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MicroRNAs show promise for revealing radiation exposure and likelihood of survival

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Ionizing radiation incidents—nuclear war, nuclear accidents or terrorist dirty bombs, for example—can cause mass fatalities. Since resources for medical countermeasures are limited, it's critically important to swiftly and accurately triage those victims most likely to benefit from treatment. A new study that published online today in *Science Translational Medicine* found that microRNAs (miRNAs) in serum may help in that effort.

The research was led by Chandan Guha, M.B.B.S., Ph.D., professor and vice chair of radiation oncology at Albert Einstein College of Medicine and Montefiore Health System, Vijay Singh, Ph.D., F. Edward Hébert School of Medicine and Medicine, Uniformed Services University of the Health Sciences, and Dipanjan Chowdhury, Ph.D., Dana Farber Cancer Institute.

First in mice and later in non-human primates (NHPs), the investigators discovered a signature of seven serum miRNAs that are expressed differently in response to total body irradiation. (miRNAs are small non-coding RNA molecules that target and bind to messenger RNA molecules to prevent protein production.)

A combination of three of these irradiation-associated miRNAs (miR-133b, miR-215, and miR-375) accurately distinguished irradiated from non-irradiated NHPs. A combination of five of the miRNAs (miR-133b, mirR-215, miR-375, miR-126 and miR-30a) could not only identify irradiated NHPs but also predict their probability of survival.

The researchers also developed a classifier based on two miRNAs (miR-30a and miR-126) that reproducibly predicted radiation-induced mortality.

Compelling evidence suggests that the same seven radiation-responsive miRNAs described in the paper are evolutionarily conserved and therefore should also help in assessing people for radiation exposure and predicting their prognosis: Genomic analysis of the miRNAs revealed that the same seven transcription factors (proteins that regulate gene transcription by binding to nearby DNA) were predicted to bind to the promoter sequences of all seven miRNAs in mice, NHPs and humans.

Serum miRNAs can be measured using relatively simple technology that provides results within 12 to 24 hours after exposure to radiation. By contrast, current techniques for assessing ionizing radiation exposure (e.g., the dicentric chromosome assay to detect DNA strand breaks in cultured lymphocytes) require several days.

"Our findings regarding radiation-responsive miRNAs in NHPs and mice make us hopeful that a combination of these miRNAs will emerge as a biomarker for precisely identifying people exposed to radiation and rapidly providing aid to those who can benefit from it," says Dr. Guha.

The study is titled "Evolutionarily conserved serum microRNAs predict radiation-induced fatality in nonhuman primates."

More information: Wojciech Fendler et al. Evolutionarily conserved serum microRNAs predict radiation-induced fatality in nonhuman primates, *Science Translational Medicine* (2017). DOI: 10.1126/scitranslmed.aal2408

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