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NEUTRALISING LLAMA ANTIBODY FRAGMENTS AS HIV-1 ENTRY INHIBITORS

Anna Forsman¹, Els Beirnaert², Marlén Aasa-Chapman¹, Willie Koh¹, Vanessa Tack², Áine McKnight¹, Agnieszka Szynol³, Theo Verrips³, Hans de Haard^{2,3} and Robin Weiss¹

¹Wohl Virion Centre, Division of Infection and Immunity, University College London, 46 Cleveland Street, London W1T 4JF, United Kingdom

²Ablynx NV, Technologiepark 4, 9052 Ghent, Belgium

³Department of Molecular and Cellular Biology, University of Utrecht, Padualaan 8, 3584 CH Utrecht, the Netherlands

Members of the *Camelidae* family produce immunoglobulins devoid of light chains. We have characterised variable domains of these heavy-chain antibodies, the VHH or Nanobodies™, from llamas immunised with HIV-1 envelope proteins in order to identify VHH that can inhibit HIV-1 interaction with its cellular receptor CD4 and block virus entry into cells. Llamas were immunised with monomeric surface glycoprotein gp120 from a Chinese HIV-1 subtype B/C chimeric isolate, 97CN54. Upon screening against envelope proteins from different HIV-1 subtypes, VHH with neutralising activity against HIV-1 primary isolates of subtype B and C were identified. These VHH bind to recombinant gp120 and gp140 derived from HIV-1 subtype A, B and C in ELISA and compete with soluble CD4 for this binding. The results indicate that heavy-chain antibody fragments have a possible use as potent HIV-1 entry inhibitors. In conclusion, since VHH are stable and can be produced at a relatively low cost, they may be considered for applications such as HIV-1 microbicide development. Anti-envelope VHH might also prove useful in defining neutralising and non-neutralising epitopes on HIV-1 envelope proteins, with implications for HIV-1 vaccine design.