

# Team Finds Stable RNA Nano-scaffold Within Virus Core

EurekAlert

CINCINNATI—With the discovery of a RNA nano-scaffold that remains unusually stable in the body, researchers at the University of Cincinnati (UC) have overcome another barrier to the development of therapeutic RNA nanotechnology.

Peixuan Guo, PhD, Dane and Mary Louise Miller Endowed Chair and professor of biomedical engineering, and his colleagues in UC's College of Engineering and Applied Sciences report the construction of a thermodynamically stable RNA nanoparticle online in the journal *Nature Nanotechnology*.

The nanoparticle, constructed from a three-way junction (3WJ) motif of packaging RNA (pRNA) molecules, can serve as a platform for building larger, multifunctional nanoparticles, says Guo, which can then be injected into the body to deliver therapeutics to targeted cells.

"RNA nanoparticles have applications in treating cancers and viral infections," he says, "but one of the problems in the field is that RNA nanoparticles are relatively unstable. Without covalent bonds or cross-linking to keep them together, the nanoparticles produced via self assembly can dissociate when injected into animal and human circulation systems, where they exist at very low concentrations."

In the work, Guo and researchers explored the unique structure of the DNA packaging motor of bacteriophage phi29, a virus that infects bacteria. The motor is geared by a ring of pRNA molecules containing interlocking loops and helical domains, which are joined together by a strong 3WJ motif.

"The pRNA is extraordinary strong," says Guo, "since it is a mechanical part that nature uses to gear a powerful motor. This strength makes it an ideal platform for constructing RNA nanoparticles. Furthermore, the core has unique and unusually stable features, such as resistance to strong denaturants like urea and the ability remains intact at ultra-low concentrations in the absence of magnesium."

Using three small fragments of RNA with high affinity for assembling into larger structures, researchers were able to recreate the 3WJ core outside the pRNA structure. In addition, each arm of the 3WJ core can be fused to siRNA molecules, receptor-binding ligands and RNA aptamers, molecular tools necessary for the nanoparticle to find a targeted cell inside the body and silence genes within it.

The resulting nanoparticle remained stable and functional in vitro and, when introduced in vivo, targeted tumors specifically without diffusing to other critical organs or normal tissues.

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"Making fusion complexes of DNA or RNA is not hard," says Guo, "but ensuring the appropriate folding of individual modules within the complex to retain their function after fusion is a difficult task. The pRNA 3WJ core directs the folding of individual functional modules, and the stability of the 3WJ core ensures that each fusion module remain folded for proper function."

Earlier this year, Guo and his team overcame another obstacle to RNA nanotechnology, the risk posed by RNase, a common enzyme that quickly degrades RNA upon contact. By replacing a chemical group in RNA's ribose ring, Guo's team was able to make the RNA resistant to degradation, while retaining its ability to assemble into nanoparticles and form appropriate 3D structure and function.

[SOURCE](#) [1]

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