

## **Full Length Single Chain, A Novel gp120-CD4 Fusion HIV Subunit Vaccine, Does Not Cause a Deleterious Autoimmune CD4 Response in Cynomolgus Macaques**

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Full length single chain (FLSC) is a novel HIV vaccine that presents conserved CD4i epitopes on HIV envelope. The constrained structure is achieved with single chain complexes of gp120 and CD4 fragments. FLSC elicits cross-reactive antibodies and heterologous protection against SHIV/SIV in three independent low-dose rectal challenge studies in rhesus macaques and is being developed as a subunit vaccine for clinical evaluation. We performed preclinical immunotoxicology studies to assess potential safety issues specifically derived from a deleterious autoimmune response to CD4. Two studies were performed in cynomolgus macaques. The presence of deleterious antibody responses to CD4 were assessed by ELISA, CD4<sup>+</sup> cell staining, as well as impact to a mixed lymphocyte reaction (MLR). CD4<sup>+</sup> T cell loss and impact to the immune response to KLH were also assessed. In study 1, we verified that depletion of CD4<sup>+</sup> cells impacted the induction of primary and secondary KLH-specific IgG and IgM antibody responses, justifying the use of the antibody response to KLH as an indicator of an autoimmune response to CD4. In study 2, immunization with multiple high doses of FLSC did not induce an autoimmune response to CD4 that had any deleterious effects in any assays that were employed. Little to no impact was seen on CD4 binding/function by flow cytometry and MLRs. Therefore, FLSC did not induce any deleterious autoimmune responses to CD4 and continues to be a promising vaccine candidate for evaluation in a Phase I clinical trial. Supported by: BMGF OPP1017606.