It takes a village: Mechanism alerts neighbors to amplify immune response

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New research reveals a clever strategy that enables a host organism to outsmart an invading bacterium by counteracting its efforts to suppress the innate immune response. The study, published by Cell Press in the November 24th issue of the journal *Immunity*, describes a mechanism by which an infected cell can quickly alert unsuspecting (and uninfected) neighboring cells that can join the fight, amplify the immune response and defeat the invader.

The pathogen *Shigella flexneri* invades the cells that line the gut and causes Shigellosis, a disorder characterized by diarrhea and sometimes even death in humans. *S. flexneri* subverts the normal immune response of the host by interfering with the ability of the infected cell to secrete chemicals called chemokines that stimulate inflammation. Inflammation is a complex response to pathogens that attracts white blood cells to destroy the bacteria. Despite the documented ability of *S. flexneri* to suppress inflammation in infected cells, intestinal cells do secrete large amounts of chemokines and exhibit substantial inflammation during Shigellosis.

Professor Cécile Arrieumerlou from the University of Basel in Switzerland led a study designed to investigate the molecular mechanisms that control inflammation during bacterial infection. Using a sophisticated microscopic technique that allowed analysis of *S. flexneri* infection at the single cell level, the researchers discovered that activation of proinflammatory signaling pathways is propagated from infected cells to adjacent uninfected cells, leading to chemokine

secretion from the bystander cells. "We found that this mechanism was mediated by specialized intercellular connections called gap junctions that allowed the infected cells to communicate with neighboring uninfected cells," explains Prof. Arrieumerlou.

Taken together, the results show that even when the immune response is suppressed in the infected cell, alerted bystanders can amplify the inflammatory response. "We have identified a novel mechanism of cell to cell communication that amplifies the immune response against bacterial infection by rapidly spreading signals via gap junctions to yet uninfected cells," concludes Prof. Arrieumerlou. "This mechanism enables the host to circumvent the immunosuppressive activity of bacteria and to massively amplify inflammation during bacterial infection."

Provided by Cell Press