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New technique records viral birthpangs

The main thing a virus does is to get in the way, says S.Ananthanarayanan.

The sole activity of a virus is reproduction. The chief components of a virus are its specific set of surface features and its formula for replication. The surface features help the virus to exactly home into a specific type of cell and once the virus is in place, the DNA, or the replication formula of the virus is injected into the cell.

The virus then uses the cell's machinery to produce its own proteins. These proteins string together to form the basic virus, complete with envelope and genetic material, capable of infecting other cells and known as the ***virion***. The cell, in the process, instead of going on with its own business, has become a factory for new viruses.

Virus action

The virus thus acts in two ways – one is to block the cell in its legitimate function, which may be to produce a particular enzyme, or to monitor the levels of other enzymes and then generate the agent that switches on other activity, etc. When this function is blocked because of the viral free-boarder, the body develops disease and whatever else.

The other virus action is to replicate and invade other cells. This ability to replicate, in fact, is the characteristic of the virus and which brings the same name to computer code that reproduces itself. The computer viruses also, except the more malicious kind, act mainly by using up memory or other computer resource because of their own expanding numbers.

The main defense against the virus is through the body's immune mechanism, which creates agents that can block the surface features of the virus and thus prevent it from attaching to target cells. The ability of the immune mechanism to respond to attack by prompt generation of defenses can be sharpened by giving the system a pre-taste of the invader, which is what happens in the protection by vaccination.

As we know, the AIDS virus is the one that targets the immune cell itself – which is why it is so difficult to deal with!

Getting to see the virions

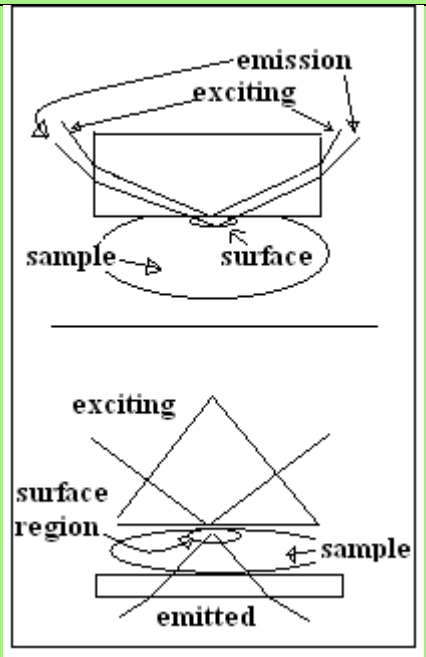
The manner in which individual virions attach, enter, and then go from cell to cell has been a subject of study. But the mechanism by which they form, by the protein components stringing together, has not been watched in action. Some properties have been deduced from studies of populations of virions or study of infected cells, but just how they get assembled has remained conjecture.

The journal, ***Nature***, this week, carries a report of the work of Sanford Simon and colleagues at the Rockefeller University, New York in developing microscopy to image detailed growth of virions of HIV-1, from start of assembly, budding and release of virions.

Total internal reflection

Events at the surface of cells can be studied with the help of fluorescence – or the property of some materials to give off light of one colour when excited with light of another, more energetic colour. This is the effect that gives us the 'cold' light from the fluorescent tube – the coating of the tube glows with near white light because of the excitation by the electric discharge inside the tube.

In microscopy, the specimen is doped with fluorescent atoms and the glow of these atoms helps form images. The problem is that the fluorescence from the portion at the ***surface*** of the cell is often masked by the strong glow that comes from deeper within. A way out has been to use a form of light that does not penetrate deep and thus excites only the targets right at the surface.



Light behaves in this non-penetrating way when it totally reflects off any surface. Total reflection takes place when light falls on a surface at a ***glancing*** angle, so sharp that no part is able to enter, because it would need to bend too steeply. When light reflects like this, the strength of its effect beyond or before the surface falls very sharply and disappears within a very short distance.

If such a light beam is used to excite fluorescent atoms near the surface, then their glow could be seen without the glare from atoms deeper within. This is the principle of the total internal reflection fluorescence microscope, a device developed in the 1980s and which has enabled very fine, real-time observation of events at the surface of cells.

Virions being born

It is known that the growth of virus-like particles, or virions, in HIV-1 depends on ***Gag proteins*** (Group specific AntiGen), an important component of HIV-1 and carrier of the information needed to form the new virus. The use of the internal reflection method has enabled watching individual virions grow, over a period of 5-6 minutes, as the level of Gag protein increases. The increase was observed with the help of fluorescent tags in the Gag protein. The technique has enabled seeing a large number of virus-like particles forming at the cell membrane and the dynamics of Gag protein appearance and motion.

Refining this methodology should allow other the role and dynamics of other components of viral reproduction to be studied.