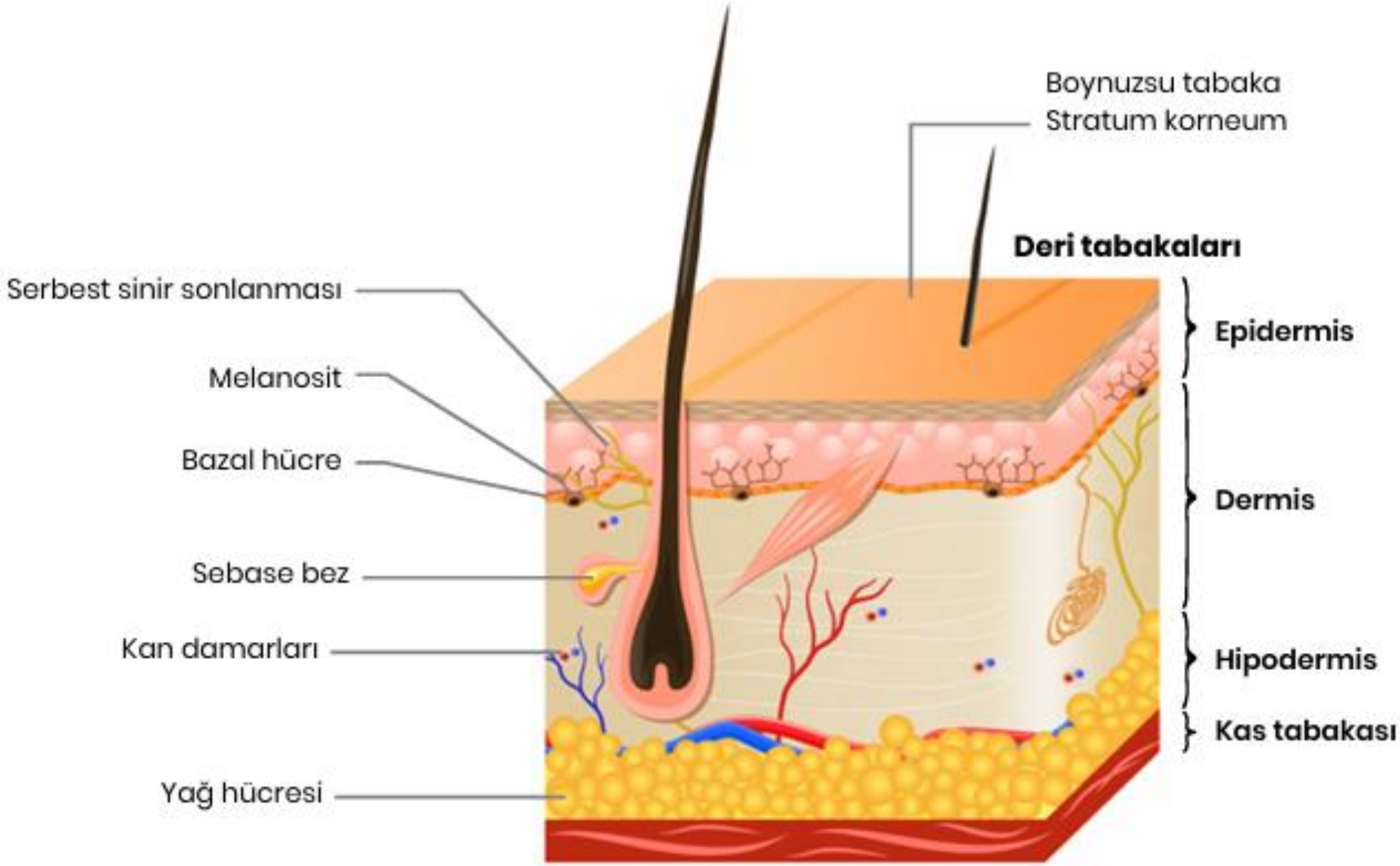
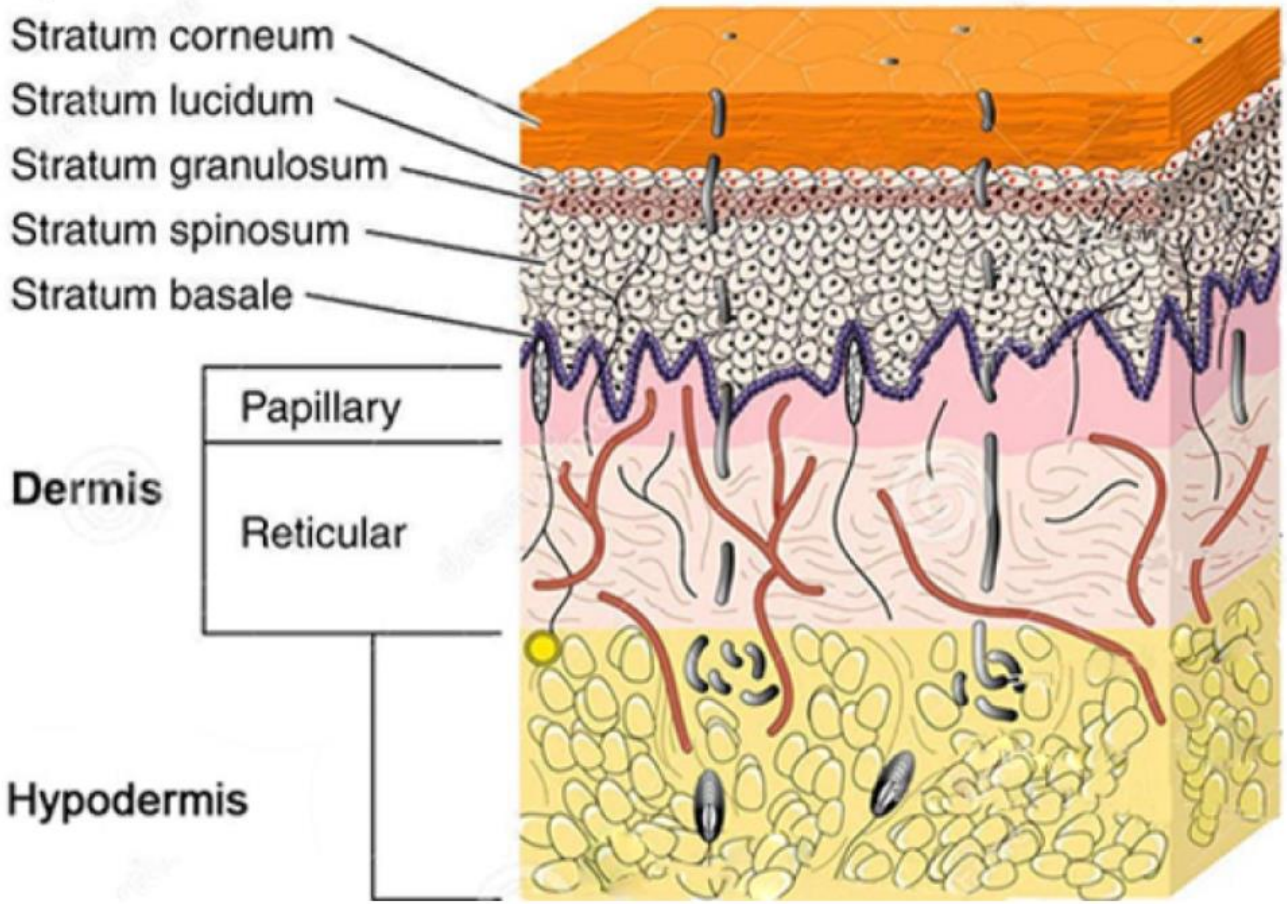
DERİ-BAĞIRSAK BAĞLANTISI

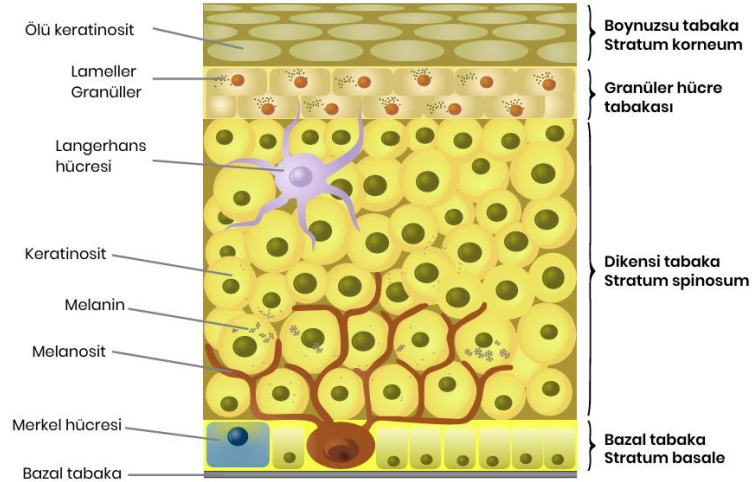
UZM DR DİLEK YAZICIOĞLU CEZAYİR
NÖROLOJİ UZMANI
dilekcezayir@gmail.com /fonksiyoneltakip@gmail.com
drdilekcezayir

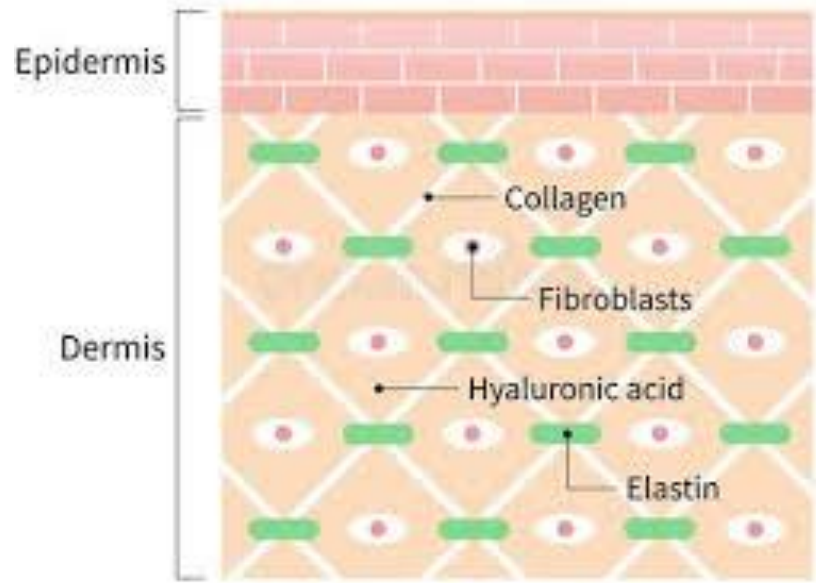
- Tüm vücudumuzu kaplayan savunma bariyeri
- Toplam yüzeyi 1,6 - 1,8 m2
- Toplam ağırlığı

yağ dokusu dahil edilmediğinde 4kg
yağ dokusu ile birlikte 9 kg


Boynuzsu tabaka
Stratum korneum
Deri tabakaları
Serbest sinir sonlanması
Melanosit
Bazal hücre
Sebase bez
Kan damarları
Yağ hücresi
Epidermis
Dermis
Hipodermis
Kas tabakası


