When intestinal bacteria go surfing

March 19 2009

The bacterium *Escherichia coli* is part of the healthy human intestinal flora. However, *E. coli* also has pathogenic relatives that trigger diarrhea illnesses: enterohemorrhagic *E.coli* bacteria. During the course of an infection they infest the intestinal mucosa, causing injury in the process, in contrast to benign bacteria.

The EHECs adhere to the surface of the mucosal cells and alter them internally: a part of the cellular supportive skeleton - the actin skeleton - is rearranged in such a manner that the cell surface beneath the bacteria forms plinth-like growths, so-called pedestals. The bacteria are securely anchored to this pedestal; the pedestals, in contrast, are mobile. This enables the bacteria, seated upon them, to surf over the cell surface and reproduce upon it, without being flushed from the intestine. But how do the bacteria bring the host cells to convert the actin skeleton? Researchers at the Helmholtz Centre for Infection Research (HZI) have now identified the signal pathway that leads to the formation of this pedestal.

"Prerequisite for this signal pathway is a special secretion system - a sort of molecular syringe, through which the bacteria insert entire proteins in the host cell," explains Theresia Stradal, head of the Signal Transduction and Motility research group at HZI. Two factors, Tir and EspFU, are brought into the host cell from the bacterium for pedestal formation. Following this, the host cell presents Tir on its surface; the bacterium recognises "its" molecule Tir and adheres to the host cell. EspFU then triggers the signal for local actin conversion.

"It has been unclear thus far how the two bacterial effectors Tir and EspFU enter into contact with one another in the host cell," says Theresia Stradal. Her research group has now found the missing link: "The molecule comes from the host cell, is called IRSp53 and gathers on the cell surface, directly beneath the bacteria sitting on it," explains cell biologist Markus Ladwein, who is also involved in the project. IRSp53, then, establishes the connection between Tir and EspFU. It ensures that actin conversion is concentrated locally. Together with the biochemist Dr. Stefanie Weiß, a former post-graduate student with the research group, Markus Ladwein also provided the counter evidence: "Cells in which IRSp53 is lacking are no longer able to form pedestals for the bacteria."

The signal pathway clarified by the Braunschweig researchers - published today in the journal *Cell Host & Microbe* - is a good example of how pathogenic bacteria develop progressively with their host. With the aid of bacterial factors, they therefore manage to simulate signals and set in motion complex processes in the host, which they then abuse for their own purposes.

More information: IRSp53 Links the Enterohemorrhagic E. coli Effectors Tir and EspFU for Actin Pedestal Formation. Stefanie M. Weiss, Markus Ladwein, Dorothea Schmidt, Julia Ehinger, Silvia Lommel, Kai Städing, Ulrike Beutling, Andrea Disanza, Ronald Frank, Lothar Jänsch, Giorgio Scita, Florian Gunzer, Klemens Rottner, and Theresia E.B. Stradal. *Cell Host Microbe*. 2009 Mar 19;5(3):244-58.

Source: Helmholtz Association of German Research Centres