SUPPLEMENTARY INFORMATION

Generation of stable monoclonal antibody-producing BCR$^+$ human memory B cells by genetic programming

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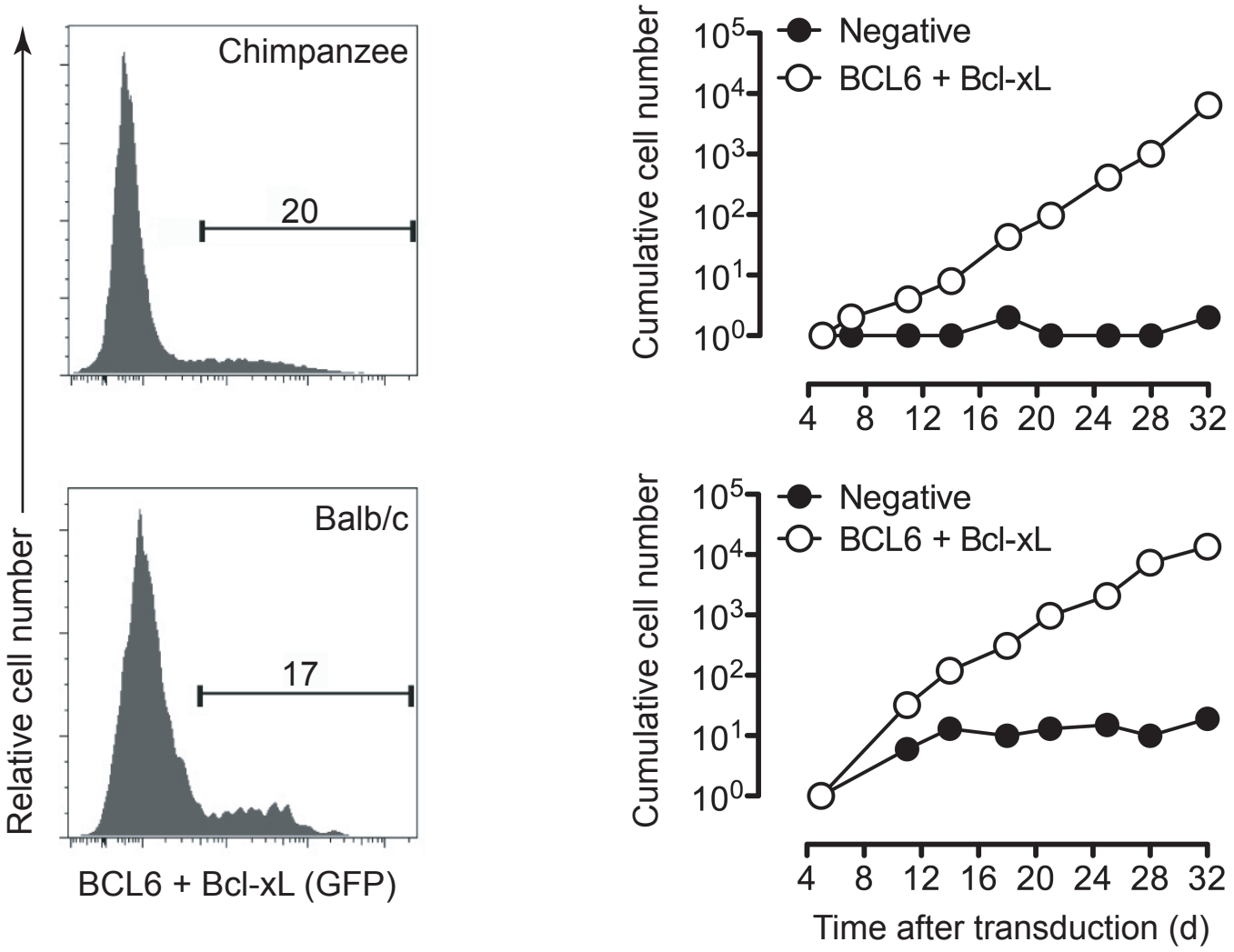
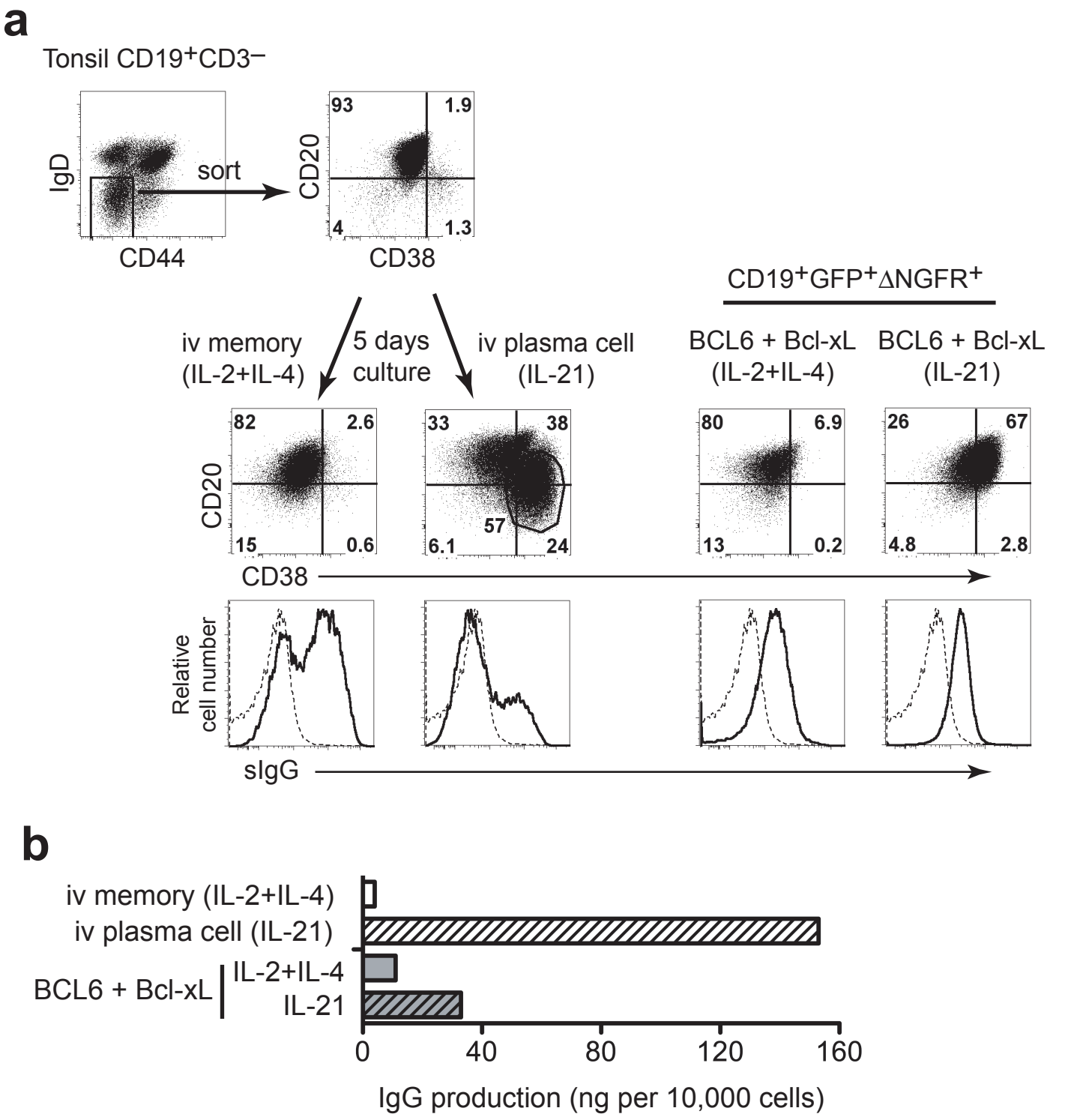


Supplementary Figure 1.

