The naked mole rat could one day save your life!

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A study recently showed that the naked mole rat possesses the ability to survive prolonged periods in the absence of oxygen, a property which could lead to the development of new strategies for reducing the damage caused by certain ischemic diseases such as heart attacks and strokes.

The **naked mole rat** (*Heterocephalus glaber*) is a very unusual rodent, due both to its appearance as well as to the number of unusual properties that it possesses. Aside from being the only cold-blooded mammal, it is also unique in that it resides in colonies organized under an enormous queen, in a style similar to that seen with social insects such as ants or bees (eusociality).

From a biological point of view, the mole rat does not show any signs of wear to the cardiovascular system or its cerebral function with aging, nor does it develop cancer, and it displays exceptional longevity: while rodents of its size generally survive 4 to 5 years, the mole rat can reach nearly 30 years of age, which is equivalent to about 600 years for a human being.

All of these characteristics make the mole rat a fascinating organism for scientists, particularly for better understanding phenomena which could slow or even prevent the development of the principal chronic diseases which occur with aging.

ABSENCE OF OXYGEN

The mole rat passes most of its existence underground digging the tunnels which allow it to reach the roots and tubercles on which it feeds. The quantity of oxygen which is present within the tunnels is evidently much less than at the surface, yet over 200 to 300 mole rats can simultaneously live there and breathe this stale air.

A study recently published in the journal *Science* sought to identify the mechanisms involved in this tolerance of mole rats to such weak concentrations of oxygen[1]. The researchers initially observed that these rodents could withstand, without any problem, an environment which contained only 5% oxygen, a condition which would suffice to rapidly kill a mouse or a human.

This adaptation to low oxygen became even more spectacular when the researchers submitted some of the rodents to an environment in which all oxygen had been removed (anoxia): the animals rapidly lost consciousness, but even after 18 minutes had passed in the complete absence of oxygen, they were capable of recuperating as if nothing had happened once the oxygen supply had been re-established.

This incredible resistance to anoxia is explained by a metabolic adaptation which had never before been observed in animals: in the absence of oxygen, the mole rats released significant levels of fructose into their blood which their cells then captured using the transport protein GLUT5 in the vital body organs, particularly the heart and the brain.

While the normal fuel for cells, glucose, requires oxygen to become transformed into energy, fructose can be metabolized in the absence of oxygen and thus can serve as a temporary source of energy for maintaining the basic functions of the organism. The metabolism of fructose occurs in plants, but had never before been identified in animals.

It thus seems that evolution has proceeded by the mole rat recycling an ancient process, developed during the appearance of plants on earth, as a way of adapting to the scarcity of oxygen in their environment. This serves as an eloquent example of the incredible plasticity of life, constantly shifting through natural selection to permit organisms to adapt to their environment.

CONQUERING ANOXIA

The strategy used by the naked mole rat to survive in an environment lacking oxygen is far from being just a scientific curiosity and could, in contrast, have important ramifications on the treatment of pathologies which result from a loss of air. During a stroke or a heart attack, for example, the brain and the heart are suddenly deprived of oxygen, which leads both to the rapid death of cells and to the deaths of people who suffer these problems in the absence of rapid medical response.

The discovery of ways to alter the normal metabolism of these cells in order that they use fructose rather than glucose would then allow us to delay the deaths of these cells and hence improve the patient's probability of survival.

(1) Park TJ et al. Fructose-driven glycolysis supports anoxia resistance in the naked mole rat. Science 2017;356:307-331.

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