Inflammation and Repair

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reaction to injurious agents- vascular, cellular and systemic
fluid and cells -> site injury protective response
sensitive activation, massive amplification, controlled down regulation

Signs:

- Calour = heat
- Rubor= redness
- Tumor = swelling
- Dolor = pain
- Loss function

Causes of Acute Inflamm

- Infections and toxins
- Trauma
- Physical and chem agents- burns, irradiation -> blisters
- Tissue necrosis: when nutrient supply cut off -> spill contents (detected) -> limit damage and clean up spillages
- Foreign bodies- splinter, dirt
- Hypersensitivity reactions

Steps for inflamm

1. Initial event – signal that response needed
2. RESPONSE: allow fluid and cells to move from circulation -> injured site- vascular system permeable
3. Cells -> correct area –only want active here – otherwise -> damage
4. Cell send signals recruiting other cells and begin action
5. Down regulation when finished

Cell action:

Phagocytosis: engulf organism/ particle -> lysosome fuses with phagosome -> phagolysosome – inject various antimicrobials etc. and kill organism
Activation: direct lysis and killing
From signals delivered from cell surface- many diff receptor pathways

- Arachadonic acid metabolite production, cytokines, modulation of adhesion molecs etc.
- E.g. CD14 reacts with lipopolysacc from bact- indicates infect

Release mediators:

Inflamm Mediators- source:

Cell-derived: act alone and active when secreted

- some pre-made in granules e.g. histamine -degranulation mast cells release histamine- reaction e.g. sneeze –rapid
- newly synth'd take longer be produced e.g. prostaglandins

Plasma mediators: act in interacting cascades and req activation

- produced constantly in liver- not when just needed i.e. clotting factors, complement

Diff stimuli -> diff courses of inflamm- resolve diff
Mediators short half-lives – degrade quickly so inflamm only persist when stimulus persists

TYPES OF INFLAMMATION:

Purulent Inflamm:
-> large amounts of pus = dead WBC/bact , caused pyogenic bact (Staph)
Lots neutrophils, necrotic cells and edema fluid
Abscess = collection of purulent inflamm tissue in confined space (deep in tissues)

- central region of necrotic cells
- preserved zone of neutrophils
- vascular dilation and fibroblast prolif

pimples and boils can occur internally- can become systemic
Fibrous Inflamm:
Fibrinogen -> tissues and cleaved -> FIBRIN (not flexible- dangerous on pericardium, also difficult to remove)
Fibrin broken down and removed (resolution)- If not removed -> scarring
Serous Inflamm:
Thin fluid from plasma or mesothelial cells in peritoneal, pleural and pericardial cavities
E.g. blisters from burns or viral infect
Ulcerous Inflamm:
Loss of ep layer- expose underlying layers
Excavation in tissue surface by shedding of necrotic inflamm tissue
Mucosa of mouth, stomach, intestines of GIT

COMPLETE RESOLUTION

Return normal permeability, drain fluid and proteins into lymph, pinocytosis into macrophages, phagocytosis apoptotic neutrophils and necrotic debris, disposal macrophages
Acute inflamm disease

- Resp distress syndrome, transplant rejection, asthma, septic shock, vasculitits

Chronic inflamm disease

- Arthritis, asthma, atherosclerosis, chronic transplant rejection

HEALING

repair = laying down collagen or elastic tissue

Inflamm and healing occur simultaneously
New tissues must be formed and must be vascularized - angiogenesis
Fibro-proliferation response patches areas of damaged tissue

- Inflamm- remove damaged and dead tissue
- prolif of CT and parenchymal cells
- Form new blood vessels and synth of new extracellular matrix proteins
- Tissue remodeling- collagen remodeling -> strength
- Wound contraction and acquire wound strength

Factors affecting Healing:

- INJURY-RELATED: nature of injury, intensity of stimulus and duration
- INFLAMM FACTORS: foreign bodies, poor vascularization, denervation, mech stress, necrotic tissue, surgical techniques
- HOST FACTORS: age, anemia, drugs, genetic disorders, hormones, diabetes, obesity, systemic infection, vitamin deficiency

Formation of Scars:

