

Altered peptide epitopes derived from the anti-apoptotic protein “survivin” may stimulate effective anti-glioma immune responses.

Lay Abstract:

Malignant gliomas (brain tumors) are among the most aggressive and devastating of all human cancers. Even with aggressive treatment, including surgery, radiation therapy and chemotherapy, survival remains poor and has not improved significantly in several decades. Evidence suggests that malignant gliomas may be treated through vaccination. Our initial observation that a DNA vaccine against a tumor protein called “survivin” inhibits the growth of these tumors in mice. Our further characterization of this DNA vaccine has led to the discovery of small portions of protein (peptides) that were responsible for recognition by the immune system. These peptides when used as vaccines by themselves were as effective as using the entire protein for an immunization. Thus we have focused on these peptides as the most basic elements of an effective vaccine. The key issue that we wish to address in this proposal is the possibility that a new approach utilizing single amino acid changes artificially introduced into the peptide vaccines changes the properties of the subsequent immune response. Particular changes can actually lead to an enhanced immune response over the of the normal peptide vaccine. We are proposing to develop these altered peptide vaccines and characterize their efficacy in mouse brain tumor models. The results of this study could directly lead to development of a clinical trial of a new vaccine for brain tumor patients.