Application of hepatitis B virus-like particles to drug delivery vehicle.

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Drug delivery systems (DDS) mean techniques for delivering needed drug to the specific cells or tissues. We focused on a viral cell-tropism as a hint of the new drug delivery vehicle. Hepatitis B virus (HBV) specifically infect human hepatocyte. We speculate that virus-like particles (VLPs) of HBV could be available as drug delivery vehicle which have the tropism to hepatocyte. VLPs do not have viral genome and capsid protein; VLPs consist of cell membrane and viral membrane-protein (cell receptor) that bind to the host cell. Previous studies shown that HBV-VLPs were produced in cells which were co-expressing HBV two surface proteins, large S (LS)- and small S (SS). LS is the cell receptor of HBV, and SS relates with particle formation. In this study, we established the optimal preparation and purification of HBV-VLP for drug delivery vehicle.

293T cells transfected with LS and SS expression plasmid were cultured for 60 hours, and the culture supernatant containing HBV-VLPs were collected. VLPs were concentrated by precipitation with PEG6000 and were labeled with the DiI, red fluorescent. DiI-labeled VLPs were purified by sucrose density gradient ultracentrifugation and were detected by Western blotting with LS and SS antibodies. We furthermore examined attachment of DiI-VLPs on cervical, lung, neuron and liver cells. In consequence, DiI-VLPs showed specificity for liver-derived HepG2 cells. Moreover, VLPs had high specificity for HepG2 cells stably expressing hepatic Na/taurocholate cotransporter (NTCP) that is an HBV receptor. These data suggested that VLPs could be used as a new drug delivery vehicle to hepatocytes. Further studies for application of our VLPs as DNA carrier are currently underway.