Non-human primate and mouse B cells can be transduced and expanded following transduction of human BCL6 and Bcl-xL. **Left panels:** Flow cytometry identification of BCL6 + Bcl-xL transduced (GFP^+) $CD19^+$ B cells from Chimpanzee and $B220^+$ B cells from Balb/c mice in culture with CD40L-L cells and IL-21 four days post transduction. The numbers indicate the percentage of transduced cells. **Right panels:** Overexpression of BCL6 and Bcl-xL confers a high proliferative capacity to transduced peripheral blood B cells from Chimpanzee and Balb/c mice. Data plotted as in Fig. 1c.



Supplementary Figure 2.

Comparison of total IgG production by BCL6 + Bcl-xL transduced cells versus *in vitro*-differentiated memory and plasma cells in a protocol adapted from Kuo *et al.*[1]. $CD19^{+}CD3^{-}IgD^{-}CD44^{-}$ tonsil GC B cells or BCL6 + Bcl-xL double-transduced cells were cultured with CD40L-L cells in the presence of IL-21 (25 ng ml^{-1}, *in vitro* [iv] plasma cell conditions) or IL-2 (100 U ml^{-1}) and IL-4 (50 ng ml^{-1}, *in vitro* [iv] memory cell conditions) for 5 days. Cells were counted and analyzed for (**a**) CD38, CD20, and sIgG expression and (**b**) supernatants were analyzed for IgG by ELISA. Total IgG production per 10,000 cells is shown.

Supplementary methods

B cell isolation. We obtained $CD19^+$ B cells from monkeys from frozen PBMC. All animals were housed at the Biomedical Primate Research Centre, Rijswijk, The Netherlands, according to international guidelines for primate care and use while study protocols were approved by the International Animals' Care and Use Committee in accordance with international ethical and scientific guidelines. We isolated Balb/c B cells by Ficoll separation from the blood of five mice and subsequently $CD3^-CD8^-$ $B220^+$ FACS sorted them.

Retroviral transduction. We transduced monkey cells with Amphotropic virus, mouse cells were transduced using Ecotropic virus encoding human BCL6 and Bcl-xL as described in the methods section.

Tonsil B cell sorting. We obtained Tonsil B cells from routine tonsillectomies performed at the Department of Otolaryngology at the Academic Medical Center, Amsterdam, The Netherlands. We separated B cells by Ficoll and sorted the $CD19^+CD3^-CD44^-IgD^-$ GC population. The use of these tissues was approved by the medical ethical committees of the institution and was contingent on informed consent.

Flow cytometry. We purchased the following mAbs against the human molecules from BD-Pharmingen unless otherwise indicated CD3 (SK7), CD10 (HI10a), CD19 (SJ25C1), CD20 (B9E9; Beckman Coulter), CD21 (B-ly4), CD22 (B-ly8; IQ Products), CD25 (BC96; eBioscience), CD27 (O323; eBioscience), CD30 (BerH8), CD38 (HB7), CD40 (MAB89; Beckman Coulter), CD70 (Ki24), CD71 (YDJ1.2.2;

Beckman Coulter), CD80 (L307.4), CD86 (2331), CD95 (DX2), CD132 (TUGh4), CD184 (CXCR4, 12G5), CD271 (LNGFR; ME20.4-1.H4; Miltenyi Biotech), CD275 (MIH12; eBioscience), HLA-DR (L243), IgA ($F(ab)_2$; DAKO), IgD (IA6-2), IgG (G18-145), IgM (G20-127) (BD), IL-21R (152512; R&D systems), Ig-kappa ($F(ab)_2$; DAKO, G20-193), and Ig-lambda ($F(ab)_2$; JDC12, DAKO).

Supplementary reference.

1. Kuo, T.C. et al. Repression of BCL-6 is required for the formation of human memory B cells in vitro. *J Exp Med* **204**, 819-830 (2007).