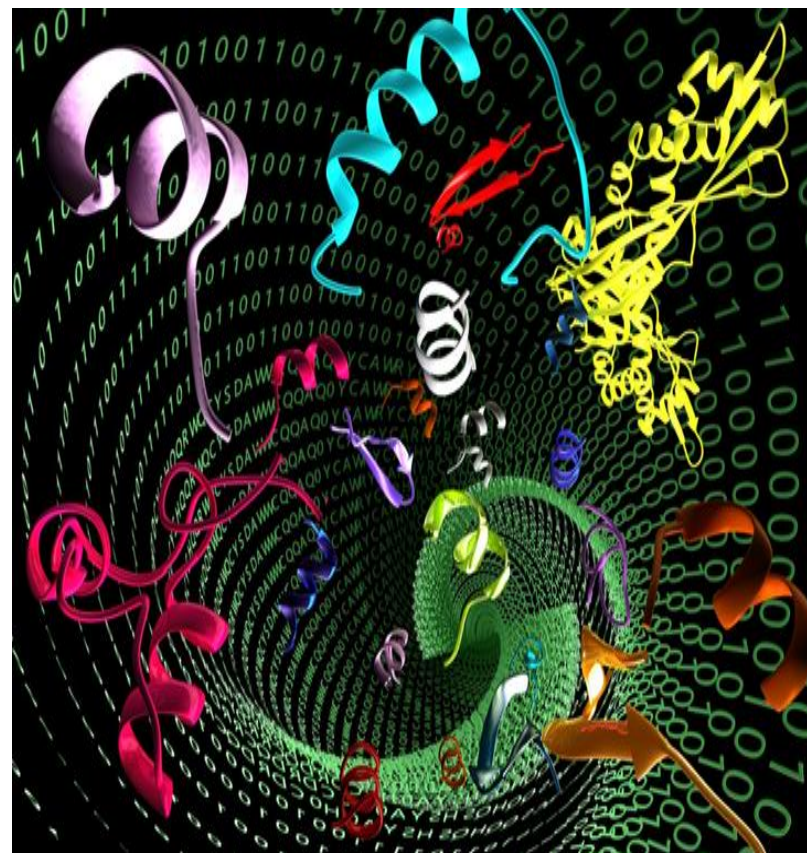


Antimicrobial Peptides and Oral Health



Prof. Dr. Batool Hassan AL-Ghurabi

What are antimicrobial peptides?

- Antimicrobial peptides- defined as polypeptide antimicrobial substances
- More than 100 of these peptides identified in fungi, insects, amphibians and humans.
- Between 12-50 amino acids;half the residues hydrophobic
- Generally cationic and amphipathic molecules
- A role in innate defense mechanism of many species

Classification of antimicrobial peptides

- Major classes include
 - (a) beta-sheets with S-S bonds
 - (b) linear alpha-helices
 - (c) extended coils
 - (d) loop structures
- Predominant class is the linear, amphipathic, α -helical peptide

What are the functions of antimicrobial peptides??

- Antimicrobial peptides participate in the innate immune system
- Can protect host from invasive microbial infections
- New evidence views antimicrobial peptides as multifunctional molecules that link innate immune response to adaptive immune system

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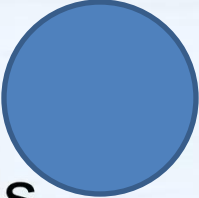
What are the functions of antimicrobial peptides??

- Mediate of cross-talk between 2 wings of immune sytem. How?
- Achieved by cytokine and chemokine production(immunomodulation)
- Also by facilitating immune and inflammatory cell migration
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What are the functions of antimicrobial peptides??

- α and β -defensins, and cathelicidin extend neutrophil lifespan (by suppression of neutrophil apoptosis)
- Induce secretion of histamine and prostaglandins from mast cells
- Induce cytokine release from T cells

Where do we find antimicrobial peptides?

- In cells- neutrophils, Paneth cells, 
- In body fluids-complement proteins
- In body secretions such as saliva and tears
- In intestinal mucus layers-peptides bound to mucins detected in rectal mucus
- B-defensin of Epithelial cells of trachea-LPS dependent production via rel/NFKappaB
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Where do we find antimicrobial peptides?

