**INVESTIGATION OF STRUCTURE AND LENGTH REQUIREMENT FOR THE DESIGN OF RNA NANOPARTICLES TO HARBOR AND RELEASE SIRNA TO FUNCTION IN CANCER CELLS**

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The field of RNA nanotechnology has developed from proof-of-concept to a contender in revolutionizing the therapeutic industry. With the large role of RNA in the human body, RNA is poised as the third milestone in pharmaceutics following small molecule and protein drugs. As such, RNA nanoparticles are able to harbor RNAinterference (RNAi) components and proven to deliver to cancer models for treatment. In this study RNA nanoparticles confirmed delivery siRNA into KB cells resulting in knockdown in of respective genes. Results demonstrated the delivery of the RNA nanoparticles led to the cleavage of mRNA substrate through RNAi-mediated mRNA degradation at the lamin specific site. The mechanism for the action of RNA nanoparticles for in vivo gene silencing was investigated. Through molecular beacon studies, it was found that dsRNA sequence representing a siRNA placed at the 5’/3’ proximate end of the phi29 pRNA-3WJ nanoparticle was released from the RNA complex by through efficient dicer processing. The length requirement of the overhanging dsRNA for the processing and release of functional siRNA was investigated and determined that more than or at least 23 nucleotides at the dweller arm is needed at the proximal 5’/3’ end of the phi29 pRNA-3WJ for release of the siRNA. This report provides a guideline for length and structure determination in the design of RNA nanoparticles for gene silencing and cancer therapy. This report demonstrates the ability of RNA nanoparticles ability to carry siRNAs for the specific gene knockdown and overcoming previous roadblocks in RNAi therapies.