Preparation and Therapeutic Evaluation of DNA-Loaded PLGA Microspheres

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To overcome the main disadvantages of non-viral gene delivery systems such as repeated administration due to the low transfection efficiency, poly(D,L-lactide-co-glycolide) was applied to encapsulate pDNA in its microsphere formulation. Free pDNA or various ratios (w/w) of chitosan / pDNA complexes was used for encapsulation, with the resulting encapsulation efficiency of 44%, 5%, and 8% for free pDNA, 0.7:1 and 1:1 ratios, respectively. Scanning electron micrographs of PLGA microspheres encapsulating pDNA or chitosan-condensed pDNA revealed a smooth spherical shape immediately after microsphere preparation and a collapsed porous shape in 41 days due to the degradation of PLGA. *In vitro* release profile showed that the 0.7:1 (w/w) ratio formulation exerted 47% release in 26 days, whereas free pDNA or 1:1 (w/w) ratio formulation did only 15% or 32%, respectively. Preliminary *in vivo* gene therapy using interleukin-12 gene (p2CMVmIL12)-loaded PLGA microsphere in colon adeno-carcinoma bearing Balb/c mice showed a significant anticancer effect, indicating that the encapsulated pDNA remained intact in the microsphere during the formulation process. The results indicate that microsphere formulation of pDNA could be useful in designing a safe and efficient gene delivery system both *in vitro* and *in vivo*.

Keywords: Microsphere, PLGA, cancer gene therapy, CT-26, chitosan