NATURE | NEWS

Wanted: cure for fatal effects of radiation

Drug that treats damage to the gut could help people undergoing radiation therapy for cancer — or victims of a terrorist attack.

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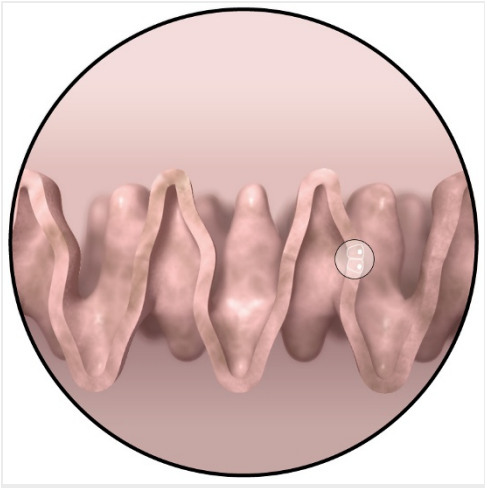
A protein that keeps gut cells alive could be key to surviving acute radiation syndrome. Tests in mice of a therapy that shores up levels of the protein in cells indicate that it limits the intestinal damage caused by exposure to radiation — such as could occur during a 'dirty bomb' attack. The drug could also prove useful for counteracting the side-effects of cancer radiation therapy.



V. Altounian/Science Translational Medicine

Exposure to intense radiation causes the death of cells in the intestinal lining within 24 hours, a process that has now been linked to the breakdown of a protein.

Drugs are already available to treat the bone-marrow damage that occurs in acute radiation syndrome. But no good drugs are available to counter the fatal gastrointestinal damage that often accompanies it, which is marked by dehydration, malnutrition and infection. Finding such drugs has become a priority of the US government since the terrorist attacks of 11 September 2001, because of the fear that terrorists might detonate dirty bombs — devices in which conventional explosives disperse radioactive material.

A group led by tumour biologist Amato Giaccia of Stanford University in California reports today in *Science Translational Medicine*[1] that gastrointestinal radiation damage might be kept at bay through stabilization of the body's supply of a protein called hypoxia-inducible factor 2 (HIF2), which helps to control the survival of cells that line the inside of the gut under the low-oxygen conditions found there. When the scientists gave mice a drug called dimethyloxallyl glycine (DMOG) to neutralize proteins that lower HIF2 levels, the mice were more resilient to radiation damage.

The scientists blasted the abdomens of eight mice with x-rays, then dosed them with DMOG 24 hours later. Six of these mice survived for at least a month, compared with only two of eleven untreated mice.

However, in mice exposed to whole-body irradiation, DMOG prevented death only in a handful of animals who also received bone-marrow transplants.

Nonetheless, says radiation oncologist David Kirsch of Duke University Medical Center in Durham, North Carolina, the findings could be useful because a dirty bomb might not affect survivors' whole bodies. “Civilians exposed to radiation may have part of their bone marrow shielded if, for example, they are in a building,” says Kirsch, who co-authored an accompanying commentary to the paper[2].

Niche market

The development of new 'countermeasures' against terrorist threats is difficult, because the market for such drugs is small, they may never be used, and it is not usually possible to test their effectiveness in people. But the US government is trying to help companies to solve these problems by funding the search for treatments through many agnecies, including the National Institutes of Health, which funded Giaccia's work, and through an agency created in the wake of the events of September 2001: the US Biomedical Advanced Research and Development Authority (BARDA).

NIH and BARDA are funding studies of a drug intended to remedy gastrointestinal effects of radiation: OrbeShield, which is being developed by Soligenix of Princeton, New Jersey. The drug has been cleared by the US Food and Drug Administration to move into animal trials that could lead to its approval.

But Giaccia does not intend to apply for BARDA funding to develop DMOG or other HIF2-stabilizing drugs. Instead, he hopes to study how these drugs — several of which are being studied as potential treatments for anaemia — might protect healthy cells from radiation

delivered during cancer treatments.

Radiation therapy is usually delivered only to the area surrounding a tumour, meaning that cancerous cells that have broken off from the tumour and travelled to distant parts of the body — metastases — are missed. It's these metastases that often prove fatal to people with cancer. Giaccia says that treatment with drugs such as DMOG might allow patients to undergo whole-body radiation, which could prove more effective.

"We're thinking about using this to transform radiotherapy from a localized type of therapy to a systemic therapy," Giaccia says. "The potential to be able to use these drugs as clinical radioprotectors is not unreasonable."

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References

1. Taniguchi, C. M. *et al*. *Sci. Transl. Med.***6**, 236ra64 (2014).
2. Lee, C.-M., Moding, E. J. & Kirsch, D. G. *Sci. Transl. Med.* **6**, 236fs20 (2014).