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aGvHD

EBMT 2018 | CCR5 and CXCR3 blockade attenuation of murine aGvHD

Anna Bartus | Mar 20, 2018

The 44th Annual Meeting of the European Society for Blood and Marrow Transplantation (EBMT) took place in Lisbon, Portugal, on 18–21March 2018. On Monday 19 March, an abstract was presented titled "Combined CCR5 and CXCR3 blockade attenuates murine aGvHD through alternating donor-derived T-cell distribution and function" by Bo Tang from Peking University First Hospital, Beijing, China.

Chemokines are important mediators to control migratory patterns and positioning of all immune cells. Chemokine receptors play an essential role in directing the migration of donor derived T-cells to target organs. CXCR3 and CCR5 are chief among these chemokine receptors. Tang *et al.* investigated whether combined CCR5 and CXCR3 blockade could attenuate murine acute graft-versus-host disease (aGvHD), and also explored the immunologic mechanism behind it.

In order to establish an allogeneic bone marrow transplantation model, BALB/c (H-2Kd) recipients received 8.0 Gy of total body irradiation (TBI) prior to transplantation, followed by the infusion of bone marrow cells (BMCs) and splenic cells (SCs) from C57BL/6J (H-2Kb) or CCR5 knockout mice (H-2Kb).

Key findings:

- CCR5 and CXCR3 are enhanced during the aGvHD process
- CCR5 and CXCR3 blockade reduced aGvHD scores from 4.67±0.33 to 1.25±0.25, $P < 0.001$
- CCR5 and CXCR3 blockade reduced aGvHD related death from 90% to 40%, $P < 0.05$
- Compared with GvHD group, combined CCR5 and CXCR3 blockade reduced
  - liver histologic score 3.3±0.3 *vs* 3±0.3, $P < 0.05$
  - lung histologic score 3.6±0.3 *vs* 3±0.3, $P < 0.05$
  - intestine histologic score 3.7±0.3 *vs* 3±0.3, $P < 0.05$

The speaker concluded by highlighting that combined CCR5 and CXCR3 blockade decreased the probability of aGvHD. Moreover, inhibition of aGvHD significantly associated with alternated donor T-cell distribution, limited donor T-cell activation and also reduced T-cell effector function in vivo. Tang further added that their data suggested that "the combined use of CCR5 and CXCR3 blockade might be applicable for aGvHD prophylaxis in clinical settings."

References

1. Tang B. *et al.* Combined CCR5 and CXCR3 blockade attenuates murine aGvHD through alternating donor-derived T cell distribution and function. Abstract OS3-7. 44th Annual Meeting of the European Society for Blood and Marrow Transplantation (EBMT). 19 Mar 2018.