Mayo Clinic study explores link between nanoparticles and kidney stones

December 19 2006

Researchers at Mayo Clinic have successfully isolated nanoparticles from human kidney stones in cell cultures and have isolated proteins, RNA and DNA that appear to be associated with nanoparticles. The findings, which appear in the December issue of the Journal of Investigative Medicine, are significant because it is one step closer in solving the mystery of whether nanoparticles are viable living forms that can lead to disease -- in this case, kidney stones.

Kidney stones are associated with pathologic calcification, the process in which organs and blood vessels become clogged with calcium deposits that can damage major organs like the heart and kidneys. What causes calcium deposits to build up is not entirely known. Medical scientists at Mayo Clinic are studying calcification at the molecular level in an effort to determine how this phenomenon occurs.

There is a growing body of scientific evidence that links calcification to the presence of nanosized particles, particles so small that some scientists question whether a nanoparticle can live and if so, play a viable role in the development of kidney stones.

The presence of proteins, RNA and DNA does not prove that nanoparticles are viable living forms because a genetic signature has not been identified, says the study's author John Lieske, M.D., a nephrologist with Mayo Clinic. A genetic signature would prove that nanoparticles are indeed living forms that replicate and can cause disease.

"We are looking at how kidney stones start as very small calcifications inside the kidney and then eventually grow into stones," says Dr. Lieske. "In the laboratory, we have isolated nanoparticles from kidney tissue and kidney stones, and have successfully propagated them in culture. This does not clearly confirm the role of nanoparticles in the formation of kidney stones, but it offers insight not otherwise known."

Approximately 12 percent of men and 5 percent of women will develop kidney stones by the time they reach 70 years old. Some $5 billion is spent in the United States each year to treat patients with kidney stones, but exactly how kidney stones form is not known. Scientists theorize that if nanoparticles become localized in the kidney, they can become the focus of subsequent growth into larger stones over months to years. Other factors, such as physical chemistry and protein inhibitors of crystal growth, also play a role. But what scientists don't quite understand is why, where and how they start growing, Dr. Lieske says.

The study cites evidence that indicates the unlikelihood that events linked to the calcification process are driven solely by physical chemistry, but instead are influenced by specific proteins and cellular responses. Understanding these events will provide clues to develop new therapy to treat kidney stones, the authors say.

"There are at least two novel hypotheses here in terms of how stones might actually form. One: an infectious agent. If that was the case, that would point us in the direction of using different kinds of treatments specific to an infectious agent. Two: the idea that cells drive calcification. That would suggest other alternative therapies," according to Virginia Miller, Ph.D., a specialist in vascular research at Mayo Clinic and a study author.

In addition, researchers examined how urine proteins alter the way crystals and cells interact in binding to cells -- the way in which cells respond to the crystals and assume more of a bone-like morphology and drive calcification over time.

In a second study, due to appear in the December issue of the *Journal of Investigative Medicine*, Drs. Lieske, Miller, and Karim Benzerara, Ph.D., of the Institut de Physique du Globe de Paris, attempted to identify a DNA chemical marker in nanoparticles. The preliminary study suggests that nanoparticles from human samples share spectroscopic characteristics with calcified bacteria that exist in freshwater lakes. However, studies could not confirm whether the nanoparticles are calcified bacteria or hydroxyapatite crystals that precipitated upon proteins present in the culture medium used to replicate the nanoparticles. Researchers did, however, identify chemical bonds between proteins and calcium in nanoparticles that were similar to those found in the bacteria that calcified in the environment.

"Right now the results are inconclusive. In some of the segments we saw a characteristic signal that might suggest DNA, but in others we did not," Dr. Miller says.

This is a relatively new area of science, so the tools and processes used in this research have yet to be perfected. "Many of these tools haven't been applied to these systems in a consistent, rigorous way. So we are still in the learning process of how to handle the material. For example, what are the ideal conditions in the laboratory in which we should study nanoparticles?

"It was disappointing that we did not find any consistent DNA information. We think the findings were inconclusive, in part, because of the inability to apply these techniques in conditions suitable to nanoparticles," Dr. Miller says.

Source: Mayo Clinic