

Interactions Between HIV Proteins GP160, Nef, and the Human Body

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INTRODUCTION

In the approximately 25 years since its discovery, HIV-1 has killed over 25 million people, and it affects another 33 million people today [1]. This deadly virus makes only 15 proteins, and so it must hijack the host cell's machinery to survive and replicate [2]. To do this, HIV-1 targets the body's CD4+ T lymphocytes, incorporates its genome into the host DNA via the enzyme *reverse transcriptase*, and activates cellular production of more viruses. This decreases the number of CD4+ T lymphocytes, which inhibits the body's capacity for immune response [1].

Current HIV-1 treatments are generally a mix of three or more drugs which serve to terminate viral DNA elongation during reverse transcription, thereby preventing meaningful incorporation into the cellular genome [1]. This treatment, however, is far from perfect; and several problems still exist.

The high replication rates of the HIV-1 virus, combined with the high error rates of RNA replication and reverse transcription, lead to the constant creation of new viral strands which may be drug resistant [1]. While current therapies allow adequate control of viral replication, another treatment problem persists: While HIV-1 reproduction may be controllable with constant drug treatment, HIV-1 remains in the CD4+ lymphocytes and can again reproduce once treatment stops [1].

Many current efforts in HIV research, then, focus on the integration of the initial HIV genome into the host cell, but this is still an area of relatively little knowledge [1]. If alternate drug targets can be identified, then more effective HIV treatments or potential cures can be produced.

METHODS

A recent siRNA screen has identified host proteins required by the HIV-1 virus for replication [2]. While it is known that certain proteins are required by the HIV virus, the precise nature of the relationship between these proteins and the virus itself remains mostly unknown [1]. Our aim is to determine the nature of relationship between these necessary human body proteins and the HIV proteins GP-160 and Nef.

To do this, we plan to use a combination of computational and traditional wet lab methods. Dr. Klein-Seetharaman and colleagues have a database which will predict protein-protein interactions (PPIs) [3]. We plan to use this database to search for predicted interactions with the GP-160 and Nef proteins to human body proteins. From the predicted matches, we plan to research the literature to determine which of the predicted matches holds the most clinical/pathological relevance to the HIV-1 life cycle. We will then order quantities of these proteins, and we will try to determine the chemical mechanism of action in the lab.

GOALS

In this method, we hope to flesh out the specific pathways between the HIV-1 virus and the human body. The identification of such pathways holds the potential for new antiviral drug targets and, in turn, for novel and more effective HIV-1 treatments.

REFERENCES

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<<http://gelato.blm.cs.cmu.edu:8080/hivPpiInvokeV2/interfaces/inter1/index.htm>>