Vaccine Watch

RSV VACCINE FAILURE EXPLAINED

A new study in *Nature Medicine* provides an explanation for a vaccine failure that occurred nearly 50 years ago, with fatal consequences.

A formalin-inactivated vaccine against respiratory syncytial virus (RSV) that was used to immunize children in the 1960s elicited a non-protective antibody response; immunized children who were subsequently exposed to RSV suffered more severe lung disease than non-vaccinated children, and two immunized toddlers died as a result of subsequent RSV infection. Previous work indicated that the failure of the vaccine was due to the inactivation of protective epitopes of RSV by formalin, but Polack and colleagues now show that a lack of affinity maturation of the antibody response to RSV might have been responsible.

The authors show that B-cell stimulation with inactivated RSV does elicit antibodies specific for protective epitopes of RSV. However, it fails to adequately stimulate Toll-like receptors (TLRs) on B cells to reach the threshold of B-cell activation that is required for a germinal centre response. Therefore, the vaccine does not stimulate affinity maturation and the production of neutralizing antibodies.

These results indicate that a safe and effective vaccine for RSV might now be within reach by the inclusion of TLR agonists in the inactivated RSV formulation.

ORIGINAL RESEARCH PAPER Delgado, M. F. *et al.* Lack of antibody affinity maturation due to poor Toll-like receptor stimulation leads to enhanced respiratory syncytial virus disease. *Nature Med.* **15**, 34–41 (2009)

HOPE FOR T-CELL-BASED HIV-1 VACCINE

The disappointing recent news reporting the failure of a recombinant adenovirus serotype 5 (rAd5) vector-based vaccine to control HIV-1 infection caused researchers to question the viability of T-cell-based vaccines against this virus. But renewed hope is now provided by Dan Barouch and colleagues, who show that a T-cell-based vaccine regimen using two distinct adenoviral vectors provided improved protection to rhesus monkeys from a high-dose infection with SIV_{MAC251}.

By testing vaccination regimens that involved priming and boosting with serologically distinct rAd vectors encoding the SIV protein Gag, they found that priming with rAd26-Gag and boosting with rAd5-Gag elicited T-cell responses of the highest magnitude, breadth and functionality. The efficient induction of Gag-specific T-cell responses by the heterologous prime–boost regimen correlated with a reduction in the peak and set point viral loads following challenge with SIV, and with decreased AIDS-related mortality of the vaccinated monkeys. Monkeys that received the rAd26–rAd5 regimen also preserved central memory $CD4^+$ T-cell numbers after challenge with SIV compared with controls. So, this study shows that durable partial immune control of pathogenic SIV infection can be achieved with a T-cell-based vaccine and should help to inform the design of the next generation of vaccines for HIV-1.

ORIGINAL RESEARCH PAPER Liu, J. *et al.* Immune control of an SIV challenge by a T-cell-based vaccine in rhesus monkeys. *Nature* **457**, 87–91 (2009)