ABSTRACT BODY

Background

Currently, cardiac myxomas are extremely rare but life-threatening tumors due to risk sudden death. Mathematical models analyzing tumor-immune interactions provide a framework that can be used to better understand tumors and specifically target tumor antigens, which can potentially be used for a cure for cardiac malignancies. Currently the overexpression of the ANXA3, ACOX2, MIA, PLA2GA2, PRKAR1, NKX2-5, MEF2, and GATA4 genes has been linked to the development of cardiac myxomas. We created a mathematical model using synthetic antigens which are tumor epitopes expressed by cardiac myxomas, to both test the strength of a model human immune system and see the immune system’s response for generation of a tumor vaccine.

Methods

We constructed a model based on the immune system model by de Pillis, one we previously used for lung cancer. MATLAB was utilized to numerically simulate all equations describing tumor-immune growth, antigen presentation, host immune response, and interaction rates. The immune system is modeled through thirteen coupled differential equations in which each equation exhibits the rate of change of a cell population in terms of growth, death, cell-cell kill, cell recruitment, and cell inactivation. This model has been modified further to introduce the addition of cardiac myxoma “vaccines” using Monte-Carlo processes to simulate an antigen stimulation response to a variety of HLA epitopes. A simulator was utilized to vary the response of an individual’s immune system when exposed to a tumor vaccine and model the immune system once a cardiac tumor is detected.

Results

We used 12 different tumor antigen epitopes from cardiac myxomas from the most over-expressed genes to test the immune system response. Our mathematical model and monte carlo simulation showed that a robust immune response can be generated if the immune system recognizes epitopes that are between 41 to 452 amino acids long.

Conclusion

We have used mathematical modeling as a tool to depict the relative strength of a host’s immune response after it has been subjected to a cardiac myxoma vaccine. Here, we showed and can infer that if a synthetic epitope is not between 41-452 amino acids long, a host will produce an immune response.

Clinical Implications

Our model for vaccines against specific cardiac myxoma tumor antigens can be used as a basis for both better understanding cardiac malignancies and to hopefully develop a cure that does not involve surgical resection.