Researchers' quest for gold

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For University of Wisconsin-Milwaukee researchers studying the toxicity of gold nanoparticles - a minuscule material with potentially big biomedical applications - the road to a new medical advance may or may not be paved with gold.

These ultrafine metallic particles hold great promise for treating diseases as diverse as cancer, diabetes or AIDS, but scientists must prove that new ways to treat disease will do no harm.

Reinhold Hutz, a professor of biological sciences at UWM, and graduate student Jeremy Larson are investigating whether gold nanoparticles target and disrupt the female reproductive tract - the only research of its kind in the United States.

Gold nanoparticles range in size from 1 to 100 nanometers; a nanometer is about one-billionth the size of a yardstick. Noting the remarkable scale of nanoparticles, Larson put the particles in perspective: "If a nanoparticle were the size of a football, a virus would be the size of a person."

What distinguishes nanoparticles from particles of other sizes is their unique physical and chemical properties. The compatibility of other biological molecules with gold nanoparticles, for example, renders them prime candidates for tissue-specific drug delivery.

"A medicine (made of nanoparticles) may one day be developed to target a specific type of cancerous tumor and limit the adverse side effects experienced by the patient," Larson said.

Focusing on the toxicity of gold nanoparticles in the reproductive tract was a natural progression for Hutz, who has devoted much of his career to understanding ovarian function. An interest in how environmental toxicants act as estrogens in females led Hutz and his former graduate student Rose Stelzer to study the toxicity of gold nanoparticles. Hutz said he and Stelzer wondered what role, if any, gold nanoparticles would play in ovarian estrogen production.

Their 2009 paper published in the *Journal of Reproduction and Development* showed that gold nanoparticles accumulate in ovarian cells that specialize in estrogen production. Furthermore, Hutz and Stelzer found that the particles alter the amount of estrogen the cells make, prompting the scientists to speculate that the particles may undermine female fertility.

Larson's work began where his predecessor left off. Larson explores the role of gold nanoparticles in the context of the intact ovary - the next logical step after studying cells in culture. Larson's preliminary findings indicate that, indeed, gold nanoparticles alter genes involved in ovarian steroid production.

In terms of these nanoparticles' potential use in drug delivery, Hutz said that altering the design of gold nanoparticles - mainly by adding small chemical groups that change the chemistry - may render them less toxic.

Hutz said future studies in his lab will look at the fate of gold nanoparticles in the whole animal, where ovarian function is influenced by an array of physiological factors not easily re-created in a dish. "We need to know how the gold nanoparticles move in the intact animal, where they go, how they are processed and what the nanoparticles do to the body's organs," Hutz said.

Robert Tanguay, a professor of environmental and molecular toxicology at Oregon State University, agreed.

"Since these studies were conducted outside the animal, more research is needed to determine if environmentally relevant exposures to engineered nanoparticles would pose a significant risk to the mammalian reproductive system," he said.

Larson said his experience in the lab consists of many "moving parts": demanding hours, uncharted territory and an ongoing hunt for research dollars.

A lack of funding, Hutz and Larson agreed, is the main obstacle to doing research. Hutz said that his lab is funded in part by money from the Children's Environmental Health Sciences Core Center, a Milwaukee-based research consortium funded by the National Institute of Environmental Health Sciences. The center aims to understand the environmental causes of childhood disease and communicate that knowledge to communities and policy makers, according to center director David Petering, a professor of chemistry at UWM.

"There are only 17 of these centers in the country, competitively awarded to academic institutions like Harvard, MIT, Johns Hopkins and the University of Wisconsin-Milwaukee," Petering said.

The center is a joint initiative of UWM, the Children's Research Institute of Children's Hospital of Wisconsin and the pediatrics department of the Medical College of Wisconsin, with scientists participating from Marquette University, UW-Madison and UW-Parkside.

"Researchers like Dr. Hutz gain access to special staff and infrastructure, funding for exploratory research, and a large community of scientists who are dedicated to working together to enhance children's health," Petering said.

As a graduate student, Larson is part of a less-visible scientific community consisting of trainees and early career scientists at universities throughout the city. Many graduate students and postdoctoral researchers remain behind the scenes, working in labs and publishing their findings out of public view. Larson, however, said he is determined to highlight research he performs at UWM. He added that he is often in competition for grants and awards with students hailing from larger, better-funded research institutions. His gold nanoparticle research has garnered several awards at national scientific meetings.

Larson noted that he enjoys opportunities to reach out beyond his lab bench and connect with others.

"In my mind, the most challenging, yet most enjoyable, aspect of our work is the collaborative, interdisciplinary effort that draws from many fields of science - physics, engineering, chemistry, biology and molecular toxicology."

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