

4. Innate immunity

1 unit Justin Perry, February 5, 2026

Immediate vs. Early induced immunity

Routes of infection (extracellular vs intracellular)

Forms of protection including:

Mucosal Barriers

Pathogen Opsonization (Complement, Antibody)

Phagocytosis

Antimicrobial Peptides

Major question: why would the innate immune response vary between extracellular and intracellular pathogens?

Microbial molecules that differ from mammalian counterparts

CpG DNA

Double stranded RNA

Lipopolysaccharide

Lipoteichoic acid

Peptidoglycan

Receptors that detect microbial molecules

TLR4 - LPS

TLR2 - heterodimerization with TLR1 and TLR6 - di- and triacylated lipoproteins

TLR3 - Double-stranded RNA

TLR5 - Flagellin

TLR7/8 - bacterial RNA in phagosome

TLR9 - CpG DNA

RIG-I and MDA-5 - cytosolic dsRNA

NOD-1/2 - cytosolic Peptidoglycan

Dectin-1 - fungal beta-glucans

Inflammasome (NLRP3, NLRP6, NLRP1, etc)

cGAS-STING

Question worth pondering: How does infection- or host-induced cell death affect self?

Paper: Juliette Lesbats, Aurélia Brillac, Julie A. Reisz, Parnika Mukherjee, Charlene Lhuissier, Mónica Fernández-Monreal, Jean-William Dupuy, Angèle Sequeira, Gaia Tioli, Celia De La Calle Arregui, Benoît Pinson, Daniel Wendisch, Benoît Rousseau, Alejo Efeyan, Leif Erik Sander, Angelo D'Alessandro & Johan Garaude. Macrophages recycle phagocytosed bacteria to fuel immunometabolic responses. *Nature* 640, 524–533 (2025). <https://doi.org/10.1038/s41586-025-08629-4>

Additional (optional) reading:

Review: Karen V. Swanson, Meng Deng & Jenny P.-Y. Ting (2019). The NLRP3 inflammasome: molecular activation and regulation to therapeutics. *Nature Reviews Immunology*. volume 19, pages477–489(2019)

Vincent R. Graziano, Jennifer Porat, Marie Dominique Ah Kioon, Ivana Mejdrová, Alyssa J. Matz, Charlotta G. Lebedenko, Peiyuan Chai, John V. Pluvina, Rafael Ricci-Azevedo, Andrew G. Harrison, Skylar S. Wright, Xinzhen Wang, Madison S. Strine, Penghua Wang, Michael R. Wilson, Sivapriya Kailasan Vanaja, Beiyan Zhou, Franck J. Barrat, Thomas Carell, Ryan A. Flynn & Vijay A. Rathinam. RNA N-glycosylation enables immune evasion and homeostatic efferocytosis. *Nature* 645, 784–792 (2025). <https://doi.org/10.1038/s41586-025-09310-6>