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| ***Alkaline Phospatase and it’s role in the Immune System - Sloot*** | **A multi-agent cell-based model for wound contraction - Boon** | **Computational Modeling of Inflammation and Wound Healing - Ziraldo** |
| Inflammation Triggering Moeties **(ITMs)** |  | "Endotoxin" is produced by simulated infectious vectors  (activates ECs, PMNs and Monos)  Cytotoxin (  1. It reduces "infection" by "cytotox." This is the bactericidal effect.  2. It reduces "oxy" by "cytotox." This is the cytotoxic effect on otherwise undamaged ECs) |
| Alkaline Phosphatase **(AP) –** *Endogenous in liver, supplemented,* |  |  |
|  |  | GCSF (  1. stimulates the bone marrow to produce granulocytes and stem cells and release them into the bloodstream  2. Inflammatory mediators such as interleukin (IL)-1, tumor necrosis factor-α (TNF), and toll-like receptor (TLR) ligands including microbial components such as lipopolysaccharide (LPS) and endogenous molecules such as the acute-phase protein serum amyloid A (12) have been shown to induce G-CSF production)  PAF (is a potent phospholipid activator and mediator of many leukocyte functions, platelet aggregation and degranulation, inflammation, and anaphylaxis  **produced by activated ECs**)  sTNFr (cytokine receptor) |
| Pro-inflammatory Cytokines | tPA  PDGF  TGFB | TNFa (**produced by both PMNs and Monos**)  IL-8 (**produced by macrophages/Monos and EC and is chemotactic for PMNs**)  IL-12 (**produced by TH1 cells**)  IL-1 (**produced by both PMNs and Monos**)  IL-6  IFNγ (is an important activator of macrophages and inducer of Class II major histocompatibility complex (MHC) molecule expression) |
| Anti-inflammatory Cytokines |  | IL-4 (**produced by TH2 cells (positive feedback) and promotes transition of TH0 cells to TH2 cells. Initial IL-4 producer unknown**)  IL-10 (**produced by Monos and TH2 cells**)  IL-1ra |
| Neutrophils – *Resting, Activated, Apoptotic, Necrotic* | Neutrophils | Neutrophils |
| Macrophages – *Activated, Resting* | Leukocytes | Macrophages |
|  | Fibres -  Collagen  Fibrin |  |
|  | Fibroblasts  Myofibroblasts | Fibroblasts |
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| Cell/cytokine/etc... | phase | Produced by | role |
| INF-g | inflammation | commonly expressed in Escherichia coli, however, the resulting product of the prokaryotic expression system is not glycosylated with a short half-life in the bloodstream after injection | IFNγ is an important activator of macrophages and inducer of Class II major histocompatibility complex (MHC) molecule expression |
| GCSF | inflammation | Inflammatory mediators such as interleukin (IL)-1, tumor necrosis factor-α (TNF) have been shown to induce G-CSF production  Monos | stimulates the bone marrow to produce granulocytes and stem cells and release them into the bloodstream |
| PAF | inflammation | activated ECs | is a potent phospholipid activator and mediator of many leukocyte functions, platelet aggregation and degranulation, inflammation, and anaphylaxis  chemotaxis for PMNs and Monos |
| sTNFr | inflammation | ? | TNFα antagonists |
| TNFa | inflammation | PMNs and Monos | PMN activation, adhesion, migration and apoptosis |
| IL-8 | inflammation | macrophages/Monos and EC | chemotactic for PMNs |
| IL-12 | inflammation | TH1 cells | transition of TH0 to TH1 cells |
| IL-1 | inflammation | PMNs and Monos | possess strongly proinflammatory effect  "IL-1" is incorporated into the calculations for "IL-8," "IL-10," "IL-12," "GCSF," and "INF-g.  PMN adhesion |
| IL-6 | inflammation | macrophages | inhibitory effects on TNF-alpha and IL-1, and activation of IL-1ra and IL-10.  responsible for stimulating acute phase protein synthesis, as well as the production of neutrophils in the bone marrow. It supports the growth of B cells and is antagonistic to regulatory T cells. |
| IL-4 | inflammation | TH2 cells (positive feedback)  **Initial IL-4 producer unknown** | promotes transition of TH0 cells to TH2 cells.) |
