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Interference of Elicited Immunity to HIV-1 Gag_{p55} by Env_{gp120}, but Not by Influenza HA, During Co-immunizations

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Immunization with more than one immunogen (co-immunization) is an efficient regimen to induce immunity to multiple antigens. However, immune interference has been reported using multi-plasmid DNA immunizations (*e.g.* co-immunization using HIV-1 Gag-Pol_{p160} and Vpr). HIV-1 envelope (Env) and Gag gene products are the most predominant immunogens used in current AIDS vaccines, although, few studies have evaluated possible immune interference when these two antigens are co-administered. Therefore, in this study, immune interference during co-inoculation was examined using DNA vaccines expressing Env_{gp120} and Gag_{p55} from gene sequences optimized for efficient expression in mammalian cells (codon-optimized). BALB/c mice vaccinated with each plasmid individually elicited high titer immune responses, however, when these same plasmids were co-inoculated, there was a reduction in the immunity elicited to Gag_{p55}. In contrast, anti-Env_{gp120} immunity was not affected. To determine if the anti-Gag immune interference was specific to Env, mice were co-immunized with plasmids expressing a soluble form of hemagglutinin (sHA) from influenza virus (A/PR/8/34) and Gag_{p55}-DNA. Similar titers of anti-Gag_{p55} immunity were observed in mice co-immunized with sHA-DNA and Gag_{p55}-DNA, as mice vaccinated with Gag_{p55}-DNA only. Gag_{p55}-DNA co-immunization did not affect anti-Env_{gp120} or anti-sHA immune responses. The Env_{gp120}/Gag_{p55} immune interference elicited during co-immunizations was not dependent on the amount of protein expressed. In addition, this induced immune interference was observed in mice even when the immunizations were performed in separate locations. Therefore, Env_{gp120} specifically interferes with the elicitation of anti-Gag_{p55} immune responses following co-immunization. Since Env and Gag are the most commonly used HIV-1 antigens in AIDS vaccine designs, future vaccine development should consider the effect of each immunogen during evaluation of the effectiveness of AIDS vaccines.