AMS values were then used as explanatory variables in statistical models of transplant failure rates in these recipients.

Highly immunogenic transplants consistently showed worse long-term survival in comparison with weakly immunogenic transplants. The continuous immunogenicity scale has allowed for reliable estimation of graft failure risk without referring to the actual number of antigenic HLA mismatches. Furthermore, measuring immunogenicity with a continuous scores scale has allowed to find weakly immunogenic transplants with high number of HLA mismatches, whose graft failure rate was comparable to the transplants with low number of HLA mismatches. As a consequence, the number of retrospective weakly immunogenic transplants exceeded the number of transplants with a single HLA mismatch. Kosmoliaptsis immunogenicity scores also showed significant association with the strength of humoral response against the transplant.

Overall, these results indicate that the HLA immunogenicity measured using the Kosmoliaptsis algorithm is a reliable predictor of the kidney transplant long-term survival.

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PUBLICATION (NON-SCIENTIFIC)

Bekbolsynov D, (2017, January 9) Better matches of kidney donors, recipients studied. *Toledo Blade.*

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AWARDS

Satellite Auxiliary Scholarship-in-need for Biomedical Science Program graduate students 2016.

FUTURE PLANS

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