S19-1 Development of gene delivery sysytem into skeletal muscles by Bubble liposomes and ultrasound

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Skeletal muscle is a promising target tissue for the gene therapy of both muscle and non-muscle disorders. Gene transfer into muscle tissue can produce a variety of physiologically active proteins and may ultimately be applied to the treatment of many diseases. A variety of methods have been studied to transfer genes into skeletal muscle, including viral and non-viral vectors. Recently, we have developed the polyethyleneglycol (PEG)-modified liposomes entrapping echo-contrast gas known as ultrasound (US) imaging gas. We have called the liposomes “Bubble liposomes” (BLs). We have further demonstrated that US-mediated eruption of BLs loaded with naked plasmid-DNA is a feasible and efficient technique for gene delivery. In this study, to assess the feasibility and the effectiveness of BLs for the gene therapy of both muscle and non-muscle disorders, we tried to deliver IL-10 expressing plasmid DNA into skeletal muscles of collagen-induced arthritis (CIA) model mice by the combination of BLs and US exposure. In this result, the gene transfer of IL-10 plasmid was associated with significant delay in arthritis onset. Moreover, arthritis severity was significantly attenuated throughout the course of the disease as compared with the control mice. TNF-alpha and IL-1beta in sera and joint tissue of CIA were decreased by the gene transfer of IL-10 plasmid.

These results suggest that gene transfer into the muscle of CIA by the combination of BLs and US exposure is an effective means to deliver anti-inflammatory cytokines. Thus, this US-mediated BLs technique for muscle gene transfer may provide an effective noninvasive method for arthritis gene therapy in clinical use. In addition, it may be applicable for the gene therapy of both muscle and non-muscle disorders.