24. TÜRK KLİNİK MİKROBİYOLOJİ VE İNFEKSİYON HASTALIKLARI KONGRESİ

Simpozyum-25
Mikrobiyatanın Hastalıklardaki Rolü̈

Nörodejeneratif Hastalıklarda Mikrobiyomun Rolü̈

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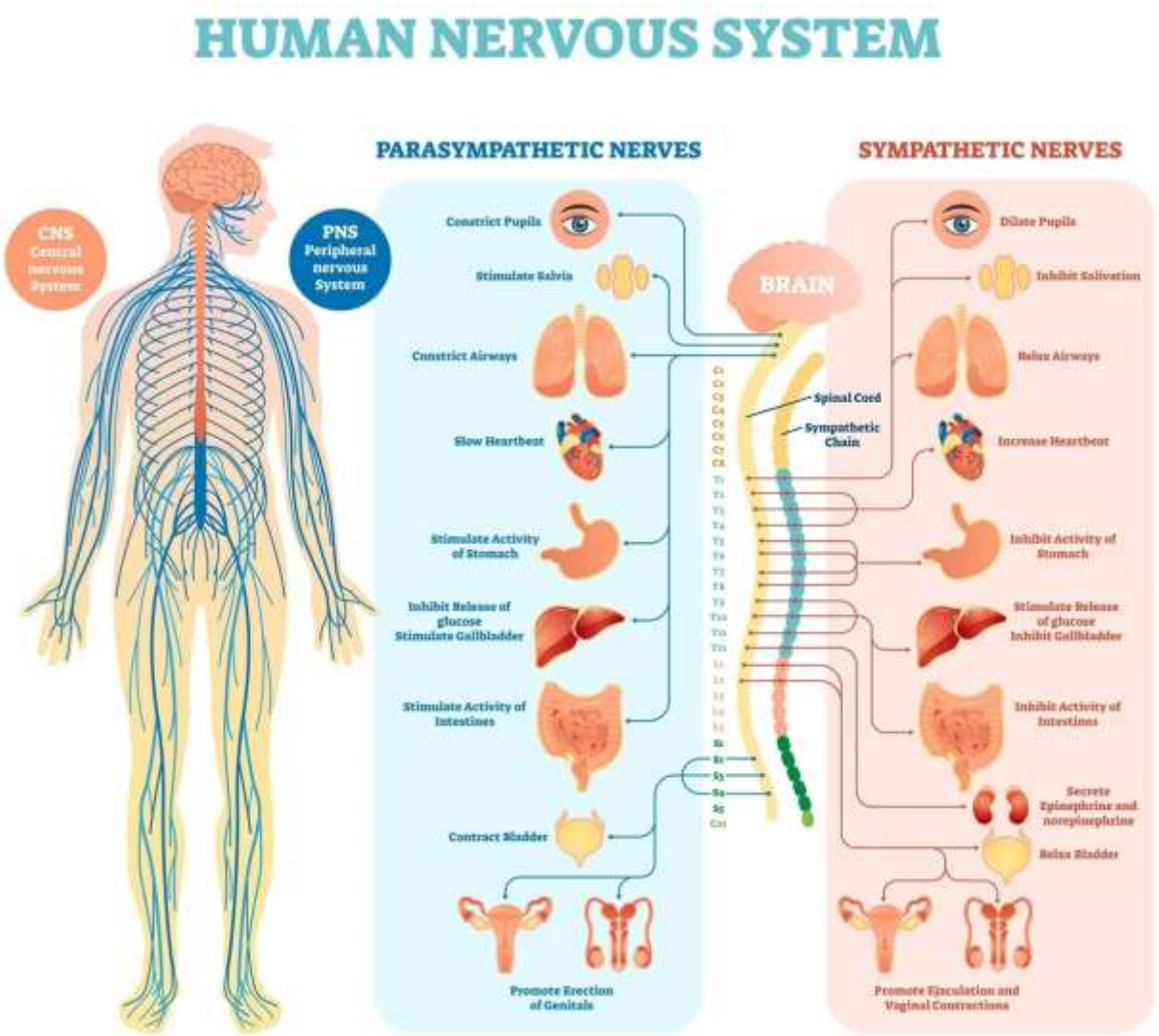
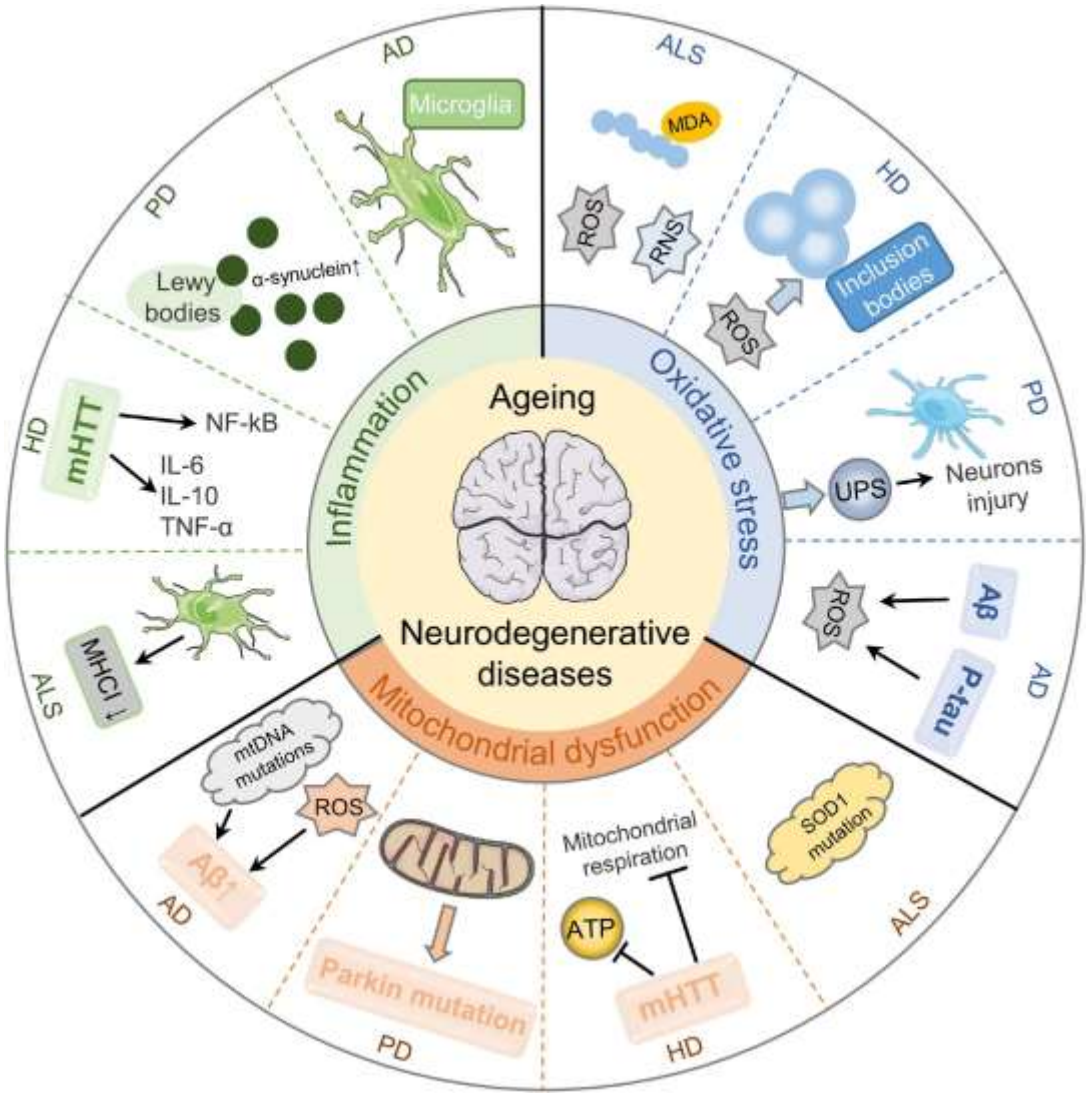
Koç Üniversitesi, Tıp Fakültesi, Tıbbi Mikrobiyoloji Anabilim Dalı,

Koç Üniversitesi, İş Bankası İnfeksiyon Hastalıkları Merkezi (KUISCID)

