Don’t Make Me Over

Why we are more than our genes

September 1, 1998 By Dave Gilden

My friend Aldyn McKean led a vigorous life for 10-plus years with a CD4 count below 200. He attributed his continued health to such daily practices as good nut-rition, adequate sleep and careful stress management. Aldyn also prioritized PCP prophylaxis, but avoided AZT and the other feeble, toxic nukes of his day.

Aldyn was an ACT UP/ New York stalwart before he passed away in 1994; he considered his activism, too, a key to extending his life. His great triumph was using ACT UP as a base to successfully pressure researchers to study the factors that keep long-term survivors immunologically healthy. (The late Michael Callen, who famously credited his own longevity to “luck, Classic Coke and the love of a good man,” was the field’s trailblazer.) But ironically, researchers have hijacked Aldyn’s legacy, reducing his complex vision of health to a roll of the genetic dice.

In the years since Aldyn died, the term long-term survivor has gradually been supplanted by slow progressor—narrowly defined as only those whose CD4 counts remain substantial for many years after infection (which would have excluded Aldyn!). Yet studies of this group have produced remarkable scientific breakthroughs. Many scientists, citing some 400 articles published since 1996, anticipate that a specific set of genetic mutations will explain most slow progression.

Those mutations interfere with the chemokine receptor—one of the key T-cell landing pads that HIV uses to nudge its way into healthy cells. Researchers are finding that people with mutations that give them low levels of chemokine receptors or high amounts of circulating chemokines (immune messenger chemicals) seem to better resist the ravages of HIV.

That is great for those with the right genetic makeup, but what about everyone else? Science can offer the great majority of people with HIV only more pills to take. Intensive research has begun on chemokine-based therapies that would ward off HIV either by binding to the critical receptors or by reducing their production.

Another target on HIV is always welcome. It offers a further option to buttress the current antiretrovirals, which fail with disturbing frequency. But the chemokine approach has many of the same weaknesses as current drugs. Besides potential problems with toxicity and adherence, the

virus could easily adapt to such new drugs by switching to another type of chemokine receptor. Such a change often happens spontaneously in late-stage HIV infection and heralds a precipitous decline in health.

Perhaps a mix of agents would block a number of receptor types. The more drugs, though, the more likely the complications. You could inadvertently turn on or off some part of the immune system, with catastrophic results. And the body would be faced with the burden of eliminating more medicines, raising the specter of new kidney and liver toxicities.

These developments would have dismayed Aldyn. His sort of survival shows that you can fight back against HIV even if your genetic luck is poor. “I am interested in the things I can control myself much more than finding out the reason I’m alive is because of a certain genetic makeup,” he told me five years ago. While a whole new chemokine industry cranks into high gear, it’s worth remembering that people with the “good” mutations may deteriorate more slowly on average, but almost all progress eventually—many at normal rates.

More relevant to Aldyn’s vision is a steady trickle of reports associating long-term survival with the ability to sustain specific HIV-targeting immune cells. Too much or too little or too narrow a defense allows HIV to gain the upper hand and slaughter the cells that oppose it. There is growing recognition that such immune balance is subject to outside influences, from sleep deprivation to psychological stress to nutritional deficiencies. Aldyn wanted large-scale studies of the way long-term survivors used medication plus nutritional supplements, exercise, stress reduction, social outreach and other health-boosting measures.

The National Institutes of Health now has a “Section on Neuroendocrine Immunology and Behavior” to study the mind-body interplay, but its AIDS funding is minimal. On the whole, divvying up the lifestyle and molecular contributions to long-term HIV survival is a field that remains largely ignored. At stake is a range of easy-to-apply strategies that—if proven—could offer PWAs powerful tools for long-term survival.
