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Oral presentation

Induction of HIV-neutralising Antibodies of the 2F5/4E10 Type

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Neutralising antibodies recognising membrane proximal epitopes of gp41 have been isolated from HIV-infected patients. Since these epitope domains are highly conserved, the corresponding antibodies 2F5 and 4E10 neutralise a broad range of HIV strains. Numerous attempts by several laboratories to generate 2F5/4E10-like antibodies by vaccination have failed, obviously because the conformation of the domain is difficult to reproduce. Recently we reported induction of neutralising antibodies against the porcine endogenous retrovirus (PERV) and the feline leukaemia virus (FeLV) by immunisation with their transmembrane envelope (TM) proteins p15E. In both retroviral TM proteins two epitope regions were identified, one located in the N-terminal part (designated E1) and the other located in the C-terminal part of p15E (E2). E2 is related to the 2F5/4E10-epitope, and is located opposite E1 when the TM envelope protein has folded. An E1 domain was identified in the C-terminal part of gp41 and two strategies were developed to induce neutralising antibodies against HIV. First, immunisation was performed with a hybrid protein based on p15E of PERV, containing the E1 domain and the E2 (2F5/4E10 epitope) domain of gp41 of HIV-1. Second, immunisation was performed with a hybrid containing the N-terminal backbone of p15E of FeLV and only the E2 (2F5/4E10 epitope) domain of gp41. With both strategies antibodies neutralising laboratory and primary strains of HIV-1 were induced. These strategies may be used to generate a vaccine inducing broadly neutralising antibodies to prevent or curtail HIV infection.