DONOR SELECTION FOR SOLID ORGAN TRANSPLANTATION GUIDED BY NGS HIGH RESOLUTION HLA TYPING IN COMBINATION WITH PIRCHE

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Introduction

The new Predicted Indirectly Recognizable HLA Epitopes (PIRCHE) algorithm predicts T cell related immune responses against HLA derived peptides after transplantation (Figure 1) and has been established to identify permissible HLA mismatches in transplantation settings. Recently, PIRCHE-II has been used to predict de-novo donor-specific antibody formation after both kidney and liver transplantation.

We hypothesize, that by combining ultra-high resolution NGS-derived HLA typing with the PIRCHE-II score in the routine organ transplant setting, the donor selection process can be improved by enabling qualified selection of the donor with least probability of subsequent antibody production in the recipient.

Methods

The HLA Twin software (Omixon) provides high resolution HLA typing originating from NGS data, and a recently introduced function has been incorporated to export the up to 4-field typing automatically to the PIRCHE web service (Figure 2), where the PIRCHE-II score per patient-donor pair can be calculated. Using this functionality, the application can be used to select the immunologically best matched related and/or unrelated living kidney donor in case of multiple and different HLA mismatches in SOT.

Furthermore, patient typing and the typings of all available donors may be exported to the PIRCHE web service, in order to generate a risk profile analysis for all potential donors. We could demonstrate that the HLA Twin software with its export of the high resolution typings to the PIRCHE application, can assist the lab's routine in selecting the patient (Figure 3). This risk profile will show the chance for the patient to find a donor with a certain PIRCHE score (based on the haplotype data of a certain population) and will predict the average PIRCHE score of potential donors.

Results

We show here that HLA high resolution typings in the HLA Twin software can easily be exported to the PIRCHE web service, in order to generate a risk profile analysis for the patient (Figure 3). This risk profile will show the chance for the patient to find a donor with a certain PIRCHE score (based on the haplotype data of a certain population) and will predict the average PIRCHE score of potential donors. Furthermore, patient typing and the typings of all available donors may be exported to the PIRCHE application (Figure 4), to calculate a PIRCHE-II score for every patient-donor pair (Figure 5).

The application can be used to select the immunologically best matched related and/or unrelated living kidney donor in case of multiple and different HLA mismatches between patient and donors. With an example of a patient receiving a second transplant, we could demonstrate that the risk profile along with PIRCHE-II scores specific for the patient-donor pair, may be employed to perform a risk assessment in multiple transplantations (Figure 6).

Discussion and Conclusion

Previous studies have shown a supportive role for PIRCHE-II in the development of de novo DSA formation after SOT and that increasing PIRCHE-II numbers appear to be a risk factor for kidney graft failure after transplantation. This supports the fact that PIRCHE-II score potentially can be used to identify acceptable mismatches in SOT.

We could demonstrate that the HLA Twin software with its export of the high resolution typings to the PIRCHE application, can assist the lab’s routine in selecting the kidney donor based on the number of mismatches, risk stratification and the level of PIRCHE score calculated per patient-donor pair.

To confirm whether a reduced PIRCHE-II score truly improves patient outcome on a broad scale, simulations and prospective studies are needed, which are currently ongoing.