Inflammasome in Wound response

The inflammatory response following wounding is often a result of innate-immune pattern-recognition receptor (PRR) activity leading to the activation of intracellular inflammasomes. Cells are equipped with a set of PRRs that recognizes the basic structural units that make up microorganisms. These receptors are located on the cell surface, endosomal membrane, and in the cytoplasm. Inflammasomes are multimeric protein complexes that are formed in a cell to orchestrate host defense mechanisms against infectious agents and physiological aberration. Assembly of an inflammasome complex requires cytosolic sensing of pathogen-associated molecular patterns or danger-associated molecular patterns by a nucleotide-binding domain and leucine-rich repeat receptor (NLR) or absent in melanoma 2 (AIM2)-like receptors (ALR).

The NLRs and ALRs have the ability to form an inflammasome. It is well established that at least five inflammasome receptors exist: NLRP1, NLRP3, NLRC4, AIM2, and Pyrin (Fig. 1) [1].
Figure 1: Established inflammasome complexes [1].

Inflammasomes have been recognized for their roles in the host defense against invading pathogens and in the development of cancer, auto-inflammatory, metabolic, and neurodegenerative diseases. The activation of an inflammasome complex of danger signals requires in most cases the adapter protein apoptosis-associated speck-like protein containing a caspase activation and recruitment domain, to catalyze proteolytic cleavage of pro-interleukin-1β (pro-IL-1β) and pro-IL-18 and drive pyroptosis [2].

Pyroptosis is a form of programmed cell death associated with antimicrobial responses during inflammation. In this process, immune cells that recognize certain danger signals within themselves produce cytokines, swell, burst and die. This releases the cytokines, attracts other immune cells to fight the infection and contributes to inflammation.

In the following picture the molecular mechanisms of pyroptosis are described.
Figure 2: signaling pathway of pyroptosis upon recognition of 'danger' signals [3]).

Summary
The inflammatory response following wounding, and in many chronic inflammatory diseases, is often a result of innate-immune PRR activity. PRRs react not only to specific pathogen molecules, the pathogen-associated molecular patterns, and to environmental irritants, but also to host-derived danger molecules involved in the processes of inflammasome activation following trauma, contact with infectious agents and physiological aberration.
The molecular organization within the inflammasome was summarized in a key review by Dagenais in memory of Dr. Jurg Tschopp [4].
Figure 3: The inflammasome. Stimulation of AIM2, RIG-I or an NLR by its cognate agonist promotes inflammasome activation and heptameric oligomerization. The active inflammasome induces caspase-1 activation, allowing processing of pro-IL-1β and pro-IL-18 into their mature forms [4].

References