even a several-orders-of-magnitude improvement in waste form (i.e., spent nuclear fuel) durability is not an important factor in performance of a repository, but the analysis they cite was not of Yucca Mountain and was published in 1983 (*9*). There has been a substantial increase in our knowledge of Yucca Mountain and our understanding of the behavior of waste form materials in a variety of geologic environments during the past 19 years. Why not use this knowledge? If we begin construction of the repository now, the financial and political investment in this site will, as it does now, drive future decisions. The well-known "sunk cost" effect echoes through the responses from our colleagues. The prospect of retrieving the waste offers little solace. There are no criteria for retrieval and no site for the retrieved waste.

What of the future? Congress will almost certainly overrule Nevada's objections, and the project will go forward. Despite this decision, surface storage of spent fuel will continue for decades. We still need to analyze the risks and take the required actions to immediately secure these surface storage facilities. The next major decision will require Congress to increase the capacity of the repository, because by 2010 the amount of spent nuclear fuel will nearly equal the legislated capacity of 70,000 metric tons. The increased capacity will further impact the design and safety analysis of the Yucca Mountain repository. Although Yucca Mountain may finally be the first geologic repository for high-level nuclear waste, it may, in the absence of a fair process and substantive analysis, be the last repository in the United States. This is a poor foundation on which to base the future of nuclear power.

**"If we begin construction of the repository now, the financial and political investment in this site will ... drive future decisions."**

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# HIV-1 Diversity and Vaccine Development

**THE INEXORABLE SPREAD OF THE HUMAN** immunodefiency virus (HIV) has prompted an urgent effort to develop an AIDS vaccine. The diversity of HIV in human populations poses an unprecedented challenge for the development of a highly effective vaccine. A recent meeting at the Vaccine Research Center at the National Institute of Allergy and Infectious Diseases, National Institutes of Health, organized in collaboration with the World Health Organization and the Joint United Nations Programme on HIV/AIDS, focused on the genetic diversity of HIV and strategies to develop vaccine candidates. More than 95% of new HIV infections occur in developing countries, and effective vaccines would no doubt help to control the epidemic. A high level of diversity of HIV exists among different populations, and vaccine trials for the developing world will also need to address factors such as concurrent infectious diseases, access to health care, and the ability to deliver and test vaccines. The relevance of HIV genetic diversity to vaccine efficacy remains unknown.

The meeting led to consensus recommendations on how best to address this scientific issue in the context of current vaccine efforts. Parallel trials of vaccine candidates from different clades are needed to address their relevance to immune protection. Although clade B is the most frequent virus type in the Americas and in parts of Asia, clade C viral strains are most prevalent in southern Africa and Asia and represent the most abundant genetic subtype worldwide. In Africa, clades A, C, and D cause the vast majority of HIV-1 infections. Recent analyses of genetic relatedness indicate that the diversity within any one clade of HIV may be no greater than the diversity between clades (*1*, *2*), although for specific gene products, such as Env, the intraclade diversity may be less than the variation between two clades. In addition, the degree of diversity varies according to viral gene product. Therefore, it is important when matching genetic sequences to consider the specific viral gene product used as an immunogen.

Although genetic diversity may affect immune responses to HIV-1, its significance for protective immunity is unknown. Significant cytolytic T lymphocyte cross-reactivity can be demonstrated between Gag proteins of clades B and C, but clade-specific epitopes are also evident. Similarly, antisera from one clade can neutralize another, and neutralization phenotype does not correlate with the clade of origin (*3*). Thus, the importance of matching clades in a vaccine candidate to the naturally occurring viruses in a geographic region has not been established. Although the genetic diversity among HIV-1 strains may be an obstacle to protective immunity, there is little scientific rationale for matching clades to the country from which they emanate. The consensus reached is that the testing of multivalent vaccines should proceed, but practical limitations dictate that vaccine candidates should be representative of clades, rather than country-specific. Extraordinary costs in dollars, man-hours, and time would result from the parallel testing of multiple parallel vaccine prototypes. At the same time, the importance of testing vaccines "relevant" to each country's HIV isolates is evident. Together, these constraints dictate a finite representation of clades in a multivalent vaccine, and the group concluded that a combination clade vaccine—for example, including clades A, B, and C—would cover the majority of HIV-1 infections worldwide.

The efficacy of a multiple-clade versus single-clade HIV vaccine candidate remains an important, unanswered scientific question. The generation of such a multiclade candidate will be of international importance and should remain high on the scientific agenda. Unprecedented international agreement and interagency coordination will be required to advance such candidate into human testing and efficacy trials.

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