MOLECULAR SNIPERS

Therapies bases on RNA interference (RNAi) typically employ one of two main platforms to route small interfering RNAs (siRNAs) through the blood and into the diseased cell. Researchers can encapsulate the inhibitory molecules into lipid nanoparticles (LNPs), which protect against degradation in the blood stream and can be decorated with surface antigens to deliver the RNA snippet to target cells, where the LNPs are taken up by endocytosis ❶. Alternatively, some drug developers are modifying the chemical backbone of naked siRNAs to make them more stable in the bloodstream and to improve cellular uptake, and conjugating the siRNAs with other molecules such as sugars to aid uptake by specific cells ❷. Once in the cytoplasm, the siRNA's antisense strand is incorporated into an RNA-induced silencing complex (RISC), where the target messenger RNA is degraded. An alternative approach is to deliver the genes encoding the inhibitory RNA sequences via a viral vector, taking advantage of the natural role of RNAi: the Dicer enzyme processes the short hairpin RNAs (shRNAs) generated after transcription of the inserted DNA into siRNAs that interact with RISC to inhibit protein translation ❸.