SCIENCE NEWS 1995 April 8, 1995
Vol. 147 No. 14 p. 214

AIDS progression fostered by dioxin?

Smokers infected with HIV-1 tend to develop AIDS more quickly than nonsmokers. Some scientists have also observed that dioxinlike compounds foster the proliferation of this AIDS virus in cultured cells. New research offers one possible explanation for both findings.

It shows that HIV-1 possesses a hitherto unrecognized docking site for a cellular protein to which dioxins and many other toxic compounds bind. When this protein binds with a pollutant and the resulting complex links with the virus, it activates HIV's genes.

TCDD, the most toxic dioxin, and a number of related compounds all bind to this protein, known as the Ah (aryl hydrocarbon) receptor, which resides in the liquid interior of cells. The binding of a pollutant to this receptor initiates a transformation that suddenly renders the duo capable of entering a cell's nucleus, where they can inappropriately turn genes on or off.

In the April Environmental Health Perspectives, researchers at the University of Cincinnati Medical Center report finding a binding site for the Ah receptor in the portion of HIV's genetic material where regulatory proteins bind to activate viral genes — an area called the long-terminal repeat.

To gauge the receptor's importance, they inserted a bacterial gene known as CAT into that long-terminal repeat as a genetic flag. They then infected mouse liver cells with the modified HIV and monitored the extent to which the virus turned CAT on when the cells were exposed to a range of toxicants.

Benzo(a)pyrene, a carcinogen present in cigarette smoke, and aflatoxin B1, a fungal poison, both quintupled CAT activity over the level seen in unstimulated cells or cells exposed to the solvent used to deliver the pollutants. TCDD and three combustion by-products doubled or tripled CAT activity.

But none of the compounds affected the activity of CAT in a mutant form of HIV lacking the Ah receptor binding site or in cells protected against reactive, biologically damaging molecular fragments known as free radicals (for their free, or unpaired, electron).

Those follow-up experiments confirm that both the receptor binding site and free radicals must be present in the cell for the activation of HIV by these types of pollutants, explains Alvaro Puga, who led the studies.

How important are these compounds to AIDS? That will depend on which cells host the virus, Puga says — specifically, whether they have Ah receptors and can foster the free radicals needed to cause damage.

— J. Raloff