Retrovirology

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Oral presentation

AIDS Vaccine Research and Development: Past, Present and Future

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Today, nearly twenty-five years since the first AIDS cases were identified, the AIDS pandemic is recognized as a global public health priority. With 14,000 new HIV infections every day, the best hope for stemming the insidious spread of HIV and for ending the pandemic remains the development of a safe and effective AIDS vaccine. The search for an AIDS vaccine can be viewed from past, present, and future perspectives. Since the identification in 1983 of HIV as the etiologic cause of AIDS, the field has gained significant knowledge on the pathogenesis of HIV relevant for vaccine development, several vaccine approaches have been designed and tested in clinical trials, and infrastructure has been established both in developed and developing countries to assess HIV incidence, molecular epidemiology, host immune response to early infection, and to conduct Phase I, II and III trials. Yet despite current global investment of nearly $650 million per year, the HIV vaccine pipeline remains inadequate. Vaccine candidates designed by empiric approaches and tested thus far in human efficacy trials have failed to prevent HIV infection or suppress HIV viral load. Current candidates approaching human efficacy trials have shown some benefit in certain monkey models but not in others. There is considerable potential that these current candidates will achieve no more than limited success if any, since they have provided little or no protection from pathogenic SIV challenge in monkeys, are markedly impeded in their capacity to elicit cell mediated immune responses in humans due to anti-vector immunity, and have not been designed to elicit effective neutralizing antibodies. In order to significantly accelerate global efforts in AIDS vaccine development and shorten the timetable for a licensed and widely accessible AIDS vaccine, the following issues should be addressed. First of all, key scientific problems, known to the field for more than a decade, need focused and direct efforts to inform rational vaccine design. These problems include: the lack of understanding of how best to design vaccines to elicit broadly neutralizing antibodies to HIV; the lack of safe and suitable candidates for clinical development which mimic the protective efficacy thus far only achieved by live attenuated SIV vaccines; and the lack of candidates in the pipeline which adequately address the hypervariability of HIV. Secondly, an "industrial model" for applied research and product development needs to be incorporated into global AIDS vaccine R&D efforts, to facilitate an expedited transfer of leading vaccine candidates demonstrating feasibility/proof of concept to major vaccine-pharmaceutical companies for advanced development. Finally, a shift from business as usual risk-benefit paradigms common to vaccine R&D needs to be established to encourage innovative product development and accelerated clinical testing of AIDS vaccine candidates without compromising safety.