STABILIZED PLASMID-LIPID PARTICLES FOR SYSTEMIC GENE THERAPY

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Gene therapies for systemic diseases such as cancer or inflammatory disorders clearly require systemic vectors. Previous work has shown that encapsulation of chemotherapeutic drugs in small, long-circulating liposomes results in preferential accumulation at tumour sites. It follows that encapsulation of plasmid in small liposomal systems should result in enhanced delivery of plasmid to tumour sites. We have developed a method for encapsulating plasmid in small (diameter~70nm) "stabilized plasmid-lipid particles" (SPLP) employing a detergent dialysis procedure [1]. These SPLP contain one plasmid per particle and are stabilized in aqueous media by the presence of a poly(ethyleneglycol) (PEG) coating. SPLP are non-toxic, exhibit extended circulation lifetimes following intravenous injection and result in delivery of up to 3% of the injected dose to a distal tumour site [2,3]. It is shown that SPLP exhibit remarkable selectivity for transfection of tumour tissue as compared to organs such as the lung, liver or spleen. Initial studies utilizing SPLP for suicide gene therapy applications employing thymidine kinase gene delivery in combination with ganciclovir will be reported. These results support the potential of the SPLP system as a systemic gene therapy vector for the treament of cancer.

REFERENCES

1. Wheeler, J.J., Palmer, L., Ossanlou, M., MacLachlan, I., Graham, R.W., Hope, M.J., Scherrer, P. and Cullis, P.R. Stabilized plasmid-lipid particles: Construction and characterization. **Gene Ther.** 6 (1999) 271-281.
2. Tam, P., Monck, M., Lee, D., Ludkovski, O., Leng, E.C., Clow, K., Stark, H., Scherrer, P., Graham, R.W. and Cullis, P.R. Stabilized plasmid-lipid particles for systemic gene therapy. **Gene Ther.** 7 (2000) 1867-1874.
3. Fenske, B.D., MacLachlan, I. and Cullis, P.R. Long-circulating vectors for the systemic delivery of genes. **Curr. Op. Mol. Ther.** 3 (2001) 153-158.