Researchers identify how Yersinia spreads within infected organs

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Researchers at Tufts University School of Medicine and the Sackler School of Graduate Biomedical Sciences at Tufts have identified how one type of bacteria, *Yersinia*, immobilizes the immune system in order to grow in the organs of mice. To do so, the researchers extended the use of a technique and suggest that it could be used to study other bacteria that use the same or similar means of infection. The study is published in the September 11 issue of *Cell Host & Microbe*.

Led by microbiologist Joan Mecsas, the research team studied a specific member of a family of effector proteins known as Yops. Like other effector proteins, Yops alter the immune system to make it possible for bacteria such as *Yersinia* to spread in infected organs and from organ to organ. The research team studied the Yop known as YopH in order to identify its specific effect within infected spleens.

Many bacteria inject proteins into cells in organs as a part of their infection process. The technique they used, called the TEM-1 reporter system, uses an enzyme and a dye to color-code cells. This enables researchers to see which of the many cells in an organ have been injected. The current study used the TEM system to identify injected cells but then, in an interesting first, gathered these cells from infected organs to study them further.

After isolating the color-coded cells from infected organs, the researchers determined how immune cells are made inactive by effector proteins, such as YopH and other Yops, by comparing cells with and

without the specific effector protein. The research team used tissue samples from two sets of mice with *Yersinia pseudotuberculosis*: those with and without functional YopH proteins. They separated tissue cells from immune cells taken from spleens and compared suspended immune cells from the two sets of mice.

The researchers determined that YopH deactivates multiple proteins and blocks calcium flows vital to normal immune cell communication. Decreased immune cell communication allows *Yersinia* to continue spreading in infected organs without an effective response from the immune system.

"Being able to pull out and study cells from infected tissues that contain bacterial proteins enabled us to see the effects of YopH in tissues infected with *Yersinia pseudotuberculosis*. Our application of this technique may also work in bacteria similar to *Yersinia*, to understand how other bacteria cause damage in organ systems," said senior author Joan Mecsas, Ph.D., an associate professor of molecular biology and microbiology at Tufts University School of Medicine and member of the immunology and molecular microbiology programs at the Sackler School of Graduate Biomedical Sciences at Tufts.

"We know that two forms of food poisoning and some forms of pneumonias caused by *E. coli*, *Salmonella*, and *Pseudomonas* respectively, as well as other types of infections depend on the same system as *Yersinia* to infect humans and animals. There are also several bacteria that use related means to infect people and animals. This includes the bacteria that cause Legionnaires' disease, ulcers, cholera, various foodborne illnesses, pneumonias and even general infections such as some ear and sinus infections. This technique could be applied to understand these other bacteria," said co-first author Enrique Durand, Ph.D., a graduate of the molecular microbiology program at the Sackler School, now teaching biology in the International Baccalaureate (honors)

program at Snowden International School at Copley in the Boston Public Schools system.

"*Yersinia* and bacteria with systems of infection like *Yersinia* can have drastic effects on organs, including inflammation that leads to appendicitis-like pain. Seeing the effect of the bacteria on specific cell types within organs, such as the spleen, has been challenging because cells grown in petri dishes cannot mimic the holistic environment of a mammalian system," said co-first author Hortensia Rolan, Ph.D., a postdoctoral scholar in the Mecsas lab.

Researchers have studied *Yersinia* since the discovery of the most well-known member of the *Yersinia* genus, *Yersinia* pestis, which causes bubonic plague (and which was found in squirrels in a national forest in Los Angeles County this summer). But *Yersinia pseudotuberculosis*, its near relative, is a standard *Yersinia* bacterium to study in labs.

Yersinia pseudotuberculosis, which is not related to tuberculosis, is a type of zoonotic bacteria, or one that can be transferred from an animal to a person. Infections in humans are rare and, like bubonic plague, it can be treated with antibiotics.

More information: Rolan, H.G., Durand, E.A., Mecsas, J. (September 11, 2013). Identifying Yersinia YopH-targeted signal transduction pathways that impair neutrophil responses during in vivo murine infection. *Cell Host & Microbe* (14:3, pp. 306-317). DOI: 10.1016/j.chom.2013.08.013

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