Fruit flies have a radical strategy for dealing with free radicals

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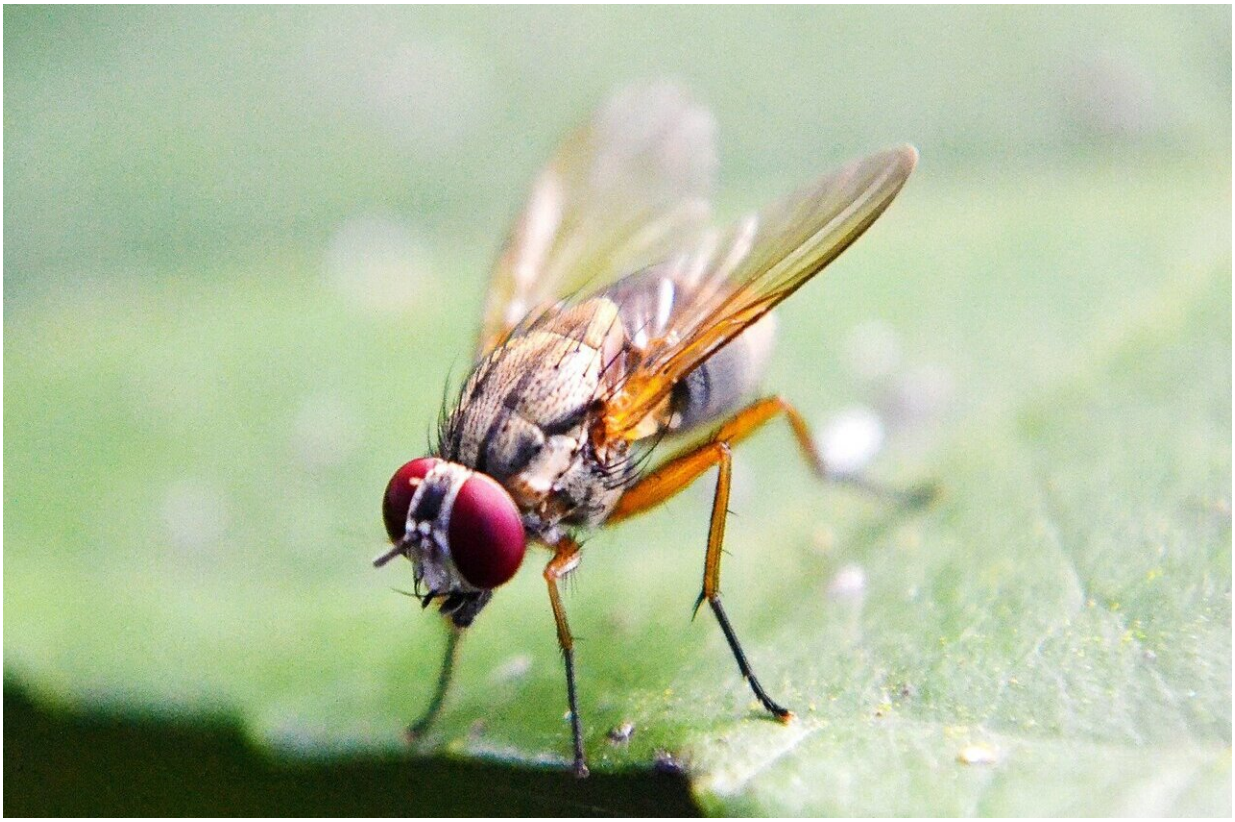

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Oxidative stress affects all living organisms, and the damage it causes is believed to play a part in cancer, diabetes, Alzheimer's disease and a number of other health conditions. Some animals have developed

remarkable, even radical strategies for combating its effects. Researchers at EPFL observed that, under acute oxidative stress, flies belonging to the genus Drosophila, commonly known as fruit flies, remove and excrete damage-causing lipids, or fats, from their blood. The team has published its findings in the journal *Immunity*.

Like humans, fruit flies produce molecules known as reactive oxygen species (ROS), a group that includes free radicals. Although they tend to get bad press for the harm they cause to our cells, these molecules also have beneficial effects, for instance alerting the immune system to an infection or repairing damaged tissue.

In normal circumstances, their harmful effects are counteracted by our cells' natural defense mechanisms, and by antioxidants such as vitamins C and E. Yet pathogens, smoking and ultraviolet light can upset this delicate balance by sending ROS production into overdrive, eventually overwhelming our body's natural defenses.

Dropping like flies

The EPFL team, led by Professor Bruno Lemaitre, happened upon a previously unknown defense strategy against ROS in fruit flies after observing that mutant individuals grown in the lab were dying a few days after exposure to a normally benign pathogen.

An initial investigation revealed the reason: fruit flies normally produce a fat-binding protein in their kidneys, but a mutated gene was depriving the genetically altered flies of this capability.

"Because the flies were dropping fast, we decided to have a bit of fun," says Prof. Lemaitre. "We named the mutated gene and the protein after Marco Materazzi, the Italian soccer player on the receiving end of Zinedine Zidane's infamous headbutt in the World Cup final."

A previously unknown mechanism

At this point, the team still hadn't made the link between the flies' death, the genetic mutation and oxidative stress. "We were baffled by what we discovered," explains Prof. Lemaitre. "Why were insects under pathogen-induced stress dying because they couldn't produce a fat-binding protein in their kidneys?"

The answer lies in a secondary mechanism of oxidative stress, by which free radicals attack lipids in the blood, producing toxic compounds and even more ROS. This self-perpetuating process, known as lipid peroxidation, has to be brought under control at all costs.

Fruit flies have a simple yet effective way of stopping this process from spiraling out of control: they remove one part of the equation altogether. Certain stressors cause the fly's kidneys to begin producing the Materazzi protein, which binds to the lipids in its blood. These are then passed out in the insect's feces.

"As we saw with our mutants, this mechanism really is a matter of life and death for a stressed insect," says Xiaoxue Li, a scientist in Prof. Lemaitre's group and the paper's lead author.

The scientists suspect this same mechanism could play an important role in other insects, and perhaps even in other animals. Previous studies have identified an allergen in cockroach droppings that bears many similarities to the Materazzi protein.

"Just like the flies in our study, all living organisms have to deal with oxidative stress damage," adds Prof. Lemaitre. "I wouldn't be surprised to see it become a major public health issue."

More information: Xiaoxue Li et al, Renal Purge of Hemolymphatic

Lipids Prevents the Accumulation of ROS-Induced Inflammatory Oxidized Lipids and Protects Drosophila from Tissue Damage, *Immunity* (2020). DOI: 10.1016/j.immuni.2020.01.008