



Big Questions for 2009 and Beyond

AIDS vaccine research has many enduring questions: Does clade matter? What constitutes an effective immune response? How can we best use the non-human primate (NHP) animal model? In these pages, we look at some of the recent research on these topics, but our *Report* is far from exhaustive. Below are some important questions that we hope will be addressed in the coming year and beyond.

1. What are the roles of various characteristics like epitope specificity and functionality in CD8 T cell-mediated viral control?
2. How does HIV genetic diversity matter for vaccine research? What systematic attempts can be made to address the relevance of clade—and at what stage in the vaccine discovery process should these take place?
3. What future directions best guide improvements in animal modeling efforts? Are current NHP vaccines and challenge viruses sufficiently predictive given their limitations?
4. What are the next steps in learning about immune activation and its impact on susceptibility to HIV infection? What clues can be gleaned from studies of nonpathogenic non-human primate models, like African Green Monkeys? How can this be applied to vaccine design?
5. If combinations of many antibodies are necessary for protection, is there a definable set?
6. What needs to happen to optimize progress in the study of adjuvants, especially for DNA products or toll-like receptors (to harness innate immunity)?
7. How can studies of candidate vaccines best elucidate the contribution of more than one type of immune response to protection?
8. Will vaccine studies evaluating candidates for their impact on virologic control take sufficient account of the effects of viral persistence and latency?