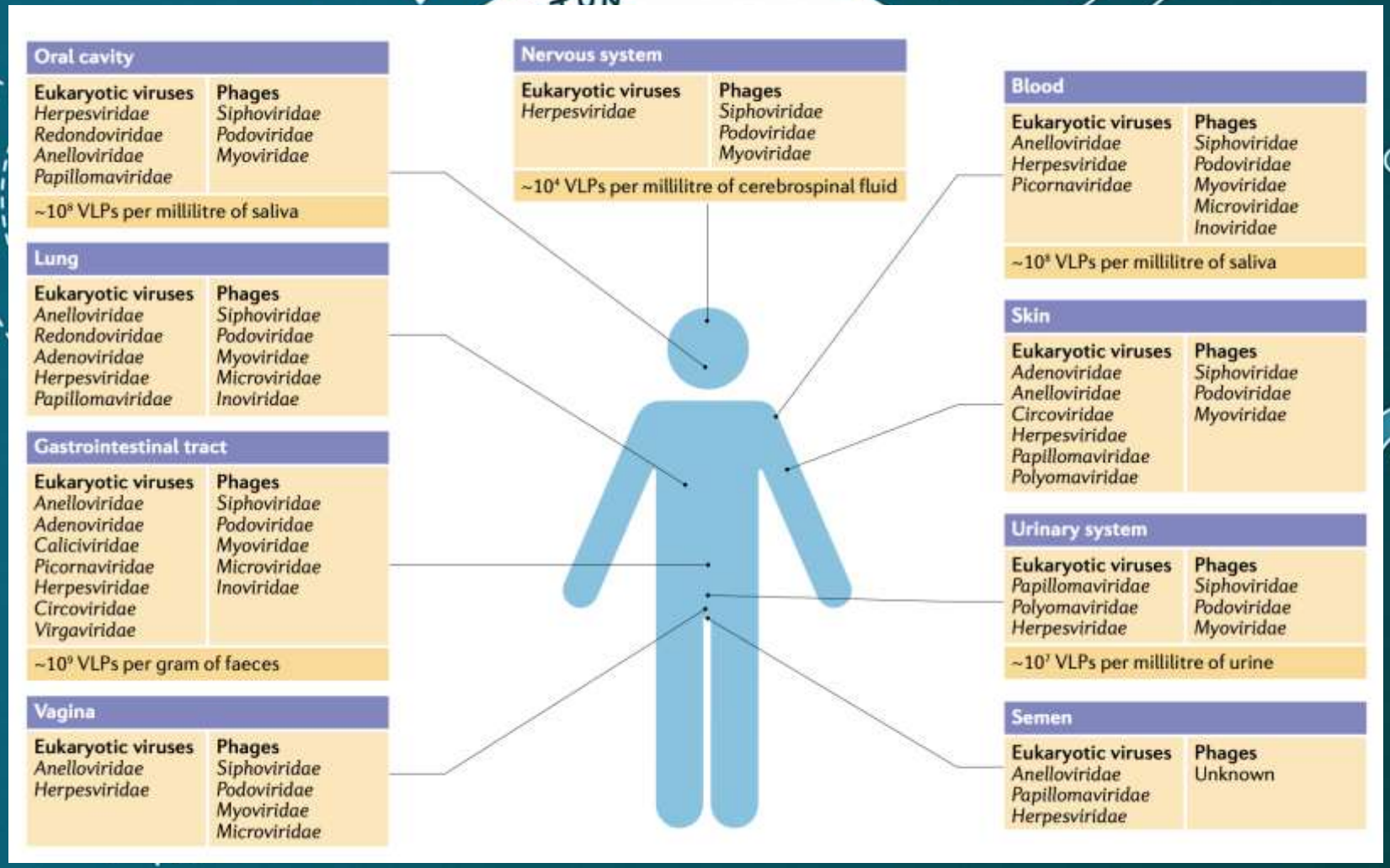
KUISCID

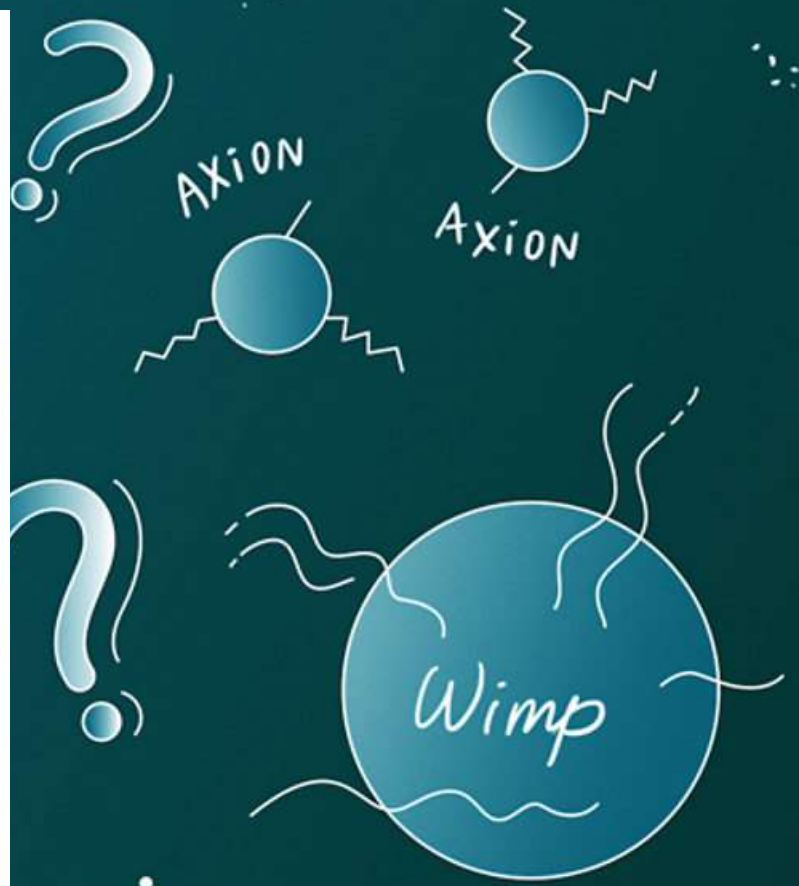
Merkezi Sinir Sistemi ; Nörodejenaratif Hastalıklar



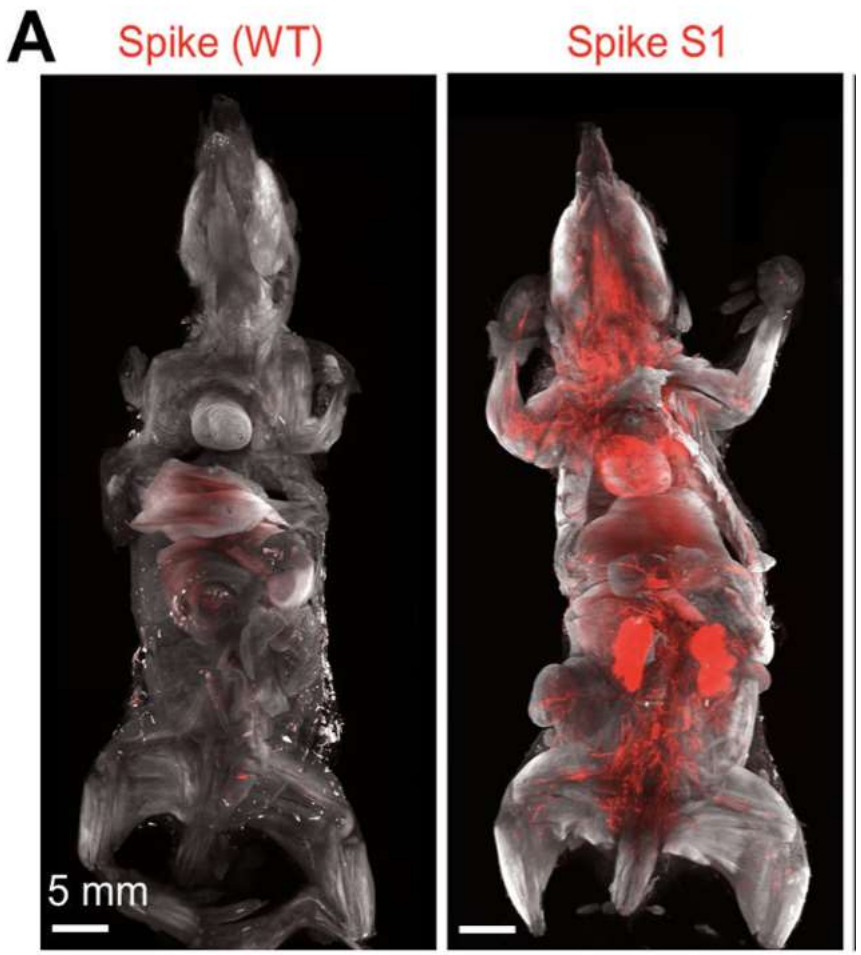


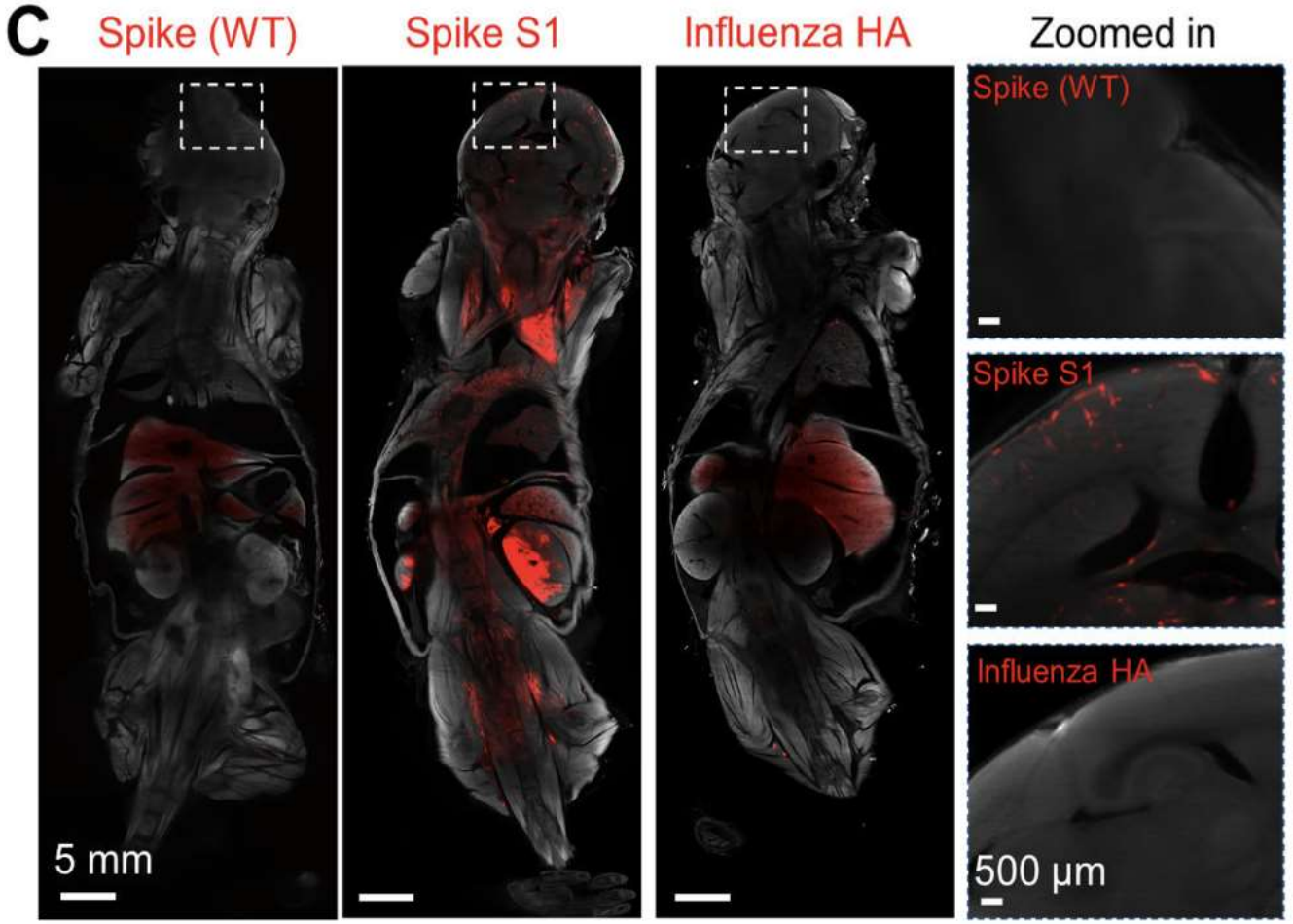
BOS, Steril, Peki ya MSS Florası Var.mı?



