Name(s)

Jessie Gan

Project Number

S0507

Project Title

Using Bioinformatics Tools to Identify Epitopes in MMP-15: A Potential Lung Cancer Drug Target

Abstract

Objectives

Immunotherapy is an emerging cancer treatment which may use techniques such as monoclonal antibodies to target cancer-specific surface proteins. Matrix Metalloproteinase 15 (MMP-15) is a surface protein implicated metastasis, however it s not well characterized. The purpose of this study is to locate epitopes for drug targeting and to elucidate features of this potentially important protein in cancer progression through use of bioinformatics analysis tools. The study was conducted for two different alignments of protein sequences: one of mammalian MMP-15 sequences and the other of Membrane Type MMP (MT-MMP) sequences. It was hypothesized that analysis of the mammalian alignment would reveal regions of conservation, implying importance and potential targets. For the MT-MMP alignment, it was predicted that analysis would identify regions of variability, which would be favorable targets to reduce toxicity due to mis-docking.

Methods

Using NCBI protein database, sequences for mammalian MMP-15 proteins and various MT-MMPs are procured and aligned using Clustal Omega. Alignment was then analyzed through production of boxshade figures, Shannon entropy plots, and structural mapping.

Results

Results from Shannon entropy plots and boxshade figure identified conserved catalytic and hemopexin domains in the mammalian alignment and variable, unique peptide regions in MT-MMP sequences. Conserved catalytic domain regions were also observed in the MT-MMP alignment.

Conclusions

The use of bioinformatics tools was able to elucidate features and potential drug targets of MMP-15. Conservation of catalytic and hemopexin domains in the mammalian alignment imply importance, and highly similar sites of this alignment may be potential drug targets. The use of Shannon entropy and boxshade plots were able to identify a MMP-15 peptide from residues 569-603 of the MT-MMP alignment, which is a viable target epitope due to its uniqueness to only MMP-15 and therefore would make the drug very specific. The next step in the project is to synthesize peptides identified in this study for monoclonal antibody production against lung cancer.

Summary Statement

Through the analysis of MMP-15 and MT-MMP amino acid sequences, I found potential epitopes for lung cancer drug targeting.

Help Received

I conducted a literature search of possible cancer proteins and performed all bioinformatics analyses myself. My mentor, Dr. Vaughn Smider, gave recommendations on cancer epitopes and bioinformatics analysis software.