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Comment on "Differentiation of IL-17–Producing Effector and Regulatory Human T Cells from Lineage-Committed Naive Precursors"

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Letters to the Editor

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Comment on "Differentiation of IL-17–Producing Effector and Regulatory Human T Cells from Lineage-Committed Naive Precursors"

In their study, Mercer et al. (1) show that IL-17–producing T cells differentiate from CCR6$^+$ naive CD4 T cells from adult peripheral blood, both conventional and T regulatory cells (nTregs). These results are in line with our recent data showing that T_H17 cells can differentiate from nTregs in adult circulating lymphocytes (2). The authors also obtained differentiation of T_H17 cells from total CD4$^+$CCR6$^+$ T cells from umbilical cord blood (UBC), although significantly less efficiently. Because of the low proportions of CCR6$^+$ cells in UBC, however, they could not assess CCR6$^+$ conventional CD4 T cells and Tregs separately. As mentioned by the authors, IL-17–secreting cells are found among Helios$^-$ Tregs that likely correspond to peripherally-induced Tregs rather than thymically-derived Tregs. As was recently reported, nTregs in adults include Helios$^+$ and Helios$^-$ cells, the latter representing ~30% of total nTregs (3). We showed, however, that Helios$^-$ Tregs are undetectable in UBC, in which nTregs are, in contrast, abundant (4). To directly assess the presence of T_H17 precursors in nTregs from UBC, we isolated them by cell sorting and differentiated them in the presence of T_H17 polarizing factors. However, we failed to obtain a significant differentiation of IL-17–secreting cells from UBC nTregs. Thus, whereas differentiation of T_H17 cells can indeed occur from phenotypically naive Tregs of adults, most FOXP3$^+$Helios$^-$ Treg precursors of T_H17 cells appear to develop in the periphery after birth, and may therefore be, despite their naive phenotype, peripherally-induced Tregs rather than thymically-derived Tregs.

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Abbreviations used in this article: nTreg, naive T regulatory cell; Treg, T regulatory cell; UBC, umbilical cord blood.

References

1. Mercer, F., A. Khaitan, L. Kozhaya, J. A. Aberg, and D. Unutmaz. 2014. Differentiation of IL-17–producing effector and regulatory human T cells from lineage-committed naive precursors. *J. Immunol.* 193: 1047–1054.
2. Valmori, D., C. Raffin, I. Raimbaud, and M. Ayyoub. 2010. Human RORγt$^+$ T_H17 cells preferentially differentiate from naive FOXP3$^+$Treg in the presence of lineage-specific polarizing factors. *Proc. Natl. Acad. Sci. USA* 107: 19402–19407.
3. Himmel, M. E., K. G. MacDonald, R. V. Garcia, T. S. Steiner, and M. K. Levings. 2013. Helios$^+$ and Helios$^-$ cells coexist within the natural FOXP3$^+$ T regulatory cell subset in humans. *J. Immunol.* 190: 2001–2008.
4. Ayyoub, M., C. Raffin, and D. Valmori. 2013. Comment on "Helios$^+$ and Helios$^-$ cells coexist within the natural FOXP3$^+$ T regulatory cell subset in humans." *J. Immunol.* 190: 4439–4440.

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