

The Neutrophil: A Beautiful Beast or a Beastly Beauty?

Neutrophils are crucial to keeping us in a healthy state, but they also play important roles in the pathophysiology of a broad spectrum of diseases [1]. Early on, they were regarded as quite primitive cells, simply executing cytotoxic functions. It has become evident, however, that they are highly sophisticated and can perform complex functions in many inflammatory contexts. Neutrophils originate from stem cells in the bone marrow where growth factors induce sequential expression of genes, resulting in a distinct phenotype, not least characterized by its different sets of cytoplasmic granule containing preformed host defense proteins ready to be released at sites of inflammation [1]. Being transported in the bloodstream, specific adhesion molecules expressed by endothelial cells and chemotactic gradients are important for neutrophil recruitment and activation [2–5].

ELR-positive CXC chemokines, including IL-8/CXCL8, are important during this process. Interestingly, there are two receptors for this group of ligands with varying affinities [6–8]. CXCL1 mediates neutrophil recruitment by binding and activating CXCR2, and inhibition of this receptor shows that dysregulation of CXCL1/CXCR2 function is correlated with the severity of disease [9]. However, the mechanisms that turn the beneficial CXCL1-mediated neutrophil functions into a destructive

phenotype are not known. In this issue, Sawant et al. [9] present highly interesting data showing that CXCL1 monomer-dimer distribution and receptor interactions are highly coupled and regulate neutrophil trafficking, and that injury in the context of disease is a consequence of inappropriate CXCR2 activation at the target tissue [10].

The classic view is that neutrophils are important in bacterial killing [11]. However, they can also recognize damage-associated molecular patterns (DAMPs) during tissue-damage and participate in viral host defense [12, 13]. Another important function is the formation of neutrophil extracellular traps (NETs), formed during an active cellular process where the neutrophil releases its DNA to the extracellular environment [14, 15]. Finally, resolution of neutrophil inflammation has to be tightly regulated to avoid accumulation of these cells, as is exemplified by the prolonged and excessive inflammation in cystic fibrosis [16–18].

The rapidly increasing knowledge regarding the immunobiology of this fascinating and important cell should attract the attention of a broad readership interested in innate immunity.

*Heiko Herwald, Lund
Arne Egsten, Lund*

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