NCI Partnership Targets RNA Research at UC

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In the decades to come, it's assumed that we'll uncover the secrets of our health and illness by studying the makeup of our DNA. But for some researchers at UC, the future of treating certain diseases lies in DNA's less famous cousin, the other macromolecular essential for life—RNA.

Professor and Dane and Mary Louise Miller Endowed Chair in biomedical engineering Peixuan Guo, PhD, has been working with RNA for decades, pioneering its use as a versatile building block for nanotechnology, or the engineering of functional systems at the molecular scale. In 1998, his lab discovered that RNA in the bacteriophage phi29 virus can self-assemble or be engineered into nanoparticles to gear a motor to package DNA into the virus's protein shell.

With a $2.4 million award from the National Cancer Institute, he will now expand that research into studying RNA's use as a nanoparticle in cancer therapy. The grant is part of the second phase of the NCI's Alliance for Nanotechnology in Cancer program, which funds researchers working to leverage the specific advantages of nanotechnology to improve the diagnosis, treatment and prevention of cancer.

The five-year award will establish a Cancer Nanotechnology Platform Partnership at UC. Guo, who serves as director of UC's NIH Nanomedicine Development Center, says RNA's unique properties will be used to explore the delivery of targeted therapies to diseased cells or tissues via nanotechnology.

"RNA is particularly attractive in nanotechnology and nanomedicine," he says. "It can be manipulated as easily as DNA, but possesses the versatility in structure and catalytic function similar to that of proteins."

As part of the award, Guo will work with an interdisciplinary team of biomedical engineering scientists, cancer biologists and RNA and DNA nanotechnology experts, including Malak Kotb, PhD, chair of UC's molecular genetics, biochemistry and microbiology department.

Kotb credits UC's nanotechnology program for helping to bring her to Cincinnati from the University of Tennessee Health Science Center in Memphis.

"The promise of Dr. Guo's technology in the diagnosis and treatment of diseases, including cancer and infectious disease, is enormous," she says. "RNA nanotechnology can create ideal therapeutic delivery molecules because RNA molecules can be bundled in different shapes and structures—this enhances their ability to interact with high specificity to molecules outside and inside cells, without causing toxicity or side effects."

In order to construct these delivery molecules, researchers will first develop new ways to screen for stable segments of RNA that can be used as nanodevices. But Kotb says RNA nanotechnology has already shown success on cancer models in her lab.

"We had been developing targeted therapeutics for leukemia and lymphoma," she says, "where we were aiming to target a specific gene that these cancerous cells depend on for their survival, but on which normal cells have less dependency. Working with Dr. Guo, we generated an effective RNA nanoparticle that not only carries the gene-silencing construct but is also decorated with another RNA nanoparticle. The second nanoparticle escorts the therapeutic nanoparticle specifically to the target cancer cells, effectively silencing the target gene and diminishing tumor growth."

"We're now eager to generate RNA nanoparticles that can affect our immune system in a way that enhances our ability to fight certain infections," says Kotb, "or that help repair damage caused by unregulated immune responses to microbes."

Spreading the Word About a Growing Field…

Though he believes the study of nanotechnology has moved "beyond imaginable possibilities," Guo says the use of RNA is still new to many in his field.

"Although the concept of RNA nanotechnology has been developed for more than 10 years, the popularity of studying RNA nanostructures has only emerged recently—90 percent of publications on RNA nanostructures were published on or after 2006," he says.

To help spread the concept and approaches of RNA nanotechnology, Guo published a "call to arms" paper, "The Emerging Field of RNA Nanotechnology" in *Nature Nanotechnology* this fall, outlining the properties of RNA nanoparticles, existing techniques and challenges for the future.

"I hope the paper will be a landmark to researchers to promote a very important new field for the treatment of cancer, AIDs and hepatitis," he says.

Guo also chaired the 2010 International Conference of RNA Nanotechnology and Therapeutics, the first event of its kind, held Oct. 23-25 in Cleveland: "With the new conference, we hope to bring together the brightest minds throughout the world to disseminate their knowledge and promote collaboration for advancing this emerging field of science," he says.