Epidermis:
Stratum corneum
Stratum lucidum
Stratum granulosum
Stratum spinosum
Stratum basale
Dermis
Papillary
Reticular
Hypodermis


Ölü keratinosit
Lameller Granüller
Langerhans hücresi
Keratinosit
Melanin
Melanosit
Merkel hücresi
Bazal tabaka
Boynuzsu tabaka
Stratum korneum
Granüler hücre tabakası
Dikensi tabaka
Stratum spinosum
Bazal tabaka
Stratum basale


Epidermis
Dermis
Collagen
Fibroblasts
Hyaluronic acid
Elastin

- DIŞTAN İÇE HİPOTEZ

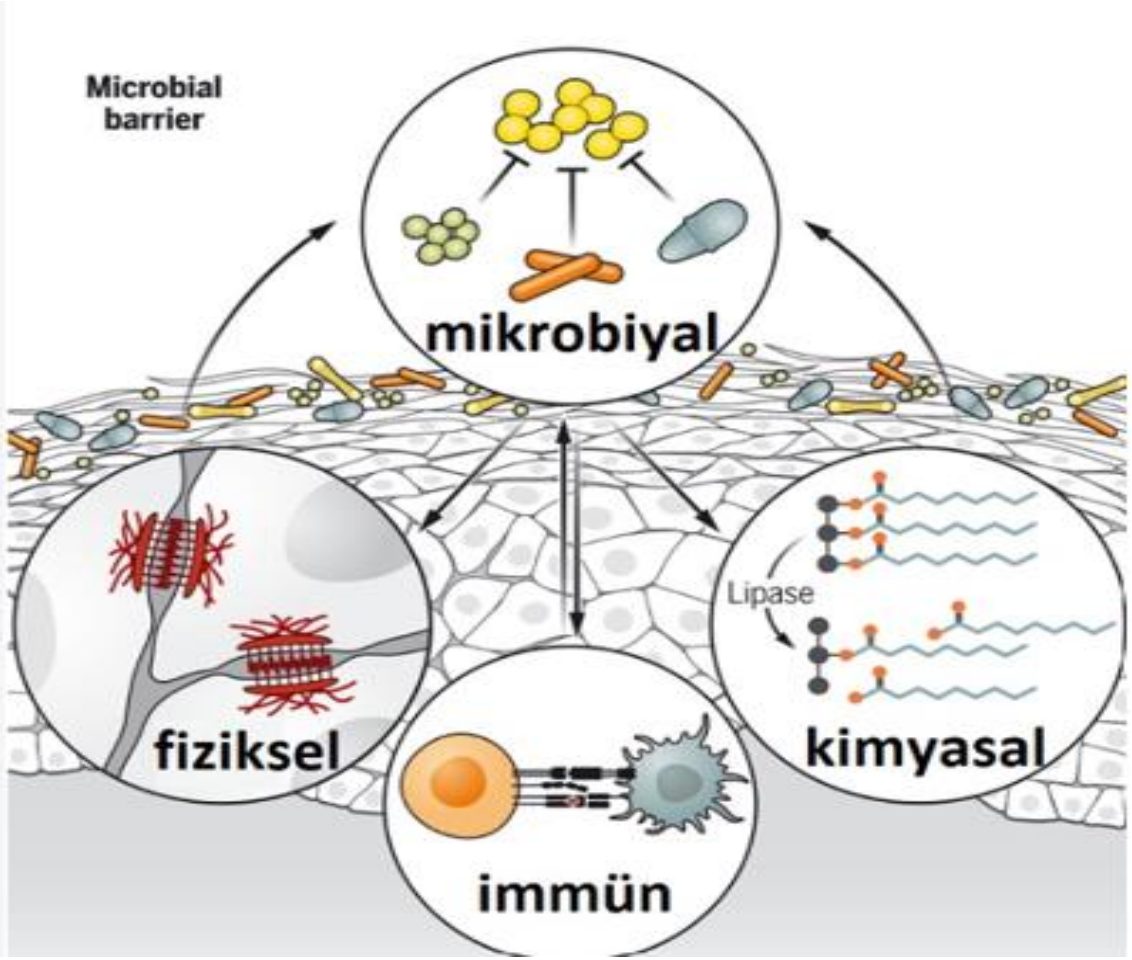
Deri bariyer bozukluğu ve deri disbiosisi ile ilişkili

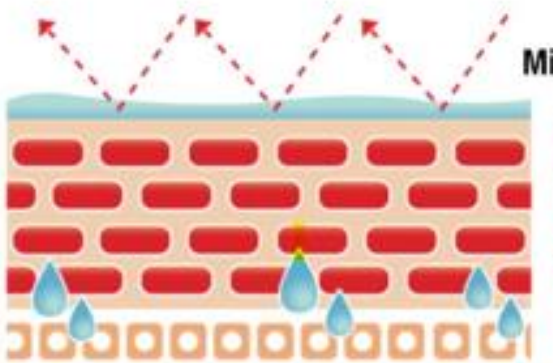
- İÇTEN DIŞA HİPOTEZ

Sistemik inflamasyon ve bağırsak disbiosisi ile ilişkili

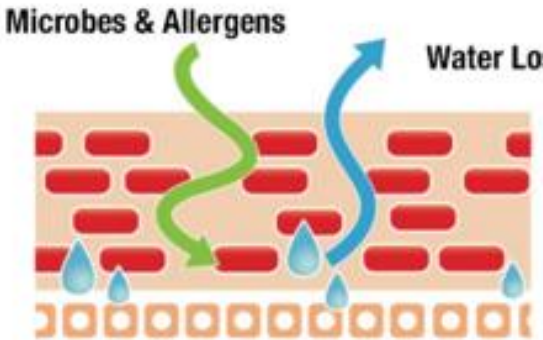
Derinin Koruyucu Bariyerleri

- Stratum Corneum
- Lipit Bariyeri
- pH Bariyeri (4.5 -5.5)
- Mikrobiyom
- Bağışıklık Bariyeri



