

1 IMMUNE MEMORY AND THE RECALL RESPONSE
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The discussion will focus on the ways that our understanding of both the acute and recall cellular immune responses have been enhanced by the recent development of tetrameric complexes of MHC class I glycoprotein+peptide (tetramers) for the direct staining of effector and memory CD8⁺ T cells. The experiments utilize mice challenged intranasally with the readily eliminated influenza A viruses, or with a murine γ -herpesvirus that establishes life-long latency in B lymphocytes and in other cell types. Application of the tetramer technology has shown us that the numbers of virus-specific CD8⁺ T cells generated in both primary and secondary responses are far in excess (>10x) of those demonstrated previously by limiting dilution analysis. All these T cells can be shown to synthesize γ -interferon following *in vitro* stimulation with high doses of the cognate peptide, but their functional status is currently unknown. Consideration will be given to the limitations of established CD8⁺ T cell memory for protection against secondary challenge with viruses.

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Abstract not submitted

3 Progress, Obstacles and Future Priorities in HIV Vaccine Development. Margaret Johnston, Assistant Director for AIDS Vaccines, NIAID, NIH, Bethesda, Maryland

Over 25 different candidate vaccines have been evaluated in human trials. Last summer the first efficacy trial of an HIV vaccine, a bivalent (B/B') gp120 vaccine, was initiated in U.S. volunteers at high risk for HIV infection. A similar trial with a different bivalent (B/E') gp120 will begin soon in Thailand. Phase II trials in the U.S. are currently focused on recombinant canarypox vectors in combination with an envelope boost (e.g. "prime-boost"). This combination has been shown to induce both neutralizing antibody and cytotoxic T lymphocytes (CTLs) in a majority of recipients. Vector, schedule and dose optimization studies are underway. Trials to evaluate canarypox vectors in other countries are also underway or planned. A series of trials to determine if vaccines can help reduce maternal-infant transmission is under discussion. Several candidate vaccines are in earlier stages of clinical development. These include DNA vaccines, vaccinia vectors, a Salmonella vector and several peptide approaches. Other promising approaches, such as modified vaccinia Ankara, VEE replicons, adenovirus vectors, recombinant BCG, and particle-based approaches are in preclinical development. The future success of HIV vaccine development hinges on many factors, including improving antigen presentation; establishing and maintaining a robust pipeline of candidate vaccines; developing international collaborations that cut across the sectors; and conducting clinical trials of the most promising candidate vaccines in populations most in need. Lessons learned to date, future priorities and new programs to stimulate the field will be presented.

4 Tribulation or Triumph: Are We Close to a Successful Malaria Vaccine?
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Recent developments in the field of vaccinology make the prospects of a safe and effective malaria vaccine for travelers brighter than they have ever been. The identification of powerful adjuvants that drive immune responses towards those believed to be required for protection against sporozoite challenge has resulted in the demonstration of convincing and reproducible protection of human volunteers with the RTS,S malaria vaccine candidate. Similarly, initial clinical results with DNA vaccine technology have been very encouraging, in particular for their ability to induce strong CD8 cytolytic responses. On the other hand, progress towards vaccines that will reduce morbidity and mortality in endemic populations (blood stage and transmission blocking vaccines) continues to lag. The field suffers from insufficient coordination and adequately focused resources as much as it does from gaps in basic science and technology. The recent demonstrated success with RTS,S and the enhanced attention to malaria by major national and international agencies suggests that a unique opportunity now exists to make real progress towards a vaccine that will have a global impact. A call to action must be linked with a technically sound, adequately resourced, and appropriately managed plan to capitalize on the current momentum.