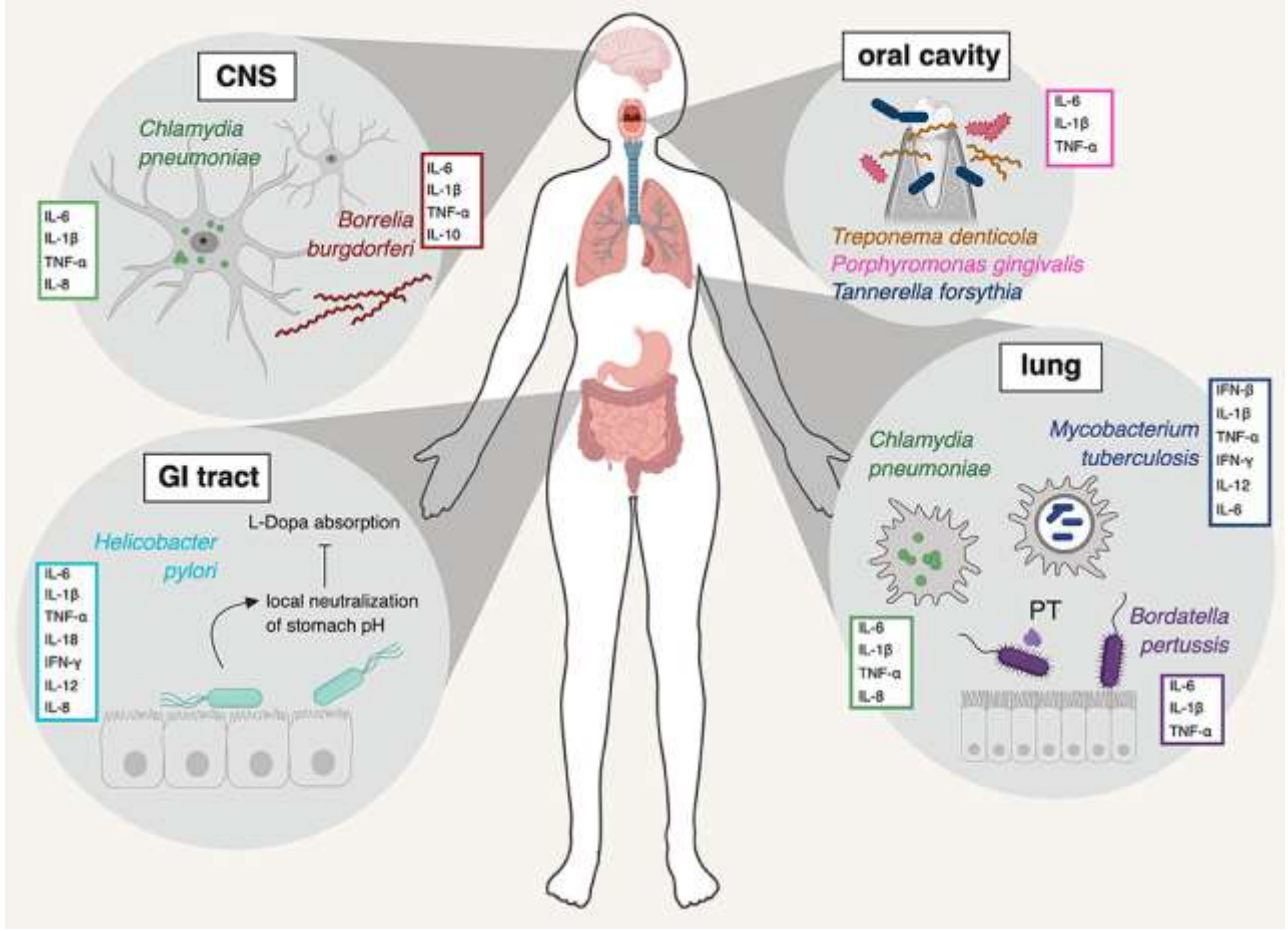


MSS, Mikrobiyota İlişkisi, Buz Dağıın Altı





MSS, Mikrobiyota İlişkisi

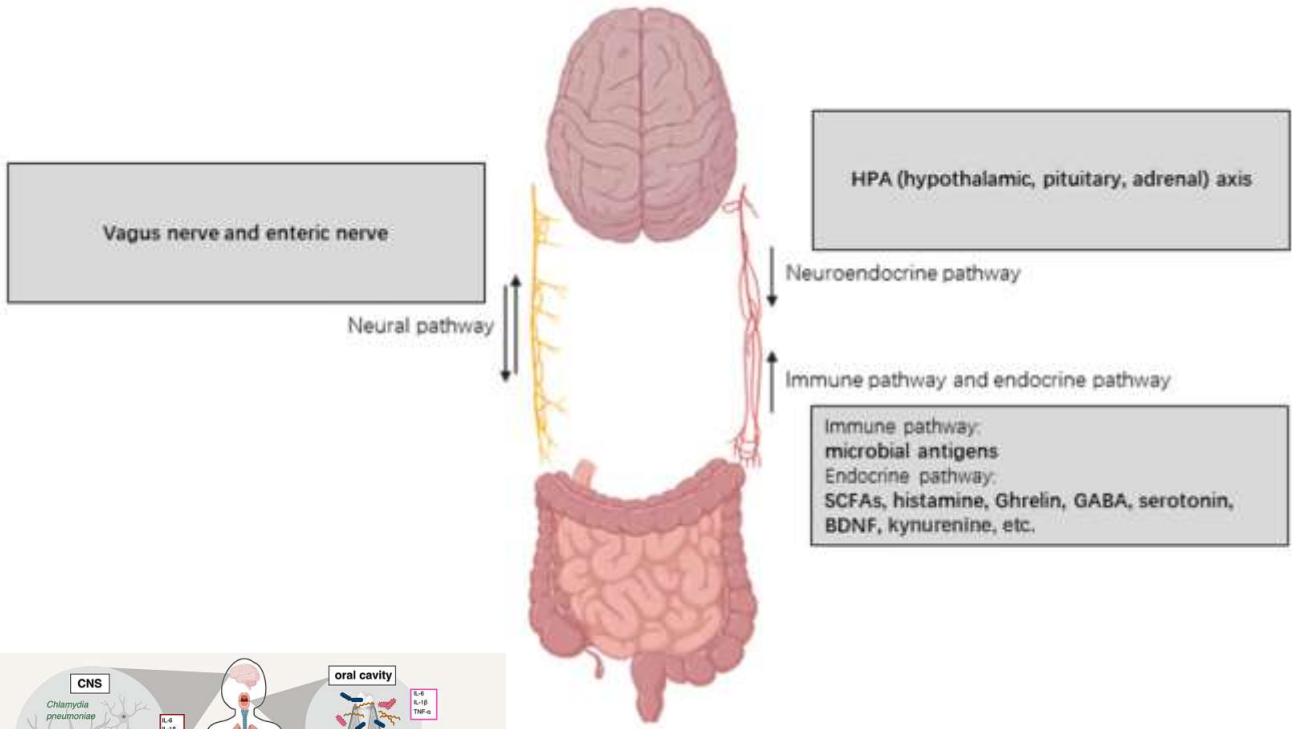


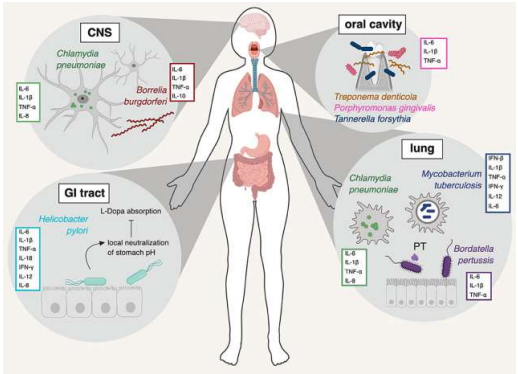
Oksidatif Hasar ve İnflamasyon

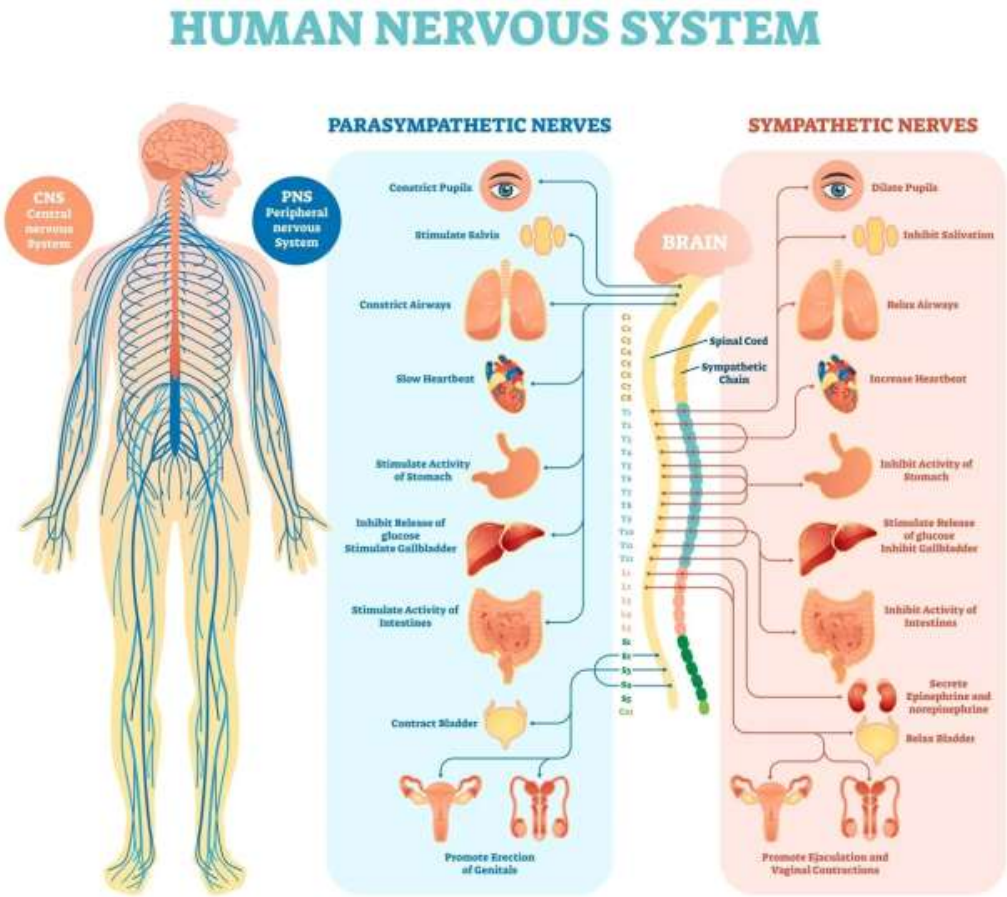
<u>Kolonizasyon-Infeksiyon-Mikrobiyom</u>

- Herpes viruslar
  - CMV
  - EBV
  - VZV, SSPE
  - HSV
- Prionlar
- Norobruselloz
- Norosfiliz
- Noroborelioz ???

MSS, Mikrobiyota İlişkisi;
