Danish researches solve virus puzzle

March 30 2007

How is virus as for example HIV and bird flu able to make the cells within a human body work for the purpose of the virus? Researchers at the University of Copenhagen shed new light on this question.

The research is a collaboration between molecular biologists and physicists. ”The molecular biologists have knowledge of how the cell functions and of the interplay between the intercellular parts, while the physicists have the expertise and the technique to be able to measure and analyze the physical processes.” says Lene Oddershede, physicist at the Niels Bohr Institute, University of Copenhagen. This interdisciplinary work between physics and biology has been very fruitful and will be published April 3rd in the prestigious scientific journal *PNAS, Proceedings of the National Academy of Sciences*.

The researchers have investigated how a virus exploits the machinery of human cells to produce the proteins which the virus needs in order to replicate to billions of new vira. The virus penetrates into the host cell where it liberates its RNA which is a copy of the heritage material, DNA. RNA is like a 'cook book' which contains the recipes of which proteins the virus needs for replication.

The work process of a virus

The cell has ribosomes, a kind of 'molecular motors', which move along the RNA and read the code for the proteins to be produced to fulfill the needs of the living cell. The task of the ribosomes is to read the code of the host cell, but the virus has the special trick that its RNA resembles

that of the host cell, and hence, the ribosomes of the host cell will start reading the viral RNA and produce the proteins requested by the virus. In order words, the virus can be viewed as a parasite, exploiting the human cell to live and replicate in.

Viral RNA resembles human RNA, but it has a tendency to curl up into 'pseudoknots', a three dimensional structure. When the ribosome walking along an RNA encounters a pseudoknot it needs to unravel the pseudoknot before it can proceed. Question is, how does it do that? Lene Oddershede at the Niels Bohr Institute, University of Copenhagen has developed optical tweezers which can investigate and manipulate molecules at the nano-meter scale. Using a tightly focussed laserbeam this instrument can grab the ends of the RNA tether and follow the process of how the pseudoknot is mechanically unfolded.

A crucial slip of the cellular motor

In their investigations the researchers use a pseudoknot which is related to bird flu. When the ribosome encounters a pseudoknot it has to unravel the knot before the reading can proceed. During this process the ribosome sometimes slips backwards and, like the letters making up a word, it now reads a new RNA sequence and hence uses another recipe to construct the protein. The researchers have found that the stronger the pseudoknot the more often this backwards slipping happens. The different protein formed is the protein needed by the virus, with possible serious consequences for the hosting organism. This is the manner in which many vira, e.g. HIV, trick the cell into producing something which it never would have done otherwise. Understanding the role of the pseudoknots can be an important step in developing a viral vaccine.

Source: University of Copenhagen