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Prime-boost AIDS Vaccine Strategies Based on Replication-Competent Adenovirus Recombinants

Bo Peng[1], Nina Malkevitch[1], L Jean Patterson[1], V Raúl Gómez-Román[1,2], David Venzon[3], Ruth Florese[1], Indresh Srivastava[2], Susan W Barnett[2] and Marjorie Robert-Guroff*‡[1]

Address: [1]Vaccine Branch, Emeryville, CA 94608-2916, [2]Chiron Corporation, Emeryville, CA 94608-2916 and [3]Biostatistics and Data Management Section, NCI, Bethesda, MD 20892-5065

Email: Marjorie Robert-Guroff* - guroffm@mail.nih.gov

* Corresponding author ‡Presenting author

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The potent, persistent immunity needed to prevent HIV infection might be best achieved by priming cellular immunity with replicating vectors and boosting antibodies with optimally designed envelopes. Replicating Ad vaccines infect epithelial cells on mucosal surfaces and thus also elicit mucosal immunity. In chimpanzees, compared to non-replicating Ad vaccines, at the same or lower dose replicating Ad vaccines were better at eliciting cellular immunity and priming antibody responses. Mismatched envelope boosts induced broad neutralizing activity to diverse R5 viruses and cross-clade ADCC activity. Multigenic Ad-SIV vaccines and SIV envelope subunit boosts elicited strong protection in 39% of rhesus macaques challenged mucosally with SIV_{mac251}. Durability of protection against a second challenge was established in 73% of previously protected animals, associated with persistent cellular immunity. Induction of memory cells and broad, strong functional antibodies illustrates the promise of this prime-boost vaccine strategy.