Utilizing Antibody Coated mRNA-LNPs for targeted delivery of cancer therapeutics

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A pervasive issue within cancer treatment is directed delivery of the therapeutic to tumor cells and not healthy cells. One such approach to address this issue involved the use of suicide gene/prodrug systems, such as the well-studied Herpes Simplex Virus Thymidine Kinase (HSV-TK) and ganciclovir system. HSV-TK can phosphorylate the acyclic nucleotide analog, ganciclovir, to its monophosphate form. The cellular kinases then convert the ganciclovir 5'-monophosphate to a triphosphate, which mimics the natural nucleotides and impairs DNA replication. In cells that do not express HSV-TK, ganciclovir is not phosphorylated and is benign. Currently, the success of suicide gene/prodrug approaches is limited by the selective delivery of the gene to the tumor site. To overcome this limitation, we are developing lipid nanoparticles (LNPs) coated with a tumor associated antibody (TAA) to deliver the mRNA corresponding to the suicide gene selectively to the cancer cells and not the healthy tissue. These TAA coated LNPs are expected to increase uptake specifically in cancer cells, resulting in the expression of prodrug activating mRNAs. Currently, through in vitro studies, the mRNA encoding the suicide gene is translatable and exerts cytotoxicity. Efforts are being made now to scale up TAA/LNP/mRNA formulations for animal studies. This approach can also be adapted to other small molecule/enzyme pairs and leaves room for mRNA delivery.