Basic Immunology

Immune components of the oral cavity.
Molecular and cellular elements of the oral immune system.

Zoltán Kellermayer

Oral cavity

Inductive site and **effector organ** of immunity

Systemic and **local** immunity (sublingual vaccines!)

Part of the mucosa-associated lymphoid tissues, with **specialized components**

Stratified squamous epithelium + “hard” tissues *(teeth)*

Chewing: causes ongoing damage

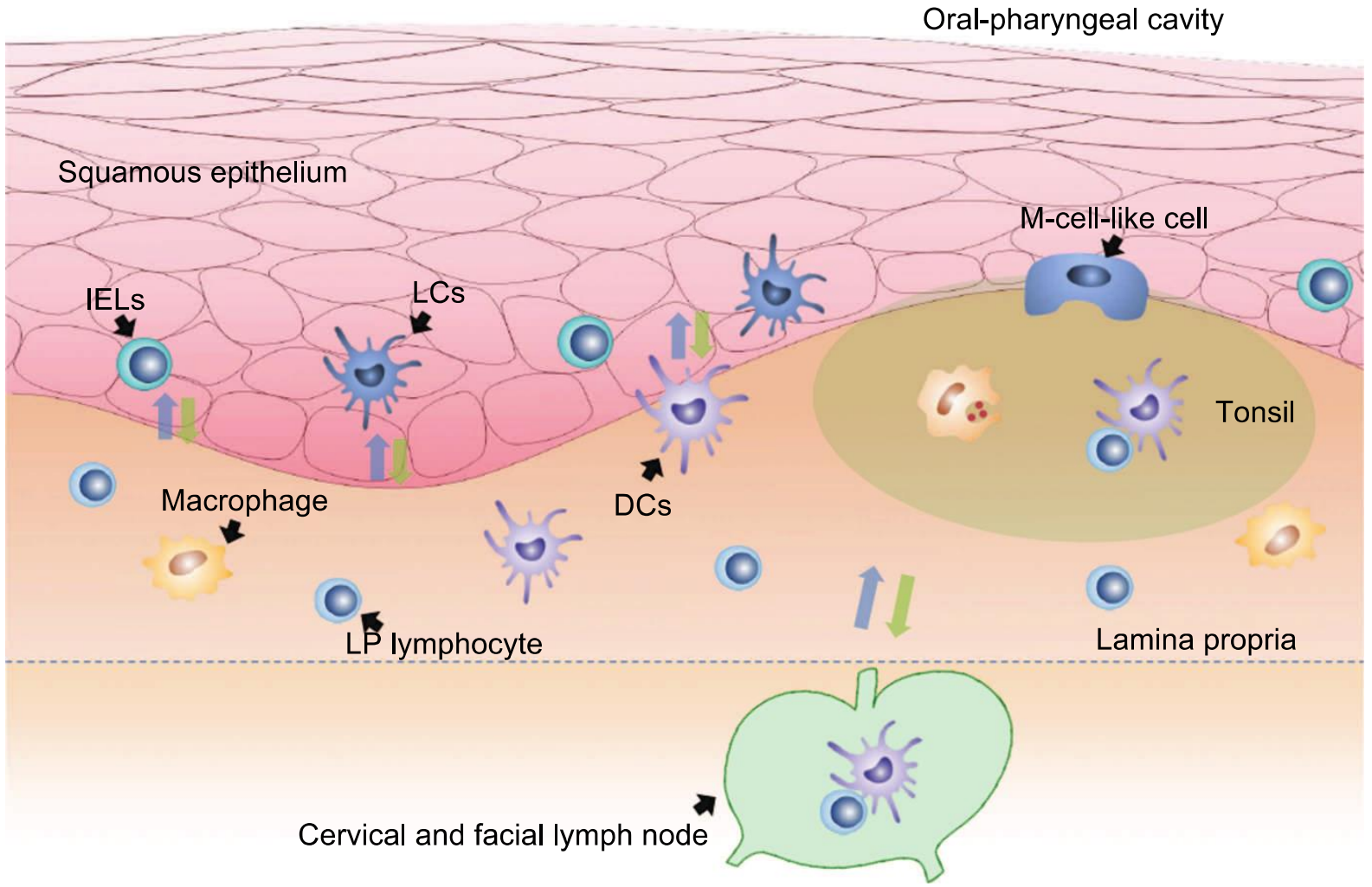
Thick and and dense physical barrier

Permeable: periodontal epithelium

Constant **antigen exposure**: ~100 million bacteria/ml of saliva (~700 species)
~500kg of food annually

