New type of bacterial protection found within cells

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UC Irvine biologists have discovered that fats within cells store a class of proteins with potent antibacterial activity, revealing a previously unknown type of immune system response that targets and kills bacterial infections.

Steven Gross, UCI professor of developmental & cell biology, and colleagues identified this novel intercellular role of histone proteins in fruit flies, and it could herald a new approach to fighting bacterial growth within cells. The study appears today in *eLife*, a new peer-reviewed, open-access journal supported by the Howard Hughes Medical Institute, the Max Planck Society and the Wellcome Trust.

"We found that these histone proteins have pan-antibacterial abilities and can have a wide-ranging effect," Gross said. "If we can discover how to manipulate the system to increase histone levels, we may one day have a new way to treat patients with bad bacterial infections."

Histones exist in large numbers in most animal cells; their primary job is to help DNA strands fold into compact and robust structures inside the nucleus. Gross said there is some evidence that histones secreted from cells protect against bacteria living outside cells. However, many bacteria enter cells, where they can avoid the immune system and continue replicating.

In principle, Gross said, histones could protect cells against such bacteria from the inside, but for many years this was thought unlikely because

most histones are bound to DNA strands in the cell nucleus, whereas bacteria multiply in the cellular fluid outside the nucleus, called cytosol. Additionally, free histones can be extremely damaging to cells, so most species have developed mechanisms to detect and degrade free histones in the cytosol.

In their study, Gross and colleagues demonstrate that histones bound to lipid (fat) droplets can protect cells against bacteria without causing any of the harm normally associated with the presence of free histones. In experiments with lipid droplets purified from Drosophila fruit fly embryos, they show that lipid-bound histones can be released to kill bacteria.

The researchers injected similar numbers of bacteria into Drosophila embryos that contained lipid-bound histones and into embryos genetically modified to not contain them. They discovered that the histone-deficient flies were 14 times more likely to die of bacterial infections. Similar results were found in experiments on adult flies. Additional evidence suggested that histones might also protect mice against bacteria.

"Because numerous studies have now identified histones on lipid droplets in many different cells – from humans as well as mice and flies – it seems likely that this system may be quite general," Gross said.

More information: Anand et al. *eLife* 2012;1:e00003. DOI: 10.7554/eLife.00003

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