- α -Defensins in neutrophils and Paneth cells
- β -defensins from epithelia of many organs including skin
- Cathelicidins in secretory granules of neutrophils and in NK cells, T cells, B cells, mast cells and epithelial cells

Defensins, histatins and cathelicidins are 3 important peptides in humans

- small, cationic and amphipathic.
- Exhibit broad-spectrum activity against Gram-positive and Gram-negative bacteria, yeasts, fungi and enveloped viruses
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Defensins

- alpha-defensins and beta-defensins
- Cationic, non-glycosylated peptides with six cysteine residue
- Cysteines form three intramolecular disulfide bridges

Histatins-saliva

- small, cationic, histidine-rich peptides
- random coil conformation in aqueous solvents
- alpha-helices in non-aqueous solvents

Cathelicidins

- random coil conformation in a hydrophilic environment
- Alpha helical in hydrophobic medium

Antimicrobial peptides from saliva

- Major secretion-submandibular glands, sublingual glands and parotid glands(these are paired glands).
- Also secreted by many minor salivary glands(in lamina propria and oral mucosa)
- Connective tissue(lamina propria)
+epithelia=mucosa
- Minor salivary glands-lingual, buccal and labial glands, palatine glands and glossopalatine folds

Antimicrobial peptides from saliva

- In body fluids

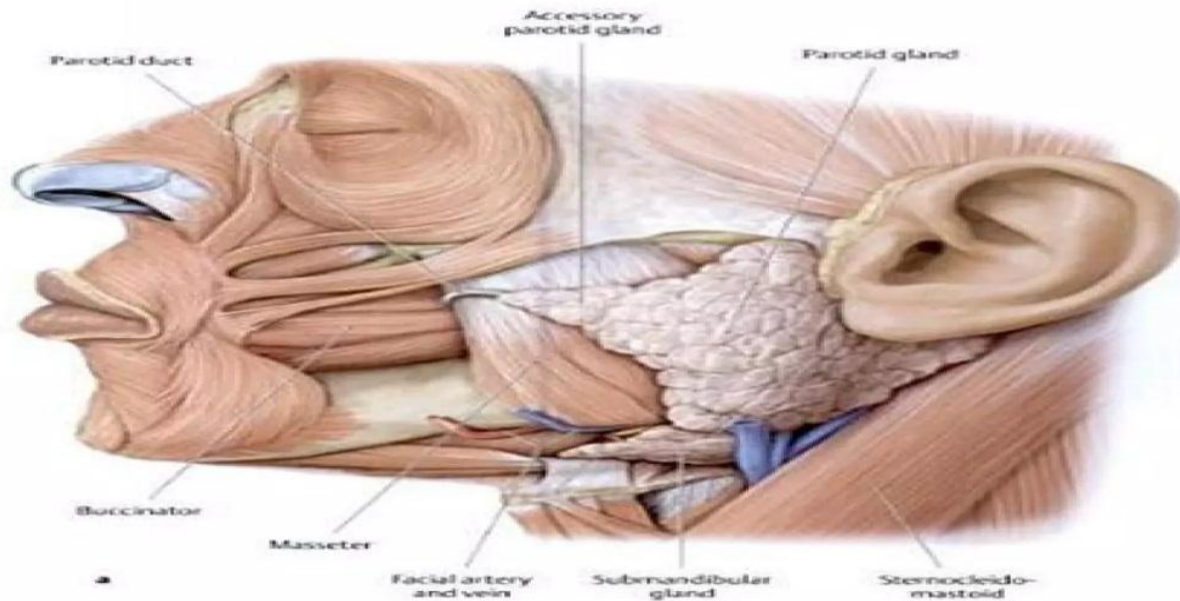
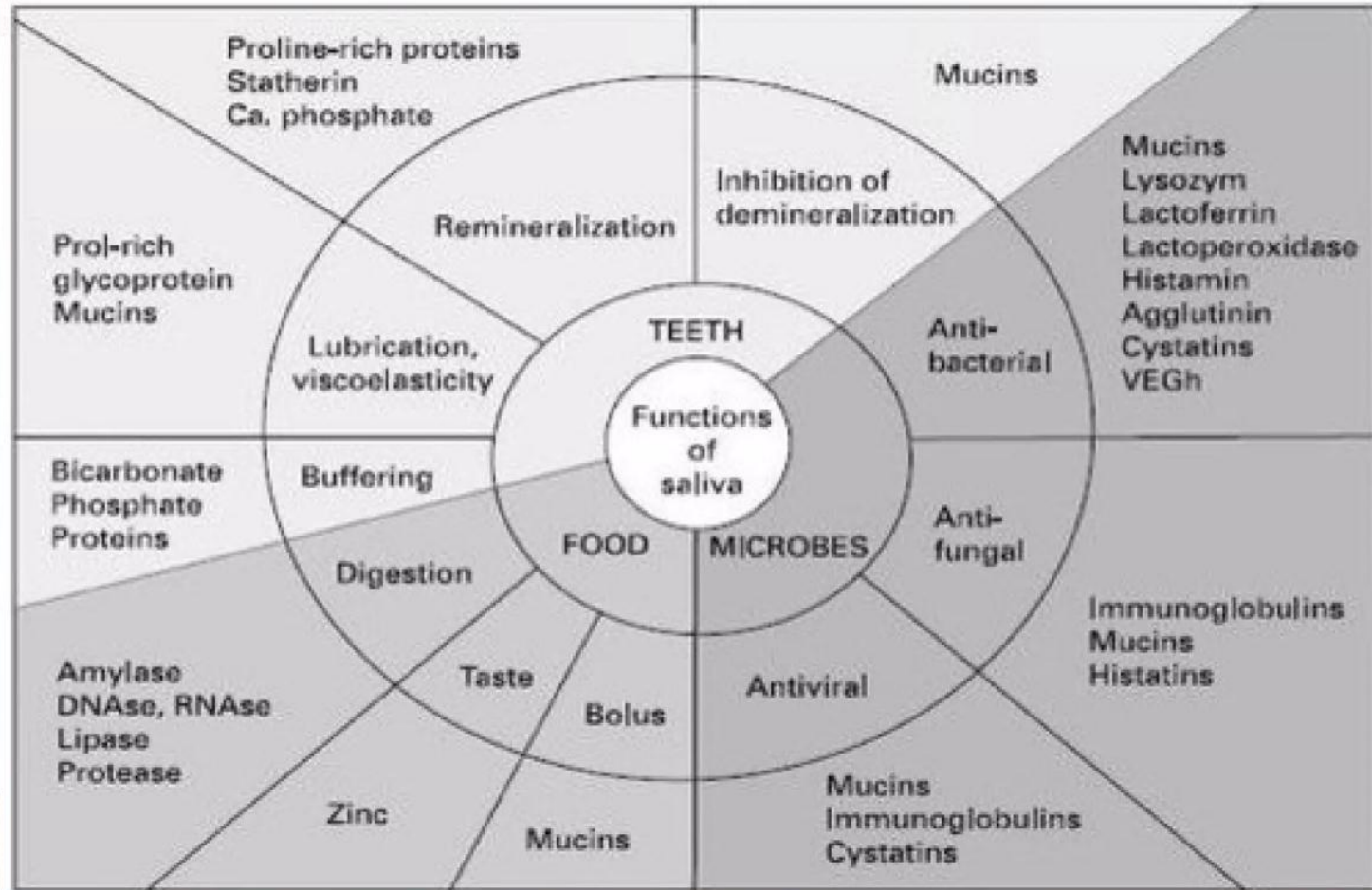