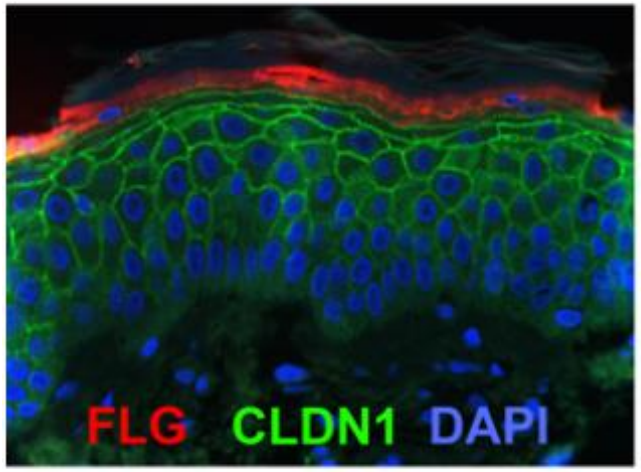


Healthy
Skin Barrier



Dysfunctional
Skin Barrier

GEÇİRGEN DERİ

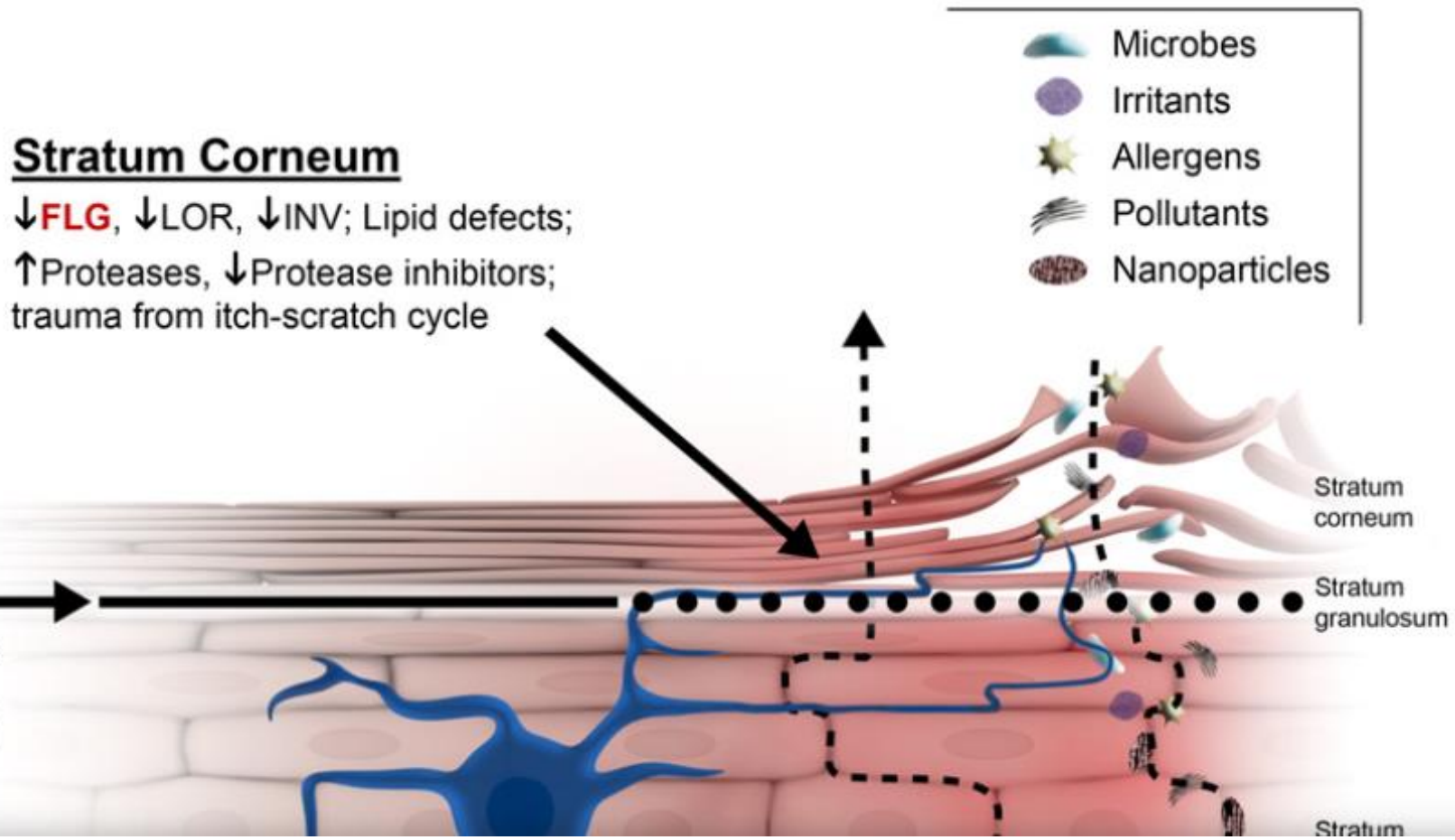


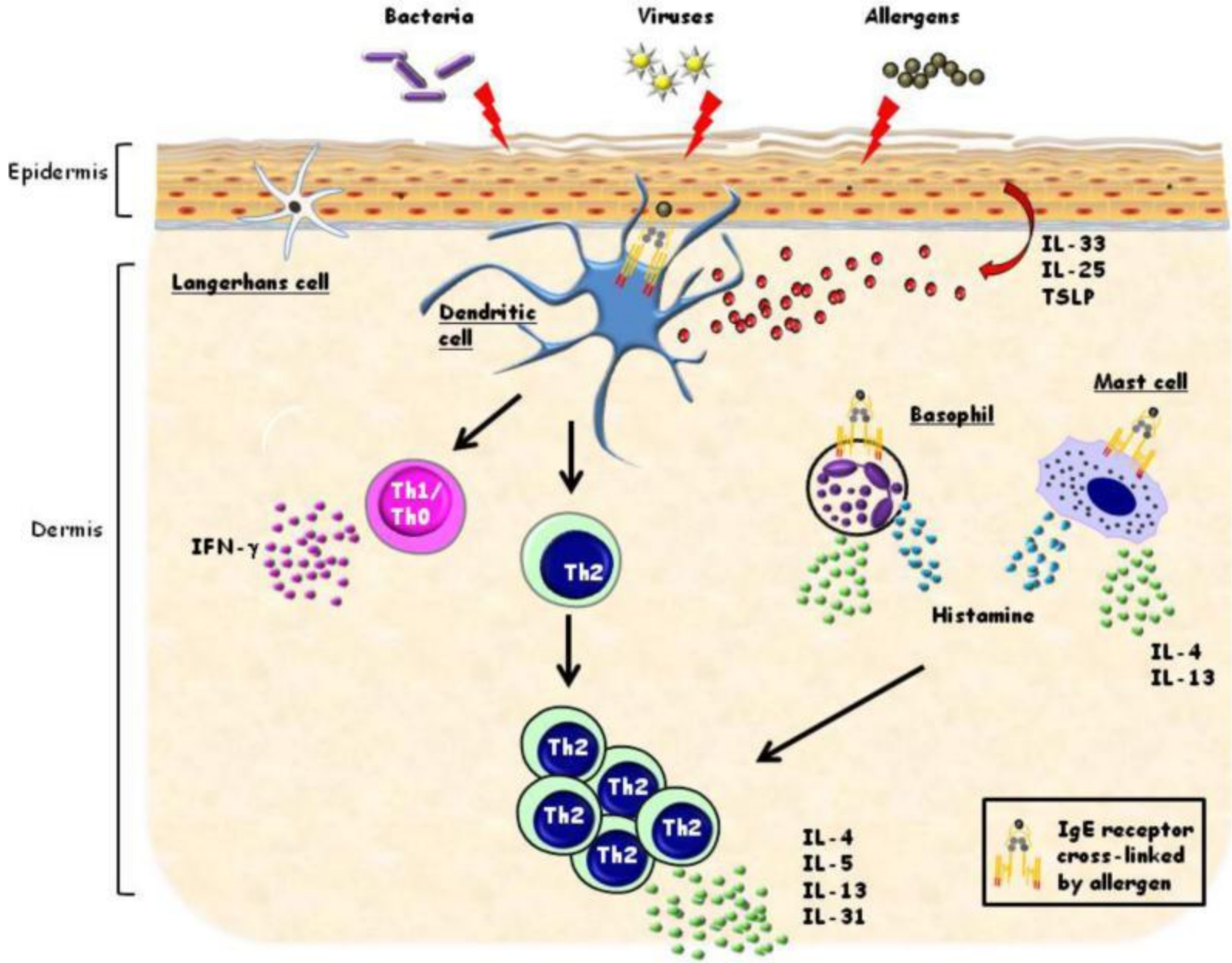
Stratum Corneum

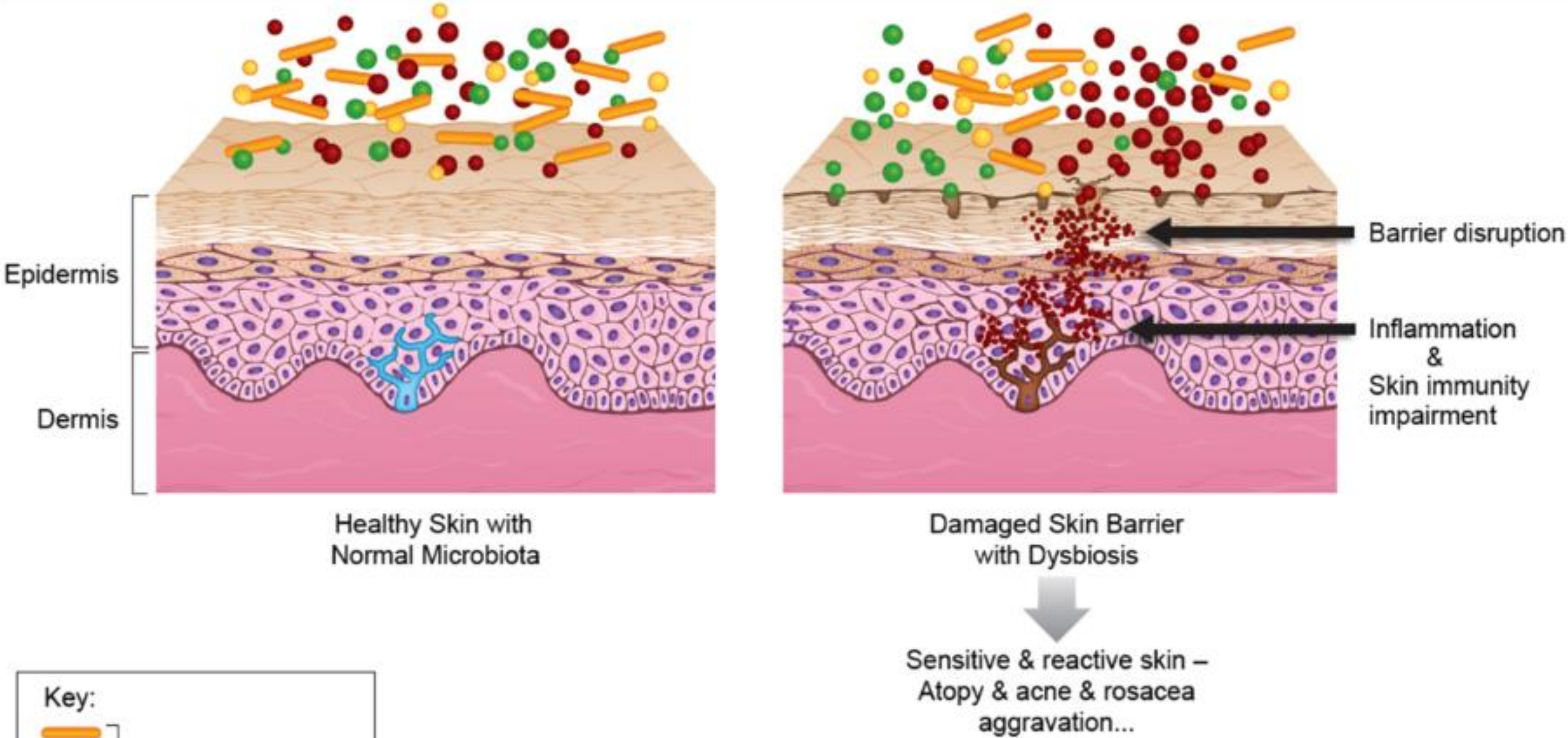
↓FLG, ↓LOR, ↓INV; Lipid defects;
↑Proteases, ↓Protease inhibitors;
trauma from itch-scratch cycle

