Mediators of inflammation

Vasoactive amine → Histamine , Serotonin

platelets, basophils, Mast cells — Vd , ↑ vascular permeability , endothelial activation

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lipid products → Membrane Phospholipids —(phospholipases)→ Arachidonic acid (mast cells, leukocytes)

Arachidonic acid → COX (⊖ aspirin) → Prostaglandins / Leukotrienes

Leukotrienes: B_4 , C_4 , D_4 , E_4 → C_4, D_4, E_4: Vasoconstriction, ↑ vascular permeability

B_4: Chemotaxis, leukocyte adhesion

Prostaglandins: PGC_4, PGD_4, PGE_4 → Smooth muscle Contraction

PGI_2, PGF_1, PGE_2, PGD_2 — imbalance → IHD & CVA

PGE_2 → pain, fever

PGI_2 → vasodilation → PI aggreg

TXA_2 → Vasoconstriction + PI aggreg

Cytokines & TNF ⇝ Stimulate expression of endothelial adhesion molecules, ↑, Systemic effects

Stimulate secretion of other cytokines

↳ IL-1 ⇝ ↗ + greater role in fever ↔ acute inflammation → chemotaxis

↳ IL-6 ⇝ acute phase response (systemic effects)

↳ IL-17 ⇝ Recruitment of neutrophils and monocytes

T_H17 ← macrophages, endothelial cells, mast cells, T lymphocytes

↳ IL-4, IL-5, IL-13 ⇝ activate eosinophils and Macs alternative pathways

T_H2

↳ IL-6, IL-12, IL-23 ⇝ activate T lymphocytes

microphages

↳ INF β ⇝ activate Macs in Classic pathway

T_H1

↳ Chemokines ⇝ Chemoattractants (40 different, 20 receptors)

↑ leukocytes, macrophages

⇝ have G protein Coupled receptors

Complement activation → inactive soluble proteins (C1–C9) → now we know more than 20

Cell lysis ← Functions → Vascular permeability, Chemotaxis, Opsonization

MAC (C9 multiples)

Vascular permeability + Chemotaxis: initial vascular phase — C3a, C5a (anaphylatoxin)

Opsonization: C3b → coating to enhance phagocytosis

C3 convertases (−), MAC (−)

C1 inhibitor deficiency → angioedema, DAF, CD59 → abnormalities → PNH → C5 deficiencies → infection susceptibility

Factor H mutations → hemolytic uremic syndrome
↳ proteolysis C3 convertases

Platelet activating factor → platelet aggregation

Protease activating receptors → platelet aggregation

Kinins → vasoactive peptide → VD, ↑ permeability, smooth muscle contraction, Pain
↳ Bradykinin (active)

Neuropeptides → Substance P and neurokinin A