High therapeutic efficacy of a new survivin LSP-Cancer vaccine containing CD^{4+} and CD^{8+} T-Cell epitopes

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The tumor antigen survivin is an attractive target to develop therapeutic cancer vaccines because of its restricted over-expression and vital functions in most human tumors. Accordingly, several clinical trials targeting survivin in various cancer indications have been conducted. Most of them relied on short peptide-based vaccines and showed promising, but limited clinical results. In this study, we investigated the immunogenicity and therapeutic efficacy of a new long synthetic peptide (LSP)-based cancer vaccine targeting the tumor antigen survivin (SVX). This SVX vaccine is composed of three long synthetic peptides containing several CD^{4+} and CD^{8+} T-cell epitopes, which bind to various HLA class II and class I molecules. Studies in healthy individuals showed CD^{4+} and CD^{8+} T-cell immunogenicity of SVX peptides in human, irrespective of the individual's HLA types. Importantly, high frequencies of spontaneous T-cell precursors specific to SVX peptides were also detected in the blood of various cancer patients, demonstrating the absence of tolerance against these peptides. We then demonstrated SVX vaccine's high therapeutic efficacy against four different established murine tumor models, associated with its capacity to generate both specific cytotoxic CD8+ and multifunctional Th1 CD^{4+} T-cell responses. When tumors were eradicated, generated memory T-cell responses protected against rechallenge allowing long-term protection against relapses. Treatment with SVX vaccine was also found to reshape the tumor microenvironment by increasing the tumor infiltration of both CD^{4+} and CD^{8+} T cells but not Treg cells therefore tipping the balance toward a highly efficient immune response. These results highlight that this LSP-based SVX vaccine appears as a promising cancer vaccine and warrants its further clinical development.

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