Basic Immunology

25th lecture:

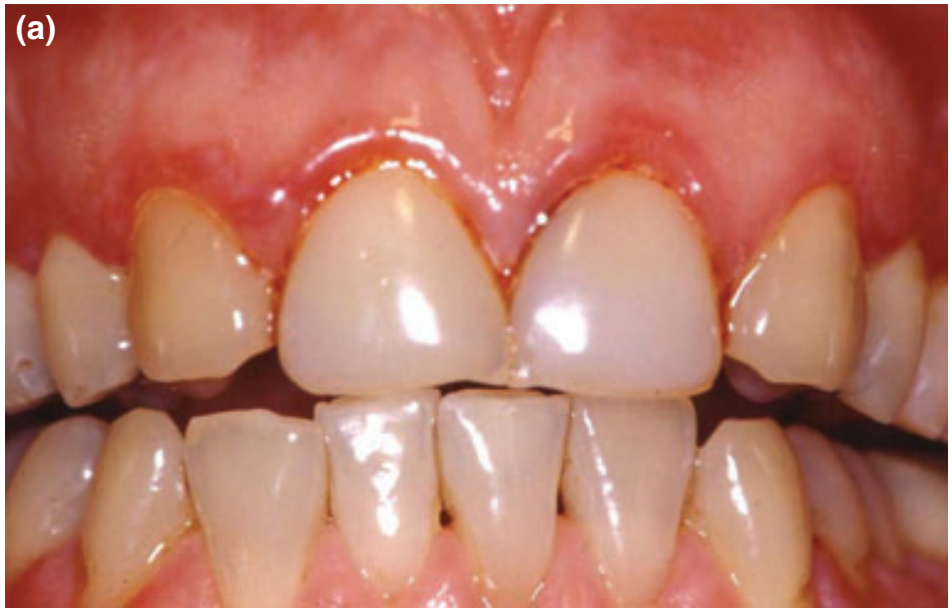
Immunology of periodontal diseases

Periodontal diseases

Diseases affecting the gingiva and supporting structures of teeth

Results in attachment loss and destruction of alveolar bone

Etiology is important for proper treatment



Marginal gingivitis

Diagnosis and classification of periodontal disease. Highfield J, Aus Dent J. 2009.

Classification of periodontal diseases (AAP, 1999)

I. Gingival diseases
    A. Plaque induced
    B. Non-plaque induced
II. Chronic periodontitis
    A. Localized
    B. Generalized
III. Aggressive periodontitis
    A. Localized
    B. Generalized
IV. Periodontitis as a manifestation of systemic disease
V. Necrotizing periodontal diseases
VI. Abscesses of the periodontium
VII. Periodontitis associated with endodontic lesions
VIII. Developmental or acquired deformities and conditions

Classification of periodontal diseases (AAP, 1999)

Most common:

-Chronic marginal gingivitis (CMG)

- Inflammatory reaction to plaques
- Reversible inflammation

-Chronic inflammatory periodontal disease (CIPD)

- Adult periodontitis
- Irreversible damage
- Smoking important exacerbating factor

Pathophysiology

Bacteria

>600 species in the oral cavity
~200 detectable in an individual

8 bacterial species have been associated with periodontal disease
- e.g.: *Prevotella intermedia* – acute necrotizing ulcerative gingivitis
  - *Porphyromonas gingivalis* – chronic inflammatory periodontal disease
- Found in both healthy and diseased sites…
- ~ 50% of plaque bacteria can be cultured, rest are unknown!

Pathogenic factors:
- -leukotoxins
- -endotoxin
- -capsular products (activators of bone resorption)
- -hydrolytic enzymes (collagenases, phospholipases, proteases… etc)

Bacteria and bacterial toxins can invade the periodontal epithelium

TABLE 1 | The predominant human oral microbiota.