Figure 1 Salivary Glands
(Picture taken from: *Thieme Atlas of Anatomy, Head and Neuroanatomy*)

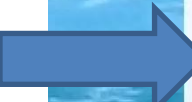
Antimicrobial peptides from saliva

- Peroxidase slows down acid production and growth of many oral microbes and fungi.
- Lysozyme promotes lysis of bacteria in conjunction with other antibacterial systems.
- Histatins from human saliva

Functions of saliva-focus on antimicrobial peptides



Release of antimicrobial peptides



- Paneth cells release antimicrobial peptides upon stimulation by the proinflammatory cytokine, interferon gamma (IFN- γ)

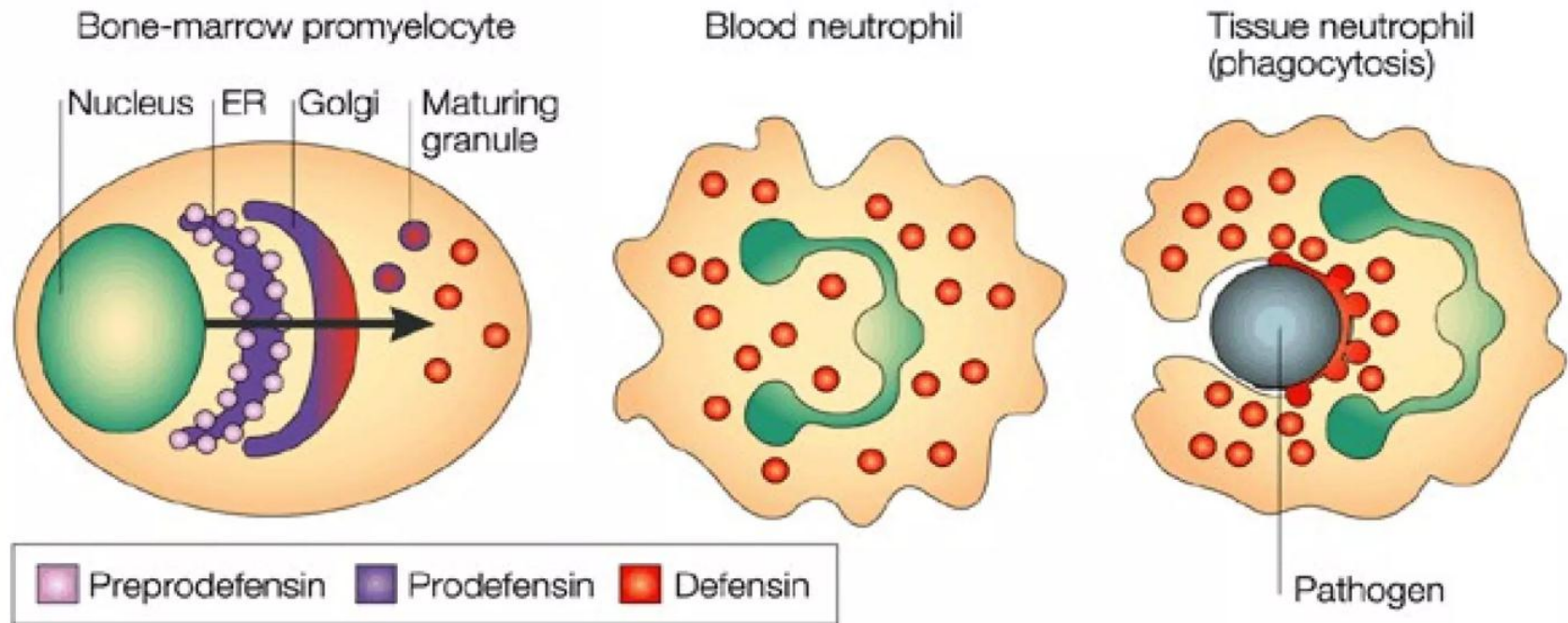


- Neutrophils-

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Antimicrobial peptides-release of defensins by neutrophils

