102b Liver Targeting of Gold Nanoparticles: Effects of Size and Surface Modification on Preferential Hepatocyte Uptake

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The rational design of synthetic gene carriers targeted to hepatocytes would facilitate the development of non-viral gene delivery strategies for the treatment of hemophilia and other diseases requiring the manipulation, replacement, or supplementation of diseased genes. However, the physicochemical properties of nanoparticles (NPs) that would promote access to and specific uptake by hepatocytes in vivo remain to be determined. We systematically examined the effects of NP size, surface modification with functionalized poly(ethylene glycol) (PEG) chains, and the addition of various targeting moieties on the ability of gold NPs to target hepatocytes. NPs were initially characterized for in vitro binding to Hepa 1-6 cells using darkfield microscopy. NPs were then injected into the tail veins of C57Bl/6 mice, and gold uptake into hepatocytes and liver nonparenchymal cells (NPCs) was measured by instrumental neutron activation analysis (INAA). Our results suggest that the physicochemical properties of NPs can be finely tuned to achieve preferential hepatocyte uptake following systemic administration. These principles can be applied to other synthetic gene delivery biomaterials to increase liver-targeted delivery.