Microbial group	Microbial genus/species
Gram-positive	
Aerobic or facultative	*Streptococcus (S. gordonii, S. mitis, S. auralis, S. salivarius)*
	Staphylococcus (S. aureus, S. epidermidis)
	Enterococcus (E. faaecalis)
	Lactobacillus (L. casei, L. fermentum)
	Corynebacterium (C. matruchotii)
	Actinomyces (A. naeslundii, A. israelli, A. viscosus)
	Arachnia (A. propionica)
	Rothia (R. dentocariosa)
Obligate anaerobes	*Bacillus (B. cereus)*
	Propionibacterium (P. acnes)
	Peptostreptococcus (P. micros, P. anaerobius)
Gram-negative	
Aerobic or facultative	*Campylobacter (C. rectus, C. concisus, C. gracilis)*
	Actinobacillus (A. actinomycetemcomitans)
Obligate anaerobes	*Fusobacterium (F. nucleatum)*
	Porphyromonas (P. gingivalis)
	Prevotella (P. melaninogenica, P. oralis, P. intermedia)

Pathophysiology

Immunogenetic factors

-*HLA association* (animal and human studies)

HLA-A9: associated with higher risk for CIPD, juvenile periodontitis, rapidly progressing periodontitis

indicate that HLA-A9 is associated with periodontal destruction

-*Genotype variants*

IL-1α, IL-1β, TNFα; IL-4, IL-10

-*Twin studies*

No difference in gingivitis, probing depth, attachment loss, and plaque in monozygous twins raised apart or together

indicate that genetic component is more important than environment

-*Antibody response*

Usually directed against Gram- bacteria; levels correlate with disease severity

e.g. increased antibody levels against *P. gingivalis* in CIPD

Both systemic and <u>local</u>

Pathophysiology

Stages *(gingivitis always precedes periodontal disease!)*

I. Initial lesion: reversible damage to gingival sulcus, polymorphonuclear cell infiltration, complement activation

II. Early lesion: still reversible, lymphocytes replace polymorphonuclear cells. Mostly T cells, few plasma cells

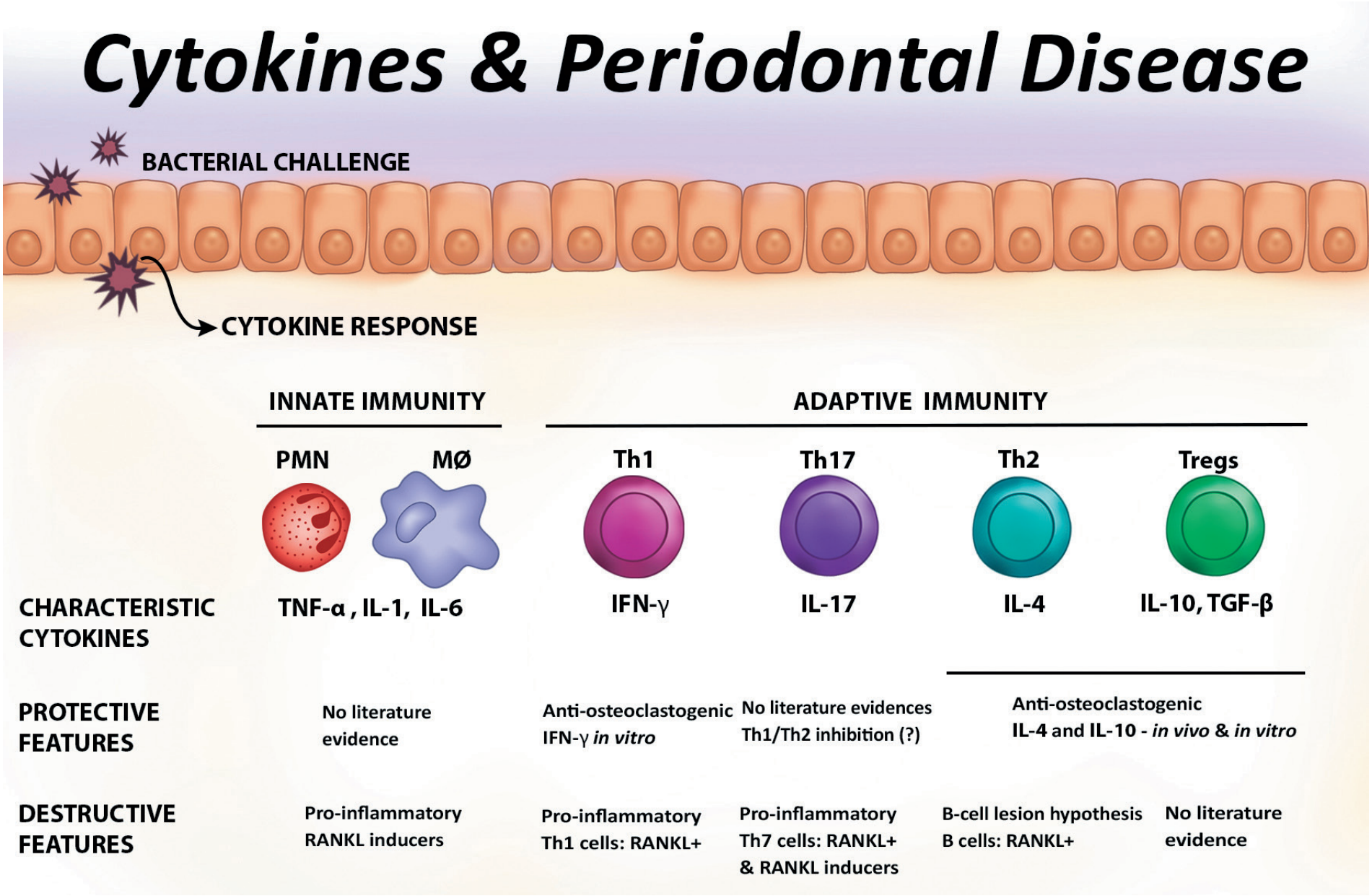
III. Established lesion: predominant plasma cell infiltration, mainly IgG^+

