CALIFORNIA STATE SCIENCE FAIR
2014 PROJECT SUMMARY

Name(s)

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Project Number

S1505

Project Title

Towards a Combination Antiviral Therapy for Flu: An Interdisciplinary Drug Discovery Effort

Abstract

Objectives/Goals

A pandemic outbreak of a highly pathogenic influenza virus such as the avian H5N1 or H7N9 strain could potentially kill millions of people before new vaccines become available. Since current antiviral drugs are losing their effectiveness as resistant virus strains emerge, new anti-influenza drugs are urgently needed. My hypothesis is that blocking the influenza cap-snatching step is a good strategy for developing the next-generation anti-flu medicine.

Methods/Materials

I performed co-crystallography to identify more potent inhibitors of PA endonuclease. I used a docking-based virtual screen followed by biological validation to discovery cap-binding inhibitors of the PB2 subunit. Using a viral transcription assay, I found inhibitors of PA and PB2 had better effect when used together than either on alone.

Results

I was able to discover new drug leads for two different subunits of the influenza polymerase that show promise for development into new flu medicine. Structural information from co-crystallography and docking also will be vital for further drug design and optimization.

Conclusions/Discussion

Therefore, the newly discovered inhibitors of PA and PB2 can potentially be used in a combination therapy to reduce the chance of developing drug resistance.

Summary Statement

A multidisciplinary approach combining crystallography, computational chemistry, and biology was used to discover new drug leads for influenza targets that show potential for application in a combination therapy.

Help Received

Used the lab equipment of Dr. Feng, Dr. Amaro, and Dr. Wilson.