Innate and **adaptive** components

Immunity of the oral cavity



DC: dendritic cell LC: Langerhans cell LP: lamina propria IEL: intraepithelial lymphocyte

The mucosal immune system in the oral cavity – an orchestra of T cell diversity. Wu RQ et al, Int J Oral Sci. 2014 6:125-32.

Cellular components

Epithelial cells

- First line (physical + chemical) barrier
- Express PRRs (TLRs, NLRs)
- Can produce inflammatory cytokines (IL-1β, IL-6, GM-CSF)
- Different types and thickness (influences permeability!)
  - keratinized, thick (>50 layers, dorsal tongue)
  - non-keratinized, thick (~30 layers, buccal mucosa)
  - non-keratinized, thin (~10 layers), rich in Langerhans cells (mouth floor)
  - junctional epithelium

NK cells

Langerhans cells, dendritic cells, macrophages: antigen presenting cells

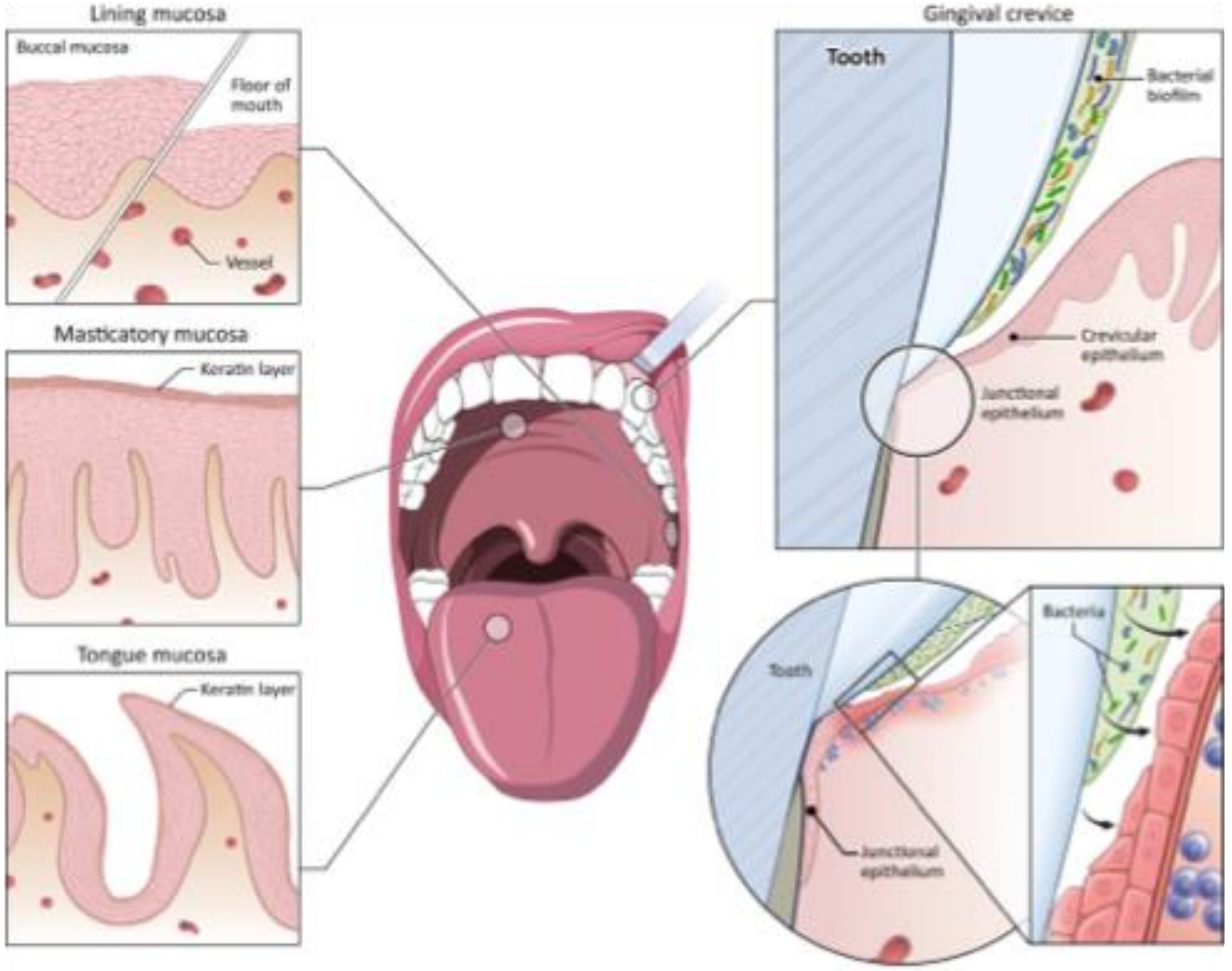
Mast cells

CD8αα+ intraepithelial lymphocytes

T cells: rare in healthy mucosa, T_H17s important in pathology (eg Candida albicans)