Beyin - Barsak Aksı ya da Akslar

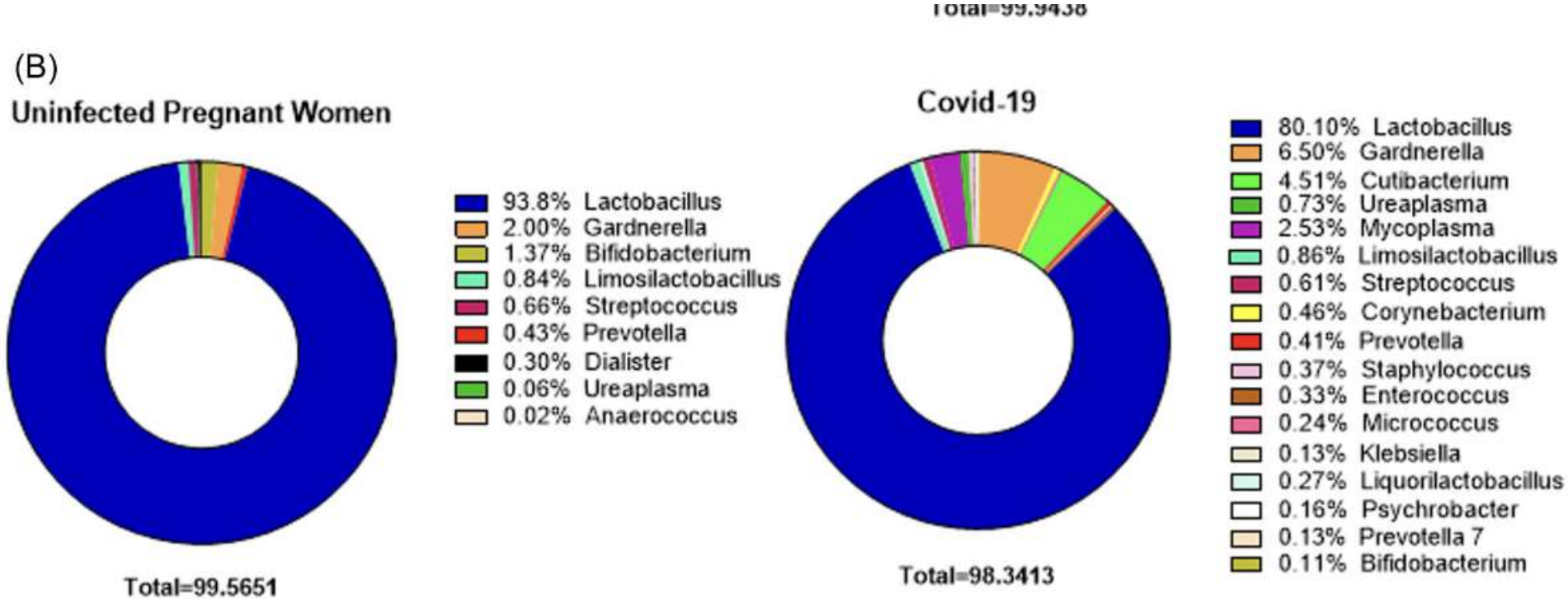






Alterations in vaginal microbiota among pregnant women with COVID-19

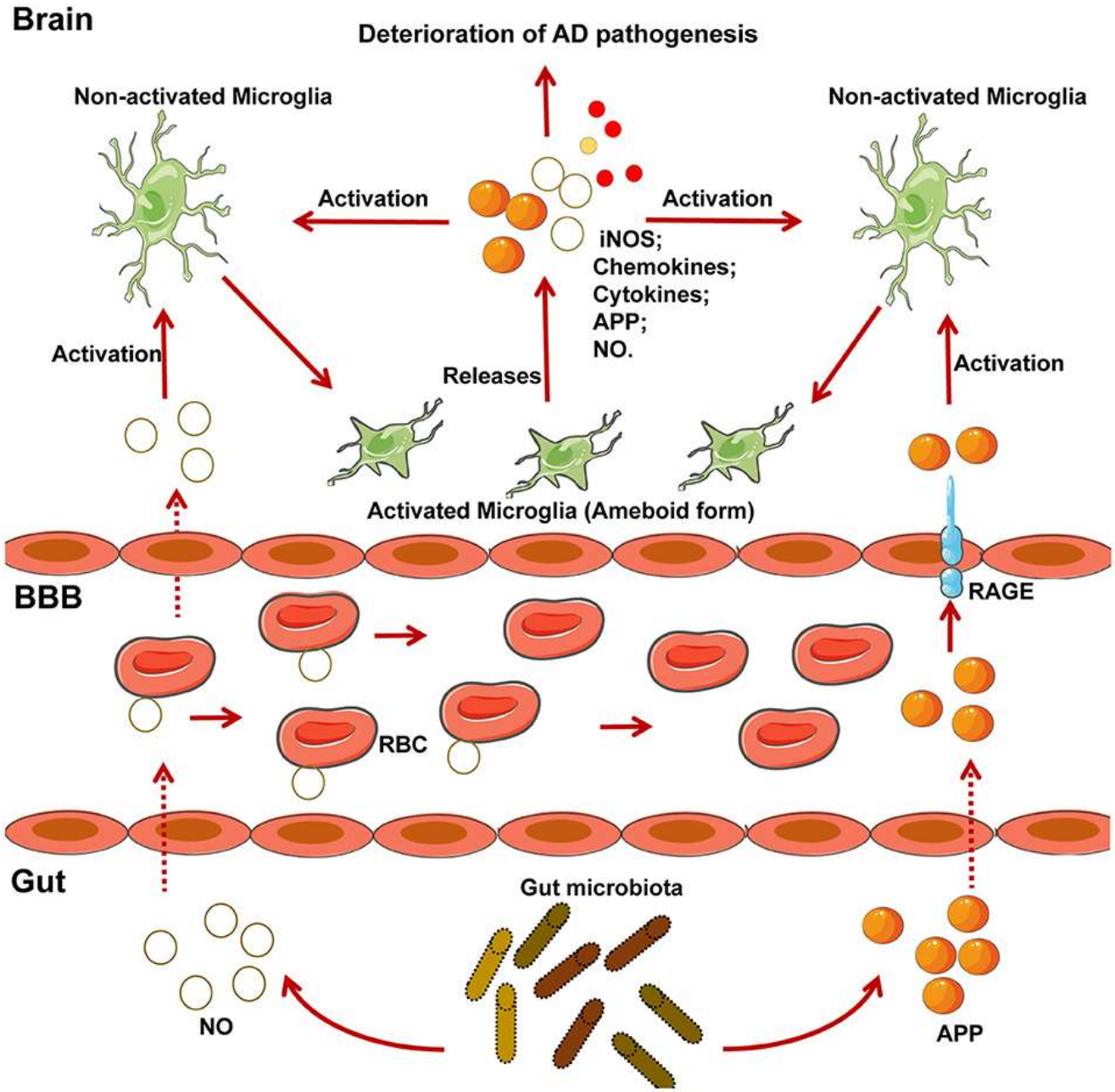
Ebru Celik M.D.[1] | Gulin Ozcan MSc[2,3] | Cansel Vatansever PhD[2,3] | Erxiati Paerhati[4] | Mert A. Kuşkucu M.D.[3,5] | Ozlem Dogan M.D:[2,3] | Sebile Guler Cekic M.D.[1] | Onder Ergonul[3,6] | Attila Gürsoy[4] | Özlem Keskin[4] | Fusun Can[2,3]



