(PF1141) LONGITUDINAL TCR SEQUENCING REVEALS DONOR-DEPENDENT IMMUNE RECONSTITUTION PATTERNS AFTER PEDIATRIC ALLOGENEIC HSCT FOR PRIMARY IMMUNODEFICIENCIES

Topic: 23. Stem cell transplantation - Clinical

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Background

Allogeneic hematopoietic stem cell transplantation (allo-HSCT) is a curative treatment for severe primary immunodeficiencies (PIDs). However, the factors influencing T-cell receptor (TCR) repertoire reconstitution post-transplant in children are not well understood, particularly regarding the interplay between donor immune diversity and recipient immune recovery.

Aims

To longitudinally characterize TCR repertoire recovery in pediatric PID patients undergoing allo-HSCT and evaluate the impact of donor factors, ATG prophylaxis, and viral reactivation.

Methods

Thirty-two pediatric PID patients and their corresponding donors (123 longitudinal samples) were analyzed pre-transplant and at 3, 6, and 12 months post-HSCT. Patients were stratified as severe combined immunodeficiency(SCID, 25%) or non-SCID (75%). TCR β-chain sequencing was performed using high-throughput methods. Repertoire diversity was assessed by Shannon index and top clonotype frequencies. Associations with donor age, donor relatedness, ATG use, and post-transplant complications were evaluated using mixed-effects models and nonparametric testing.

Results

SCID patients had significantly lower baseline TCR diversity compared with non-SCID patients ($P<0.05$). Post-transplant, SCID patients demonstrated progressive increases in TCR diversity over 12 months, whereas non-SCID patients showed an early decline at 3 months followed by gradual, but incomplete, recovery over 12 months.
Recipients of pediatric donors and related donors (including haploidentical family donors) exhibited significantly higher TCR diversity at 6 and 12 months compared with adult or unrelated donors (all $P<0.05$). ATG prophylaxis was associated with delayed repertoire diversification, particularly in non-SCID patients. In contrast, letermovir administration did not significantly affect global TCR diversity at any time point.
Lower pre-transplant recipient TCR diversity was associated with subsequent acute GVHD ($P<0.05$), while chronic GVHD and CMV or EBV reactivation were not significantly correlated with overall diversity. Clonal tracking demonstrated predominant replacement by newly generated donor-derived clonotypes. Viral reactivation was associated with enrichment of CMV- and EBV-related clonotypes without sustained contraction of global diversity.

Summary/Conclusion

In pediatric PID patients undergoing allo-HSCT, TCR repertoire reconstitution is influenced by baseline immune status, donor age and relatedness, and ATG exposure. Newly generated donor-derived clones dominate long-term recovery, while virus-associated expansions reflect adaptive immune remodeling. TCR sequencing may support immune monitoring after pediatric transplantation.