Antigen-armed antibodies targeting B lymphoma cells effectively activate antigen-specific CD4+ T cells.

The treatment of non-Hodgkin lymphomas has benefited enormously from the introduction of monoclonal antibody-based therapies. However, the efficacy of these treatments varies with lymphoma subtypes and typically decreases with subsequent relapses. Here, we report on antigen-armed antibodies (AgAbs) as a potential treatment of B-cell lymphoma. AgAbs include antigens from ubiquitous pathogens, such as Epstein-Barr virus (EBV), that persist in their host and elicit strong lifelong T-cell responses. They act as vectors by introducing antigen directly into tumor cells to induce an antigen-specific CD4(+) T-cell response against these cells.

We have fused antibodies targeting human B-cell surface receptors (CD19-22) to immunodominant T-cell antigens from EBV proteins, including EBNA1, EBNA3B, and EBNA3C. Exposure of EBV-transformed B cells and of Burkitt lymphoma cells to AgAbs led to antigen presentation, T-cell recognition, and target cell killing. The efficiency of AgAb action paralleled the abundance of the targeted molecules on lymphoma cells as well as their HLA class II expression levels. AgAbs can also induce activation and proliferation of EBV-specific memory CD4(+) T cells ex vivo. These studies show the potential of AgAbs as an effective therapeutic strategy against B-cell lymphomas.