

## a walk on the rough side

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Life can be hard. There are times when you find yourself in the most unfriendly circumstances and, more often than not, the best way to deal with the situation is to find your own solution and wriggle your own way out. Living species are the most imaginative of beings when it comes to designing defence mechanisms. Some release nasty smells to ward off predators, or melt into the landscape and become invisible to them. While others live in protective shells, inject toxins that paralyse, or are simply wise enough to walk away from danger. Many species have also chosen to live in places no one would ever dream of settling down in and, over time, have developed ways to flourish in severe temperatures, faced with complete dehydration and under crushing pressures. Among these are tardigrades, also known as water bears or moss piglets. One tardigrade in particular, *Ramazzottius varieornatus*, lives in very harsh conditions and even seems to have found a way to survive harmful radiation. Thanks to a protein which has been dubbed damage suppressor protein.



waterbear, by Thomas Shahan

Courtesy of the artist

The first tardigrade was described in 1773 by the German zoologist Johann August Ephraim Goeze (1731-1793), and the name *tardigrada* – literally meaning *slow stepper* – was coined three years later by the Italian priest and biologist Lazzaro Spallanzani (1729-1799). Tardigrades are tiny cylindrical eight-legged invertebrates that measure up to 2.1mm in length. They are divided into five segments. The first is the head, followed by four others from which protrude a pair of legs frequently punctuated by a set of claws. Despite its littleness, a tardigrade's internal structure is surprisingly complex: it has a complete

digestive system and a well-developed nervous system consisting of rings around a mouth. About 1,200 different species are known to date, though it is thought that there are many more. As for their lifespan, adult tardigrades live an average of several months.

Water bears are scattered across the globe where they live in freshwater environments, marine environments but also terrestrial habitats such as in moss. Like many other multicellular extremophiles, they can survive harsh conditions – very high pressures, austere temperatures and lack of water – by slowing down their physiology and almost bringing to a standstill their vital organs to preserve them. In this dehydrated state, tardigrades literally shrivel up and decrease in size, and can remain in this state for as much as 20 years. Tardigrades are particular, however, in that they can survive extreme conditions both in their dehydrated (inactive) and active forms. And *R.varierornatus* seems to be fitted out with the best survival kit of them all.

How did *R.varierornatus* acquire such skills? Some claim that, over millions of years, tolerance-specific genes have been pumped into the tardigrade's genome by a process known as horizontal gene transfer, or HGT. So much so that up to 17.5% of its genes would be of foreign origin. This theory has met with much controversy, however. The genome of *R.varierornatus* is certainly expected to carry

stress-related genes if it is to survive in the environments it does, however its genome does not seem to carry more foreign genes than would be expected – i.e. about 1.2% of the total genome. What is more, besides acquiring tolerance-specific genes, *R.varierornatus* would have lost a few metabolic pathways that respond to stress – which is an unexpected state of affairs but must also have its say in protecting the tardigrade.

Fierce dehydration or radiation can do a lot of harm to molecules: they can, for example, shred DNA apart. *R.varierornatus* seems to be particularly protected against high-dose radiation. How? This faculty could simply be a side-product of the tardigrade's capacity to tolerate complete dehydration. Nevertheless, the recently characterized damage suppressor protein, or Dsup, may well have a central role in protecting DNA. When inserted into genetically engineered human cells, Dsup improved their radiotolerance by a staggering 40 to 50%. Dsup is a nuclear protein and expressed abundantly during the tardigrade's embryonic stage – precisely when DNA is being replicated and is hence vulnerable. So far, the protein has been found in no other living organism.

How exactly, though, does Dsup protect the tardigrade's DNA? Its middle region is long and alpha-helical; its C-terminal is needed to locate the protein to the nucleus, and associate with nuclear DNA. It is thought that Dsup literally huddles around the tardigrade's DNA thus creating a sort of protective shield against radiation. In most instances, when a protein clings onto DNA there is a great chance that it

will inhibit, or at least interfere with, DNA replication and transcription. But this doesn't seem to be the case with Dsup. It could be that the amino-terminal and middle regions of Dsup both have roles in somehow relieving the adverse effects that are expected when Dsup associates with DNA.

Unique creatures such as tardigrades, which live under unique circumstances, are bound to develop unique ways to survive, and hence acquire molecules and pathways that are also unique to them. This makes them a potential source of genes and mechanisms involved in protection that could be of interest to scientists. Compared with control cells, Dsup-expressing human cultured cells saw a reduction of up to 50% in DNA damage caused by X-rays. Transferring Dsup into genetically-engineered animals should therefore increase resistance to radiation damage. By extrapolation, patients undergoing radiotherapy during cancer treatment or indeed people who work in radiation-rich environments could benefit from the doings of a protein such as Dsup – though it is always far more tricky to know in advance how a whole organism will react. What is more, there are undoubtedly other systems in *R.varierornatus* that contribute to its radiotolerance – one of which could be a DNA repair system for instance. Needless to say, astrobiologists also have a keen interest in tardigrades, and have had so since the early 1960s. If these invertebrates can put up with such hostile conditions, could they not survive in outer space? And if so, would they not give us clues as to what may already be living out there? An intriguing thought.

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## Cross-references to UniProt

Damage suppressor protein Dsup, *Ramazzottius varieornatus* (Tardigrade) : P0DOW4

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