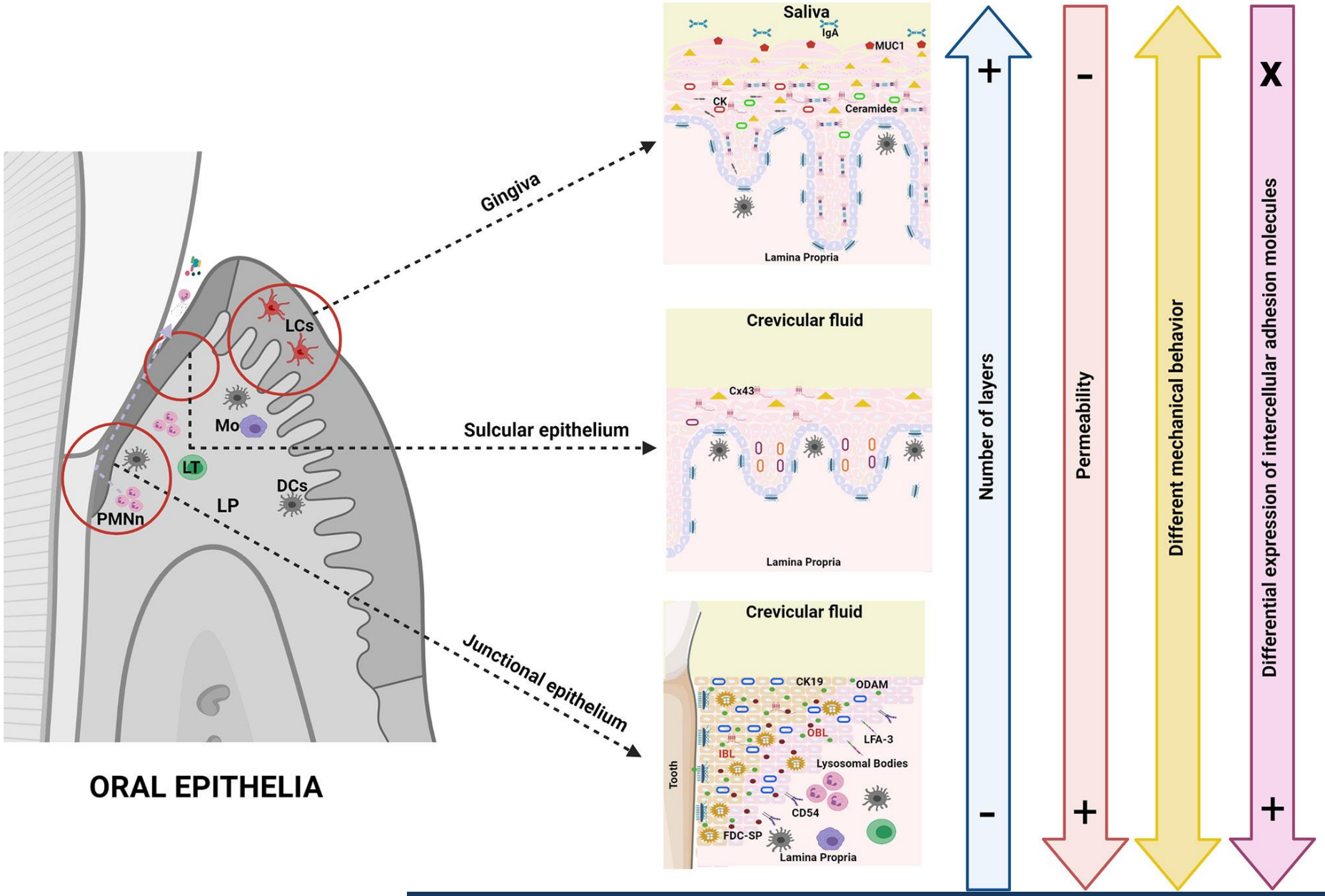
B cells: mainly IgA^+, few IgG^+

Oral epithelial barriers



Tissue-specific immunity at the oral mucosal barrier. Moutsopoulus N et al. Trends Immunol 2018

Oral epithelial barriers



Oral versus Gastrointestinal Mucosal Immune Niches in Homeostasis and Allostasis. Suarez LJ et al. Front Immunol 2021.

Saliva

750-1000 ml/day

3 pairs of major glands (parotid, submandibular, sublingual) + several minor glands

Important in:

- physico-chemical protection of teeth
- immunity of oral mucosa
- mucosal healing

Contains lots of proteins with innate and adaptive immunologic features

Low concentrations of the various factors, but synergistic effect

Xerostomia: Increased susceptibility to oral candidiasis, worse dental caries

Salivary antibodies

Types

IgA: usually dimer (from the salivary gland),
IgG: lower amounts (from serum or local plasma cells)
IgM and IgE: very low amounts

IgA$^+$ B cells

Activated in NALT (nasopharynx-associated lymphoid tissue, tonsillae + adenoids, *Waldeyer's ring)*

Migrate to salivary gland stroma (and mucosa)

IgA

Transported across epithelial cells via polymeric Ig receptor + secretory component
Constitutively secreted into saliva

Salivary IgA function

Neutralization

Agglutination

Surface immune exclusion

Opsonization (FcαRI) – antigen presentation, degranulation, cytokine production

Catalyze oxygen burst

Salivary antimicrobial proteins

Defensins
Disrupt pathogen membranes; antibacterial, antifungal, antiviral activity

Lactoferrin
Iron-binding protein; neutralizes bacteria and viruses, disrupts bacterial membrane

