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Developing Precise Nanoparticles that Can be Used to Deliver Drugs

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Introduction

The development of nanoparticles has led to a wide range of clinical applications in recent years. Nanoparticles have been made to get around the limitations of free therapies and get around biological barriers—systemic, cellular and microenvironmental—that is different for different patient populations and diseases. Precision therapeutics, in which personalized interventions have increased therapeutic efficacy, has also been successful in overcoming this patient heterogeneity. However, a one-size-fits-all approach to platform optimization continues to be the primary focus of nanoparticle development. We argue that intelligent nanoparticle design can improve efficacy in general delivery applications while enabling tailored designs for precision applications, thereby improving patient outcome overall. Our focus is on advancements in nanoparticle design that overcome heterogeneous barriers to delivery.

Description

Due to liver accumulation, although lipid nanoparticles (LNPs) are a clinically mature technology for the delivery of genetic medicines, their therapeutic applications are limited. By allowing the delivery of messenger RNA (mRNA) and gene editing systems to non-liver tissues, our group has recently developed selective organ targeting (SORT) nanoparticles that expand the therapeutic applications of genetic medicines. We investigated the mechanistic factors that define SORT nanoparticles' organ-targeting properties in order to comprehend how they overcome the delivery barrier of liver hepatocyte accumulation [1]. We found that the compound idea of the additional SORT atom controlled biodistribution, worldwide/obvious pKa and serum protein associations of SORT nanoparticles. In addition, we provide evidence for an endogenous targeting mechanism that involves 1) the desorption of poly(ethylene glycol) lipids from the surface of the LNP,) the binding of distinct proteins to the surface of the nanoparticle as a result of recognition of exposed SORT molecules) interactions between surface-bound proteins and cognate receptors that are highly expressed in particular tissues. These results suggest that the recruitment of specific proteins to a nanoparticle's surface can enable drug delivery beyond the liver, establishing a crucial link between the molecular composition of SORT nanoparticles and their unique and precise organ-targeting properties [2].

New approaches to gene targeting based on RNA oligonucleotides were developed following the discovery of RNA interference (RNAi). Mammalian cells' endogenous RNAi machinery has been extensively studied in recent years, resulting in the discovery of molecular mechanisms that enable precise dsRNA-mediated gene expression regulation. These RNA duplexes are delivered from a stem-circle structure called the forerunner miRNA and are handled into short dsRNAs by Dicer [3,4]. Because of the short acknowledgment length necessity, an individual miRNA can tie to numerous mRNAs and thus it can direct various qualities because of decreased restricting particularity. When compared to siRNAs, this also results in less effective gene silencing for any given gene. In contrast, shRNAs are engineered as plasmids in the laboratory. The plasmid is used to express RNA molecules with a tight hairpin turn, making it easier to use RNAi to silence target genes over time. Therefore, intra-cellular delivery of a plasmid containing specific shRNA sequences, capable of targeting mRNA strands after Dicer processing, is typically required for shRNA expression in cells. Because they are based on DNA, shRNA plasmids outperform dsRNAs in terms of resistance to degradation. However, additional transcriptional steps are required prior to the generation of dsRNA because shRNAs necessitate the use of an expression vector.

The behavior of mucus in the lungs is also altered by disease. High levels of MUC5AC and MUC5B polymers characterize lung mucus, a barrier that significantly affects NPs inhaled 118,157. However, because cystic fibrosis mucus has a higher viscosity, which encourages biofilm formation by entrapping pathogens and limiting neutrophil mobility157,158, increased MUC5B expression and excessive cross-linking of polymers in the mucus results in decreased pore size and low rates of mucus clearance [5,6].

Conclusion

Primary ciliary dyskinesia and cigarette smoke-induced chronic bronchitis both has elevated MUC5B concentrations.asthma158 has elevated MUC5AC. Overall, it has been discovered that the properties of mucus vary greatly depending on patient factors like diet, lifestyle and disease, making it difficult to deliver NP through inhalation.

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Conflict of Interest

There are no conflicts of interest by author.

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