Peptide Labeled Gold Liposomal nanoparticles for drug delivery into the Brain

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The blood brain barrier (BBB) represents the greatest obstacle in neurological related diseases. Most available treatments fail to reach the brain; thus the physician has to deal with invasive procedures endangering patients' health. For this reason, our research project is focused on developing RNA interference (RNAi) treatments that can be administered in a non-invasive manner. Here, we developed RNAi carrying gold liposome nanoparticles that were conjugated to the brain targeting peptides: Apolipoprotein E (ApoE) and Rabies Virus Glycoprotein (RVG). We hypothesize that these nanoparticles can improve RNAi delivery into brain tumor cells. Here, we pegylated each peptide to 1,2-Distearoyl-sn-Glycero-3-Phosphoethanolamine-Polyethylene-Glycol-Maleimide (DSPE-PEG-Maleimide) molecules, forming micelle conjugates that were then mixed with cholesterol and 1,2-Dioleoyl-sn-glycero-3-phosphocholine (DOPC). Afterwards, we encapsulated gold-nanoparticles—previously conjugated to oligonucleotide microRNA inhibitors (OMIs)—with our lipid mixture. We also encapsulated standard OMIs into each nanoliposome formulation as controls. Characterization for these nanoparticles led to a DSPE-PEG-maleimide-peptide labeling efficiency of 85% and 90% for ApoE and RVG respectively. Both nanoparticles resulted in a slightly negative charge. ApoE-Liposome-Gold-OMIs and RVG-Liposome-Gold-OMIs turned out to have an average size in diameter of 37.7 nm and 36 nm respectively. For all nanoparticle formulation, we obtained encapsulation efficiencies that were greater than 60% and a 50/1 OMIs to gold loading capacity. *In vitro* experiments showed that gold nanoparticles carrying RNAi negative controls are not toxic and can internalize brain tumor cells effectively. Likewise, ApoE-Liposome-Gold-OMIs and RVG-Liposome-Gold-OMIs significantly increased RNAi delivery and thus, effectively downregulated the expression of a microRNA of interest in comparison to non-treated and liposome controls. Moreover, in vivo experiments proved our hypothesis, we observed a significant increase in our nanoparticles' accumulation in brain tumor tissues of mice compared to non-treaded and liposome controls. Developing viable RNAi-based therapeutics is a rigorous task, but they are crucial to assure the patient a non-invasive therapy that could improve their quality of life and overall survival.