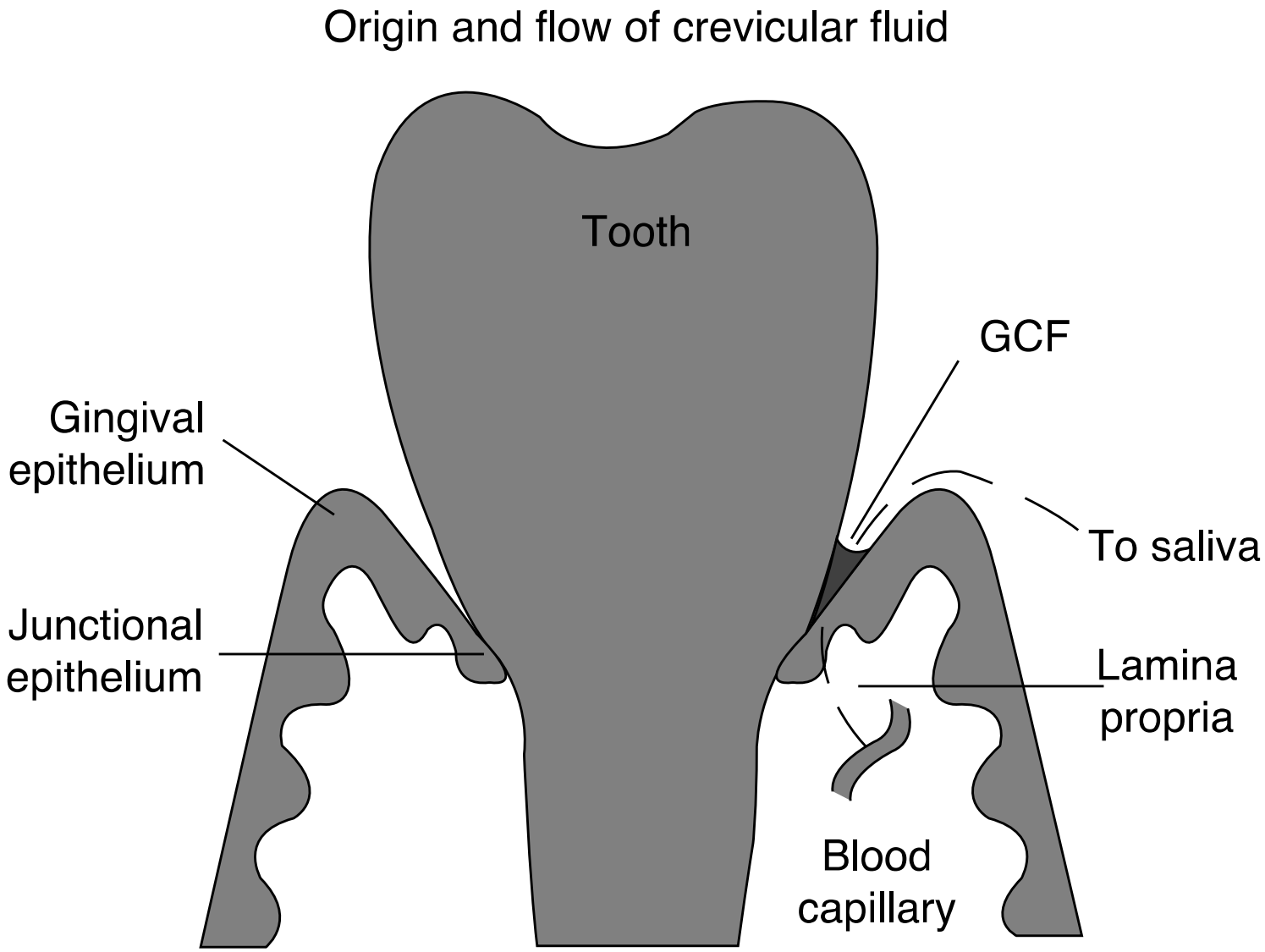
Cathelicidins
Destruct bacterial membranes; bind LPS

Lysozyme
Hydrolyzes peptidoglycan, effective mainly against Gram+ bacteria

α-Amylase
Cleaves the α-1,4-glycosydic bond; can bind LPS, influences bacterial adhesion

Mucins
Secretory and membrane-bound form, entrap and agglutinate pathogens

Gingival crevicular fluid (GCF)