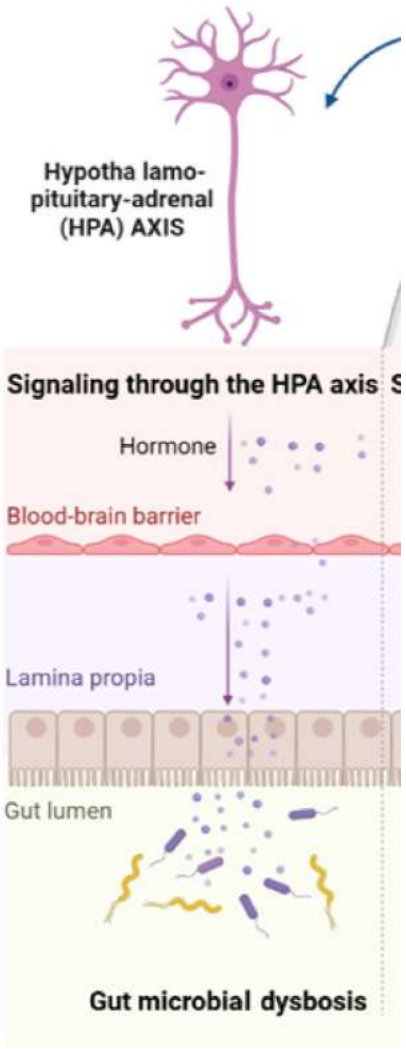
Nitrik Oksit, Mikroglieal Aktivite

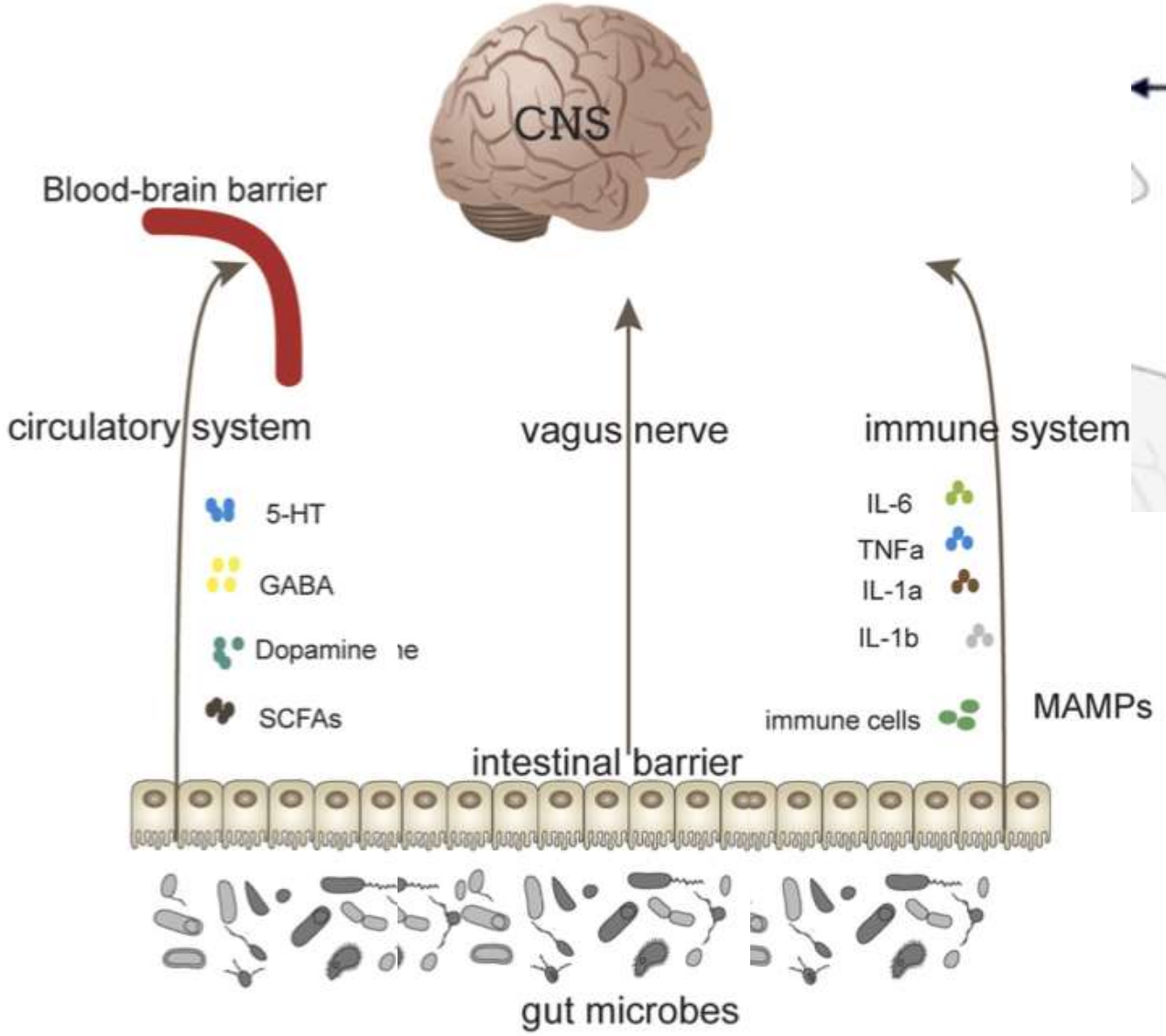
L-arjinin, L-sitruline ➔ NO ➔

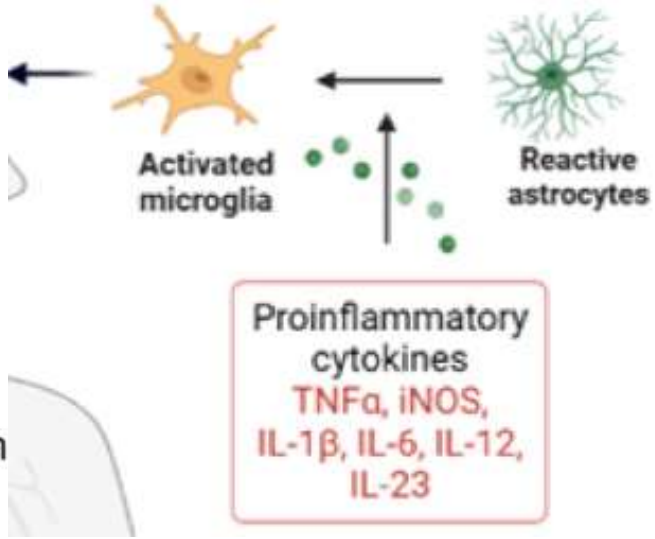
Akt ve CREB (Siklik AMP-Responsif-element bağlayıcı protein)
Hücre Sağlığı
fazlası ; RNS, ROS