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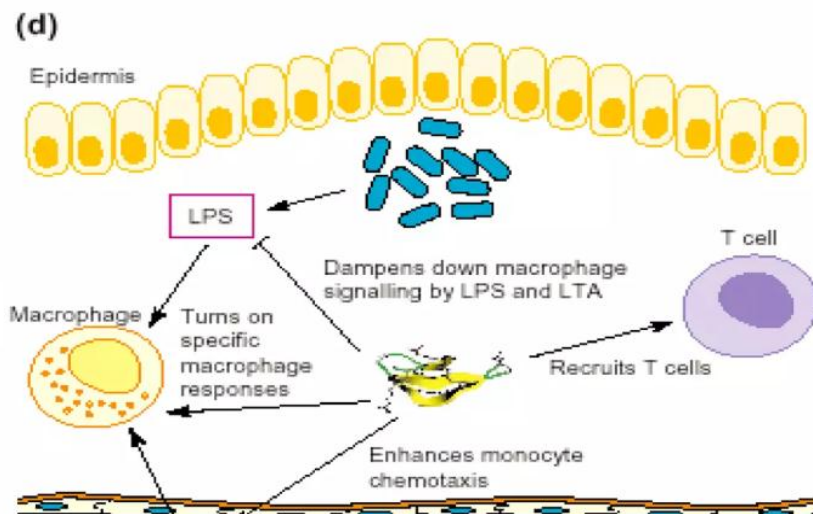
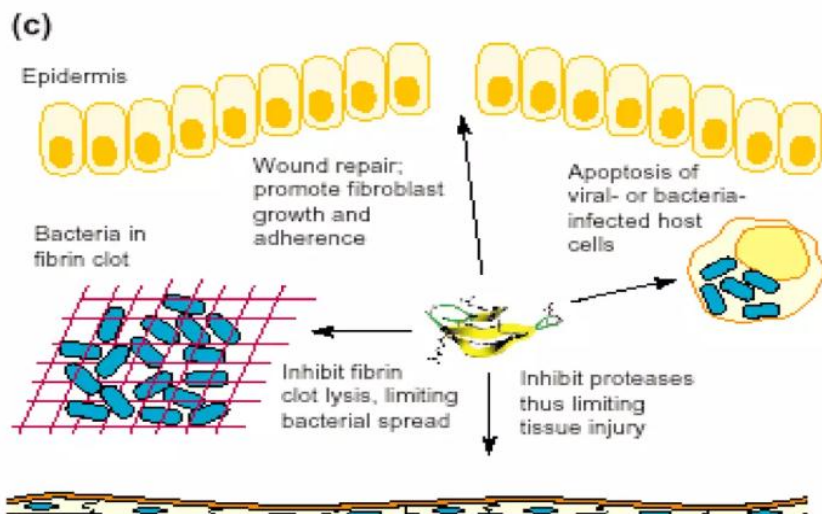
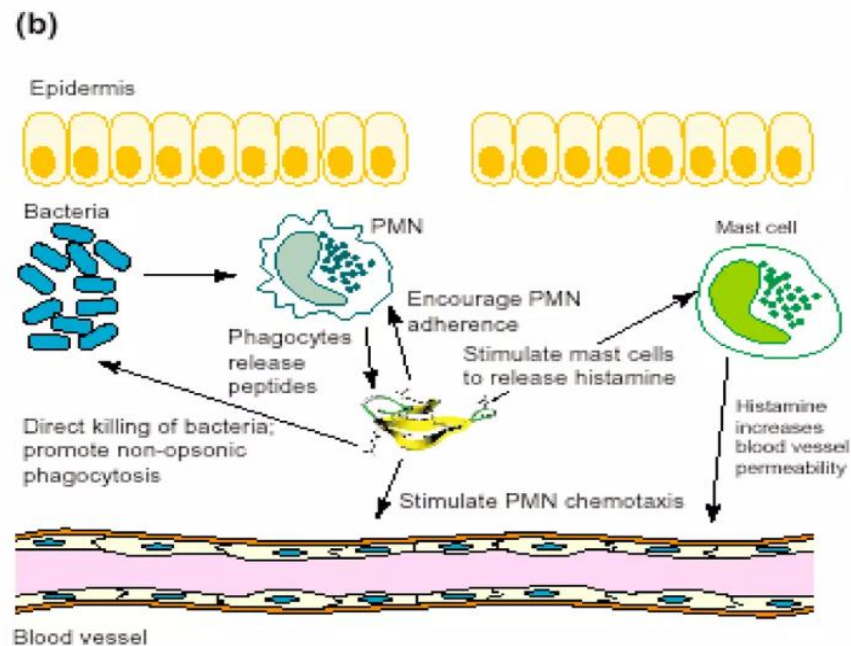
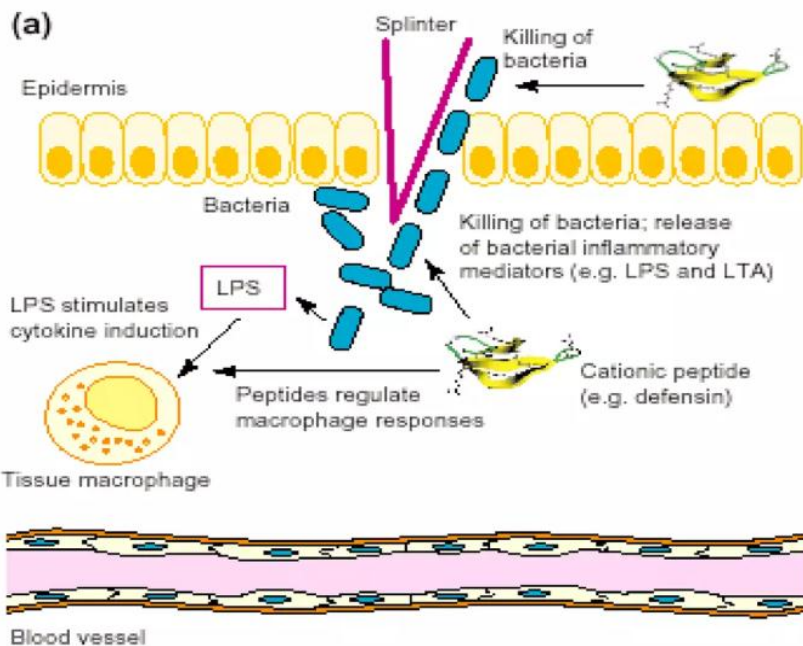
How do they work?

Acute inflammation

- Killing of bacteria, release of bacterial inflammatory mediators (LPS, LTA), regulation of macrophage response.
- Adherence of PMN and chemotaxis, stimulation of mast cells to release histamine.
- fibroblast growth and adherence, apoptosis of viral- or bacteria- infected host cells, inhibition of fibrin clot lysis (thereby limiting bacterial spread), inhibition of proteases (thus limiting tissue injury).

Chronic inflammation

- Recruitment of T cells, enhancement of monocyte chemotaxis,
- Regulation of macrophage response.



Antimicrobial peptides differ from peptide antibiotics of bacteria

- These peptides differ from most (but not all) peptide antibiotics of bacteria
- Also differ from peptide antibiotics from fungi
- Fungi synthesize peptide antibiotics by specialized metabolic pathways