To the editor:

Granulocyte colony-stimulating factor mobilization alters dendritic cell cytokine production and initiates T helper 2 polarization prior to host alloantigen presentation

The recent paper by Arpinati et al. elegantly demonstrates that the numbers of T helper 2-inducing dendritic cells (pre-DC2s) are increased in granulocyte colony-stimulating factor (G-CSF)-mobilized allografts. Pre-DC2s on subsequent activation lead to polarization of naive CD4 T cells toward a Th2 phenotype. In the accompanying Focus on Hematology article, Liu and Blom suggest that acute graft-versus-host disease (GVHD) may be diminished due to activation of donor DC2s by host alloantigens resulting in Th2 production. Missing from Liu and Blom’s article and in their accompanying figure, however, is the information that Th2 polarization is initiated in the donor, prior to host alloantigen activation of pre-DC2s.

Our following recent findings on the effects of G-CSF on dendritic cell cytokine profile and other studies on GVHD may clarify the timing of donor Th2 differentiation and the role of host antigen-presenting cells (APCs) in GVHD:

1. We have recently demonstrated that G-CSF–mobilized DCs produce less interleukin-12 (IL-12) in response to endotoxin or lipopolysaccharide (LPS), compared with unmobilized DCs. Because IL-12 secretion by DCs is central to Th1 differentiation, reduced IL-12 production by DCs is likely the mechanism by which naïve T cells are polarized toward a Th2 phenotype.

2. G-CSF–mobilized DCs have an altered response to LPS resulting in a suppressed release of tumor necrosis factor α (TNFα). TNFα is a key inflammatory cytokine implicated in the activation of DCs and in the etiology of acute GVHD.1,3,5

3. It is well established from experimental GVHD models that G-CSF polarizes donor T cells toward a Th2 phenotype prior to entering the host and before any activation of donor DC2s by host alloantigens.5,6

4. Finally, Shlomchik et al have recently demonstrated in a murine transplant model that host APCs, and not donor APCs, are responsible for the initiation of GVHD.7 In their model, inactivation of host APCs prevented GVHD despite the presence of numerous donor APCs.7

Therefore, in addition to the extremely important findings by Arpinati et al that increased DC2s after G-CSF mobilization lead to Th2 production, the above studies suggest that host alloantigens are not required for DC2s actions on helper T cells. It is likely that host alloantigens further activate pre-DC2s and promote rather than initiate the ongoing Th2 proliferation, leading to reduced severity of acute GVHD.

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References
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