

Correspondence

Reply

To the Editor:

We would like to thank Paquin-Proulx et al¹ for their comments on our report of invariant natural killer T (iNKT) cells in patients with common variable immunodeficiency (CVID)² and their additional data on iNKT cells in treatment-naïve patients with CVID.¹ We welcome the additional description of iNKT cell differences in patients with CVID and the possible role of intravenous immunoglobulin (IVIg) in altering cellular phenotypes after initiation of treatment.³ Our observation, through rare event flow cytometric evaluation, that a large proportion of patients with CVID manifested an apparent deficit of iNKT cells led us to the culture-based approach to discriminate an absolute deficiency of iNKT cells in this cohort. The identification of a functional deficit of iNKT cell expansion after this assessment extended our phenotype in the CVID population compared with the control subjects. It is possible that the expansion of iNKT cells alters their functional phenotype, with the reduction of CD161 on iNKT cells being one such recognized change of long-term NKT cell culture. All of our functional assays with CD1d ligands were undertaken in the presence of blocking antibodies to CD1d, and the cytokine responses were shown to be absent, supporting our view that iNKT cells were critical to their production. We believe the use of complementary techniques for the evaluation of cellular effector functions (ELISPOT assay, ICS, RT-PCR, and cytokine arrays) will be important for the complete characterization of iNKT cells in the future.

All of our patients with CVID were receiving immunoglobulin (subcutaneous and intravenous) at the time of their cellular evaluation, with a treatment period of 2 to 32 years. We recruited a separate cohort of patients with X-linked agammaglobulinemia to evaluate any effect of long-term IVIg on iNKT cells in a representative primary antibody deficiency control group and found that this patient group was most similar to healthy control subjects, suggesting that long-term immunoglobulin did not have a direct effect on iNKT cells. The longitudinal follow-up of

different primary antibody deficiency patient groups, including those with a pediatric onset, who are IVIg treatment naïve will better define the direct and indirect effects of disease management, including antibiotics, physiotherapy, and immunoglobulins, on cellular subsets over time.

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