Attacking AIDS

Tackling the AIDS virus as it tries to make proteins to reproduce itself could lead to the development of a whole new class of drugs to attack the condition.

Professor Warren Tate from the University of Otago Department of Biochemistry says that existing therapies are expensive, requiring varying combinations of three classes of drugs to combat two different aspects of HIV biology.

It is this combination that converts their infection from being a fairly rapidly lethal disease to one where it is held as a chronic infectious disease. But the cost of these drug combinations means that therapy is not getting to the people in the most infected areas such as Africa and Asia.

Professor Tate’s group is looking at another aspect of viral biology which hasn’t been examined in great detail but is unique in that it targets the way the virus makes its proteins.

AIDS uses an unusual mechanism, called translational frameshifting, just at one point of protein synthesis.

“What that means is that the human ribosome reads the viral RNA, to decode it and make proteins,” Professor Tate explains. “It reads the viral RNA in group of three letters, just like it reads its own RNA, but it gets to a point where it slips backwards by one letter and is now in a new frame.”

Professor Tate discovered the mechanism in a bacterial gene in the 1980s. So when HIV was found to use it, this allowed his team to apply a lot of their resources and skills from their earlier HRC supported research on what has been called genetic recoding, or the unusual events genes use in their expression.

One of the strengths of this strategy is that they are targeting an aspect of the virus for which it cannot readily develop resistance.

“What we are doing is targeting a host function, namely the part of the human cell where proteins are made and the indication is that you don’t have to mess it up too much to dramatically affect the ability of the virus to re-infect other surrounding cells.”

Professor Tate says that the advantage of this is that we might be able to use known compounds like antibiotics, which can be produced at low cost.

At this stage his group have established proof of principle using model systems, first in a test tube and now with cells and tissue cultures. They have also tested a number of compounds that can affect this event.

Professor Tate says that there is a huge need for a cheaper form of therapy with 30 million people worldwide not on any effective treatment at the moment.

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