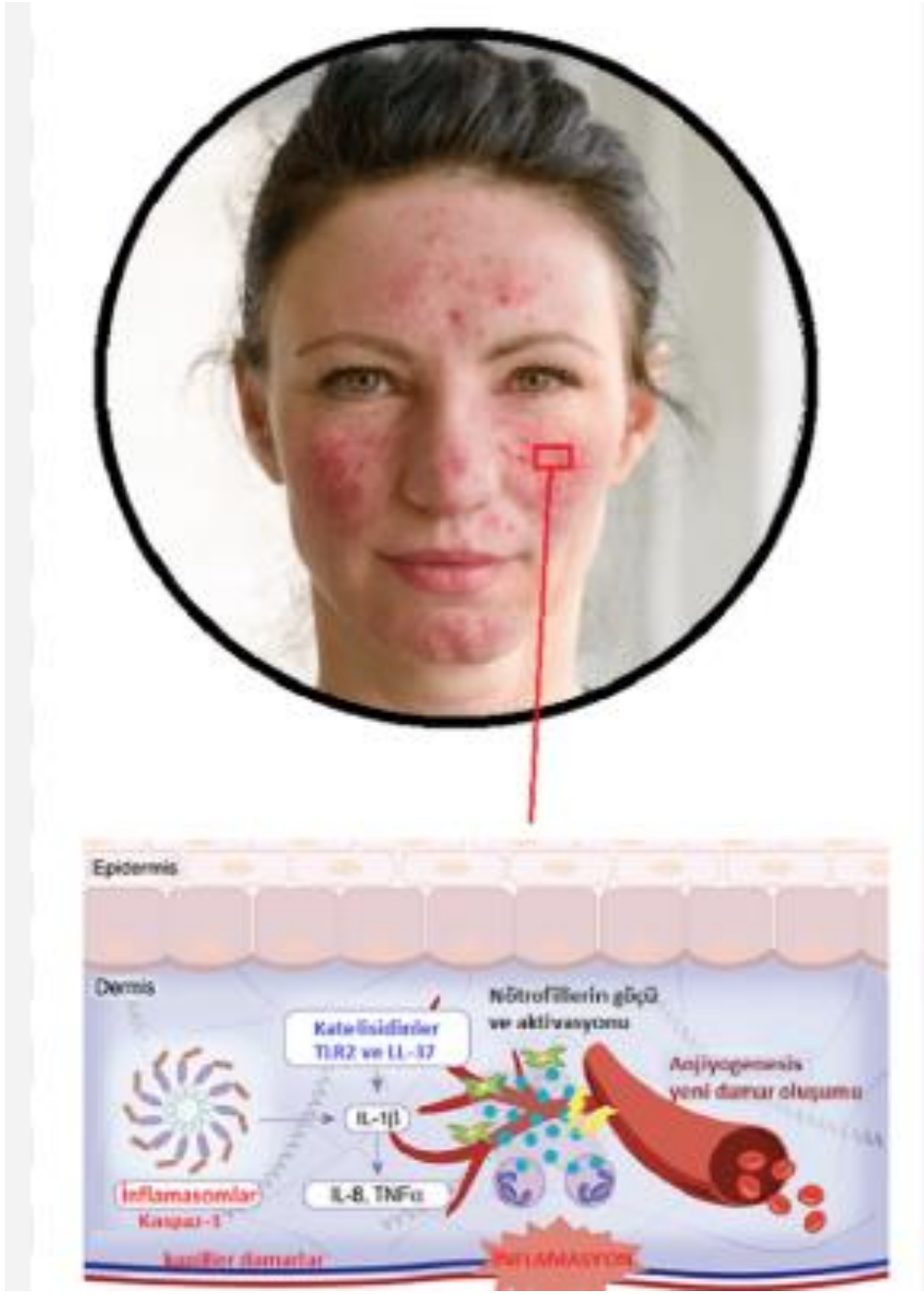
Tight Junction

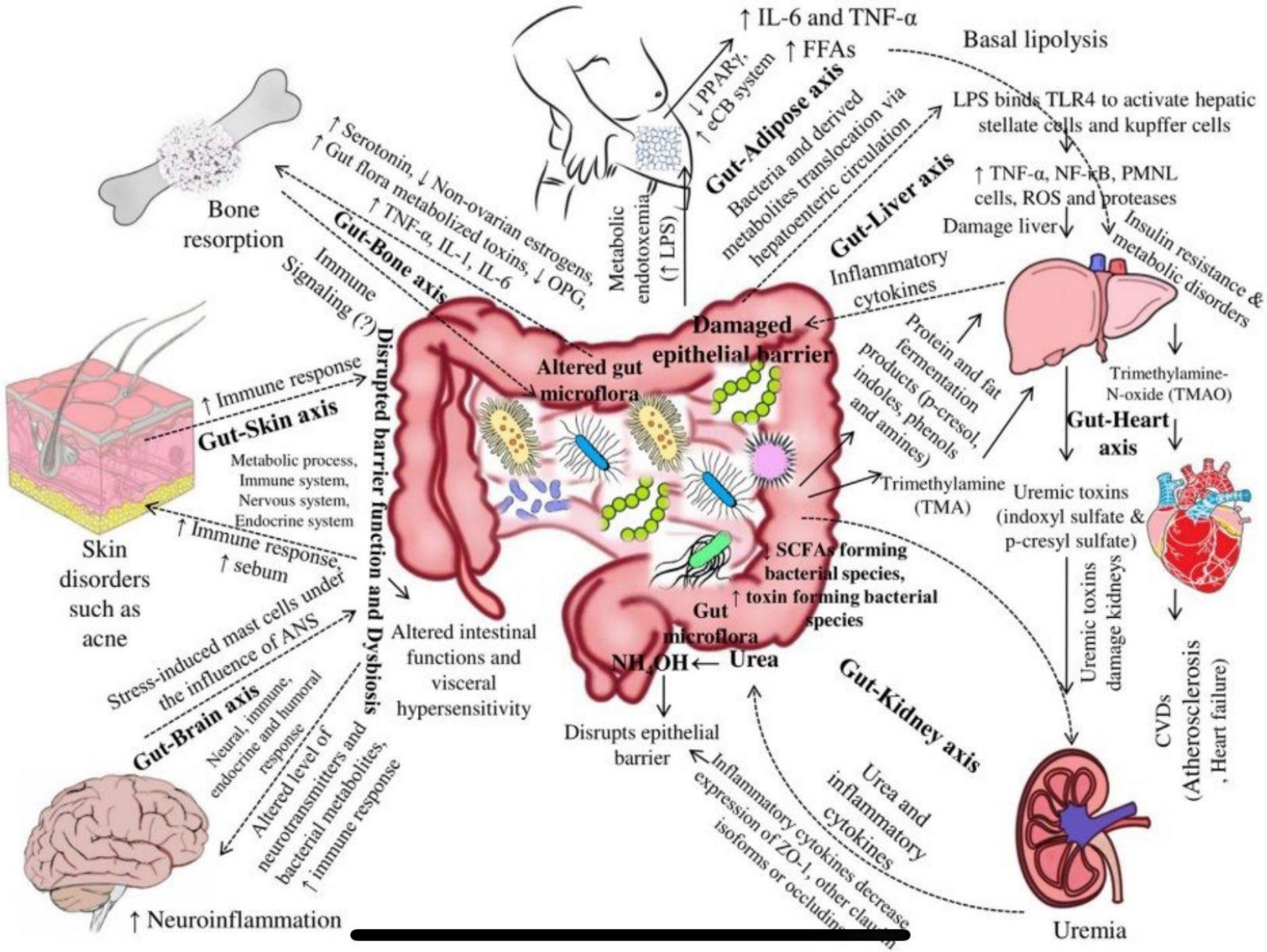
↓CLDN1,
Cleavage of TJ proteins by proteases
(endogenous, allergen-associated,
microbe-associated)

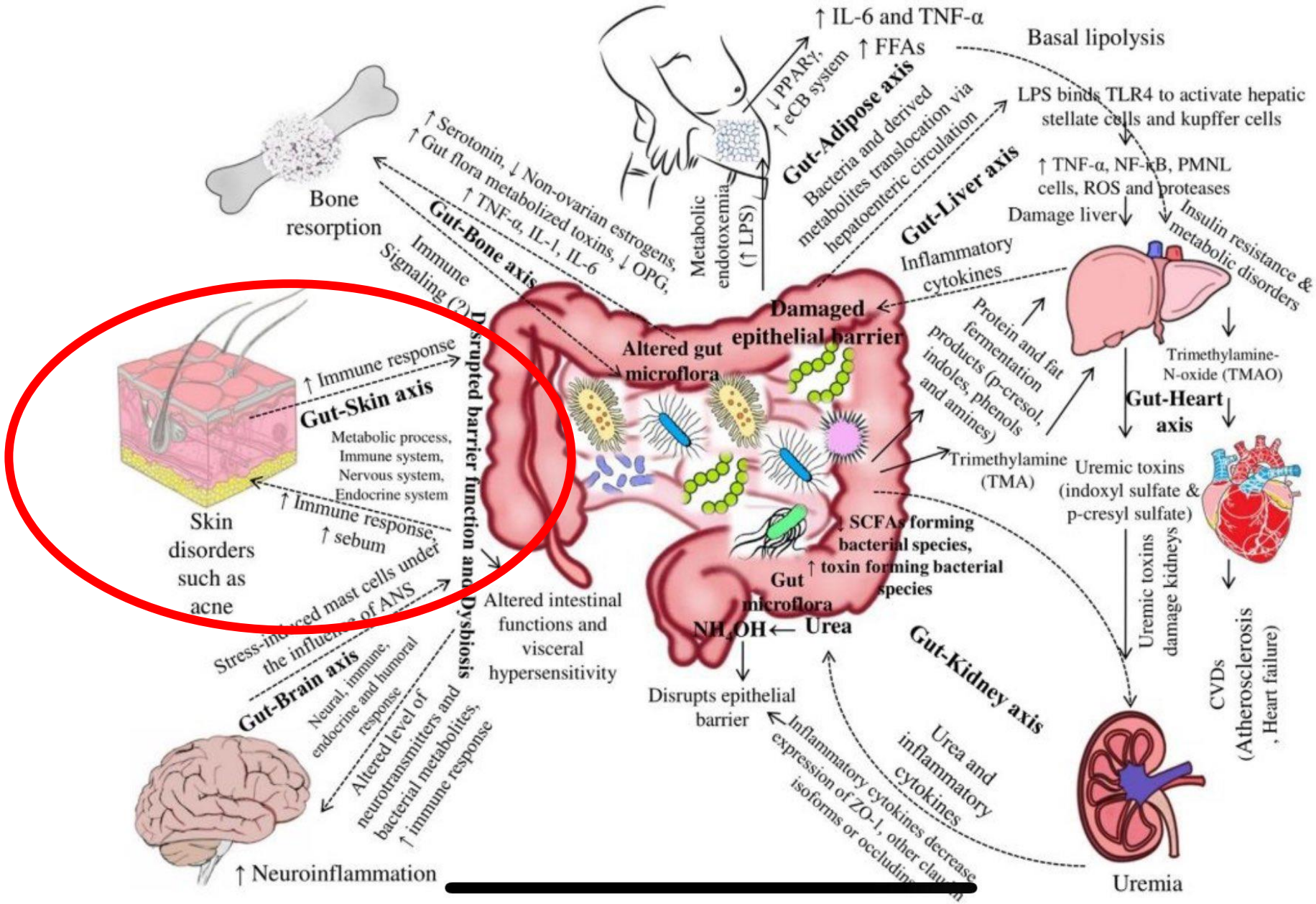


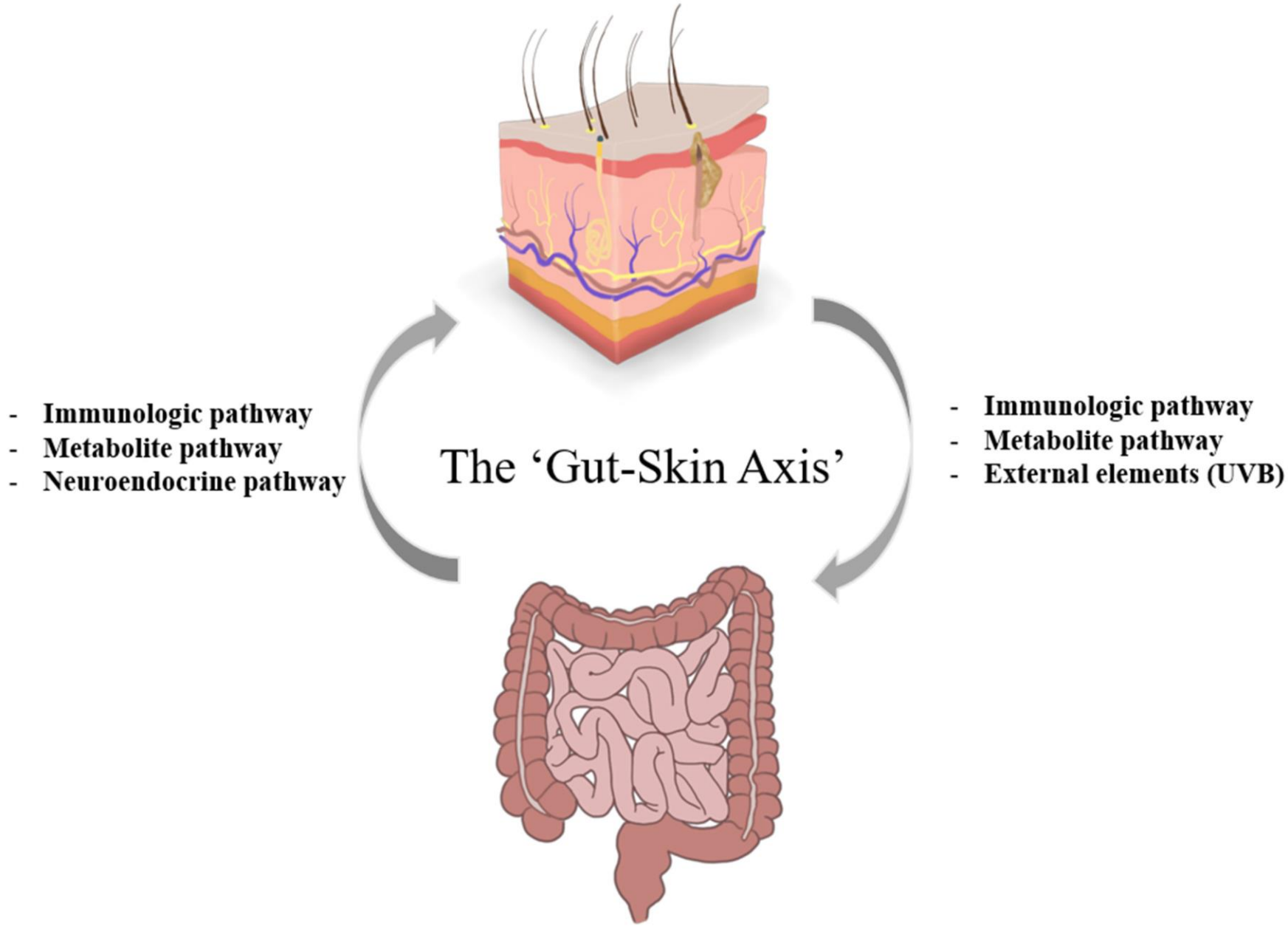

Bacteria
Viruses
Allergens
Epidermis
Dermis
Langerhans cell
Dendritic cell
IL-33
IL-25
TSLP
Th1/ Th0
IFN-γ
Th2
Basophil
Mast cell
Histamine
IL-4
IL-13
Th2
Th2
Th2
Th2
Th2
IL-4
IL-5
IL-13
IL-31
IgE receptor cross-linked by allergen

