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Long-lasting humoral immunity: existence of memory B-cell-independent long-lived plasma cells in humans

Cynthia Umukoro | Jul 25, 2016

G. Bhoj, *et al.*, investigated the survival of plasma cells (PCs) and their antibodies in adult and pediatric patients who have received chimeric antigen receptor (CAR)-based adoptive T-cell immunotherapy targeting CD19 to treat B-cell lineage malignancies (CTL019). Their investigations were carried out in order to further elucidate the mechanism of humoral immunity in humans. The results of this study were published in Blood in 2016.

The key findings were:

- After CART therapy, some vaccine/pathogen-specific IgG and IgA titers remain relatively stable for 6 and 12 months respectively
- Analysis of bone marrow biopsies after CTL019 revealed persistence of antibody-secreting PCs at least 25 months post-CTL019 infusion despite absence of CD19+CD20+ B-cells, in 8 patients

In conclusion, these data provided evidence of the existence of memory B-cell–independent, long-lived PCs in humans that contribute to long-lasting humoral immunity.

Abstract

The mechanisms underlying the maintenance of long-lasting humoral immunity are not well understood. Studies in mice indicate that plasma cells (PCs) can survive up to a lifetime, even in the absence of regeneration by B cells, implying the presence of long-lived PCs as a mechanism for long-lasting immunity. Evidence from humans treated with anti-CD20, which depletes circulating B cells, also suggests B-cell–independent long-term survival of some PCs. On the other hand, antibody responses may be sustained solely by short-lived PCs with repopulation from clonally related memory B cells. To explore PC longevity and humoral immunity in humans, we investigated the fate of PCs and their antibodies in adult and pediatric patients who received chimeric antigen receptor–based adoptive T-cell immunotherapy targeting CD19 to treat B-cell lineage malignancies (CTL019). Treatment with CTL019 is frequently associated with B-cell aplasia that can persist for years. Serum antibody titers to vaccine-related antigens were measured, and quantitative assessment of B cells and PCs in blood and bone marrow was performed at various time points before and after CTL019 therapy. While total serum immunoglobulin concentrations decline following CTL019-induced B-cell aplasia, several vaccine/pathogen-specific serum immunoglobulin G and A (IgG and IgA) titers remain relatively stable for at least 6 and 12 months posttreatment, respectively. Analysis of bone marrow biopsies after CTL019 revealed 8 patients with persistence of antibody-secreting PCs at least 25 months post-CTL019 infusion despite absence of CD19+CD20+ B cells. These results provide strong evidence for the existence of memory B-cell–independent, long-lived PCs in humans that contribute to long-lasting humoral immunity.

References

1. Bhoj V.G. *et al*. Persistence of long-lived plasma cells and humoral immunity in individuals responding to CD19-directed CAR T-cell therapy. Blood. 2016 May 10. DOI: blood-2016-01-694356. [Epub ahead of print].