Abstract


STUDENT: My N Bui

DEGREE: Master of Sciences

COLLEGE: Sciences and Humanities

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PAGE: 6

RNA nanotechnology is rapidly emerging field and has recently received wide interest in the scientific community. The field is focused on design, synthesis, and assembly of artificial RNA nanoparticles with wide spectra applications in synthetic biology and medicine (1,2). This work demonstrates the robust properties of in-silico designed RNA tetra-uracil (tetra-U) structural 3D motifs for the construction of nanometer-scale nucleic acid geometries (Figure 1). The artificial tetra-U motif is unique and advantageous to the previous reports (3,4) in that it possesses the special property of self-assembly and can be controlled to predictably build structures of defined size, shape, and stoichiometry. Particularly, we demonstrate the fabrication of economically favorable RNA triangular nano-scaffolds based on RNA, DNA, and hybrid

Figure 1. Fabrication of de-novo RNA, RNA/DNA and DNA nanoparticles or different sizes and shapes based on in-silico designed tetra-U helix linking module.
RNA-DNA strands, the geometries of which were confirmed by atomic force microscope. Each of the triangle nanoparticles was thoroughly analyzed and their physicochemical properties were compared using well-established assays, including UV-melting, enzymatic degradation, immunostimulatory activity, and gene-silencing implementing RNAi technology. We found that the modulation of RNA and DNA strand composition makes it possible to engineer, in a de novo fashion, nanometer-scaled particles that are enzymatically resistant, thermodynamically stable, and potentially instrumental in the delivery of fluorescent probes and gene-silencing agents to cancer cells. Furthermore, the triangular nano-scaffolds show great promise for biomedical applications due to their tunable immunostimulatory properties.

Overall, the system shown here for a simple design to precisely tune physicochemical and biostimulatory properties adds a new angle to exploiting RNA/DNA hybrid nanoparticles in a clinical setting. We have also obtained preliminary data demonstrating that tetra-U motif can be used to construct other polygons made of RNA and DNA including squares, pentagons, and hexagons. Further work is currently under investigation. We are planning to evaluate nucleic acid polygon’s physicochemical properties including assembly efficiency at isothermal conditions, thermodynamic stabilities, and enzymatic resistance. This data will be crucial to further demonstrate the importance of such economically advantageous and fine-tunable hybrid RNA/DNA nanostructures to fulfill the needs of the rapidly developing field of RNA nanotechnology.

References
