Cardiac Myxoma Tumor Dynamics: A Monte Carlo Simulation As a Basis for a Tumor Vaccine

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INTRODUCTION

- 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 multiple malignancies.
- An important aspect of tumor-immune surveillance to consider is elimination of tumor cells.
- 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 evaluate the immune system’s response.
- Utilizing multi-organ mapping and the lack of division by heart cells, the antigens of the heart and the tumor antigens of cardiac myxomas can be studied together to better understand tumor-immune dynamics.
- Currently the overexpression of the ANXA3, ACOX2, MIA, PLA2GA2, PRKAR1, NNX2-5, MEF2, and GATA4 genes has been linked to the development of cardiac myxomas.

METHODOLOGY

- We constructed a model based on the immune system model by de Pillis, one that we previously used to examine lung cancer\(^1\).
- MATLAB was utilized to numerically simulate and 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.

- The strength of binding depended on the generated values of two variables from the Monte Carlo process.
- 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.
- The resultant model is composed of cardiac myxoma epitopes of different fragment sizes (41-452 amino acids long).

RESULTS AND DISCUSSION

- Cardiac myxomas are encountered three times more often in women\(^1\). It is more common in the fourth to seventh decades of life, mostly diagnosed in adults.
- 60 to 80% arise in the left atrium typically in the fossa ovalis, 15-28% in the right atrium, 12% in ventricles or valves\(^2\).
- About 755 of cardiac myxomas are in the left atrium and 25% in the right atrium\(^2\).
- We used a total of 12 different tumor antigen epitopes from cardiac myxomas to test the immune system response:
  - 5 from the ANXA3 gene, 1 from ACOX2, 1 from MIA, 1 from PLA2GA2, 1 from PRKAR1, 1 from NNX2-5, 1 from MEF2, and 1 from GATA4.
- 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.
- The model can be utilized to simulate the strength of a host’s immune response after a host is inoculated with a cardiac myxoma vaccine.
- Results from the model are in silico, meaning that results from this model can be applied to a clinical setting.

CONCLUSION

- 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.
- Here, we showed and can infer that if a synthetic epitope is not between 41 to 452 amino acids long, a host will produce an immune response.

REFERENCES

- DoPillis et al. in 2005

DISCLOSURES: NONE