



Forum in immunology
Editorial

Introduction: rational vaccine strategies against AIDS

Vaccines based on viral structural products (Env/Gag/Pol) alone have failed to prevent infection by human immunodeficiency virus (HIV)/simian immunodeficiency virus (SIV). More recently, vaccines based on viral regulatory gene products (Tat/Rev/Nef) have been shown to contain virus replication and to prevent disease onset. A vaccine combining both regulatory and structural viral antigens (combined vaccine) is likely to be superior to single modalities since it can induce immune responses targeting both early and late viral products, thereby reducing virus entry and virus replication at both early and late stages. In addition, the combined vaccine can exploit known immunomodulatory functions of HIV regulatory genes/products, which can improve immune responses (intensity, breadth) against structural antigens. In this regard, novel Env variants appear to be superior to previous Env products. On these premises, novel vaccine candidates based on the rational combination of early/regulatory and late/structural genes/products of HIV should be designed and tested. This represents the mission of the AIDS Vaccine Integrated Project (AVIP), an EU-awarded consortium of seven countries (France, Finland, Germany, Italy, South Africa, Sweden, UK) aimed at these goals. In particular, the mission of AVIP is to develop novel combined vaccines and to test them in phase I trials in HIV-infected and non-infected individuals in Europe, and to further develop them for future testing in phase II/III trials in developing countries (DC). This also requires the fostering of training, technology transfer and community involve-

ment between EU and DC. To ensure a rapid implementation of the program, priority has been given to vaccine combinations containing antigens for which, singly, efficacy has been demonstrated in animal models, GMP production has been accomplished and phase I studies have been completed or are ongoing. The rational vaccine design and development are expected to bring new products in the vaccine pipeline for advanced clinical testing upon rigorous selection of the most successful candidate based on standardized and harmonized criteria of clinical, preclinical and laboratory procedures and assays. This Forum will focus on the new and rational vaccine design and development of four novel vaccine candidates within the AVIP program and on the steps required to arrive at advanced clinical testing in DC.

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