Life After Birth

Anne-christine d'Adesky on mom's little helper: a placenta protein promising a new entry block*er*

June 1, 2001 By Anne-christine d'Adesky

Why do 70 percent of moms with HIV deliver HIV negative babies? What mystery confers protection? Bruce Patterson, MD, of Northwestern University's Children's Memorial Hospital may have found a major piece of this baffling puzzle. Mother Nature, it seems, offers us a home-grown anti-HIV weapon: Leukemia Inhibitory Factor (LIF), a natural protein that flourishes in the rich soil of women's placentas. Based on Patterson's test-tube studies, LIF may be "up to a thousand times more potent against HIV than AZT," despite being a miniscule molecule measured in picograms. If LIF's natural power can be harnessed, a little will go a long way.

How does LIF work? The natural protein is, according to Patterson, a cytokine-like molecule -- essential not only to cell-to-cell communication but to implantation of the fetus. Patterson hypothesizes that it attacks HIV right after the virus enters the cell, just before reverse transcription (the point at which AZT and other nukes muck up the virus' lifecycle). So LIF "might be a whole new area of entry inhibition," says Patterson.

An admitted "techie" with a background in virology and molecular biology, the 38-year-old Patterson stumbled across LIF with his own home-grown technology using gene chips to compare viral RNA in the placentas of women who transmitted HIV to their babies and those who didn't. To his surprise, LIF popped off the charts. "There were cytokine, chemokine-receptor, hormonal differences, but the one thing that we really noticed was LIF," Patterson says. In a poster session at February's Retrovirus Conference in Chicago, Patterson showed that the placentas of women who *did not* pass on the virus had much higher levels of LIF. Patterson cultured the placenta and then tested LIF against HIV. Pow! "It's a very active little molecule," Patterson says.

LIF is directly linked to progesterone, a hormone that kicks in during pregnancy. "Progesterone is used in fertility, so if you agree that HIV transmission occurs in the placenta during the first trimester, then you're talking about being able to provide additional protection," he says, adding that he is planning the first clinical trial to study the LIF-progesterone link.

He also found high expression of LIF in the thymus, a key organ in CD4 cell immunity to HIV. Since the destruction of thymic tissue is linked to AIDS progression, this finding could be important, especially for HIV positive children with budding thymuses. Meanwhile, a Swedish team has reported high LIF levels in the lymph nodes of acutely ill HIVers. "Is it the chicken or the egg?" Patterson asks. "Is LIF increased by some mechanism to fight HIV, or is HIV itself inducing LIF

expression?”

Patterson recently got word that an Australian research group, Amrad, is testing LIF in Phase II clinical trials for treatment of neuropathy related to chemo. “We may be able to go right into human clinical trials,” he reports. “So far, those data show that LIF appears to be safe in humans.”

Peering past the placenta, Patterson sums up the big picture: “If human proteins that perform other functions in the body can also fight off viruses, there may be natural ways to increase the normal level of these proteins to fight HIV.” Maybe Mother knows best after all.

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