NATURE | NEWS

Tardigrade protein helps human DNA withstand radiation

Experiments show that the tardigrade's resilience can be transferred to cultures of human cells.

Jason Bittel

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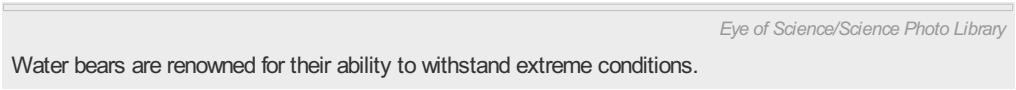

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Water bears are renowned for their ability to withstand extreme conditions.

Tardigrades, or water bears, are pudgy, microscopic animals that look like a cross between a caterpillar and a naked mole rat. These aquatic invertebrates are consummate survivors, capable of withstanding a host of extremes, including near total dehydration and the insults of space.

Now, a paper[1] published on 20 September in *Nature Communications* pinpoints the source of yet another tardigrade superpower: a protective protein that provides resistance to damaging X-rays. And researchers were able to transfer that resistance to human cells.

"Tolerance against X-ray is thought to be a side-product of [the] animal's adaption to severe dehydration," says lead study author Takekazu Kunieda, a molecular biologist at the University of Tokyo. According to Kunieda, severe dehydration wreaks havoc on the molecules in living things. It can even tear apart DNA, much like X-rays can.

The researchers wanted to know how tardigrades protected themselves against such harsh conditions. So Kunieda and his colleagues began by sequencing the genome of *Ramazzottius varieornatus*, a species that is particularly stress tolerant. It's easier to study processes within the tardigrade's cells when the animal's genome is inserted into mammalian cells, says Kunieda. So researchers manipulated cultures of human cells to produce pieces of the water bear's inner machinery to determine which parts were actually giving the animals their resistance.

Eventually, Kunieda and his colleagues discovered that a protein known as Dsup prevented the animal's DNA from breaking under the stress of radiation and desiccation. And they also found that the tardigrade-tinged human cells were able to suppress X-ray induced damage by about 40%.

Genomic treasure trove

"Protection and repair of DNA is a fundamental component of all cells and a central aspect in many human diseases, including cancer and ageing," says Ingemar Jönsson, an evolutionary ecologist who studies tardigrades at Kristianstad University in Sweden.

This makes the new paper's findings "highly interesting for medicine", says Jönsson. It opens up the possibility of improving the stress resistance of human cells, which could one day benefit people undergoing radiation therapies.

Kunieda adds that these findings may one day protect workers from radiation in nuclear facilities or possibly help us to grow crops in extreme environments, such as the ones found on Mars.

Bob Goldstein, a biologist at the University of North Carolina at Chapel Hill who helped to sequence the genome of another tardigrade species[2], says the research is exciting and clever. He also thinks that the study's authors are correct in predicting that this is probably just the first of many such discoveries.

"The tardigrade is resistant to a lot of different kinds of extremes," says Goldstein. And this means that the animals must have many different ways of protecting themselves.

"We are really just at the beginning of exploring the genetic treasure that the tardigrade genome represents," says Jönsson.

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References

1. Hashimoto, T. *et al. Nature Commun.* http://dx.doi.org/10.1038/ncomms12808 (2016).
2. Boothby, T. C. *et al. Proc. Natl Acad. Sci. USA* **112**, 15976–15981 (2015).

2 comments

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Keith Baverstock • 2016-09-23 07:52 AM

This paper represents a prodigious amount of work, but nevertheless I believe the authors are “barking up the wrong tree” in trying to account for the tardigrade’s extraordinary resistance to stress, particularly ionising radiation, in terms of DNA repair or its protection from stress damage. I think that the single most significant property of the adult tardigrade in relation to stress resistance is that its somatic cells are eutelic, that is, after hatching as an adult, the somatic cells do not divide. This means that the DNA in the cells is functionally dormant and stress damage is of no consequence. Thus, except for replication, the tardigrade is functionally a multi-cellular protein-only organism. Its cells are similar to red blood cells in humans, which have no genomic DNA. Indeed, the dose of radiation required to kill tardigrades is comparable to that required to kill red blood cells, namely a few thousand Gy. This conclusion is further reinforced by the observation that the embryonic tardigrade (where the DNA is being used for replication) is considerably more sensitive to ionising radiation, LD50 being a few hundred Gy, similar to other similarly sized organisms, such as C. elegans and in contrast to much larger mammalian cells, where LD50 is of the order of a few Gy only. It may be the case that the protein Dsup, by binding to the DNA, does increase radio resistance of human cells, but the extent of this effect (40% improvement) is “small beer” compared to the difference between tardigrade embryonic cells (where Dsup is strongly expressed) and adult somatic cells. Incidentally, it is also the case that heavily irradiated tardigrades are able to produce eggs, but these do not hatch. Thus, all the functions, or “machinery”, of the cell, which are carried out by proteins, remain intact, while replication, which relies on the integrity of the DNA sequence, is destroyed by high doses of radiation. A fuller account of how the tardigrade might uniquely contribute to our understanding of biology can be found at: http://inference-review.com/article/genes-without-prominence.

Sujai Kumar • 2016-09-20 07:27 PM

Dear Jason Bittel Thanks for placing this fantastic research by Hashimoto et al in context. However, it seems a bit odd that you also cite a previous tardigrade genome paper claiming 17% horizontal gene transfer, when that research has been roundly refuted as an artefact of bacterial contamination by 4 independent labs: http://www.ncbi.nlm.nih.gov/pubmed/27035985/ http://www.ncbi.nlm.nih.gov/pubmed/27069789/ http://www.ncbi.nlm.nih.gov/pubmed/27173901/ http://www.ncbi.nlm.nih.gov/pubmed/27173902/ In fact, Hashimoto et al 2016 also refute the extensive HGT finding in tardigrades: "Extensive HGT is thus not a common feature in the phylum Tardigrada and is also not correlated with extremotolerance, because R. varieornatus has superior tolerability compared with H. dujardini without extensive HGT."