MSS, Mikrobiyota Beyin - Barsak Aksı



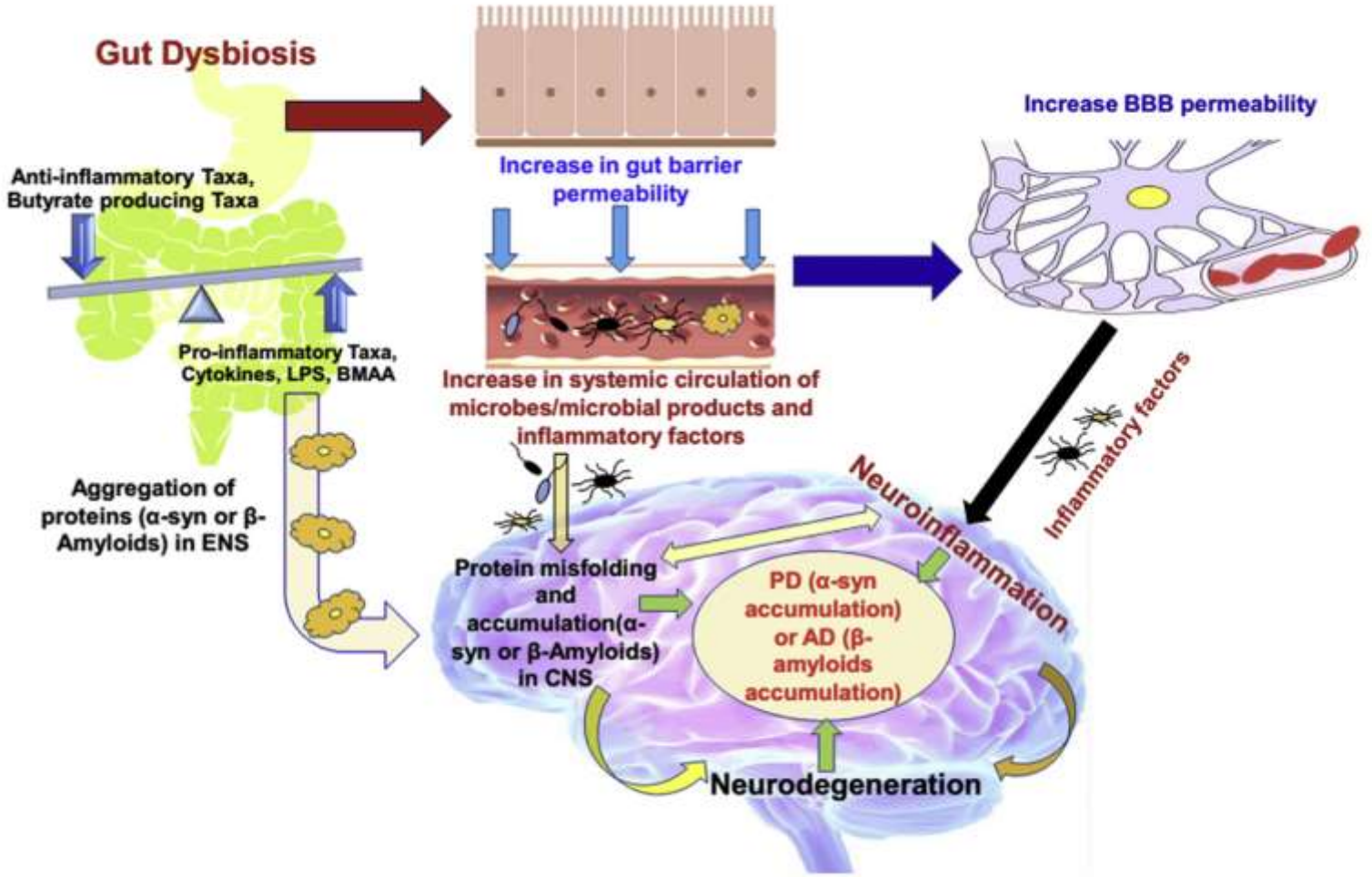




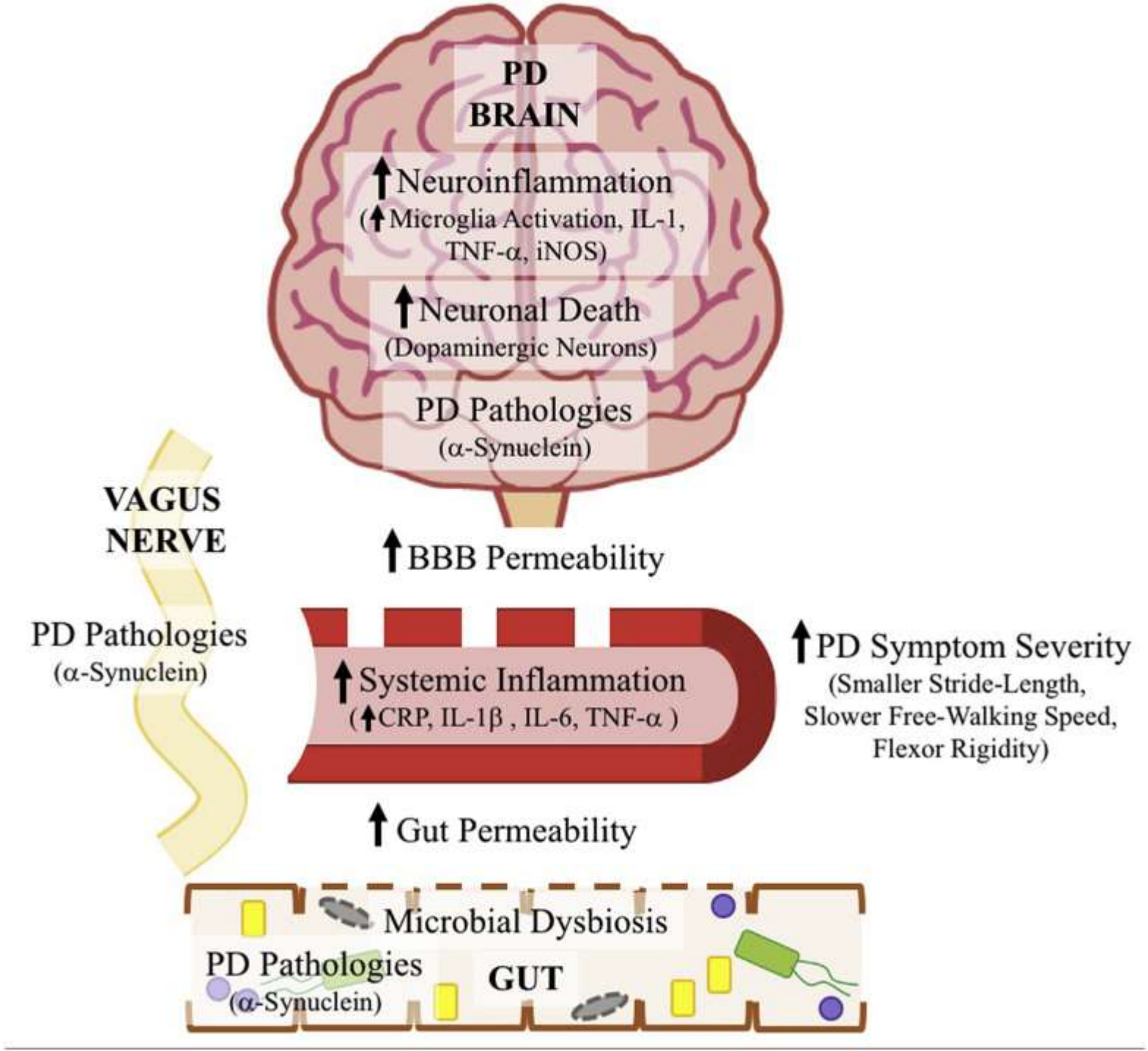
Çok Bilinen Hastalıklar, Olası Patogenez; Parkinson ve Alzheimer; Biriktirme

Parkinson: Striatal dopaminerjik hücre ölümü ve motor defisitlerle sonuçlanan nörotoksik alfa-sinüklein inklüzyonlarının varlığı ile karakterize.

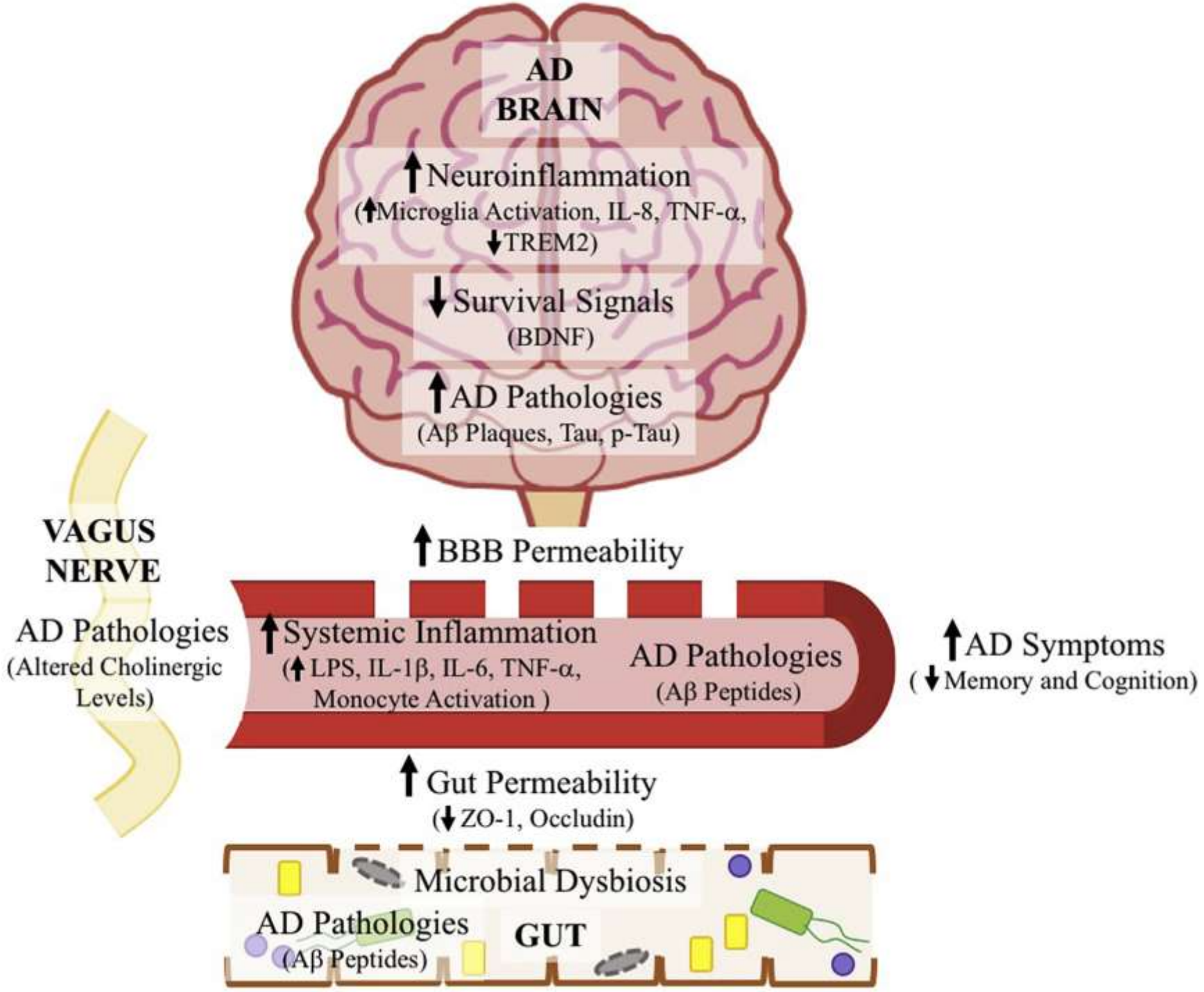
Alzheimer ayırt edici özelliklerinden biri hücre dışı Aβ plaklarının birikmesidir



