CASE STUDY: MARCH 2014

T-cell repertoire following autologous stem cell transplantation for multiple sclerosis

BACKGROUND
• Autologous hematopoietic stem cell transplantation (HSCT) is commonly employed for hematologic and non-hematologic malignancies and is being evaluated for severe autoimmunity to ‘reset’ the immune system
• In a Phase II study of HSCT for poor-prognosis multiple sclerosis, immune reconstitution post-transplant was monitored and correlated with outcomes

AIM
To understand the relationship between diversity of T-cell repertoire after HSCT and outcomes

METHODS
Peripheral blood samples were collected from 24 subjects with multiple sclerosis and peripheral blood mononuclear cells (PBMCs) were obtained

1. Before HSCT: PBMCs → gDNA extraction → immunoSEQ™
2. HSCT
3. 2 months: PBMCs → gDNA extraction → immunoSEQ
4. 1 year: PBMCs → gDNA extraction → immunoSEQ

RESULTS

Subjects largely developed a new CD4+ repertoire after treatment

The reconstituted CD8+ repertoire was created by clonal expansion of cells present before treatment

Subjects who failed to respond to treatment had less diversity in their T-cell repertoire early during the reconstitution process

CONCLUSIONS
• These results underpin the notion that repertoire complexity is critical for the re-establishment of immune tolerance
• Low T-cell diversity may be an early indicator of inadequate immune reconstitution and may be used to tailor monitoring and therapy post-transplant