cells that causes virtually no side effects. Both CD22 immunotoxin constructs (the IgG-dgA and the Fab'-dgA) have been produced in gram quantities in a GLP-P3 laboratory at the University of Texas. These highly potent, endotoxin-free, reagents have received FDA approval for phase I clinical trials. In these trials, toxicity, pharmacokinetics, antibody response and efficacy are being determined. Our findings in the first 20 patients will be described.

* S.fr.41.2

Receptor-mediated gene delivery and expression in hepatocytes

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Foreign genes have been introduced into mammalian cells *in vitro* by accomplished previously by a variety of methods. Techniques that have been developed for transfection of mammalian cells in vivo, are technically difficult or lack cell specificity.

We have recently developed a soluble, targetable delivery system consisting of an asialoglycoprotein covalently coupled to a polycation. The strategy was based on: 1) unique receptors on hepatoyytes which internalize galactose-terminal (asialo-)glycoproteins 2) polycations can bind in a non-covalent non-damaging interaction.

A gel retardation system was developed and optimal binding of the asialoglycoprotein-polysine conjugate to DNA was determined.

Using chloramphenicol acetyltransferase (CAT) as a marker gene, specific delivery and expression of CAT was demonstrated *in vitro* using asialoglyceprotein receptor (+) and (−) cell lines.

Because of the solubility and targetability of the delivery system, the possibility of targeted gene delivery *in vivo* was investigated. Intravenous injection of conjugate-DNA complexes in rats resulted in detection of CAT DNA sequences in liver 15 min later by dot blots with a CAT cDNA probe. CAT enzyme activity 24 hrs later was found specifically in liver but no other tissues or control livers.

A construct consisting of mammalian regulatory elements driving the CAT gene also resulted in foreign gene expression targeted to hepatocytes, indicating that natural mammalian regulatory sequences can function after receptor-mediated delivery *in vivo*. However, targeted hepatic CAT expression was transient, maximal between 24 and 48 hrs. The CAT activity declined to barely detectable levels by 96 hrs.

In an attempt to obtain persistence of foreign gene expression, stimulation of hepatocyte replication was employed. Injection of complex followed by 67% partial hepatectomy resulted in levels of hepatic CAT activity that increased following surgery and remained detectable through 11 weeks post-hepatectomy.

Conclusions: A targetable gene delivery system can permit *in vivo* expression of an exogenous gene after simple intravenous injection. The foreign gene expression can be enhanced and made to persist by induction of hepatocyte replication. This system may be useful in the evaluation of the effects mammalian regulatory sequences and in the study of models of genetic diseases.