Nanoparticle Orientation to Control RNA Loading and Ligand Display on Exosomes for Cancer Regression

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Nanotechnology offers many benefits, and here we report an advantage of applying RNA nanotechnology for directional control of motion. The orientation of arrow-shaped RNA was altered to control ligand display on exosome membranes for specific cell targeting, or to regulate the loading of siRNA or miRNA. Placing a membrane anchoring lipid at the tail of the arrow results in display of the ligands including RNA aptamer or folate on the outer surface of the exosome. In contrast, placing the lipid molecule at the arrowhead results in loading of therapeutic RNA into the exosome. Taking advantage of the RNA ligand for specific targeting and exosome for efficient membrane fusion, the resulting ligand-displaying exosomes were capable of specific delivery of siRNA or miRNA to cells, and efficiently blocked tumour growth in three cancer models. Exosomes that display an aptamer that binds to prostate-specific membrane antigen, and loaded with survivin siRNA, inhibited prostate cancer xenograft. Exosomes instead displaying EGF aptamer inhibited orthotopic breast cancer models. Likewise, survivin siRNA-loaded and folate-displaying exosomes inhibited patient-derived colorectal cancer xenograft.