

# Antibody therapy prevents gastrointestinal damage following radiation exposure in mice

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A new study offers the first evidence of a drug capable of preventing lethal damage to the gastrointestinal (GI) tract caused by exposure to high levels of ionizing radiation, such as those occurring during a nuclear incident. There are currently no FDA-approved treatments or prophylactics available to manage the condition, known as radiation gastrointestinal syndrome (RGS), which is associated with weight loss, vomiting, diarrhea, dehydration, systemic infection, and – in extreme cases – septic shock and death.

The research was conducted in mice by investigators at Memorial Sloan-Kettering Cancer Center and The University of Texas MD Anderson Cancer Center and will be published in the May 2012 issue of *The Journal of Clinical Investigation*.

The GI system is maintained through the continuous infusion of epithelial cells produced by specialized stem cells located in gland-like structures called crypts found in the epithelial lining of the small intestines and colon. High-dose irradiation kills these stem cells and destroys the protective epithelial barrier, or mucosa, resulting in onset of RGS within days of exposure.

According to the study, administration of a drug called 2A2 anti-ceramide antibody inhibited cell death (apoptosis) in blood vessels within the [GI tract](#) and improved 90-day survival from 0 percent to 80 percent among mice exposed to 15 Gy whole-body irradiation.

"We discovered that using this monoclonal antibody to inhibit blood vessel damage and dysfunction led to a dose-dependent increase in the number of surviving stem cells, which are highly active and responsible for repopulation of the damaged GI epithelium," said the study's corresponding author Richard N. Kolesnick, MD, a member of Memorial Sloan-Kettering's Molecular Pharmacology and Chemistry Program whose laboratory conducted the research experiments.

Developed by investigators at MD Anderson, the drug works by interfering with ceramide — a lipid molecule that plays a role in apoptosis — generated on the surface of the endothelial cells that make up the smallest blood vessels of a tumor.

The US Department of Health and Human Services has placed significant emphasis on the development and deployment of new therapies and countermeasures to protect first responders, military personnel, and others who are required to enter into areas of potential radiation contamination. Dr. Kolesnick and colleagues are working to develop anti-ceramide antibody as an agent used not only to protect against the damaging effects of radiation prior to exposure, but also to mitigate those effects after exposure.

Provided by Memorial Sloan-Kettering Cancer Center

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