Strategies for enhancing the safety and efficacy of recombinant vaccines and technology transfer to developing nations

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We have taken a number of approaches to improve the safety and efficacy of recombinant vaccines for use in humans and animals, including: choice of the strain of vaccinia virus (VACV) used as a vector, insertional inactivation of virulence and immunoregulatory genes of VACV, and expression of cytokine genes that attenuate the vector by more than a million-fold without reduction in immunogenicity. These strategies are illustrated by providing examples of recombinant VACV (rVACV) vaccines; we have developed for rinderpest, vesicular stomatitis, simian immunodeficiency virus, smallpox, and Rift Valley fever. Additionally, we have exploited the advantages of recombinant vaccines and developed diagnostic kits that permit one to distinguish between vaccinated and infected individuals. We constructed rVACVs expressing an interferon gamma (IFNγ) and lacking the immune-modulating genes B8R, B13R, and B22R. IFNγ is a cytokine with potent immunoregulatory, antineoplastic, and antiviral properties. These rVACVs replicated to high titers in tissue culture, yet were avirulent in both immunocompromised and immunocompetent mice with no detectable viral replication in these animals. A single immunization elicited potent humoral, T-helper, and cytotoxic T-cell immune responses in mice despite the absence of any detectable virus replication in vivo. IFNγ co-expression and the inactivation of one or more VACV immune-modulating genes provide an optimized method for increasing the safety while maintaining the efficacy of rVACV vaccines for use in humans and animals. Finally, the ILMB has facilitated and implemented the transfer of technologies in molecular biology to developing countries in Africa that has led to self-sufficiency.

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