

Role of danger and microbial signals in neutrophils subpopulations recruitment during infection.

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Abstract:

Neutrophils are the first line of defence against bacteria and fungi and help fight parasites and viruses. Recently, neutrophil subpopulations with distinct functions have been reported under homeostatic and pathological conditions, although their role and their mechanisms of recruitment during inflammation and infections have not been clarified.

To this purpose we used a model of skin infection with *Candida (C.) albicans*, *Pseudomonas (P.) aeruginosa* and *Staphylococcus (S.) aureus* and we performed a multi-parametric flow-cytometry analysis. We identified aged and fresh neutrophils as CXCR4+CD62Llow and CXCR4- CD62L+/high respectively. Moreover, we employed mice lacking key Pattern Recognition Receptors (PRRs), PRR signalling molecules or alarmins to study the mechanisms of neutrophil subsets' recruitment both through flow-cytometry and qPCR.

We actually found the existence of two waves of neutrophil recruitment. The first one mediated exclusively by an LTB₄ (Leukotriene B 4)-IL-1 α (Interleukin 1 α)-CXCL1 axis, regardless of the type of infection, and the second wave mediated by both danger molecules and PAMPS (Pathogen Associated Molecular Patterns). We also observed an early accumulation of all neutrophils' subpopulations, with a prevalence for aged and activated (CD62L-CXCR4-) ones at late time points.

Our data suggest an early a-specific neutrophils recruitment mediated by danger molecules, which is necessary to contain a local infection. Later on, during an infection, pathogen-specific mechanisms come in action and drive pathogen clearance, with the presence of neutrophils subpopulations with a more "effector" and phagocytic activity.