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Determining the Efficacy of Antigen-armed Antibody in B Cell Lymphoma

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In this thesis, a new type of antibody, so-called antigen-armed antibodies (AgAbs), has been generated, in which the peptide of an immunodominant T cell epitope of a common pathogen such as EBV has been incorporated into antibodies targeting B cell specific surface receptors (CD-19, -20, -21 and -22). AgAbs directed against four B cell surface receptors (CD19, 20. 21 and 22) efficiently targeted HLA-matched LCLs and Burkitt's lymphoma (BL) cell lines, resulting in antigen presentation and activation of EBV epitope-specific CD4+ T cells. These activated CD4+ T cells could kill the LCL and BL target cells. The antigen presentation efficiency of AgAbs was superior to treatment with the corresponding peptides alone. The action of AgAbs depended on both surface receptor expression and HLA class II expression levels. In CD21 negative DG75 cells, CD21-targeted antigen presentation could be restored by stable transfection of CD21, and the absence of CD21 was shown to be beneficial for CD19-targeted antigen presentation. AgAb treatment demonstrates potential as a therapeutic strategy against B cell lymphoma and this strategy warrants further investigation in additional B lymphoma subtypes, especially for those that retain a high expression of HLA class II, and in a mouse model of B cell lymphoma.