Nanoparticle shows promise in reducing radiation side effects

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Using transparent zebrafish embryos, researchers at Jefferson Medical College have shown that a microscopic nanoparticle can help fend off damage to normal tissue from radiation. The nanoparticle, a soccer ball-shaped, hollow, carbon-based structure known as a fullerene, acts like an "oxygen sink," binding to dangerous oxygen radicals produced by radiation.

The scientists, led by Adam Dicker, M.D., Ph.D., associate professor of radiation oncology at Jefferson Medical College of Thomas Jefferson University in Philadelphia and at Jefferson's Kimmel Cancer Center, and Ulrich Rodeck, M.D., professor of dermatology at Jefferson Medical College, see fullerenes as a potentially "new class of radioprotective agents."

They present their team's results November 15, 2005 at the AACR-NCI-EORTC International Conference on Molecular Targets and Cancer Therapeutics in Philadelphia.

While chemotherapy and radiotherapy are the standard treatments for cancer, they take their respective toll on the body. Radiation can damage epithelial cells and lead to permanent hair loss, among other effects, and certain types of systemic chemotherapy can produce hearing loss and damage to a number of organs, including the heart and kidneys. Some other side effects include esophagitis, diarrhea, and mouth and intestinal ulcers.

Only one drug, Amifostine, has been approved to date by the federal Food and Drug Administration, to help protect normal tissue from the side effects of chemotherapy and radiation, and researchers would like to develop new and improved agents.

Dr. Dicker and his group were exploring the molecular mechanisms responsible for cellular damage from radiation. They collaborated with a Houston-based drug company, C Sixty, and its radiation-protective agent, CD60_DF1.

To test how well it worked, they turned to tiny zebrafish embryos, which are transparent and allow scientists to closely observe damage produced by cancer treatments to organs. Zebrafish usually have most of their organs formed by day three of life.

They gave the embryos different doses of ionizing radiation as well as treatment by either Amifostine, which acted as a control agent, or CD60_DF1. They found that CD60_DF1 given before and even immediately after – up to 30 minutes – exposure to X-rays reduced organ damage by one-half to two-thirds, which was as good as the level of protection given by Amifostine.

"We also showed that the fullerene provided organ-specific protection," Dr. Dicker notes. "It protected the kidney from radiation-induced damage, for example, as well as certain parts of the nervous system."

He explains that one way that radiation frequently damages cells and tissues is by producing "reactive oxygen species" – oxygen radicals, peroxides and hydroxyls. The research team showed that zebrafish embryos exposed to ionizing radiation had more than 50 percent fewer reactive oxygen species compared to untreated embryos.

He says that the company also has technology enabling certain molecules to be attached to the nanoparticles, which will allow targeting to specific organs and tissues.

Next, Dr. Dicker and his colleagues would like to plan studies looking at another animal model system to find out if fullerene not only protects the entire animal from radiation, but to also examine organ-specific effects, such as protecting the lungs, for example. They also are interested in exploring its ability to prevent some of the long-term side effects of radiation, such as fibrosis in the leg. He and his co-workers also want to determine better ways to target the agent to protect specific tissues and organs.

Source: Thomas Jefferson University

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