In Vivo Pinpoint Drug/Gene Delivery System

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Conventional gene delivery systems (GDS) rely on viral infection (e.g., AdV, AAV, HIV) or cellular endocytosis (e.g., liposome, plasmid). These GDS have been used in various clinical trials; however all systems lack the ability for *in vivo* pinpoint targeting and most viral vectors introduce the fragment of its genome along with therapeutic genes into host cells. Recently, a new carrier, bio-nanocapsules (BNC), was developed by our group (Yamada et al., *Nat. Biotech.* 2003). BNC is about 100-nm nanocapsules based on a hepatitis B virus surface antigen (HBsAg) particle, which can be efficiently synthesized in yeast cells. Since the HBsAg S and M particles have been used for long time in humans as a recombinant HB vaccine, BNC is also considered as a safe material for humans. Various materials (gene, drug, siRNA, protein, 100-nm polystyrene bead, etc) can be introduced inside BNC by electroporation or liposome fusion. Since original BNC displays pre-S1 region, a human liver-specific receptor, on its surface, we already succeeded in the *in vivo* pinpoint delivery of genes and drugs to the human liver-derived tumors in xenograft models by the intravenous injection of BNC. The infection efficiency of BNC is comparable to that of viral vectors. Moreover, various bio-recognition molecules (antibody, sugar chain, receptor, ligand, homing peptide, etc) can be easily displayed on the surface of BNC instead of pre-S1 region for the re-targeting of BNC from human liver to other tissues *in vivo*.