Rhesus in Pieces

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A single HIV mutation -- not monkeying around -- killed a Harvard University primate in a promising vaccine trial. When researchers reported it in the January *Nature*, headlines in the popular press were quick to pen the obituary of all experimental vaccines using genetic strategies. But experts dismissed the rumors of death as exaggerated.

The Harvard vax uses synthetic viral proteins to imprint immune cells with an HIV ID so that if the real culprit shows up, the body can search and destroy. This so-called therapeutic vaccine is intended to help those already infected keep the virus in check. Due to the extraordinary complexity of conferring immunity to all of HIV's different strains, a therapeutic vaccine is considered a more realistic goal in the short term than a vaccine that prevents infection outright.

Eight Rhesus monkeys in the study were infected with SHIV, the simian version of HIV, about three years ago. They all were doing well on the vaccine until the virus in one primate, known affectionately as No. 798, abruptly pulled a genetic switcheroo so that the SHIV-imprinted T cells could no longer recognize it as the enemy.

The death of a single monkey looms larger than might at first appear in a field so specialized that only a dozen or so genetic vaccines have been tested. Still, some of the candidates have been successful in animal studies for more than two years. Scientists dubbed the death "sobering," but they deny that it's a major setback in AIDS vaccine development. "Certainly it's not a reason to slow down or lose enthusiasm," said Dan Barouch, MD, lead author of the study. In fact, Merck & Co. researchers reported very promising results with their AIDS vaccine in the same issue of *Nature*.

IAVI, the leading nonprofit fundraiser for global vaccine research, did some predictable damage control. "Problems with the Harvard vaccine may be a rare fluke," IAVI honcho Seth Berkeley, MD, said, "or they may be symptomatic of serious shortcomings. Time will tell."

Vax researchers have long known that HIV's genius for genetic mutation poses one of the highest hurdles to any successful vaccine strategy. "It was bound to happen," said Jeffrey Laurence, MD, amfAR's science consultant. But Laurence added that the Harvard vaccine and its counterparts, however flawed, will still be useful in regions of the world decimated by AIDS and devoid of meds. "You have to hope that any little bit can help," he said. A vaccine that would prolong lives would "make a big dent" in the death toll.