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Intranasal immunization with a multigene vaccine in combination with a novel adjuvant, N3, induces systemic and mucosal immune responses

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Background: We have developed a multigene/multisubtype HIV-1 vaccine that is currently being tested in two clinical phase I trials. The vaccine contains genes encoding multiple subtypes of envelope, gag and RT. We are currently investigating ways to enhance the vaccine specific mucosal immune response. In order to enhance the delivery and immunogenicity of the plasmids we are using a novel cationic lipid, N3, as adjuvant.

Objectives: To evaluate, in mice, intranasal delivery of the genetic vaccine in combination with the adjuvant N3 and assess the systemic and mucosal responses elicited.

Methods: Young C57/BL6 mice (2 weeks old at the start of the experiment) were immunized 3 times with the multigene vaccine intranasally or intramuscularly with or without the adjuvant N3. The mice received 20 μg of plasmid at each immunization. The production of vaccine-specific antibodies, both IgG and IgA, was measured in sera as well as in vaginal washes and feces. The cellular responses were assessed by IFN-γ and IL-2 ELISpot on PBMCs.

Results: After the second immunization all animals immunized with the addition of the adjuvant N3, either intranasally or intramuscularly, responded with significant titers of anti-gp160env and anti-p55gag IgG in sera. Furthermore, animals immunized intranasally with addition of N3 had significant vaccine-specific IgA titers in both vaginal washes and feces. Following the third DNA immunization the humoral responses were boosted even further in the adjuvanted animals. The cellular responses, as measured by IFN-γ and IL-2 reactivity of PBMCs following the third immunization, were directed against both gag and env with the broadest responses detected in the animals adjuvanted by N3.

Conclusions: By immunizing with a low dose genetic vaccine in formulation with a novel cationic adjuvant, N3, we could induce broad humoral and cellular anti-HIV responses. Furthermore, intranasal immunization resulted in a mucosal IgA response directed against both envelope and gag. Our results are encouraging since the immune responses in mucosal surfaces is believed to be highly important in order to inhibit sexual transmission of HIV.