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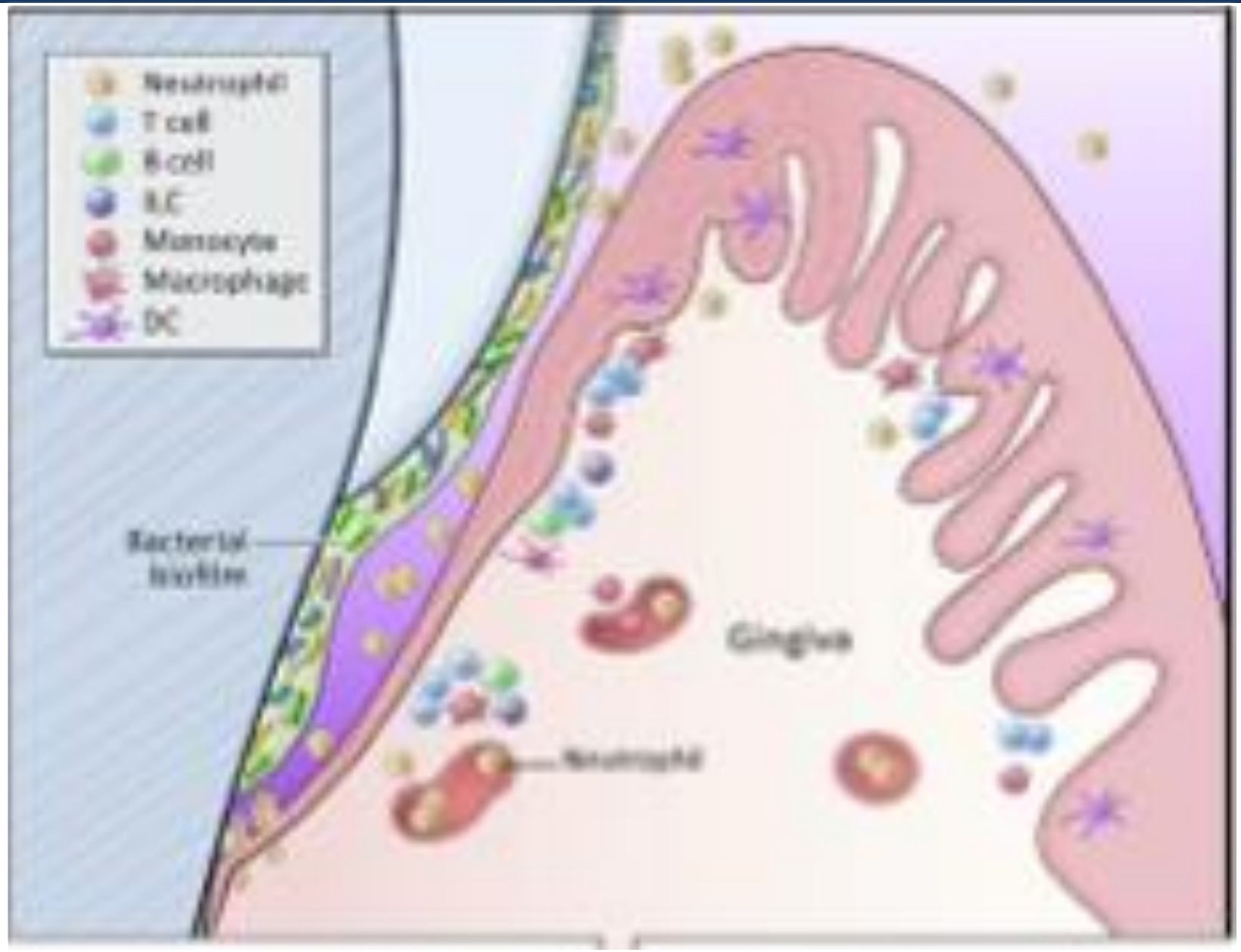

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Gingival crevicular fluid (GCF)