| IL-10 | inflammation | Monos and TH2 cells | PMN migration and apoptosis, activation status of Monos, and the transition of TH0 to TH2 cells |
| IL-1ra | inflammation |  | IL-1ra levels tend to increase later than IL-1 levels, suggesting that IL-1ra functions to block further IL-1 activity and has a role in the termination of the inflammatory response.  preventing IL-1 from sending a signal to that cell. |
| Endotoxin | inflammation | infectious vectors | activates ECs, PMNs and Monos.   In monocytes and macrophages, three types of events are triggered during their interaction with LPS:   1. Production of cytokines, including IL-1, IL-6, IL-8, tumor necrosis factor (TNF) and platelet-activating factor 2. affect neutrophil chemotaxis and accumulation. The result is inflammation. 3. Activation of the coagulation cascade |
| Cytotoxin | inflammation |  | 1. It reduces "infection" by "cytotox." This is the bactericidal effect.  2. It reduces "oxy" by "cytotox." This is the cytotoxic effect on otherwise undamaged ECs) |
| Endothelial Cells (EC) | Inflammation/ contraction | activated by Endotoxin >= 1 or oxy < 60 | Allowing white cells to move through blood vessel. |
| Neutrophils (PMNs)  *Resting, Activated, Apoptotic, Necrotic* | Immune system/ inflammation/ contraction | "PAF," "endotoxin" and "IL-8" as the PMN chemotactic factors | PMNs are mobile agents |
| Alkaline Phosphatase **(AP)** | Immune system |  |  |
| Macrophages – *Activated, Resting* | Immune system/ inflammation | cytokines and bacterial endotoxins  IFN-γ is the most potent macrophage-activating factor | Activated macrophages also release proteases, neutrophil chemotatic factors; reactive oxygen species such as nitric oxide and superoxide; cytokines such as tumor necrosis factor-alpha (TNF-alpha), interleukin one and eight (IL-1 and IL-8), eicosanoids, as well as growth factors. These products of activated macrophages result in the tissue destruction which is a hallmark of inflammation |
| TH0-cells | Inflammation | [10.1371/journal.pone.0179015](https://dx.doi.org/10.1371%2Fjournal.pone.0179015) | represent progenitor cells for the two cell types above |
| TH1 cells represent the pro-inflammatory T-cells; they are Blue. | Inflammation | are activated in the presence of "IL-12."  mainly develop following infections by intracellular bacteria and some viruses | produce interferon-gamma, interleukin (IL)-2, and tumour necrosis factor (TNF)-beta, which activate macrophages and are responsible for cell-mediated immunity and phagocyte-dependent protective responses |
| TH2 cells represent anti-inflammatory T-cells | Inflammation | are activated in the presence of "IL-10.  predominate in response to infestations by gastrointestinal nematodes | type 2 Th (Th2) cells produce IL-4, IL-5, IL-10, and IL-13, which are responsible for strong antibody production, eosinophil activation, and inhibition of several macrophage functions, thus providing phagocyte-independent protective responses. |
| TGFB | Contraction | secreted by many cell types, including macrophages (leukocytes),   * **Activation by protease and metalloprotease**   Plasmin and a number of Matrix metalloproteinases (MMP) play a key role in promoting tumor invasion and tissue remodeling by inducing proteolysis of several ECM components.   * **Activation by pH** * **Activation reactive oxygen species (ROS)** * **Activation by thrombospondin-1** | Attracts macrophages and fibroblasts  Stimulates resting monocytes – upregulates inflammatory response  While also ***downregulating*** cytokine production in monocytes and macrophages  inhibits activated macrophages |
| tPA | Contraction | Which is released by the endothelial cells | This cytokine breaks down the clot and  hence it decays the fibrin |
| PDGF | Contraction | platelets upon activation, it is also produced by other cells including smooth muscle cells, activated macrophages, and endothelial cells | Attractant leukocytes |
| Collagen | Contraction |  |  |
| Leukocytes | Contraction |  |  |
| Fibrin | Contraction |  |  |
| Fibroblasts | Contraction |  |  |
| Myofibroblasts | Contraction |  |  |
|  | Contraction |  |  |