Spotlight on HLA: Current Aspects in Transfusion and Transplantation Medicine

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The HLA system is the major histocompatibility complex in humans. The identification of alloantibodies in sera of polytransfused patients led to the definition of the first HLA antigens. Their importance in transfusion and transplantation medicine has been immediately recognized. The HLA system is the most polymorphic region of the human genome. HLA molecules play a key role in adaptive immune reactions against pathogens but also initiate immune responses against alloantigens leading to graft rejection or graft-versus-host responses. Molecular technologies in HLA typing and the sequencing of the human genome have boosted our knowledge about the diversity and organization of the HLA system. Particularly due to the advent of next-generation sequencing technologies, HLA typing can now be done with a hitherto unknown quality and reliability.

This issue of *Transfusion Medicine and Hemotherapy* is dedicated to the selection of some currently relevant aspects of HLA immunology and immunogenetics in the field of transfusion and transplantation medicine. Particularly for hematopoietic stem cell transplantation, the requirements for HLA typing are high and have extended considerably over time. The review by Fürst et al. [1] summarizes the clinical evidence for HLA matching and donor selection in unrelated hematopoietic stem cell transplantation according to the resolution and loci of different HLA mismatches and also discusses special situations such as unidirectional mismatches, permissible HLA mismatches, and HLA matching in cord blood transplantation. As numbers of transplants are increasing, the

problem of HLA alloimmunization is recognized more and more, and a section of this review is devoted to risks associated with the presence of HLA antibodies in patients and donors.

High-throughput molecular typing methods demand the employment of appropriate bioinformatic procedures for processing of raw data and integrative data analysis. The laboratory of the DKMS has been involved in the development of bioinformatic procedures and HLA typing automatization from the very beginning. Klasberg et al. [2] summarize their perspective on the current methodology for HLA-associated data analysis in next-generation sequencing typing. Their review spans challenges arising from different library preparation procedures as well as regarding the specifications of different sequencing platforms. Central to their paper is the discussion and comparison of different alignment and HLA allele assignment methods applicable in HLA typing workflows.

The review by Eyrych and Schulze [3] concerns the involvement of HLA typing and matching procedures focusing on pediatric stem cell transplantation and includes practical recommendations for finding a suitable donor. The special case of haploidentical donor selection, which traditionally was a field of pediatric hematopoietic stem cell transplantation but continues to gain importance in adult hematopoietic stem cell transplantation, is also discussed.

The introduction of Luminex single-antigen bead identification of HLA antibodies had a considerable impact on the assessment of immunized patients awaiting

organ transplantation. However, there is no clear consensus regarding the management of patients before and after lung transplantation with respect to HLA alloimmunization. Dick et al. [4] summarize their procedures for the detection and treatment of immunized patients registered for lung transplantation in one of the largest centers in Germany, discussing their experience in the context of the evidence available from the literature. HLA alloimmunization poses challenges in the provision of safe and efficacious blood products for patients in need of transfusion. Alloimmunization on both the patient and the donor side must be considered in this situation. Weinstock and Schnaidt [5] give a comprehensive overview of the sources and mechanisms of HLA sensitization, summarize preventive measures, and detail the available techniques for antibody screening and identification. Finally, the management of immunized patients is discussed and an outlook on future developments is given.

Predicted Indirectly ReCognizable HLA Epitopes (PIRCHE) is a bioinformatic approach to predict poten-

tially immunogenic peptides deriving from mismatched HLA allotypes in patients and their donors in transplantation medicine, which are presented in shared HLA molecules. In theory, low numbers of PIRCHE may correlate with reduced alloreactivity as compared to high numbers of PIRCHE. Ayuk et al. [6] investigated the PIRCHE model in a retrospective cohort of 424 adult patients with 9/10 HLA-matched unrelated donors. A bioinformatic tool for the assessment of HLA mismatches and a predictive classification into permissive and nonpermissive mismatches would improve donor selection for patients where no related or unrelated matched donor is available. Still, this group makes up a significant proportion of patients at about 25% of all unrelated donor searches, a number which has been decreasing only slightly over the last years.

In summary, this special issue of *Transfusion Medicine and Hemotherapy* gives a broad overview of current relevant issues in transfusion and transplantation medicine from a diagnostic perspective but also regarding clinical management.

References

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