TRANSPLANT IMMUNOLOGY

Gut bugs and grafts

The intestinal microbiota has been implicated in the regulation of a growing number of immunological processes. Now, scientists reporting in the *Journal of Experimental Medicine* show how gut commensals influence the severity of graft-versus-host disease (GVHD) following allogeneic bone marrow transplantation (BMT).

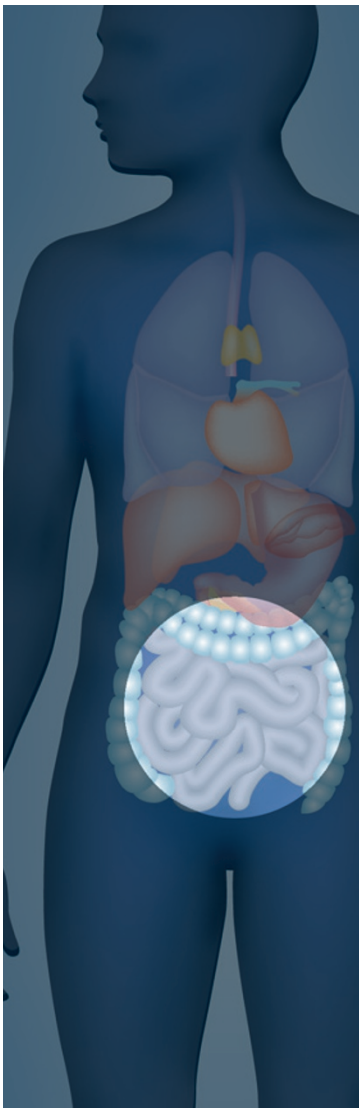
Although a role for the intestinal microbiota in GVHD manifestations in the gut is suspected, previous studies have had inconsistent results. To explore the link further, Jenq *et al*. used a well-known mouse model of acute GVHD following allogeneic BMT — the B10.BR→B6 model. After BMT, there was an increase in the bacterial load in the ilea of mice with or without GVHD. However, analyses of the composition of the gut flora indicated that recipient mice that developed GVHD had a dramatic loss of bacterial diversity and a distinct composition compared with recipient mice that did not develop GVHD. In the setting of GVHD, there were notable increases in the order Lactobacillales and decreases in the order Clostridiales and in other members of the phylum Firmicutes in the ileum. In particular, sequencing of 16S ribosomal RNAs revealed the expansion of populations of the commensal *Lactobacillus johnsonii*.

To determine whether the association between *L. johnsonii* and GVHD had clinical implications, the authors treated recipient mice with antibiotics and then recolonized the gut with *L. johnsonii* prior to BMT. Antibiotic-treated mice showed a loss of Clostridiales and an emergence of *Enterococcus* spp. (order Lactobacillales), and this was associated with exacerbated GVHD. By contrast, antibiotic-treated mice that received *L. johnsonii* showed no expansion of *Enterococcus* spp. populations and were protected from increased GVHD lethality and pathology. The authors suggest that *L. johnsonii* (a species found in probiotic preparations) may reduce GVHD severity by preventing the expansion of *Enterococcus* spp., which may exacerbate GVHD in the gut.

Interestingly, an analysis of stool samples from patients receiving bone marrow transplants revealed similar GVHD-associated changes in the commensal flora to those seen in mice. This and the finding that antibiotic exposure prior to BMT (which occurs commonly in BMT recipients) could be a risk factor for GVHD have important implications for the future management of patients receiving BMT.

Lucy Bird

ORIGINAL RESEARCH PAPER Jenq, R. R. *et al.* Regulation of intestinal inflammation by microbiota following allogeneic bone marrow transplantation. *J. Exp. Med.* **209**, 903–911 (2012)



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