Alarmin

Mediators of inflammation are substances that regulate the course of inflammatory reaction.

Among them we include:
* alarmins (DAMPs and PAMPs),
* vasoactive amines (histamine, serotonin),
* eicosanoids (prostaglandins, prostacyclin, thromboxanes, leukotrienes),
* cytokines,
* reactive forms of oxygen and nitrogen,
* complement,
* coagulation,
* fibrinolytic system,
* kinin system.

==Alarms==
Substances that are released first during an inflammatory reaction (signal 0). Their function is primarily **modulation of the immune response'**. They are followed by cytokines and subsequently acute phase reactants.

Significant for earlier laboratory diagnosis of incipient inflammation than for acute phase reactants.

DAMPs (*damage associated molecular patterns*)

Molecules that are **released from damaged cells** for example during necrosis or other cell death (except apoptosis – phagocytosis of apoptotic bodies). It participates in the inflammatory reaction even when the microbe is no longer present.

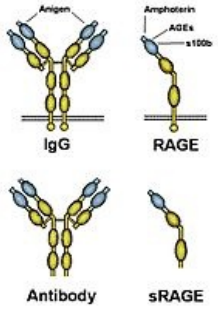
These include, for example, **ATP**, **DNA**, **RNA** (extracellular usually not present), **S100 proteins**, **HMGB1** (an intracellular protein capable of remodeling chromatin, usually produced by necrotic cells, macrophages, NK cells and dendritic cells), **adenosine**, **uric acid**.

===PAMPs (*pathogen associated molecular patterns*)===
Substances that are specific to microbes - **dsRNA'' *and* bacterial DNA', *lipopolysaccharide, lipoteichoic acid,* 'peptidoglycan**.

===Receptors for alarmins - PRRs (*pattern recognition receptors*)===
Very important receptors for the proper functioning of the immune system. They regulate the **immune response'**, **cell death** or **cell differentiation**. They are proteins expressed on the surface of cells of the immune system (neutrophils, monocytes, macrophages, dendritic cells, epithelial cells). They recognize DAMPs and PAMPs molecules.

====*Toll-like receptors* (TLR)====

An extracellular receptor that is able to recognize foreign (potentially dangerous) structures. They occur mainly on the surface of cells of the immune system and surface epithelia. It belongs to the first line of defense against pathogens. Its stimulation leads to the production of cytokines and chemokines (activation of a specific immune response).



====RAGE (*receptor for advanced glycation end products*)====
A receptor for advanced glycation end products. It is a multiligand extracellular receptor capable of binding multiple alarmins. It is involved in a number of pathological conditions - inflammation, Alzheimer's disease, diabetic complications, complications of renal failure and vascular wall damage.

Physiologically, it participates in the development of muscles and bones in embryogenesis.

Nod-like receptors (NLRs)

Intracellular cytoplasmic proteins. After activation by phagocytosed bacterial peptidoglycans and cellular stress, they initiate an immune response.

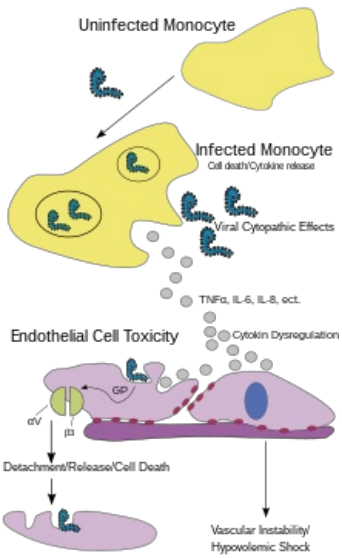
==Cytokines==

It serves to regulate the immune response. They are produced mainly by activated macrophages and T-helpers after stimulation by immune complexes or microbial products. Furthermore, they are important for the communication of cells of the immune system.

The main functions of cytokines include:
* fever stimulation,
* influence on the synthesis of acute phase reactants (in the liver),
* complement activation, opsonization,
* stimulation of myelopoiesis and release of leukocytes from the bone marrow,

* increase in the synthesis of *heat shock* proteins (chaperones) – affecting the configuration of newly synthesized proteins.

Among the cytokines in the inflammatory reaction, we include mainly **IL-1, IL-6, TNF-α'** and others.



🔎 *For more information see Cytokines.*

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