IV. Advanced lesion: destructive state; pocket formation, epithelial ulceration, periodontal ligament destruction, bone resorption

P. gingivalis important!

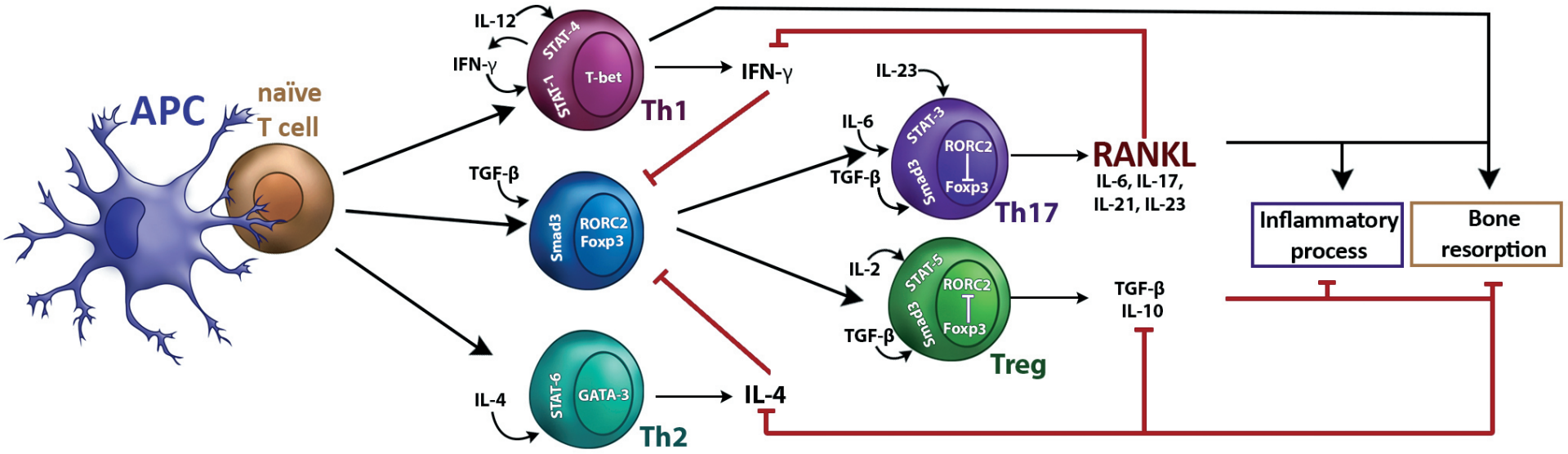
"PSD" model: polymicrobial synergy and dysbiosis

Cytokines



Host response mechanisms in periodontal diseases. Silva N et al, J Appl Oral Sci. 2015.

