Study of what makes cells resistant to radiation could improve cancer treatments

October 18 2017

A Johns Hopkins University biologist is part of a research team that has demonstrated a way to size up a cell's resistance to radiation, a step that could eventually help improve cancer treatments.

Jocelyne DiRuggiero's laboratory provided some of the microorganisms used in the study, in which an instrument that works a bit like an electron microscope spotted the telltale molecular structures associated with resistance to the harmful effects of ionizing radiation, or IR. The tests, which use a method called electron paramagnetic resonance spectroscopy, show that the same molecular structures provide resistance for every type of living cell found on Earth, from microorganisms to human cells.

Results of the research were just published in *Proceedings of the National Academy of Sciences*.

Led by Michael J. Daly, a biologist at Uniformed Services University of the Health Sciences in Bethesda, Maryland, the study looked at samples of bacteria, yeast, human cells, and a domain of single-celled organisms called archaea. For all of these, the molecular structures they had identified for examination were shown to be "the strongest known gauge of biological IR resistance between and within organisms representing all three domains of life."

Daly had years ago disproven the longstanding idea that the harm of radiation exposure lay in the damage to strands of DNA alone. He showed that the problem was not the DNA damage itself, but the inability of cells to repair the damage. In IR resistant organisms, proteins remained functional to repair the DNA damage, allowing the cells to survive the radiation exposure.

Daly had also shown, in a 2004 study, that radiation resistance was associated with the presence in the cell of manganese ions associated with small organic molecules, forming powerful antioxidant complexes. DiRuggiero discovered the same manganese complexes in archaea and other bacteria, supporting the idea of a universal mechanism for IR resistance. The complexes were found to have potent antioxidant properties that supported the proteins in the cell, which in turn bolstered the cell's ability to repair DNA damage.

The new study reports a method of identifying the active form of these manganese ion complexes and demonstrates that they are associated with radiation resistance. For example, the highly IR resistant bacterium, Deinococcus radiodurans, is shown as a .94 in an index of the manganese complexes, while the radiation sensitive E. coli has a value of .17. Human cells have an index of .95, which is remarkably resistant given the large genome size and so many targets for DNA damage.

DiRuggiero—who provided samples for three types of microorganisms in the archaeal and bacterial domain—said the electron paramagnetic resonance spectroscopy used in this study could be used to examine cancer cells to determine their resistance to radiation, and to tailor radiation therapy accordingly.

She said it's also possible that the manganese ion complexes could be developed in a form that could be given to people to boost their resistance to radiation.

More information: Ajay Sharma et al. Across the tree of life, radiation resistance is governed by antioxidant Mn2+, gauged by paramagnetic resonance, *Proceedings of the National Academy of Sciences* (2017). DOI: 10.1073/pnas.1713608114

Provided by Johns Hopkins University