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## Response

## Is CD103 a good surface marker for in vivo–activated effector/memory Treg cells in patients with chronic inflammation? Unknown yet

We observed that the percentage of CD103<sup>+</sup> cells among CD4+FoxP3+ regulatory T (Treg) cells of donor DBA/2 mice was less than 10% before transplantation, and the percentage of CD103<sup>+</sup> cells among donor-type CD4<sup>+</sup>Foxp3<sup>+</sup> Treg cells increased to more than 55% in BALB/c recipients with chronic graft-versus-host disease (GVHD) and 70% in recipients without chronic GVHD after hematopoietic cell transplantation (HCT).<sup>1</sup> We also observed that the percentage of CD103<sup>+</sup> cells among Foxp3+CD4+ Treg cells in donor C57BL/6 mice was approximately 20% (mean  $\pm$  SE: 20.7  $\pm$  1.7%, N = 4) before HCT, and the percentage of CD103<sup>+</sup> Treg cells increased to around 40% (mean  $\pm$  SE: 44.3  $\pm$  2.0%, N = 4) in BALB/c recipients with acute GVHD. These results indicate that inflammation, especially chronic inflammation, can augment the expression of CD103 on mouse Foxp3<sup>+</sup> Treg cells, although the percentage of CD103<sup>+</sup> cells among Foxp3<sup>+</sup> Treg cells can differ up to certain levels in different mouse strains or different housing environments, because the percentage of CD103<sup>+</sup> Treg cells in our DBA/2 mice is around 10%, but the percentage of our C57BL/6 mice is around 20%; the percentage of CD103<sup>+</sup> Treg cells in our C57BL/6 mice is approximately 20%, but the percentage in C57BL/6 mice in Hühn's reports is approximately 30%.<sup>2</sup>

It has been well documented that the percentage of CD103<sup>+</sup> cells among Foxp3+CD4+ Treg cells in healthy humans is low, around 5%.3-5 However, it is still unknown whether Fopx3+ Treg cells in human HCT recipients express CD103. It has been shown that the percentage of CD103<sup>+</sup> cells among CD25<sup>hi</sup>CD4<sup>+</sup> T cells was significantly higher than that among CD25<sup>-</sup>CD4<sup>+</sup> T cells in patients with multiple sclerosis.<sup>6</sup> In addition, in vitro TGF-Binduced Treg cells were all CD103<sup>+</sup>.<sup>7</sup> TGF-β secretion is usually up-regulated in patients with chronic inflammation.<sup>8</sup> Therefore, although most of the Foxp3<sup>+</sup> Treg cells in normal humans do not express CD103, we cannot exclude the possibility that Foxp3<sup>+</sup> Treg cells in patients with chronic inflammation (such as chronic GVHD) will up-regulate CD103 expression. Because it has been reported that effector/memory Foxp3+ Treg cells express CCR6 in mice<sup>9</sup> and they express CD39 in multiple sclerosis patients,<sup>10</sup> comparison of expression of CD103, CCR6, and CD39 by Foxp3+ Treg cells in patients with chronic inflammation is required to find out which one is best for identifying the Foxp3 Treg cells.

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