Failure Is Sweet

July 1, 2002 By Emily Bass

April’s Keystone Symposium in Colorado played a kind of winter games to this summer’s 13th International AIDS Conference in Barcelona. Both meetings mix a luxe setting -- a ski resort, sun-splashed Gaudi cathedrals -- with new findings from AIDS’ top researchers.

Keystone 2002 featured a variety of promising results, but the gold medal for relevance to HIVers went to Goldilocks -- the so-called Goldilocks Hypothesis floated by Mike McCune, MD, of the Gladstone Institute in California (see "Once Upon a Time"). San Francisco General Hospital’s Steven Deeks has long noted that some patients whose regimens are failing nonetheless continue to have high CD4s and good health. McCune’s study of SF General HAART-users who stayed on combos despite viral breakthroughs yielded provocative data. While these folks did not fare better than the undetectables, they were far healthier -- and for much longer -- than would be expected. It seems that HIV’s genetic mutations -- shaped by pressure specifically from protease inhibitors -- creates a less harmful virus.

But that’s not news. What’s exciting is McCune and Deeks’ discovery that some of those who stuck with therapy despite this protease-resistant viral rebound in fact had *stronger* HIV-specific immune responses than those with undetectable virus. Why? The immune system needs a certain threshold of virus to remain active; reducing viral load to near nothing “starves” immune cells of the necessary antigen stimulation. These responses are a homegrown weapon against HIV -- and may mean that the detectable virus does not equal a failed regimen.

That’s where Goldilocks enters, that picky girl who wanted her bed, chair and porridge *just so*. McCune stresses that it takes *“just the right amount of virus of just the right type”* to get these beneficial effects. He observed the boost in HIV-specific CD4 and CD8 cells only in people with viral loads of 1,000 to 10,000. Above and below this range, the immune responses dropped away. A toast to Deeks and McCune for questioning received wisdom.

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