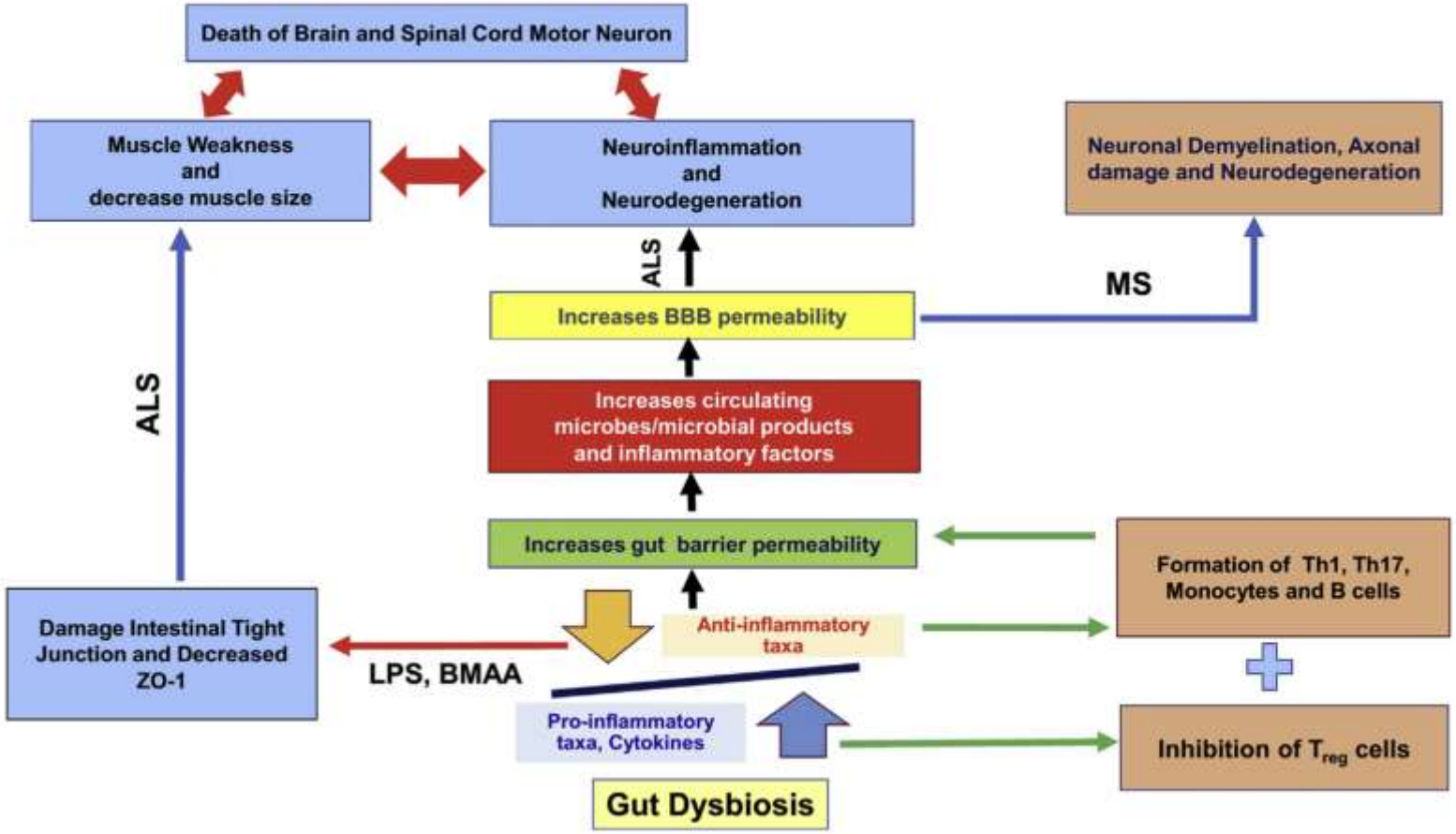
Parkinson


PD
BRAIN
Neuroinflammation
(Microglia Activation, IL-1,
TNF-α, iNOS)
Neuronal Death
(Dopaminergic Neurons)
PD Pathologies
(α-Synuclein)
VAGUS
NERVE
BBB Permeability
PD Pathologies
(α-Synuclein)
Systemic Inflammation
(CRP, IL-1β , IL-6, TNF-α)
PD Symptom Severity
(Smaller Stride-Length,
Slower Free-Walking Speed,
Flexor Rigidity)
Gut Permeability
Microbial Dysbiosis
PD Pathologies
(α-Synuclein)
GUT

Alzheimer


AD
BRAIN
↑Neuroinflammation
(↑Microglia Activation, IL-8, TNF-α,
↓TREM2)
↓Survival Signals
(BDNF)
↑AD Pathologies
(Aβ Plaques, Tau, p-Tau)
VAGUS
NERVE
↑BBB Permeability
AD Pathologies
(Altered Cholinergic
Levels)
↑Systemic Inflammation
(↑LPS, IL-1β, IL-6, TNF-α,
Monocyte Activation)
AD Pathologies
(Aβ Peptides)
↑AD Symptoms
(↓Memory and Cognition)
↑Gut Permeability
(↓ZO-1, Occludin)
Microbial Dysbiosis
AD Pathologies
(Aβ Peptides)
GUT

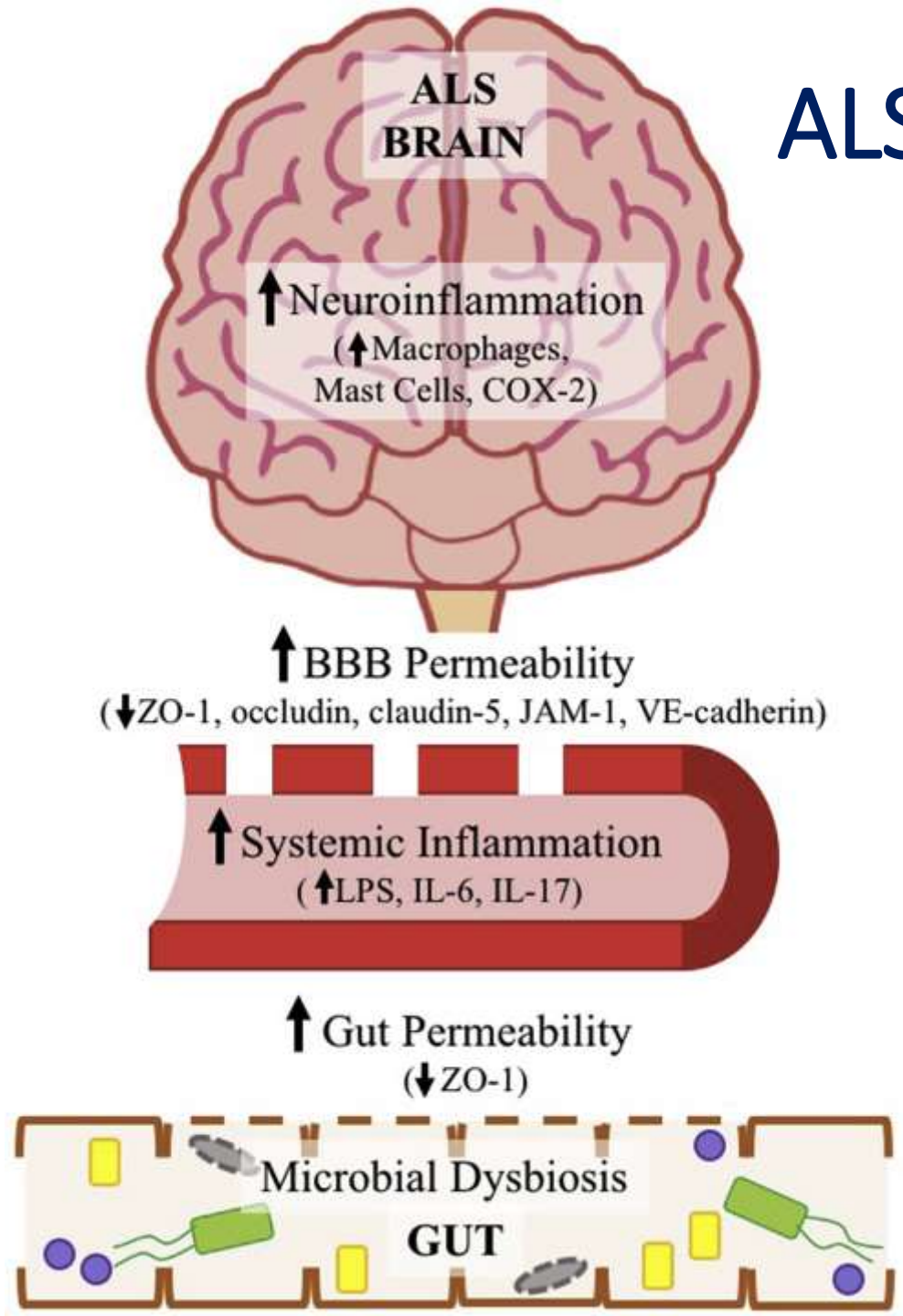
Çok Bilinen Hastalıklar, Olası Patogenez; ALS ve MS

