*Her life's work took a hairpin turn in 1981, when this researcher's immunology lab described the immune impairment in four patients with a mysterious illness soon to be known as AIDS. Now, with a grant from the Bill and Melinda Gates Foundation, her team is using sophisticated techniques to find out if a portion of the virus—the V3 loop, shaped like a hairpin—could be the key to developing a novel vaccine against HIV.*

# A Hairpin Turn

**Susan Zolla-Pazner, Ph.D.**
Professor of Pathology;
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"A chill spread through all of us in the lab…When we saw that one-third of our healthy test group had the same strange T-cell syndrome as the four patients identified with Kaposi sarcoma, we knew something enormous was circulating in the gay community," said long-time AIDS researcher Dr. Susan Zolla-Pazner, recalling the start of the epidemic.

That moment was also the start of a career-long search for the specific part of the HIV virus' protein coat that elicits antibodies that block HIV infection. Although many scientists turned away from this "antibody path" when early attempts to develop vaccines failed, as an immunologist, Dr. Zolla-Pazner remained convinced of the importance of pursuing antibodies in general, and V3 antibodies in particular. Her lab has already produced powerful antibodies from cell lines of individuals infected with HIV.

In 2006, Dr. Zolla-Pazner was the recipient of a three-year grant to participate in the Collaboration for AIDS Vaccine Discovery, an international network of highly collaborative research projects funded by the Gates Foundation. Dr. Zolla-Pazner has assembled an interdisciplinary team of researchers that builds on her own strength in immunology, including scientists specializing in virology, crystallography, and structural and computational biology. This team brings together scientists from eleven institutions in the United States, India, and Cameroon in West Africa, where HIV subtypes B, A and C, respectively, are predominant.

"When I came to New York for a two-year post-doc, I could never have imagined all this," she said. "The intellectual stimulation. The human catastrophe. The sense that maybe you can make a difference in your lifetime. The opportunity to pass on to students what you know—and show them how basic science can really impact on the human condition."

The HIV-1 virus surface V3 loop (rendered here as an orange ribbon) captured by the broadly neutralizing human monoclonal antibody 447-52D (colored surfaces). The sequences of amino acids that make up the V3 loop vary, but the fundamental structure with its distinctive hairpin turn remains the same, and is widely recognized by a powerful group of antibodies. Using special assays, these antibodies are being tested for neutralizing activity, and the most broadly acting are being crystallized along with the V3 loops that they recognize. The crystals are providing the basis for sophisticated molecular modeling studies that are helping researchers identify the features of the V3 loop that elicit protective antibodies.