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INSIDE JEB

Cancer-defying blind mole rats are super DNA repairers

A blind mole rat (*Spalax carmeli*). Photo credit: Andrey V. Galkin.

Although blind mole rats have not discovered the route to eternal youth, they do seem to enjoy a cancer-free old age, and the secret behind their resilience seems to be their subterranean existence. Imad Shams, from the University of Haifa, Israel, explains that the rodents encounter dangerously low oxygen levels (hypoxia) and are exposed to internally produced DNA-damaging substances that are released when the burrows are ventilated, yet they seemed to suffer no ill effects. It was assumed that they had evolved efficient DNA repair mechanisms to protect themselves from the damage – which could also protect them from cancer – although Shams says, 'to date, no direct experimental evidence was provided for this assumption'. As the issue was unresolved, he and his colleagues Vered Domankevich, Hossam Eddini and Amani Odeh began to search for direct evidence of the blind mole rat's powers of molecular self defence.

First, the team collected skin cells from baby blind mole rats (*Spalax carmeli*) and grew them in isolation in the lab before exposing the cells to hydrogen peroxide – one of the toxins produced by oxygen that breaks DNA strands – to find out how well they survived. Impressively, the mole rat cells survived the damaging effects well, with high proportions of healthy cell survival in contrast to rat skin cells, which suffered high death rates. In addition, when the team checked how much damage the mole rat DNA incurred, they were impressed to see that the mole rats accumulated significantly fewer DNA breaks than rat skin cells.

However, Shams says, 'It was still unclear whether this was due to efficient DNA repair and maintenance mechanisms or other reasons', so the team exposed the cells to increasing doses of damaging UV radiation and a chemotherapy drug, etoposide – both of which also break the DNA chain – to find out how well the mole rat cells survived. Impressively, the mole rat cells that were treated with the chemotherapy drug were almost unaffected, in contrast to skin cells from rats, which barely survived 2 days after the highest dose of chemotherapy. Meanwhile, the UV-exposed mole rat cells suffered some damage, but nowhere near as severe as the damage incurred by the rat skin cells. In addition, Shams and colleagues injected DNA that had been damaged by UV into the mole rat cells to find out how well the rodents could repair the damage, and found that the mole rats' DNA damage repair capacity was 36 times higher than that of the rat skin cells.

Shams says, 'We show that the DNA repair capacity of hydrogen peroxide-induced lesions is five times higher in *Spalax* than in the rat' and he adds that the results suggest 'the involvement of the nucleotide excision repair, base excision repair and other pathways'. He also hopes that the lessons learned from these remarkable cancer-defying rodents could offer hope of a genuine cure for cancer: 'Understanding the mechanisms evolved by *Spalax* over millions of years not only has implications for understanding aging and cancer development but may also have therapeutic importance', he says.

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