

Naked mole-rats bear chili pepper heat

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Pity the tiny naked mole-rat. The buck-toothed, sausage-like rodent lives by the hundreds in packed, oxygen-starved burrows some six feet under ground. It is even cold-blooded -- which, as far as we know, is unique among mammals. You can feel their pain. But, they can't feel ours.

Evolution has benefited naked mole-rats by ridding them of a body chemical called Substance P, a neurotransmitter released by pain fibers that send signals to the central nervous system in mammals after making contact with things that cause long-lasting, achy pain.

A better understanding of how Substance P works in the strange rodents may lead to new analgesic drugs for people with chronic pain who do not respond well to current medication, according to Thomas Park, associate professor of biological sciences at the University of Illinois at Chicago, and Gary Lewin of the Max-Delbrück Center for Molecular Medicine in Berlin, principal authors of a study appearing Jan. 29 in the free-access journal *PLoS Biology*.

Park, Lewin and their laboratory teams in Chicago and Berlin used a modified herpes cold sore virus to carry genes for Substance P to the rodents' nerve fibers.

"We were able to rescue their ability to feel pain," said Park. His research group restored Substance P and the naked mole-rats' ability to sense the burning sensation other mammals feel when subjected to capsaicin, the active ingredient in chili peppers.

The restored sensitivity was limited to just one rear foot of each tested rodent. "They'd pull their foot back and lick it," in response to the stimulus, said Park. Other feet were impervious to the sting of capsaicin.

"Capsaicin is very specific for exciting the fibers that normally have Substance P," said Park. "They're not the fibers that respond to a pin prick or pinch, but the ones that respond after an injury or burn and produce longer-lasting pain."

But the researchers found that mole-rats remained completely insensitive to acids, indicating a fundamental difference in how their nerves respond to this stimulus.

"Acid acts on the capsaicin receptor and on another family of receptors called acid-sensitive ion channels," Park said. "Acid is not as specific as capsaicin. The mole-rat is the only animal that shows completely no response to acid."

Park said the research adds to knowledge about the neurotransmitter Substance P.

"This is important specifically to the long-term, secondary-order inflammatory pain. It's the pain that can last for hours or days when you pull a muscle or have a surgical procedure," he said.

Park said naked mole-rats provide a new model system that is different from all other animals he has studied.

"We're learning which nerve fibers are important for which kinds of pain, so we'll be able to develop new strategies and targets."

Naked mole-rats, native to east-central Africa, developed a protective reaction to acids through evolution. Living in tight underground quarters,

the mole-rats exhale high levels of carbon dioxide, which becomes acid when it touches skin and mucous tissue in the nose, eyes and mouth. But the mole-rats have evolved to become desensitized to the stinging pain of acid.

The UIC biologist plans to study other animals, both closely related and unrelated -- such as Alaskan marmots that burrow in high CO₂ environments -- to examine how they have evolved similar strategies to cope with acid-rich living conditions.

Source: University of Illinois at Chicago

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