1. Migration and prolif of Fibroblasts:
    a. Macroscopic- soft, pink and granular
    b. Microscopic- angiogenesis and fibroblast prolif
    c. New vessels leaky -> edematous
        Fibrinogen and plasma fibronectin -> early stroma
    - Fibroblasts attracted by TGFβ,PDGF,EGF,FGF, IL1 and TNF
    - Macrophages produce GF's, clear debris, fibrin and foreign material
2. ECM Deposition:
    a. Fibroblasts = maj source of ECM components
        i. Collagen synth and deposition
    - Granulation tissue -> scar
        - Spindle shaped fibroblasts, dense collagen, elastic tissue fragments
    - Vascular regression -> scar becoming pale

Complications of healing

Deficient Scar formation: mech stress or poor vascularization, can rupture and/or ulcerate
Excessive formation of repair components: excess collagen -> raised scars – HYPERTROPHIC
Scar beyond original borders = KELOID (genetic components evident)
Contractures: too much contraction deforms surrounding tissue

L3: Intro to Immunity

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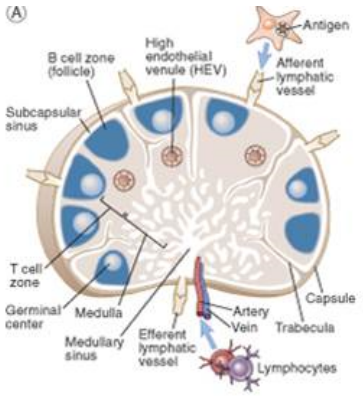
Non-specific mechanisms: resisting barriers, skin, ciliated ep, sebaceous glands, digestive enz and normal microbiota

Innate system: phagocytosis and intracellular killing, NK cells, complement, natural AB, TLR's

Adaptive: Humoral (B cell) response -> AB and memory B cells,

- Cellular (t cell) response: T cells (CD8 and CD4), reg T cells and memory T cells



Lymphatics

Ag captured from site infect -> transport to draining LN where immune response is initiated

- Follicle (Blue area) = B-cell rich

T cell response:

Ag Shown epitope -> activated and makes cytokines -> activate macrophage

CD8 cells only activated by cells present internal Ag- kill cells similar those activated it

Dendritic Cells:

Immature DC in skin = *Langerhans cells*

During migration DC mature -> efficient APC

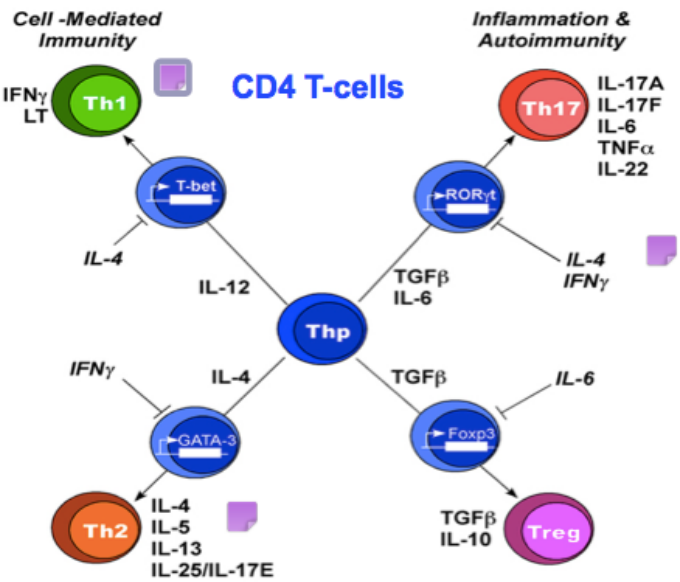
	Immature DC	**Mature DC**
Function	Ag capture	Ag presentation
Expression FC, mannose receptors	Y	N
Molecs involved in T cell activation	N or low	Y
Class II MHC moec – half life on surface	10 hours	>100 hours
Number class II molecs on surface	10^6	7 x 10^6

T- cell activation – Danger Signal

DANGER SIGNAL

- Prevents reaction with novel host proteins (breast milk) delivered through TLR
- -> cascade of kinase reaction that reach nucleus and activate cell

Th1 subset -> intracellular bacteria



Th2 -> allergies and parasites
Pathways antagonists – turn each other off
Transcription factors (blue) help in this