

# We are IntechOpen, the world's leading publisher of Open Access books Built by scientists, for scientists

6,900

Open access books available

185,000

International authors and editors

200M

Downloads

Our authors are among the

154

Countries delivered to

TOP 1%

most cited scientists

12.2%

Contributors from top 500 universities



WEB OF SCIENCE™

Selection of our books indexed in the Book Citation Index  
in Web of Science™ Core Collection (BKCI)

Interested in publishing with us?  
Contact [book.department@intechopen.com](mailto:book.department@intechopen.com)

Numbers displayed above are based on latest data collected.  
For more information visit [www.intechopen.com](http://www.intechopen.com)



# Introductory Chapter: Background Summary Regarding Neutrophils

*Maitham Khajah*

## 1. Neutrophils: important immune cells in health and diseases

Neutrophils are key players in the innate and the adaptive immunity and contribute to the pathogenesis of various infectious and noninfectious conditions. These cells have the capability of performing various effector functions and therefore are considered an important therapeutic target for many conditions. They are considered the fastest immune cells in our body and the first to arrive to the inflammatory site. This occurs in response to a wide variety of chemoattractive agents, such as CXC chemokines [keratinocyte-derived cytokine (KC), macrophage inflammatory protein-2 (MIP-2)], lipid mediators [leukotriene B<sub>4</sub> (LTB<sub>4</sub>) and platelet-activating factor (PAF)], the complement split product (C5a), and the bacterial toxin formyl-met-leu-phe (fMLP)] [1]. Neutrophils use different intracellular signaling pathways in their migrative behavior which are dependent on the type of chemoattractant they encounter [1–3].

These immune cells also play an important role in the recognition of various pathogens through specific cell surface and cytoplasmic receptors including toll-like receptors (TLRs) and nucleotide oligomerization domains (NODs). In addition, they can also recognize opsonized particles through the complement receptors and mediate antibody-dependent cell cytotoxicity (ADCC) through their interaction with immunoglobulin receptors [4–6]. They can also mediate microbial killing through oxygen-dependent and oxygen-independent mechanisms. In response to various ligands, this results in a dramatic increase in oxygen consumption due to the activation of nicotinamide adenine dinucleotide phosphate (NADPH) oxidase system leading to the generation of various reactive oxygen (e.g., superoxide anion radical) [7] and nitrogen (through nitric oxide synthase; NOS) intermediates [8]. This can not only aid in microbial killing but also contribute to the pathogenesis of various inflammatory and cancerous conditions (through the generation of peroxynitrite). The non-oxidative arm of neutrophil killing is mediated through the action of antimicrobial peptides and proteases present in various compartments of azurophilic (primary), specific (secondary), gelatinase, and secretory granules [9–13].

This book provides recent evidence regarding the role of cannabinoid receptors (CR-1 and CR-2) and different subtypes of the immunoglobulin receptor FcγRs in the pathogenesis, diagnosis, and treatment of various diseases of infectious and noninfectious origin. Furthermore, the differential expression pattern of CD16 + CD11b + receptors on the surface of neutrophils and their role in the diagnosis of acute viral and bacterial infections will also be highlighted. Finally, the utility of using different chemiluminogenic probes for the detection of NADPH activity for the circulating blood neutrophils and their role in determining the in vivo state of host inflammatory activation will be highlighted in this book.

IntechOpen

IntechOpen

### **Author details**

Maitham Khajah  
Department of Pharmacology and Therapeutics, Faculty of Pharmacy,  
Kuwait University, Kuwait

\*Address all correspondence to: [maitham@hsc.edu.kw](mailto:maitham@hsc.edu.kw)

### **IntechOpen**

---

© 2019 The Author(s). Licensee IntechOpen. This chapter is distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/3.0>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited. 

## References

- [1] Heit B, Tavener S, Raharjo E, Kubes P. An intracellular signaling hierarchy determines direction of migration in opposing chemotactic gradients. *The Journal of Cell Biology*. 2002;**159**(1): 91-102. Epub 2002 Oct 7
- [2] Khajah M, Andonegui G, Chan R, Craig AW, Greer PA, McCafferty DM. Fer kinase limits neutrophil chemotaxis toward end target chemoattractants. *Journal of Immunology*. 2013;**190**(5):2208-2216
- [3] Heit B, Robbins SM, Downey CM, Guan Z, Colarusso P, Miller BJ, et al. PTEN functions to 'prioritize' chemotactic cues and prevent 'distraction' in migrating neutrophils. *Nature Immunology*. 2008;**9**(7):743-752. DOI: ni.1623 [pii]10.1038/ni.1623
- [4] Hayashi F, Means TK, Luster AD. Toll-like receptors stimulate human neutrophil function. *Blood*. 2003;**102**(7):2660-2669
- [5] Lee WL, Harrison RE, Grinstein S. Phagocytosis by neutrophils. *Microbes and Infection*. 2003;**5**(14):1299-1306
- [6] Stuart LM, Ezekowitz RA. Phagocytosis: Elegant complexity. *Immunity*. 2005;**22**(5):539-550
- [7] McCord JM, Fridovich I. The biology and pathology of oxygen radicals. *Annals of Internal Medicine*. 1978;**89**(1):122-127
- [8] Kruidenier L, Kuiper I, Lamers CB, Verspaget HW. Intestinal oxidative damage in inflammatory bowel disease: Semi-quantification, localization, and association with mucosal antioxidants. *The Journal of Pathology*. 2003;**201**(1):28-36. DOI: 10.1002/path.1409
- [9] Belaaouaj A, McCarthy R, Baumann M, Gao Z, Ley TJ, Abraham SN, et al. Mice lacking neutrophil elastase reveal impaired host defense against gram negative bacterial sepsis. *Nature Medicine*. 1998;**4**(5):615-618
- [10] Reeves EP, Lu H, Jacobs HL, Messina CG, Bolsover S, Gabella G, et al. Killing activity of neutrophils is mediated through activation of proteases by K<sup>+</sup> flux. *Nature*. 2002;**416**(6878):291-297
- [11] Tkalecic J, Novelli M, Phylactides M, Iredale JP, Segal AW, Roes J. Impaired immunity and enhanced resistance to endotoxin in the absence of neutrophil elastase and cathepsin G. *Immunity*. 2000;**12**(2):201-210
- [12] Pham CT. Neutrophil serine proteases: Specific regulators of inflammation. *Nature Reviews. Immunology*. 2006;**6**(7):541-550
- [13] Faurschou M, Borregaard N. Neutrophil granules and secretory vesicles in inflammation. *Microbes and Infection*. 2003;**5**(14):1317-1327