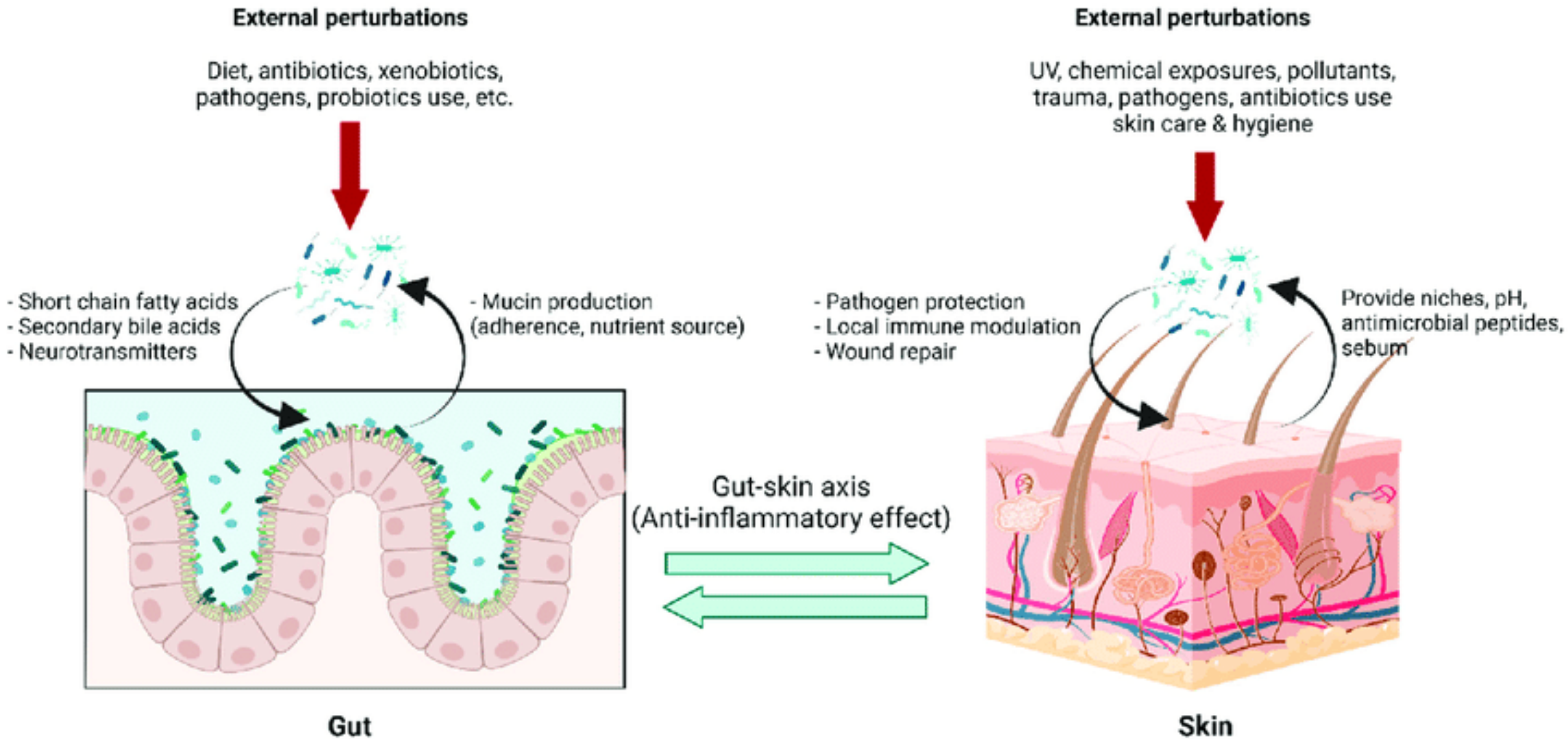

Epidermis
Dermis
Barrier disruption
Inflammation
&
Skin immunity
impairment
Healthy Skin with
Normal Microbiota
Damaged Skin Barrier
with Dysbiosis
Sensitive & reactive skin –
Atopy & acne & rosacea
aggravation...
Key:
Commensals
Pathogenic Bacteria

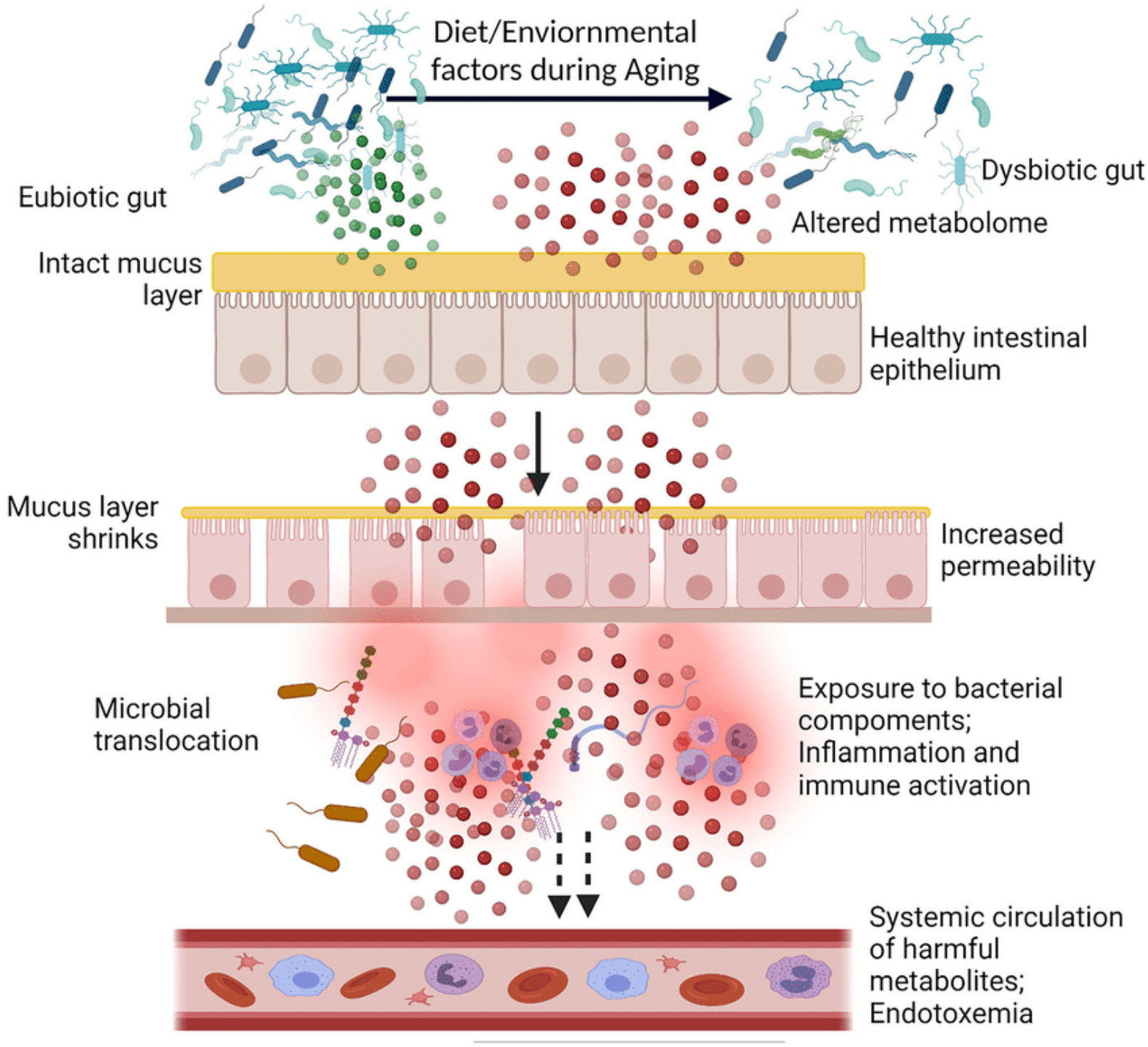

Epidermis
Dermis
Nötrofillerin göçü
ve aktivasyonu
Katelisidinler
TLR2 ve IL-17
IL-1β
İnflamasomlar
Kaspaz-1
IL-8, TNFα
Anjiyogenesis
yeni damar oluşumu
İNFLAMASYON


↑ IL-6 and TNF-α
↑ FFAs
Basal lipolysis
↓ PPARγ, ↑ eCB system
Gut-Adipose axis
Bacteria and derived metabolites translocation via hepatoenteric circulation
Metabolic endotoxemia (↑ LPS)
LPS binds TLR4 to activate hepatic stellate cells and kupffer cells
↑ TNF-α, NF-κB, PMNL cells, ROS and proteases
Damage liver
Insulin resistance & metabolic disorders
Gut-Liver axis
Inflammatory cytokines
Bone resorption
↑ Serotonin, ↓ Non-ovarian estrogens, ↑ Gut flora metabolized toxins, ↓ OPG, ↑ TNF-α, IL-1, IL-6
Gut-Bone axis
Immune Signaling (?)
Damaged epithelial barrier
Altered gut microflora
Protein and fat fermentation products (p-cresol, indoles, phenols and amines)
Trimethylamine-N-oxide (TMAO)
Gut-Heart axis
↑ Immune response
Gut-Skin axis
Metabolic process, Immune system, Nervous system, Endocrine system
↑ Immune response, ↑ sebum
Skin disorders such as acne
Disrupted barrier function and Dysbiosis
Trimethylamine (TMA)
Uremic toxins (indoxyl sulfate & p-cresyl sulfate)
↓ SCFAs forming bacterial species, ↑ toxin forming bacterial species
Gut microflora
Altered intestinal functions and visceral hypersensitivity
Stress-induced mast cells under the influence of ANS
Gut-Brain axis
Neural, immune, endocrine and humoral response
Altered level of neurotransmitters and bacterial metabolites, ↑ immune response
NH4OH ← Urea
Disrupts epithelial barrier
Gut-Kidney axis
Uremic toxins damage kidneys
CVDs (Atherosclerosis, Heart failure)
Urea and inflammatory cytokines
Inflammatory cytokines decrease expression of ZO-1, other claudin isoforms or occludin
↑ Neuroinflammation
Uremia

