Gene Pool

July 1, 1999 By Lark Lands, PhD

There’s a new numbers game in town: Counting mutations to forecast how well salvage therapy may work. A Swiss study recently found that among 62 PWAs whose HAART had failed, the only significant predictor of response to a new regimen containing nelfinavir was the number of resistance mutations present before starting the new therapy.

Participants had been heavily pretreated, averaging almost three years on nucleoside analog reverse transcriptase inhibitors (NRTIs, or “nukes” of the AZT class) and more than a year on protease inhibitors (PIs). Three people had tried nonnucleoside reverse transcriptase inhibitors (NNRTIs). Using genotypic resistance testing, researchers found that nine out of 10 participants had NRTI resistance mutations at the outset, with four mutations the norm. An equal proportion had PI mutations, with the same median of four. NNRTI mutations were comparatively low—7 percent —but after all, only 5 percent of participants had taken that class of antiretrovirals.

Alas, no one with more than three PI or five RTI (either nuke or non) resistance mutations achieved a significant (greater than one log or 10-fold) drop in viral load within four to 12 weeks, the response designated to indicate success. No other factor—medical history, duration of prior antiretroviral therapy, number of drugs used, starting-point CD4 count or viral load—was found to be a significant predictor of response to the new combo.