Osteoimmunology



Osteoblast – Osteoclast balance:

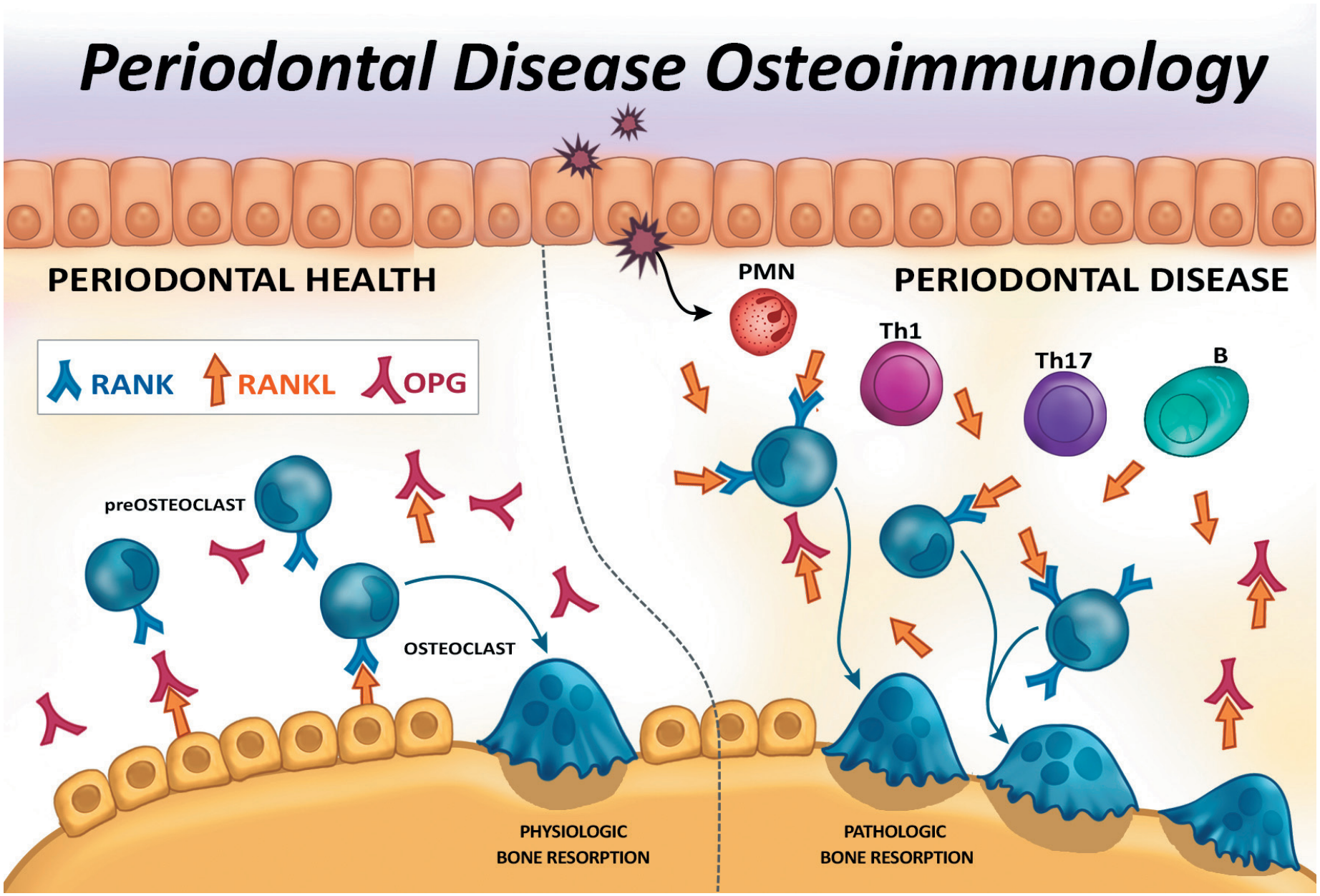
-RANKL: binds to RANK → Osteoclast differentiation, activation

-Osteoprotegerin: binds RANKL → inhibits osteoclast activation

-T_H17 cells can produce RANKL

Host response mechanisms in periodontal diseases. Silva N et al, J Appl Oral Sci. 2015.

