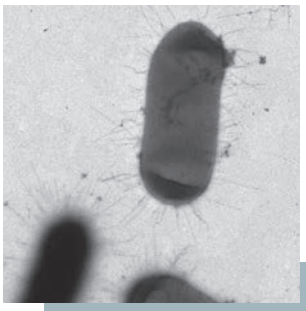

salk
Where cures begin.

Janelle Ayres

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The Problem

Our main tool for fighting infections is antimicrobials, such as vaccines, antivirals and antibiotics. But there are limitations to this approach: besides not working for all diseases, antibiotics also kill good bacteria that inhabit our bodies and contribute to multi-drug resistant, harmful bacteria ("super bugs"). An additional limitation to this method is that killing an infection does not ultimately determine if a patient will survive. Fixing the physiological impairment (such as tissue and metabolic damage) that occurs during infections is critical to an organism's health as well.

The Approach

In a new approach to therapeutics, Janelle Ayres studies how the body controls and repairs the collateral damage generated during interactions with bad microbes. She is taking an innovative approach grounded in mathematical and evolutionary predictions that uses the beneficial microbes that inhabit our digestive system for damage-control therapeutics. In pivotal work, Ayres showed that those damage-control mechanisms are just as important as an animal's immune system in surviving infection. Her revelation of an entirely new set of defense mechanisms will likely lead to novel therapies that bacteria won't be able to evolve resistance to. And because pathologies that arise during infection are similar to those created by non-infectious diseases, therapies that manipulate damage-control mechanisms could also have broader applications than antibiotics. Ultimately, by leveraging those damage-control mechanisms, Ayres aims to develop treatments for infectious and non-infectious diseases (such as pathologies associated with cancer and aging) without the need for antibiotics.

The Innovations and Discoveries

- Ayres provided the first evidence that an animal's ability to survive an infection is not solely dependent on the ability of the immune system to kill bacteria. Rather, she determined that damage-control mechanisms are just as important in the animal's recovery.
- Ayres gave fruit flies a dose of *Listeria* bacteria and tested what variables—from diet to genetics—allowed the flies to survive the infection. She found that distinct sets of genes in the flies encode mechanisms to prevent, limit and repair damage that occurs during infection.
- Ayres showed that when mice consume a strong antibiotic, they're more prone to developing a lethal, body-wide *E. coli* infection. The reaction, Ayres demonstrated, was dependent on the inflammasome, a particular complex of immune system proteins that becomes activated when the bacterial environment in the intestines shifts.

For more information, please visit:
www.salk.edu/scientist/janelle-ayres

Digestive Disorders, Immunology, Infectious Disease, Inflammation, Metabolism, Microbiology