ToC

00 **Pyroptosis: host cell death and inflammation**

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Microorganism- and host-derived signals can stimulate formation of a multiprotein complex called the inflammasome, which activates the cysteine protease caspase 1. In turn, caspase 1 triggers an inflammatory programmed cell death pathway known as pyroptosis. Numerous pathogens have evolved a mechanism to subvert pyroptosis and persist within infected cells.

Biographies

Tessa Bergsbaken received her B.S. in medical microbiology and immunology from the University of Wisconsin-Madison, USA, and she recently completed her Ph.D. in microbiology at the University of Washington, USA, for her work on the mechanism of caspase 1 activation in response to *Yersinia* infection.

Susan L. Fink received her Ph.D. in molecular and cellular biology at the University of Washington, USA, where she studied caspase 1 activation and the mechanism of pyroptosis. Her research interests are in the diagnosis, treatment and prevention of infectious and inflammatory diseases and she is currently engaged in medical training at the University of Washington.

Brad T. Cookson is Professor of Laboratory Medicine and Microbiology at the University of Washington in Seattle, USA. Improving the diagnosis and treatment of human diseases is his primary motivation for discovering the mechanistic details and immunopathogenesis of host–pathogen interactions. His scientific training includes bacterial genetics (University of Utah, with John R. Roth), microbial pathogenesis (Washington University, with William E. Goldman), cellular immunology (University of Washington, with Michael J. Bevan) and board certification in pathology.

Online-only summary

- Life or death of individual cells determines health and disease in multi-celled organisms. Cell death is crucial for organogenesis *in utero* and successful control of host cell populations in healthy tissues, but can also play a part in disease that occurs in response to toxic insults or microbial infection.
- The cysteine protease family called caspases is composed of both initiators and effectors, have crucial roles in cell death and drive mechanistically distinct modes of cellular demise. The physiological consequences of cell death are determined by the mechanisms employed, which range from relatively benign cellular destruction to alarm-ringing inflammatory recruitment of additional cells and biochemical processes.
- Microorganism- and host-derived 'danger' signals stimulate formation of a multiprotein complex, termed the inflammasome, which leads to processing and activation of caspase 1. Active caspase 1 causes pyroptosis and is responsible for proteolytic maturation of the inflammatory cytokines interleukin-1β (IL-1β) and IL-18.
- Pyroptosis is characterized by caspase 1-dependent formation of plasma-membrane pores, which leads to pathological ion fluxes that ultimately result in cellular lysis and release of inflammatory intracellular contents.
- During microbial infection *in vivo*, caspase 1-dependent processes control pathogen replication, stimulate adaptive immune responses and enhance host survival; however, inappropriate activation of caspase 1 can lead to pathological inflammation.
- Pathogens have a range of mechanisms for preventing the activation of caspase 1, highlighting its antimicrobial role during infection. Pathogens can directly inhibit caspase 1 activation, induce alternative forms of cell death or regulate production of caspase 1-activating ligands.