Osteoimmunology



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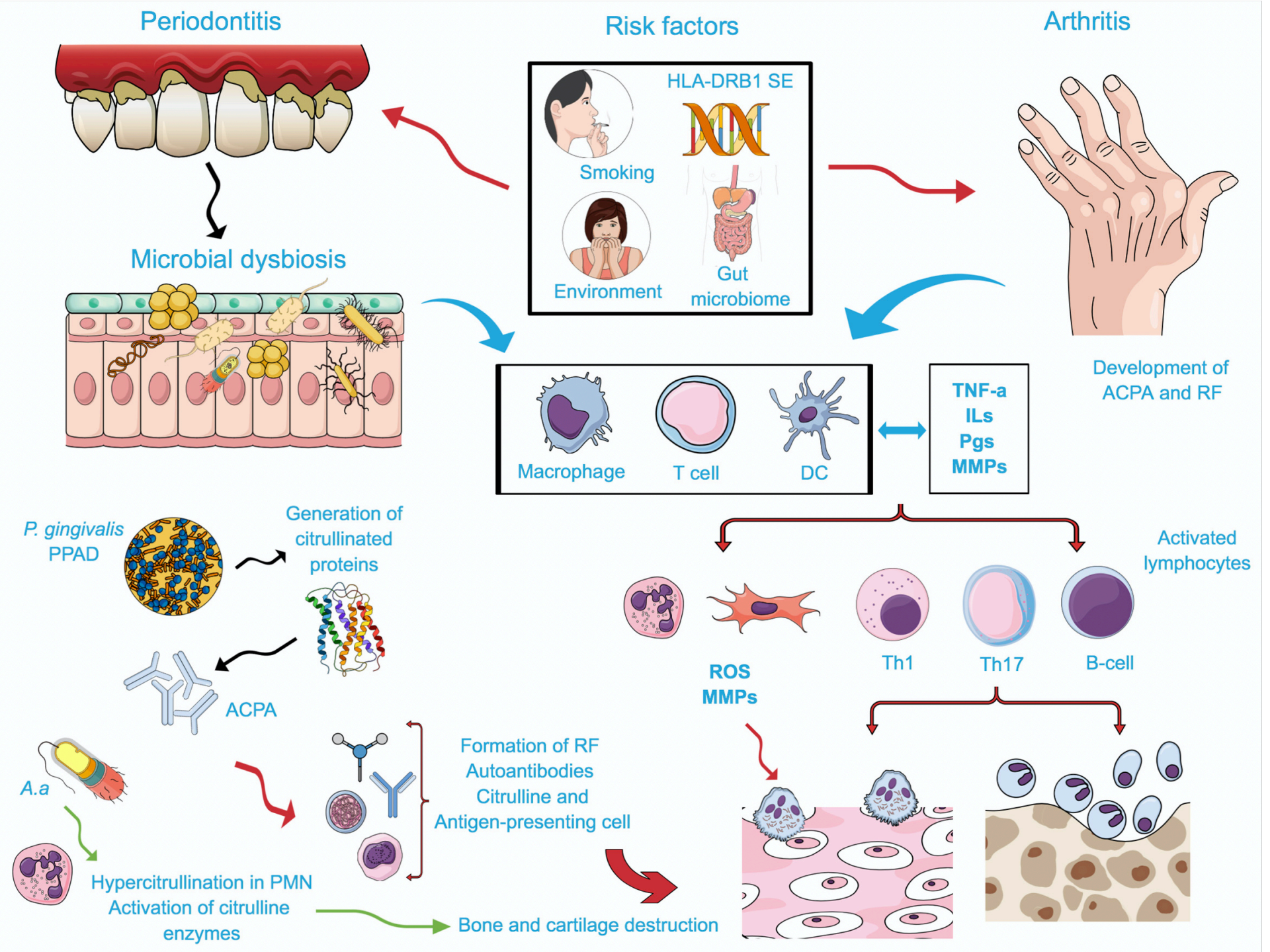
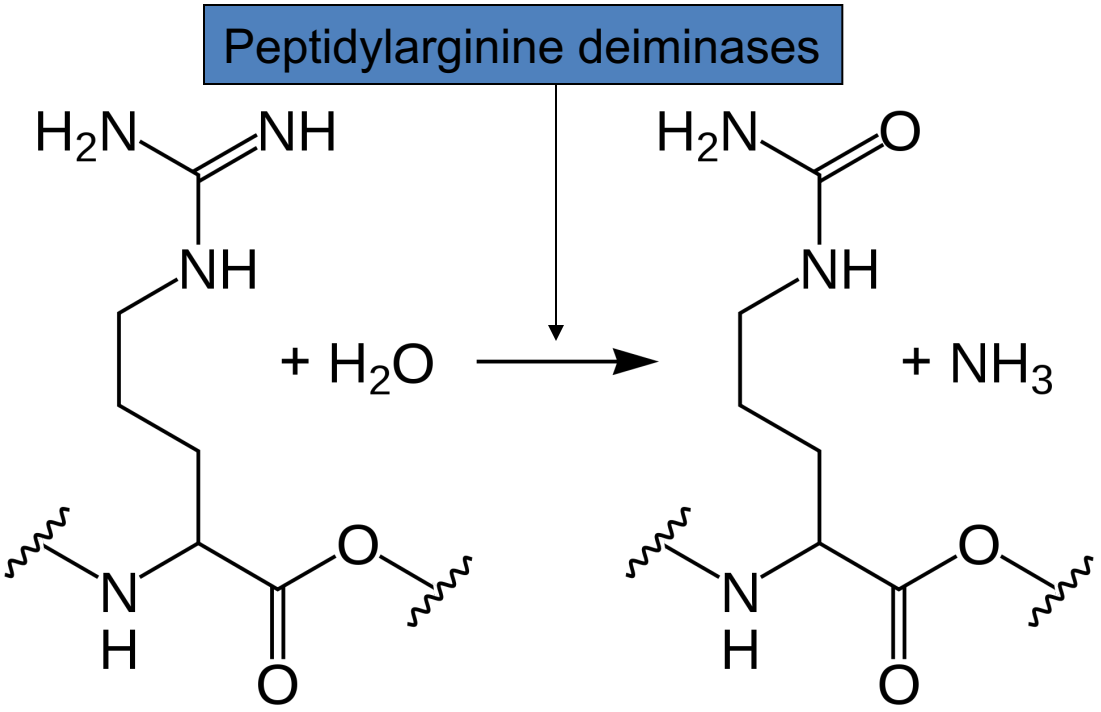

