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Cryo-EM Studies of An Engineered Small Interfering RNA Nano-Ring Used as a Gene Silencing Therapeutic

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Specific small interfering RNAs (siRNAs) designed to silence oncogenic pathways can be used for cancer therapy. Three-dimensional nanoscale RNA scaffolds functionalized with therapeutic siRNAs have the potential for broad use in nanotechnological and biomedical applications. The design strategies of RNA scaffolds employ assembly principles borrowed from natural RNA structures. We functionalized an RNA nanoscaffold with six therapeutic siRNAs, visualized the structure with electron cryo microscopy, and tested the therapeutic constructs in vitro and in cell lines. Our Cryo-EM reconstruction was in agreement with the nanoscaffold design and confirmed the correct formation of the siRNA functionalized nanoring. Cell culture experiments showed significant gene silencing with the siRNA nanoscaffold. Our results demonstrate that RNA-based therapeutic nanoparticle have high potential for siRNA silencing.