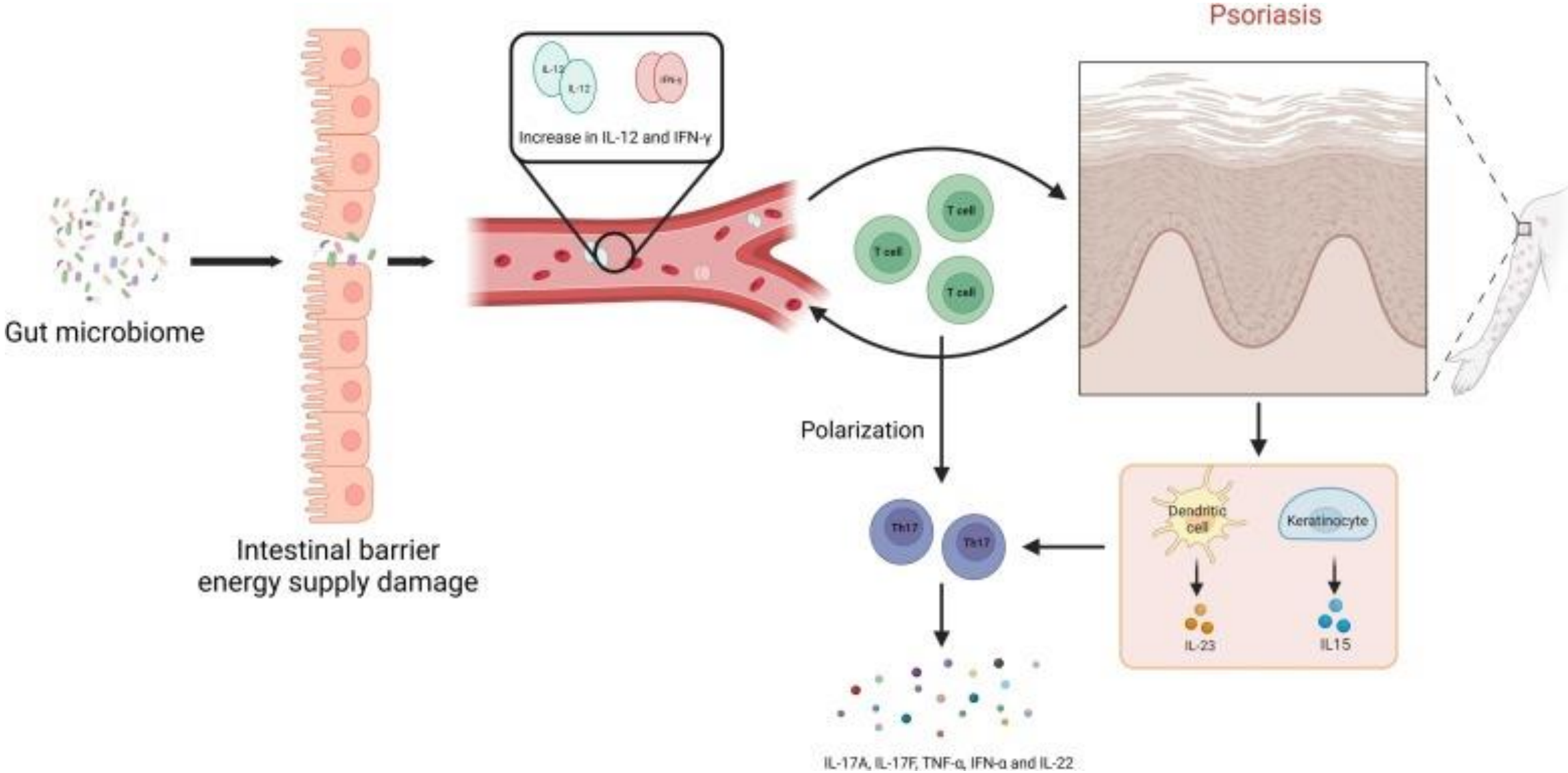

↑ IL-6 and TNF-α
↑ FFAs
Basal lipolysis
↓ PPARγ, ↑ eCB system
Gut-Adipose axis
Bacteria and derived metabolites translocation via hepatoenteric circulation
Metabolic endotoxemia (↑ LPS)
LPS binds TLR4 to activate hepatic stellate cells and kupffer cells
↑ TNF-α, NF-κB, PMNL cells, ROS and proteases
Damage liver
Gut-Liver axis
Insulin resistance & metabolic disorders
Inflammatory cytokines
Bone resorption
↑ Serotonin, ↓ Non-ovarian estrogens, ↑ Gut flora metabolized toxins, ↓ OPG, ↑ TNF-α, IL-1, IL-6
Gut-Bone axis
Immune Signaling (?)
Damaged epithelial barrier
Altered gut microflora
Protein and fat fermentation products (p-cresol, indoles, phenols and amines)
Trimethylamine-N-oxide (TMAO)
Gut-Heart axis
↑ Immune response
Gut-Skin axis
Metabolic process, Immune system, Nervous system, Endocrine system
↑ Immune response, ↑ sebum
Skin disorders such as acne
Trimethylamine (TMA)
Uremic toxins (indoxyl sulfate & p-cresyl sulfate)
↓ SCFAs forming bacterial species, ↑ toxin forming bacterial species
Gut microflora
Altered intestinal functions and visceral hypersensitivity
Disrupted barrier function and Dysbiosis
Stress-induced mast cells under the influence of ANS
Gut-Brain axis
Neural, immune, endocrine and humoral response
Altered level of neurotransmitters and bacterial metabolites, ↑ immune response
NH4OH ← Urea
Gut-Kidney axis
Uremic toxins damage kidneys
CVDs (Atherosclerosis, Heart failure)
Disrupts epithelial barrier
Inflammatory cytokines decrease expression of ZO-1, other claudin isoforms or occludin
Urea and inflammatory cytokines
↑ Neuroinflammation
Uremia


- Immunologic pathway
- Metabolite pathway
- Neuroendocrine pathway
The ‘Gut-Skin Axis’
- Immunologic pathway
- Metabolite pathway
- External elements (UVB)

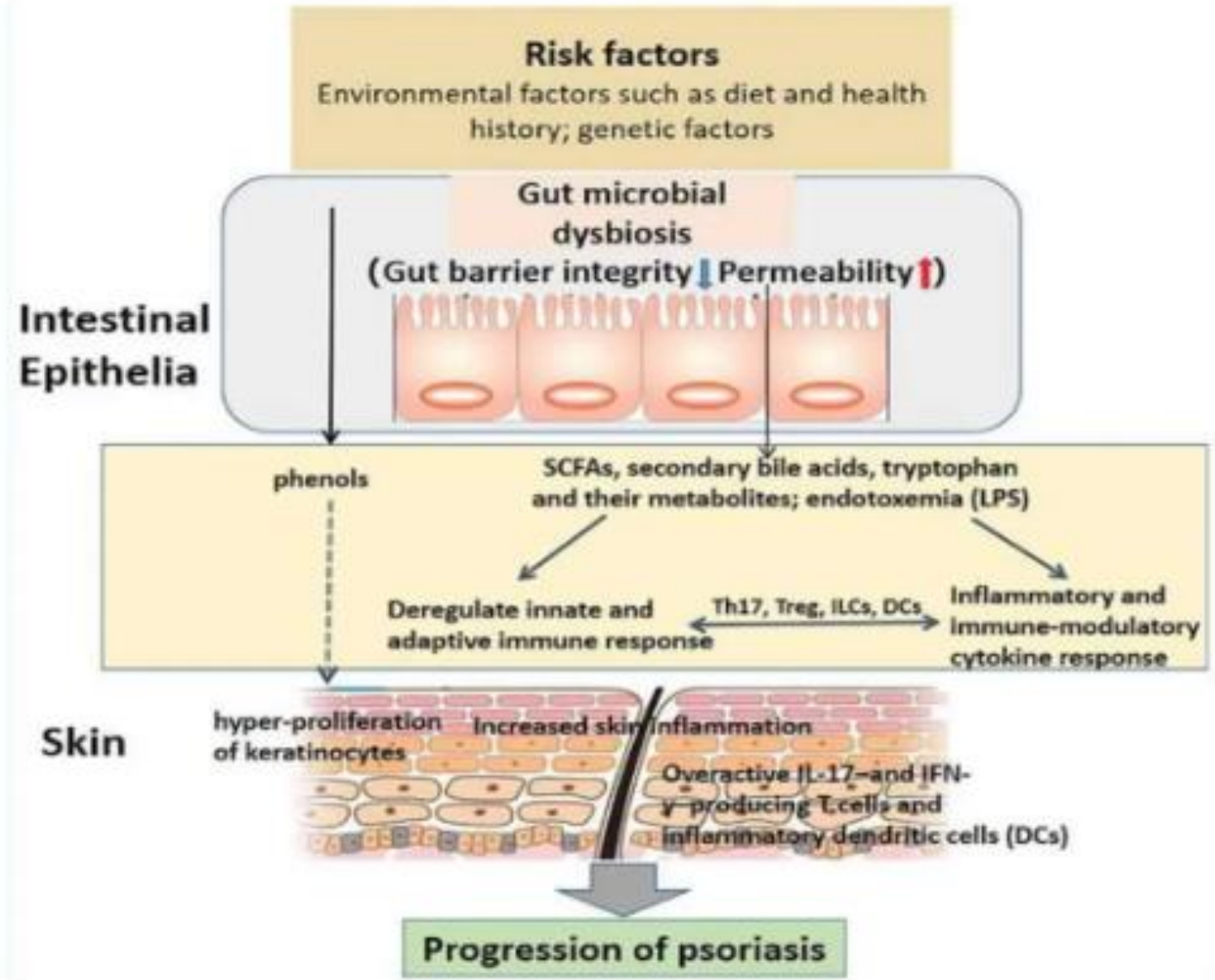

External perturbations
Diet, antibiotics, xenobiotics, pathogens, probiotics use, etc.
- Short chain fatty acids
- Secondary bile acids
- Neurotransmitters
- Mucin production (adherence, nutrient source)
Gut
Gut-skin axis (Anti-inflammatory effect)
External perturbations
UV, chemical exposures, pollutants, trauma, pathogens, antibiotics use skin care & hygiene
- Pathogen protection
- Local immune modulation
- Wound repair
Provide niches, pH, antimicrobial peptides, sebum
Skin

