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Investigation of autoimmunogenic potential of GX-12, a New anti-HIV DNA Vaccine, by popliteal lymph node assay and autoantibody induction.

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GX-12 is a naked DNA vaccine developed by Dong-A Pharmaceutical Company, Green Cross Company and Genexine for the treatment of HIV infection. GX-12 consists of four separate plasmids. This study was performed to investigate the autoimmunogenic potential of GX-12 using primary and secondary PLNA method, and to examine the induction of autoantibodies in mice immunized with GX-12.

In primary popliteal lymph node assay (PLNA), GX-12 was injected into the right footpad at a dose level of 12.5 μg, 50 μg or 200 μg/head. Seven days after administration, The PLN weight, cellularity and LPR (lymphoproliferative reaction) indices were determined. In results, there was no increase in PLN weight, cellularity or LPR indices in groups treated with 12.5 or 50 μg of GX-12. However, in the highest dose group, GX-12 induced a significant increase in cellularity index, and also provoked slightly increased in LPR and PLN indices. Secondary PLNA was routinely used to discriminate the antigen-specific reaction from irritant effects. Therefore, we performed the secondary PLNA to examine that the positive result in primary PLNA was due to the antigen-specific reaction or irritant effects of GX-12. In all groups treated with GX-12, there was no inter-group difference in PLN, cellularity and LPR indices when compared with the control group. On the contrary, trinitrobenzenesulfonate dihydrate (TNBS), a well-known allergic compound, showed marked increase in LPR, PLN and cellularity indices. In addition, sodium dodecyl sulfate (SDS), a known irritant, did not show an increase of all three indices as expected. The production of anti-DNA or anti-muscle cell autoantibodies was also investigated in this study. Balb/c mice were immunized and boosted with GX-12 four times at 2-week interval. GX-12 had no effect on the number of B cells secreting IgG antibodies reactive with the mammalian DNA and the muscle cell antigen myosin. Immunization with GX-12 also did not affect the absorbance against mDNA and myosin antigen in all groups. These results

demonstrate that the number of B cells secreting immunoglobulin G (IgG) against mDNA and myosin were not increased in spleen, and the anti-DNA or anti-myosin autoantibody titer also did not increased in serum. Histologically, there was no evidence of the development of myositis or immune complex deposition in muscle. Kidneys from vaccinated mice also showed no evidence of glomerulonephritis or immune complex deposition. Based on these results we concluded that GX-12, an anti-HIV DNA vaccine, has little risk of autoimmunogenic potentials.

Keyword : GX-12, autoimmunogenic potential, autoantibody, PLNA