Periodontitis
Risk factors
Arthritis
HLA-DRB1 SE
Smoking
Environment
Gut microbiome
Microbial dysbiosis
Development of ACPA and RF
Macrophage
T cell
DC
TNF-a
ILs
Pgs
MMPs
P. gingivalis
PPAD
Generation of citrullinated proteins
ACPA
Activated lymphocytes
Th1
Th17
B-cell
ROS
MMPs
A.a
Formation of RF
Autoantibodies
Citrulline and
Antigen-presenting cell
Hypercitrullination in PMN
Activation of citrulline enzymes
Bone and cartilage destruction

Citrullination (deimination) 1.

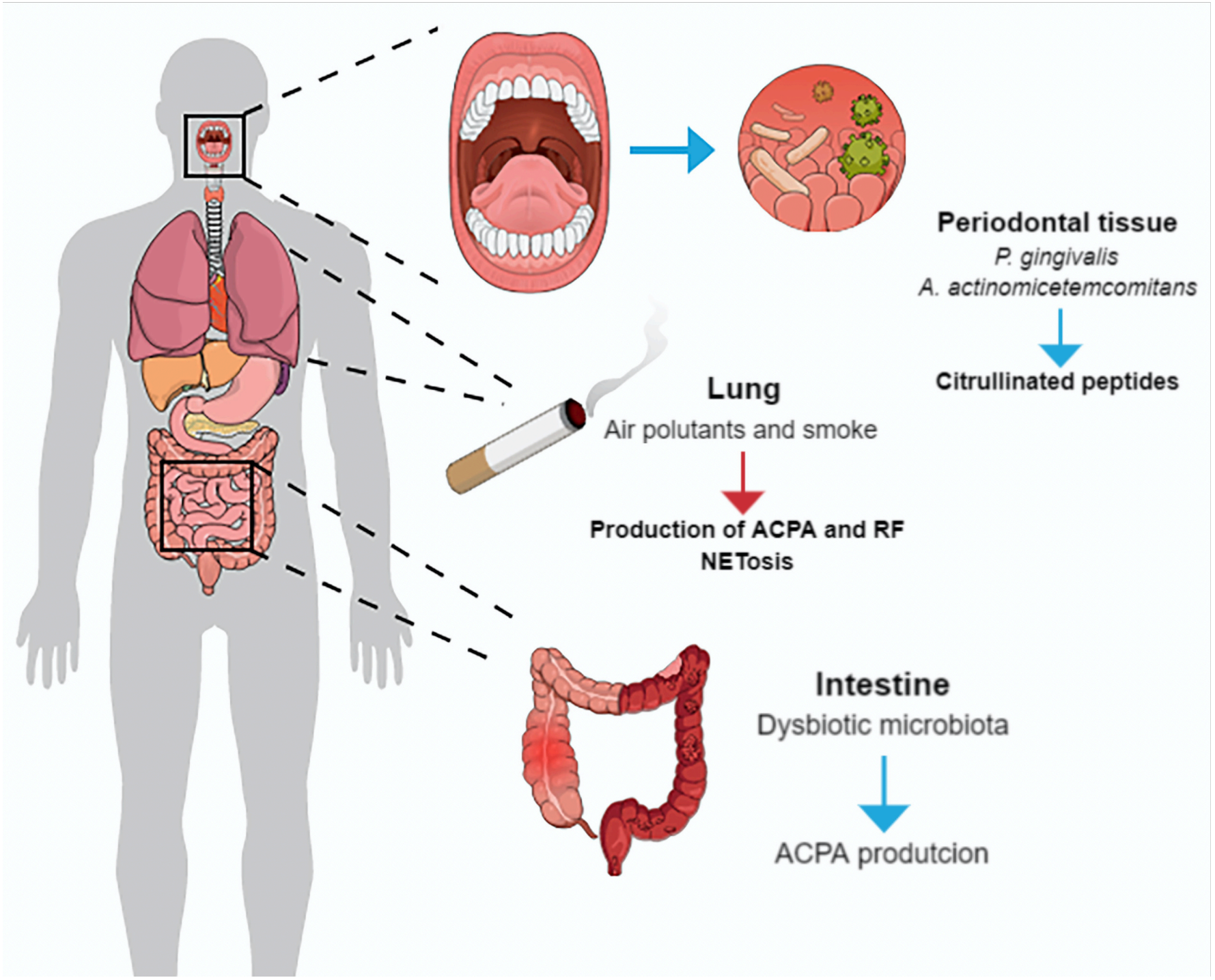


Arginine Citrulline

Citrullinated proteins:
MBP, filagrin, histon proteins, **vimentin**, fibrin, firbrinogen

MCV=modified citrullinated vimentin

Intermediate filament family - connective tissue, cytoskeleton


Periodontal tissue
P. gingivalis
A. actinomicetemcomitans
Citrullinated peptides
Lung
Air polutants and smoke
Production of ACPA and RF
NETosis
Intestine
Dysbiotic microbiota
ACPA produtcion