Transudate from gingival capillaries

Accumulates around the necks of the teeth

Normally ~1ml/day, significantly increases in periodontitis and gingivitis

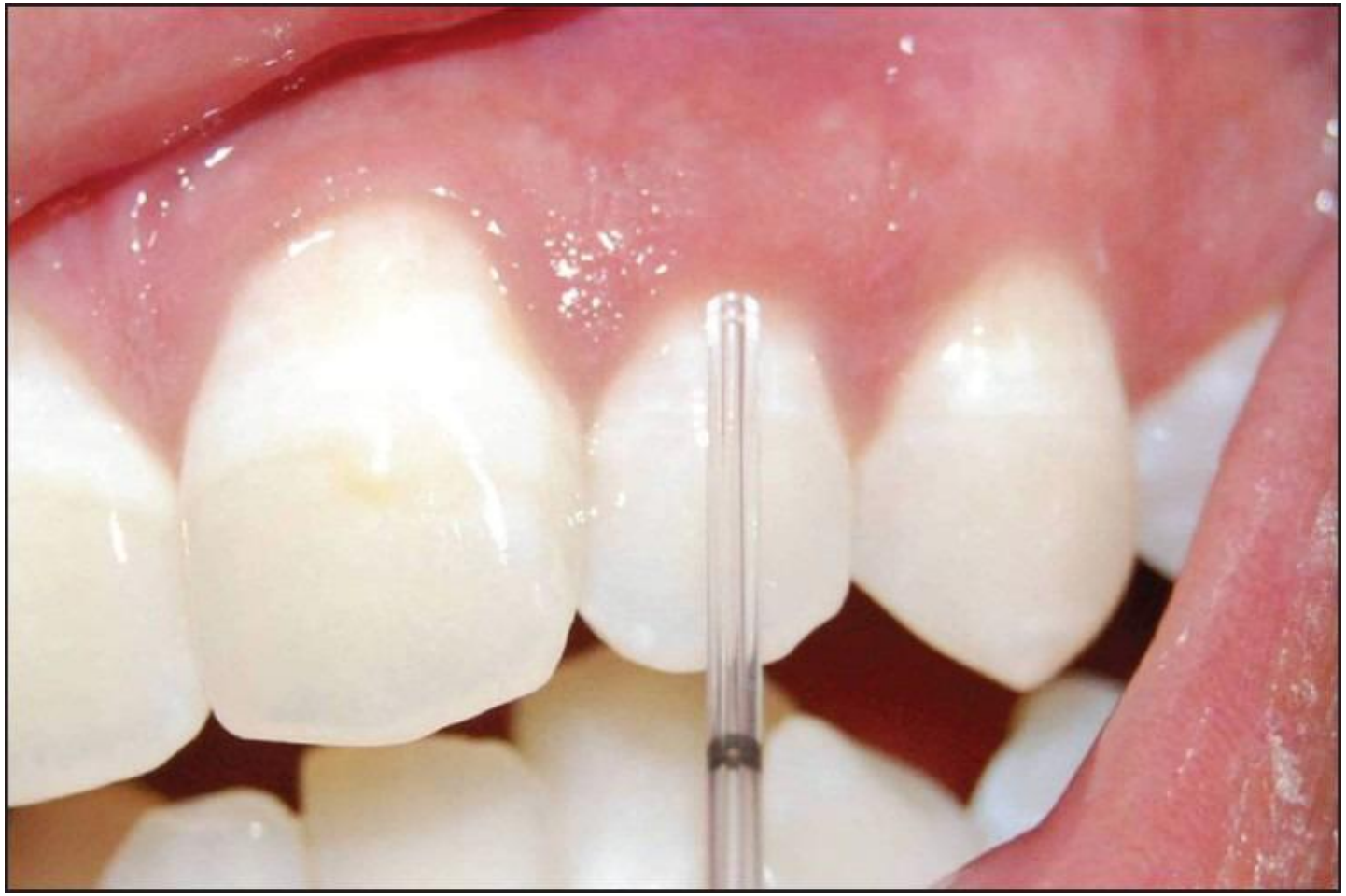
Content:

- humoral components: antibodies (IgG), cytokines, digestive enzymes, antimicrobial proteins
- cellular components: leukocytes, lymphocytes

Function: cleans the crevice between the tooth and the gingival epithelium

Gingival crevicular fluid (GCF)

Collection of GCF



Comparison of matrix metalloproteinase-3 and tissue inhibitor of matrix metalloproteinase-1 levels in gingival crevicular fluid in periodontal health, disease and after treatment: a clinico biochemical study. 2013. Kumar PM et al, Dent Res J.