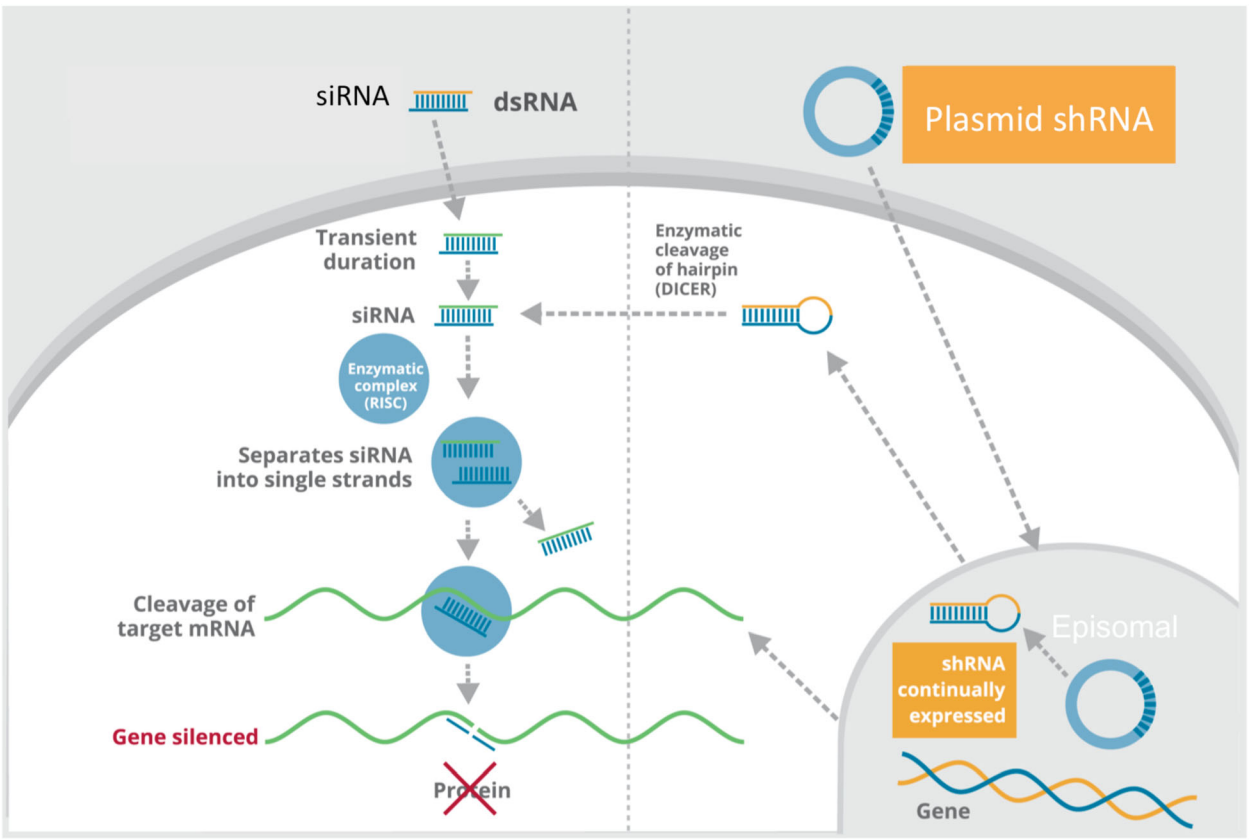
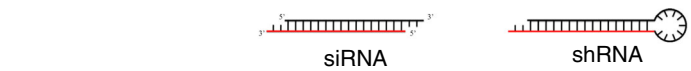


Fig. 2 Mechanisms of siRNA versus shRNA. shRNA may be episomal or integrate into the genome via lentiviral transfection for greater stability. Both pathways converge at the RISC complex



	siRNA	shRNA
Nomenclature	Small Interfering RNA	Short Hairpin RNA
Source	Laboratory synthesis	Nuclear expression
Delivery to the cell	Via synthetic/natural polymers and lipids to the cytoplasm	Via viral and other gene therapy vectors to the nucleus.
Persistence	99% degraded after 48 hours	Expressed for up to 3 years.
Administration	Local or limited systemic injection	Local and systemic injection
Dosage	High (low nM)	Low (5 copies)
Likelihood of specific 'off target' effects	Higher than shRNA	Lower than siRNA
Likelihood of non-specific 'off targets' effects	Higher immune activation, inflammation and toxicity	Lower immune activation, inflammation and toxicity
Application	Acute disease conditions; Where high doses are tolerable	Chronic, life threatening diseases or disorders; Where low doses are desirable

Fig. 3 Comparison of shRNA and siRNA. Notably, shRNA does not require regular dosing that siRNA-based therapeutics do