Neutrophils

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Neutrophilic granulocytes or **polymorphonuclear neutrophils** (PMNs) are the most abundant white blood cell in humans and mice. They are characterised by the multi-lobed shape of their nucleus (**Figure 1, left**) which distinguished them from other white blood cells of lymphoid or myeloid origin, such as **lymphocytes** and **monocytes**.

Neutrophils are the first white blood cells recruited to sites of acute inflammation, in response to chemotactic cues such as **CXCL8** (interleukin-8, **IL-8**) produced by stressed tissue cells and tissue-resident immune cells such as **macrophages**. Neutrophils therefore comprise a large proportion of the early cellular infiltrate in inflamed tissues and are the major constituent of pus.

Microbial clearance

Neutrophils represent the first line of defence in response to invading microbes, by **phagocytosis** of pathogens and/or release of antimicrobial factors contained in specialised granules. Phagocytosis is an active, receptor mediated process during which a pathogen is internalised into a specialised vacuole, the phagosome (**Figure 1, right**).

The interaction with the pathogen can be direct, through recognition of **pathogen-associated molecular patterns** (PAMPs) by neutrophil **pattern recognition receptors** (PRRs), or indirect, through recognition of **opsonised microbes** by **Fc receptors** or **complement receptors**. The **phagosome** undergoes a rapid maturation process that involves the fusion with neutrophil granules and the targeted delivery of **antimicrobial molecules** and generation of **reactive oxygen species** (ROS).

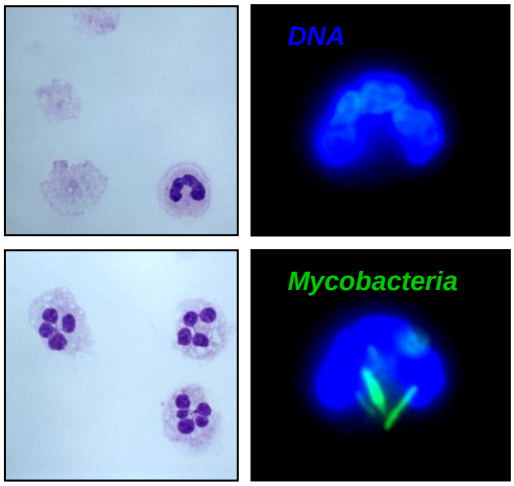

Figure 1. Left: Giemsa-stained human neutrophils as seen under the microscope; either freshly isolated (top) or cultured together with cytokines (bottom). Right: Human neutrophils harbouring phagocytosed mycobacteria as analysed by fluorescence microscopy.

Degranulation of specific granules on the neutrophil surface and the extrusion of nucleic acids to form **neutrophil extracellular traps** (NETs) create an antimicrobial milieu at the inflammatory site and contributes to killing of extracellular pathogens.

Neutrophils at the interface between innate and adaptive immunity

Neutrophils have historically been viewed as short-lived effector cells of the innate immune system as they undergo spontaneous apoptosis *in vitro* unless rescued by survival signals such as inflammatory cytokines or microbial compounds (**Figure 1, left**). However, this view rarely takes into account the notion that neutrophils make important contributions to the recruitment, activation and programming of other immune cells. Recent studies demonstrate that neutrophils themselves secrete an array of pro-inflammatory and immunomodulatory cytokines and chemokines capable of enhancing the recruitment and effector functions of other cells. Neutrophils engage in mutual interactions with a range of immune and non-immune cells, such as dendritic cells (DCs), B cells, NK cells, CD4, CD8 and γδ T cells as well as mesenchymal stem cells, and can be found in draining lymph nodes and the spleen.