



Can valproic acid lure HIV out of hiding?

by Julie Schneiderman

New research suggests we might finally have the ability to tap into latent HIV reservoirs. Results from a proof-of-concept study published in August 2005 in the *The Lancet* led to a flurry of attention over the potential effects of valproic acid (Depakene). Valproic acid is presently on the market and approved for use as an anticonvulsant.

The team of Texas-based researchers set out to assess the efficacy of a standard clinical dose of valproic acid to deplete HIV from resting CD4 cells. Unlike highly active antiretroviral therapy (HAART), which attacks the virus but cannot access and block the latent reserves, their pilot study showed that in three out of the four participants the amount of resting cell infection was reduced by an average of 75 percent.

Researchers believe that once valproic acid has flushed out and isolated the virus, a combination of antiretroviral therapy, vaccines, and other interventions might be able to effectively purge the virus from the body. The methods used to treat HIV in the future, then, might not be much different from strategies currently used to treat certain types of cancers.

To further test these concepts, Canadian HIV Trials Network (CTN) investigators Drs. Jean-Pierre Routy, Cecile Tremblay, and Rafick-Pierre Sékaly and their team at McGill University have proposed a clinical trial using valproic acid to lure latent HIV reserves out of cells and then block their re-entry (CTN 205). Since reservoirs have continued to be one of the most complex elements of the disease, valproic acid could be the key

to unlocking some of the mysteries. As Dr. Routy explained: "It used to be a mission impossible to play with reservoirs and now this is a first step."

Routy and his colleagues had initially planned a single-site study with approximately 50 participants. However, following the CTN's semi-annual meetings in Montreal, new sites have agreed to participate. In addition to Montreal Chest and Hôtel Dieu (CHUM), they include: Dr. Julio Montaner, St. Paul's Hospital, Vancouver; Dr. Danielle Rouleau, Notre-Dame Hospital, Montreal; Dr. Benoît Trottier, Clinique Médicale l'Actuel, Montreal; Dr. Jonathan Angel, Ottawa General Hospital; Dr. Jean Guy Baril, Clinique Médicale du Quartier Latin, Montreal. These sites could increase participation to at least 75 people. The study expects to begin enrolling in early 2006.

Research on valproic acid is not without its critics who are hesitant to point to results until further research is done. Others caution that while resting CD4 T-cells remain an important hiding spot for HIV, it is still unclear whether reservoirs of the virus can stay latent elsewhere in the body. Despite the skepticism and words of warning, Dr. Routy is optimistic about the study and its long-term potential for furthering research: "It is amazing to see that something can even begin to crack the enormous wall of HIV." ⊕

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Trials enrolling in BC

CTN 147 — Early Versus Delayed Pneumococcal Vaccination
BC sites: Downtown Infectious Disease Clinic (IDC) and St. Paul's Hospital, Providence Health Care, Vancouver

CTN 167 — OPTIMA: Options with Antiretrovirals
BC sites: Viron Health, Downtown IDC, and St. Paul's Hospital, Vancouver, Cool Aid Community Health Centre, Victoria and Medical Arts Health Research Group, Kelowna

CTN 178 — Effect of Rosiglitazone Maleate (Avandia) on Blood Vessels
BC site: St. Paul's Hospital, Vancouver

CTN 189 — 3TC or No 3TC for HIV with 3TC Resistance
BC sites: St. Paul's Hospital, Vancouver; and Cool Aid Community Health Centre, Victoria

CTN 190 — SMART: Strategies for Management of Antiretroviral Therapy
BC site: Downtown IDC, Vancouver

To find out more about these and other trials, check out the **Canadian HIV Trials database** at www.hivnet.ubc.ca/ctn.html or call Sophie at the CTN 1.800.661.4664.