Advancement of the Field of RNA Nanotechnology for Cancer Therapy

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The field of RNA nanotechnology has advanced rapidly during the past decade. A variety of programmable RNA nanoparticles with defined shape, size, and stoichiometry have been developed for diverse applications. RNA nanotechnology is the construction of nano-architectures by bottom-up self-assembly with a scaffold, ligands, therapeutics, and regulators, comprised mainly or exclusively of RNA. RNA nanoparticles can self-assemble into a homogeneous structure with defined stoichiometry. These nanoparticles with 2'- modifications are thermodynamically and chemically stable, non-toxic, and highly soluble; display favorable biodistribution and PK/PD profiles; and retain authentic folding and independent functionalities of all incorporated modules (i.e. RNA aptamer, siRNA, miRNA or ribozyme). Although I proved the concept of RNA nanotechnology by bottom-up self-assembly of engineered RNA fragments in 1998 (Cell 1998; Molecular Cell 1998; https://www.google.com/search?q=Molecular+Cell+Peixuan+Guo&source=lnms&tbm=isch&sa=X&ved=0ahUKEwjQyKSGpePTAhVh64MKHXooDXwQ_AUIBygC&biw=1104&bih=540#imgrc=5V7JQF2dd3IH8M), it was not until recently that three major challenges became resolved concerning RNase degradation, *in vivo* dissociation, and immune responses. The rising popularity of RNA nanotechnology is mainly due to the following achievements: (1) introducing chemical modifications into nucleotides without significantly altering the RNA folding or self-assembly; (2) confirming the concept that RNA structures have very high thermodynamic stability and is suitable for *in vivo* circulation and other applications; (3) developing methods to control shape, size, and stoichiometry of RNA nanoparticles; (4) proving that the immunogenicity of RNA nanoparticles is size, shape, structure and sequence dependent and is tunable to produce either a minimal immune response that can serve as safe therapeutic vectors, or a strong immune response for cancer immunotherapy or vaccine adjuvants; (5) decreasing cost of RNA production by chemical synthesis; (6) demonstrating the production of safe and specific targeting therapeutic RNA nanoparticles for cancer and other diseases with little or no accumulation in vital organs.

Further reading:

1) ***ACS Nano***. 2018; in press. **2)** ***Journal of Control Release***. 2018; 276:17. **3)** ***Nature Nanotechnology***. 2018; 12:82. **4)** ***Advanced Materials.*** 2016; 28:7501. **5)** ***Molecular Therapy***. 2016; 24:1267. **6)** ***ACS Nano***. 2015; 9:9731. **7)** ***Advanced Materials***. 2016; 28:100. **8)** ***Nature Nanotechnology***. 2011; 6:658. **9)** ***Nature Nanotech***. 2010; 5:833. **10)** ***Mol. Cell.*** 1998. 2:149 (first paper to prove of concept of RNA Nanotechnology, featured in ***Cell***). **11)** ***Science***. 1987; 236:690. **12)** ***Nano Today***. 2015; 10:631.