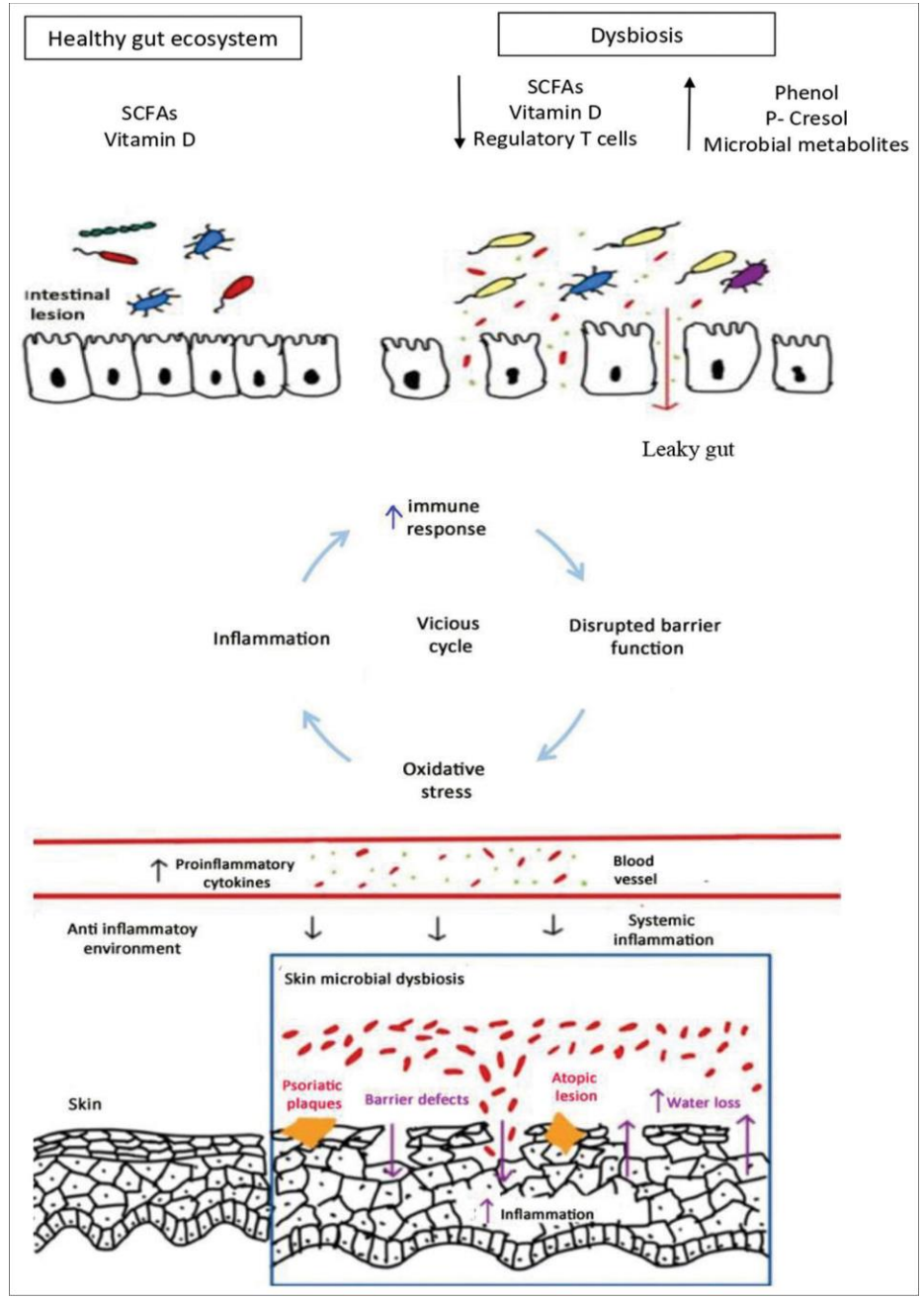

Diet/Enviornmental factors during Aging
Eubiotic gut
Dysbiotic gut
Altered metabolome
Intact mucus layer
Healthy intestinal epithelium
Mucus layer shrinks
Increased permeability
Microbial translocation
Exposure to bacterial compoments; Inflammation and immune activation
Systemic circulation of harmful metabolites; Endotoxemia

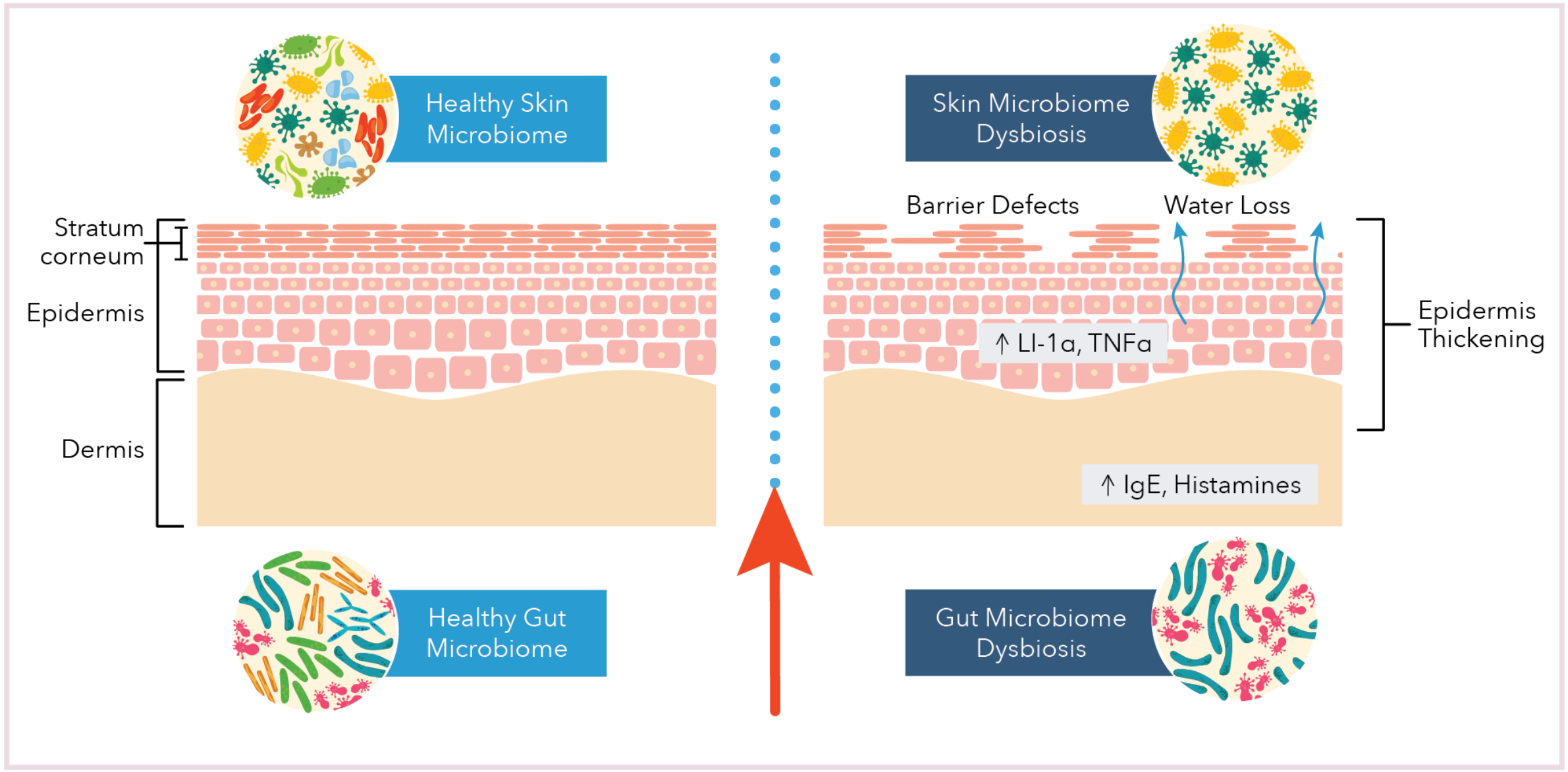
- BAĞIRSAK MİKROBİYOTA DENGESİZLİKLERİ
- GEÇİRGEN BAĞIRSAK
- KRONİK İNFLAMASYON (YANGI)
- BAĞIŞIKLIK SİSTEMİNİN ANORMAL YANITI (OTOİMMUNİTE, ALERJİK REAKSİYON)


Psoriasis
Increase in IL-12 and IFN-γ
Gut microbiome
Intestinal barrier
energy supply damage
T cell
T cell
T cell
Polarization
Th17
Th17
Dendritic cell
Keratinocyte
IL-23
IL15
IL-17A, IL-17F, TNF-α, IFN-α and IL-22

Gut –Skin Axis and Pathogenesis of psoriasis

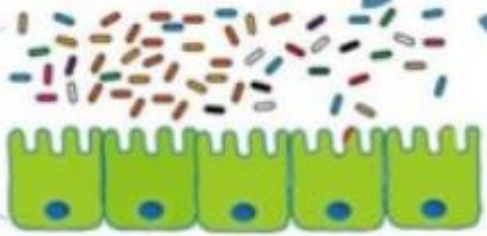



Healthy gut ecosystem
Dysbiosis
SCFAs
Vitamin D
SCFAs
Vitamin D
Regulatory T cells
Phenol
P- Cresol
Microbial metabolites
Intestinal lesion
Leaky gut
immune response
Disrupted barrier function
Oxidative stress
Inflammation
Vicious cycle
Proinflammatory cytokines
Blood vessel
Anti inflammatoy environment
Systemic inflammation
Skin microbial dysbiosis
Skin
Psoriatic plaques
Barrier defects
Atopic lesion
Water loss
Inflammation

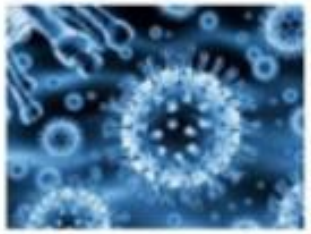

Healthy Skin Microbiome
Skin Microbiome Dysbiosis
Barrier Defects
Water Loss
Stratum corneum
Epidermis
Dermis
↑ Ll-1a, TNFa
Epidermis Thickening
↑ IgE, Histamines
Healthy Gut Microbiome
Gut Microbiome Dysbiosis

