

National Jewish Health Researchers Discover How Virulent Bacteria Sabotage Immune Response Against I

FEBRUARY 01, 2010

Denver, CO — Researchers at National Jewish Health have discovered how the virulent food-borne bacteria *Listeria monocytogenes* induces infected immune cells to sabotage their own defensive response. The studies offer insight into host-pathogen interactions and suggest potential therapeutic targets for food poisoning, tuberculosis and autoimmune diseases.

In the Feb. 15 issue of the *Journal of Experimental Medicine*, Laurel Lenz, PhD, and his colleagues report that macrophages infected by the bacteria *Listeria* release interferon- $\alpha\beta$ (IFN- $\alpha\beta$), which makes them and nearby immune cells unresponsive to activation signals. This reduces immune resistance to the bacteria, which causes thousands of cases of food poisoning -- and more than 500 deaths -- each year in the United States.

"*Listeria* appears to benefit by triggering an endogenous pathway of the host that dampens its own immune response," said Dr. Lenz. "Our findings suggest that *Listeria* increases its survival in infected individuals by inducing cross-talk between host interferon signaling pathways."

When patrolling immune-system cells encounter non-pathogenic microbes, they normally engulf and destroy them. However, certain pathogens such as *Listeria* can grow within immune cells, which then release alarm signals to other nearby cells. One of these alarms is IFN- $\alpha\beta$. IFN- $\alpha\beta$ protects host cells from viral infection. However, IFN- $\alpha\beta$ also increases growth of *Listeria* and certain other bacteria.

Dr. Lenz and his colleagues showed that IFN- $\alpha\beta$ does this by down-regulating expression of receptors for interferon- γ (IFN- γ). With its receptors down-regulated, IFN- γ cannot drive resting macrophages into an activated state that is especially effective against bacterial pathogens inside the cell.

"IFN- $\alpha\beta$ acts as a sort of anesthetic to numb the response of immune cells to IFN- γ ," said Dr. Lenz.

The research highlights the crosstalk that exists between the antibacterial and anti-viral arms of the immune response. Dr. Lenz's findings demonstrate that IFN- $\alpha\beta$, well known to stimulate antiviral defenses, dampens anti-bacterial activity as well.

He speculates that this may be a way for the immune system to more efficiently defend against viral pathogens, while avoiding collateral damage caused by an overactive immune cells. In fact, interferon- β , a medication widely used for multiple sclerosis, may do just that. Dr. Lenz speculates that this medication may act in part by down-regulating expression of IFN- γ receptors on myeloid cells, thus reducing the stimulation of autoimmune T cells.

The next step will be to define more precisely how IFN- $\alpha\beta$ mediates down-regulation of the IFN- γ receptors, and to determine whether prevention of these effects improves resistance to infection by *Listeria* and other bacterial pathogens.

National Jewish Health is known worldwide for treatment of patients with respiratory, cardiac, immune and related disorders, and for groundbreaking medical research. Founded in 1899 as a nonprofit hospital, National Jewish remains the only facility in the world dedicated exclusively to these disorders. Since 1998, U.S. News & World Report has ranked National Jewish the #1 respiratory hospital in the nation.

National Jewish Health is the leading respiratory hospital in the nation. Founded 120 years ago as a nonprofit hospital, National Jewish Health today is the only facility in the world dedicated exclusively to groundbreaking medical research and treatment of patients with respiratory, cardiac, immune and related disorders. Patients and families come to National Jewish Health from around the world to receive cutting-edge, comprehensive, coordinated care. To learn more, visit the

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Media Contacts

Our team is available to arrange interviews, discuss events and story ideas.

William Allstetter

303.398.1002

allstetterw@njhealth.org

Adam Dormuth

303.398.1082

dormutha@njhealth.org