A Pair of Genes

June 1, 2002 By Mike Barr

The future of HIV therapy is near, and it's called pharmacogenetics. So says an editorial in the March *Lancet*, featuring a scenario straight out of *Gattica*: Having recently tested positive, you visit your doctor for a quick genetic analysis of your body's tissues. No needle pricks -- a single strand of hair or sloughed-off skin cell will do. A computer generated result spits out a personally tailored prescription for the best time to start therapy, the most effective drug combo and the combo least likely to cause side effects. Price? $350 to $500. Turnaround time: one week.

Call it better living through technology. Our current "one size fits all" approach to HAART is, at best, an art and, at worst, the cause of needless drug failure and side effects. But a group of Swiss immunologists at the Lausanne-based lab of longtime AIDS researcher Giuseppe Pantaleo hopes to turn this art into a science -- to begin with, by accepting that "genetic differences play a major role in determining the success of therapy," as the group put it in a *Lancet* commentary.

Take the protease inhibitors. Two lone genes seem to control your body's response to that class of meds: If you have a version of these, chances are that the amount of drug making it into your blood and your cells will not be as high as it needs to be. Why? Blame it on your DNA, which affects the body's metabolism of the drugs, determining how much is actually utilized. Higher drug levels mean lower risk of resistance.

Or consider abacavir (Ziagen), one of the three Glaxo drugs in Trizivir. Some 5 to 10 percent of patients on abacavir develop a potentially life-threatening hypersensitivity reaction -- fever, rash and gastrointestinal symptoms in the first six weeks of treatment. Genetic testing, however, is on the verge of ID'ing who will develop this reaction. A team of Australian researchers recently reported results from their screening system, effective in ferreting out 72 percent of the at-risk cases. (A second study by Glaxo, however, was only 50 percent successful.) Australia's Simon Mallal, MD, cautions that his data do not yet constitute a diagnostic test for the abacavir reaction: Of the 18 people who developed the reaction, four did not have the genetic markers. Meantime, Glaxo's Seth Hetherington, MD, notes only that the results demonstrate "the potential" of pharmacogenetics in maximizing treatment strategies.

Clearly we are a long way from using this fledgling technology in clinical practice: The consensus seems to be that while the assay's "sensitivity" will soon improve, its "specificity" will lag -- meaning too many false positives. Still, if insurers can be pressured to cover it, the new gene test, once up to speed, is likely to help HIVers use their meds better.