Immunomodulation

Gut microbiota homeostasis



Digestion and absorption of nutrients



Resistance to pathogens

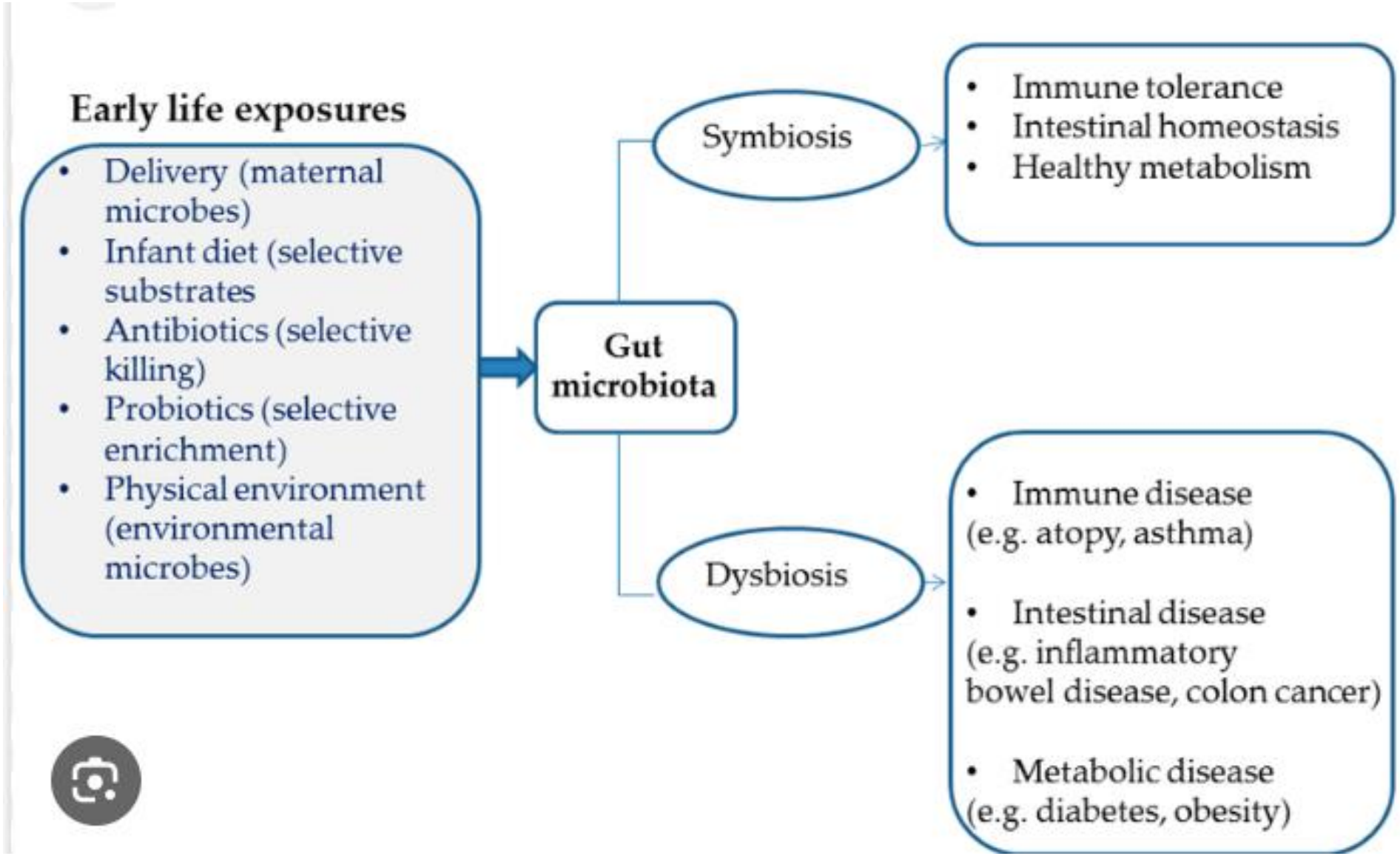
Intestinal mucosal barrier

İMMUNMODÜLASYON

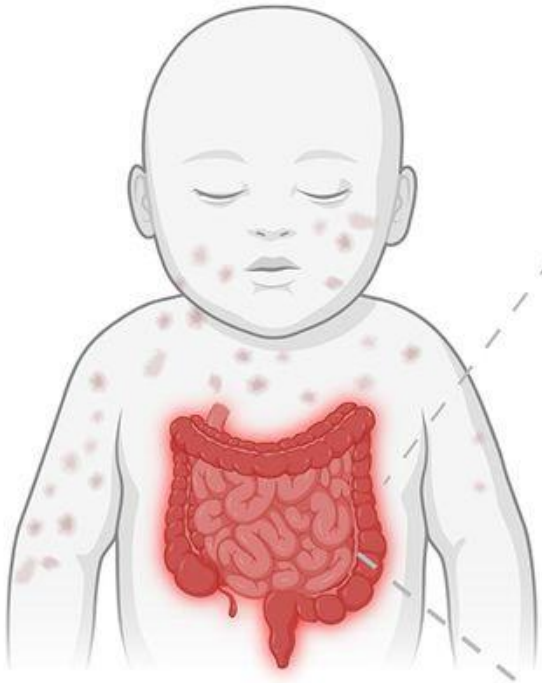
- Bağışıklık sisteminin programlanması

(zararsız antijenlere karşı **tolerans gelişmesinde** önemli)

- Uzak organdaki immun yanıtı da etkilemekte
- T hücrelerinin hangi tarafa yöneleceği genetik yatkınlık ve mikrobiyom ile düzenlenmekte (özellikle ilk 1000 gün önemli)
- Bağırsak disbiosisi, konakçı hassasiyetini artırabilir ve mukozal immünolojik toleransı bozabilir, bu durum da alerjik hastalıklara zemin hazırlayabilir


Early life exposures
Delivery (maternal microbes)
Infant diet (selective substrates
Antibiotics (selective killing)
Probiotics (selective enrichment)
Physical environment (environmental microbes)
Gut microbiota
Symbiosis
Immune tolerance
Intestinal homeostasis
Healthy metabolism
Dysbiosis
Immune disease (e.g. atopy, asthma)
Intestinal disease (e.g. inflammatory bowel disease, colon cancer)
Metabolic disease (e.g. diabetes, obesity)

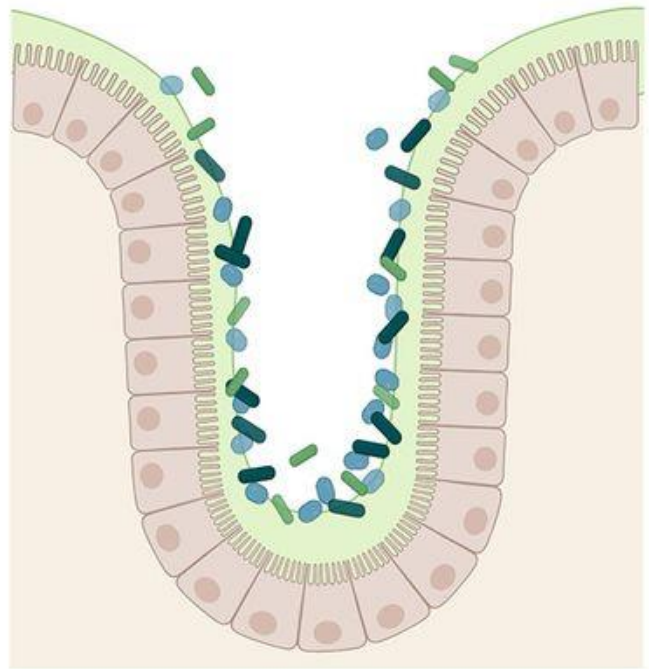
Relationship between gut microbiome and infantile atopic dermatitis



Infant

Up to 12 months of age

Changes in the gut microbiome



Bacteria with elevated abundance

Enterobacteriaceae:
Escherichia/Shigella
Klebsiella
Enterobacter

Bacteria with decreased abundance

Akkermansiaceae:
Akkermansia muciniphila
Lachnospiraceae:
Coprococcus


Bağırsaklarınızın
söyleyemediğini
Cildiniz
söyler!

KAYNAKLAR

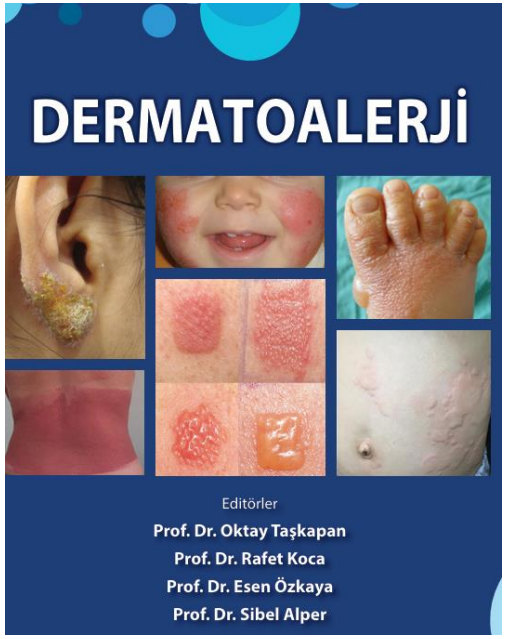
Review > Microorganisms. 2021 Feb 11;9(2):353. doi: 10.3390/microorganisms9020353.

Gut–Skin Axis: Current Knowledge of the Interrelationship between Microbial Dysbiosis and Skin Conditions

Britta De Pessemier [1], Lynda Grine [2], Melanie Debaere [1], Aglaya Maes [1], Bernhard Paetzold [3], Chris Callewaert [1]

Affiliations + expand

PMID: 33670115 PMCID: PMC7916842 DOI: 10.3



Deri-Bağırsak-Akciğer Epitel Geçirgenliği

Yana Kost , ... Vivian Y. Shi , içinde Atopik Dermatit: İçeriden Dışarıya mı, Dışarıdan İçeriye mi?, 2023

Cilt geçirgenliği

Epidermal bariyer, stratum korneum ve sıkı bağlantılardan (TJ) oluşur ( ). Atopik dermatitte epidermal bariyer bozukluğu, değişen lipid bileşimi , işlevsiz ve azalmış yapısal proteinler, artan cilt pH'ı ve azalmış cilt mikrobiyom çeşitliliğinden kaynaklanabilir . Cilt geçirgenliği kusurları, hastalığın şiddetiyle ilişkili olan transepidermal su kaybının ölçülmesiyle değerlendirilebilir (Baldwin, Bhatia, Friedman, Eng ve Seite, 2017 Hon, Leung ve Barankin, 2013 ; Weidinger ve Novak, 2016).

GUT MICROBES
2022, VOL. 14, NO. 1, e2096995 (29 pages)
https://doi.org/10.1080/19490976.2022.2096995

Taylor & Francis
Taylor & Francis Group

REVIEW

OPEN ACCESS Check for updates

Impact of gut microbiome on skin health: gut-skin axis observed through the lenses of therapeutics and skin diseases

Md. Rayhan Mahmud [a], Sharmin Akter [b], Sanjida Khanam Tamanna [b], Lincon Mazumder [b], Israt Zahan Esti [b], Sanchita Banerjee [b], Sumona Akter [b], Md. Rakibul Hasan [b], Mrityunjoy Acharjee [c], Md. Sajjad Hossain [d], and Anna Maria Pirttilä [e]

[a]Department of Production Animal Medicine, Faculty of Veterinary Medicine, University of Helsinki, Helsinki, Finland; [b]Department of Microbiology, Jagannath University, Dhaka, Bangladesh; [c]Department of Bioscience, Graduate School of Science and Technology, Shizuoka University, Shizuoka, Japan; [d]Institute of Biology, Eötvös Loránd University, Budapest, Hungary; [e]Ecology and Genetics, Faculty of Science, University of Oulu, Oulu, Finland

Aile Hekimliğinde
Dermatolojik
Hastalıklara Yaklaşım

Editör: **Doç. Dr. Yasemin Korkut Kurtoğlu**

Türkiye Klinikleri

nutrients

MDPI

Review

The Role of Probiotics in Skin Health and Related Gut–Skin Axis: A Review

Ting Gao, Xiaoyu Wang, Yixuan Li and Fazheng Ren *

- TEŞEKKÜRLER