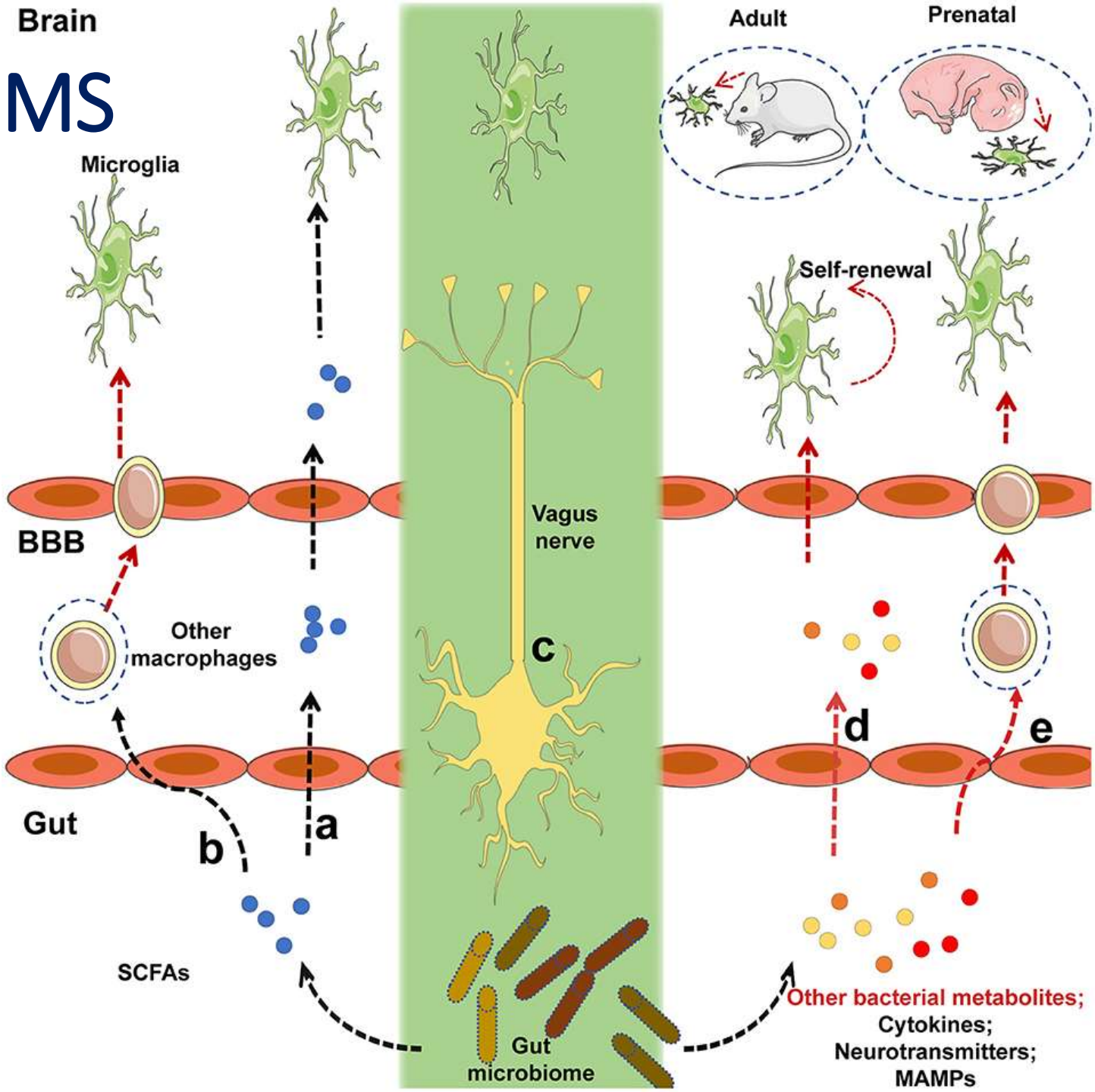


Bağırsak mikrobiyotasında Clostridium, Bacteroidetes, Prevotella, Parabacteroides ve Lactobacillus varlığı SCFA'ların üretimini indükleyebilir

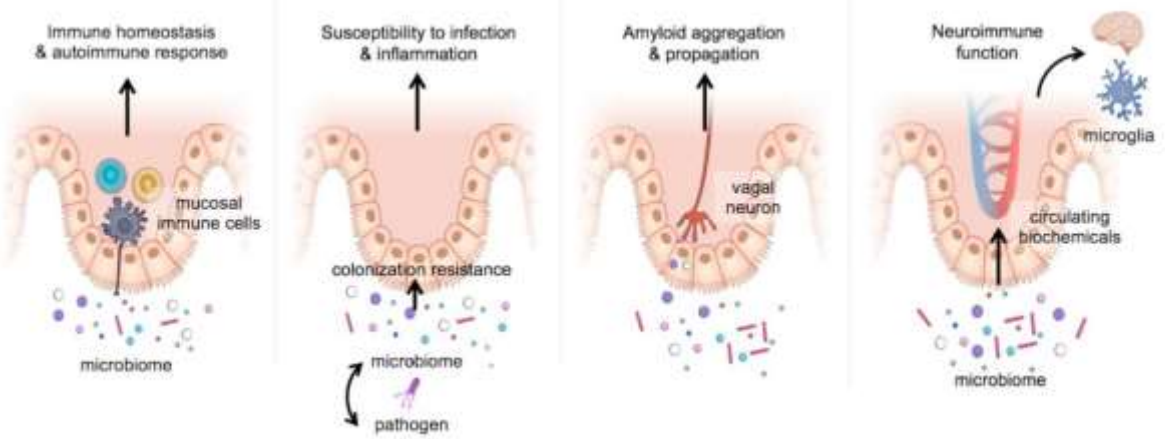
Bununla birlikte, MS hastalarında Firmicutes kolonizasyonunun arttığı Faecalibacterium'un göreceli bolluğunda azalma olduğu bildirilmiştir bütirat üreten bakteridir Treg'leri
MS hastalarında Clostridium perfringens tip B'nin bağırsak kolonizasyonunun epsilon toksin seviyelerinde artışa neden olduğu bildirilmiştir Bu toksin BBB'yi bozar

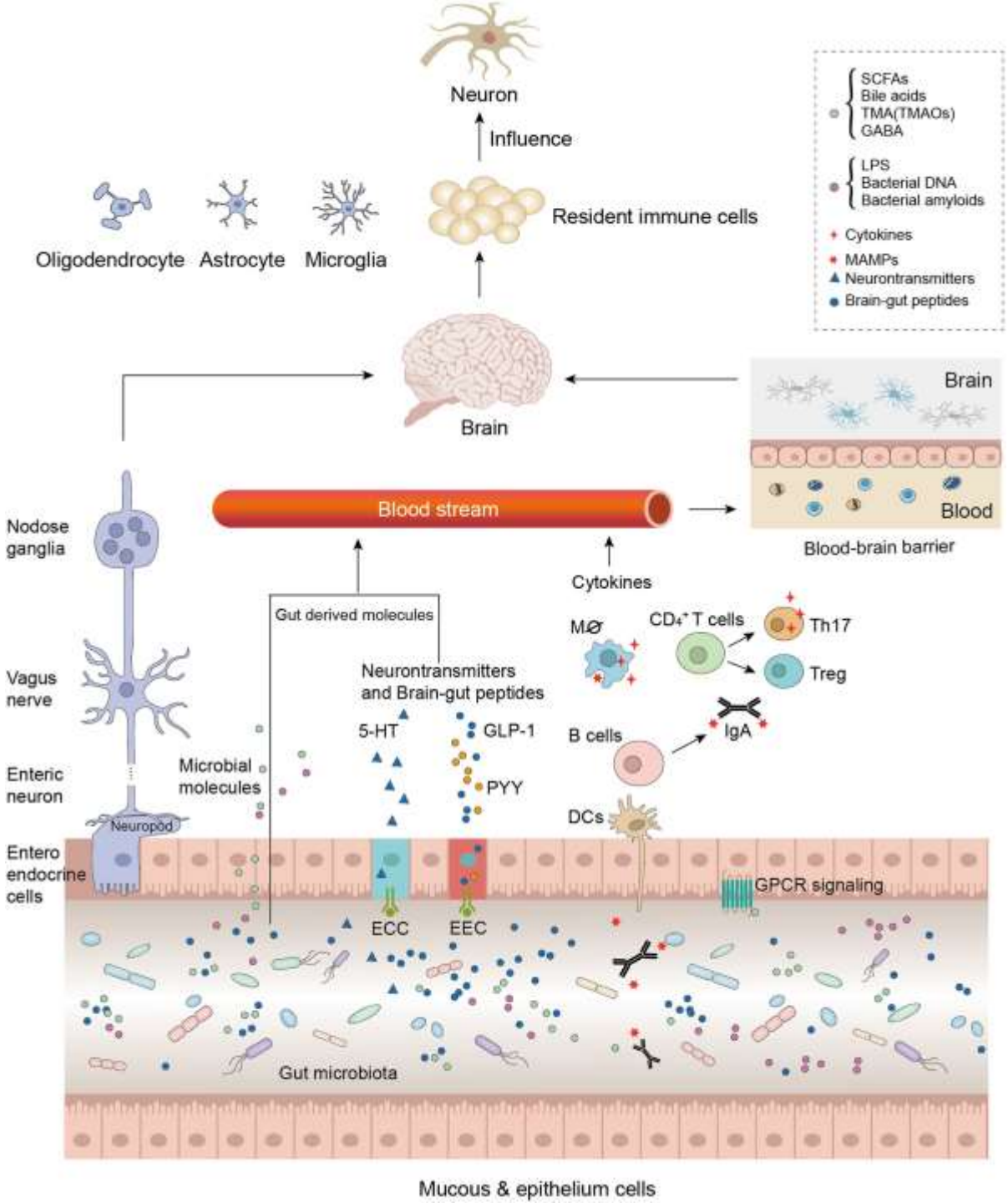
ALS&MS


ALS
BRAIN
Neuroinflammation
(Macrophages,
Mast Cells, COX-2)
BBB Permeability
(ZO-1, occludin, claudin-5, JAM-1, VE-cadherin)
Systemic Inflammation
(LPS, IL-6, IL-17)
Gut Permeability
(ZO-1)
Microbial Dysbiosis
GUT


Brain
Adult
Prenatal
Microglia
Self-renewal
BBB
Vagus
nerve
Other
macrophages
c
d
e
Gut
b
a
SCFAs
Gut
microbiome
Other bacterial metabolites;
Cytokines;
Neurotransmitters;
MAMPs

Temel Etkileşim

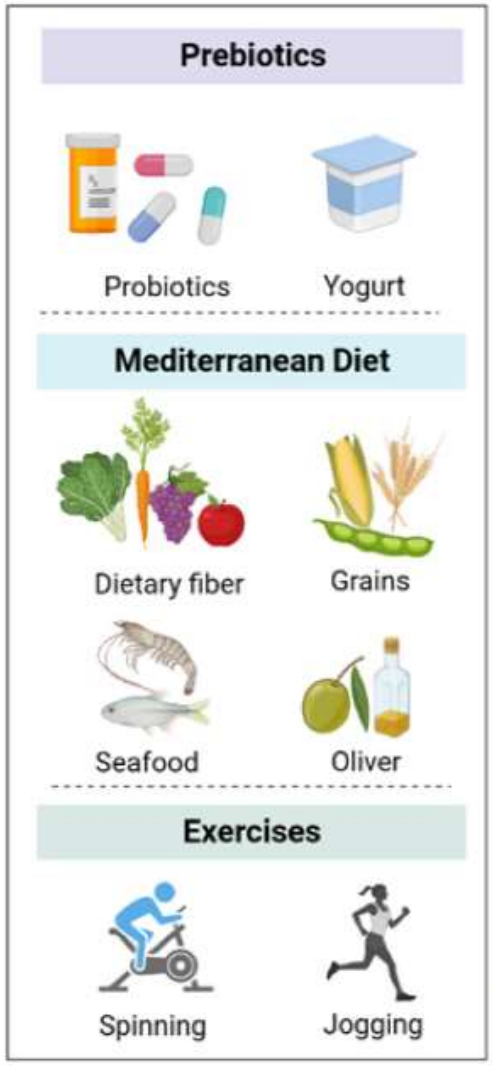


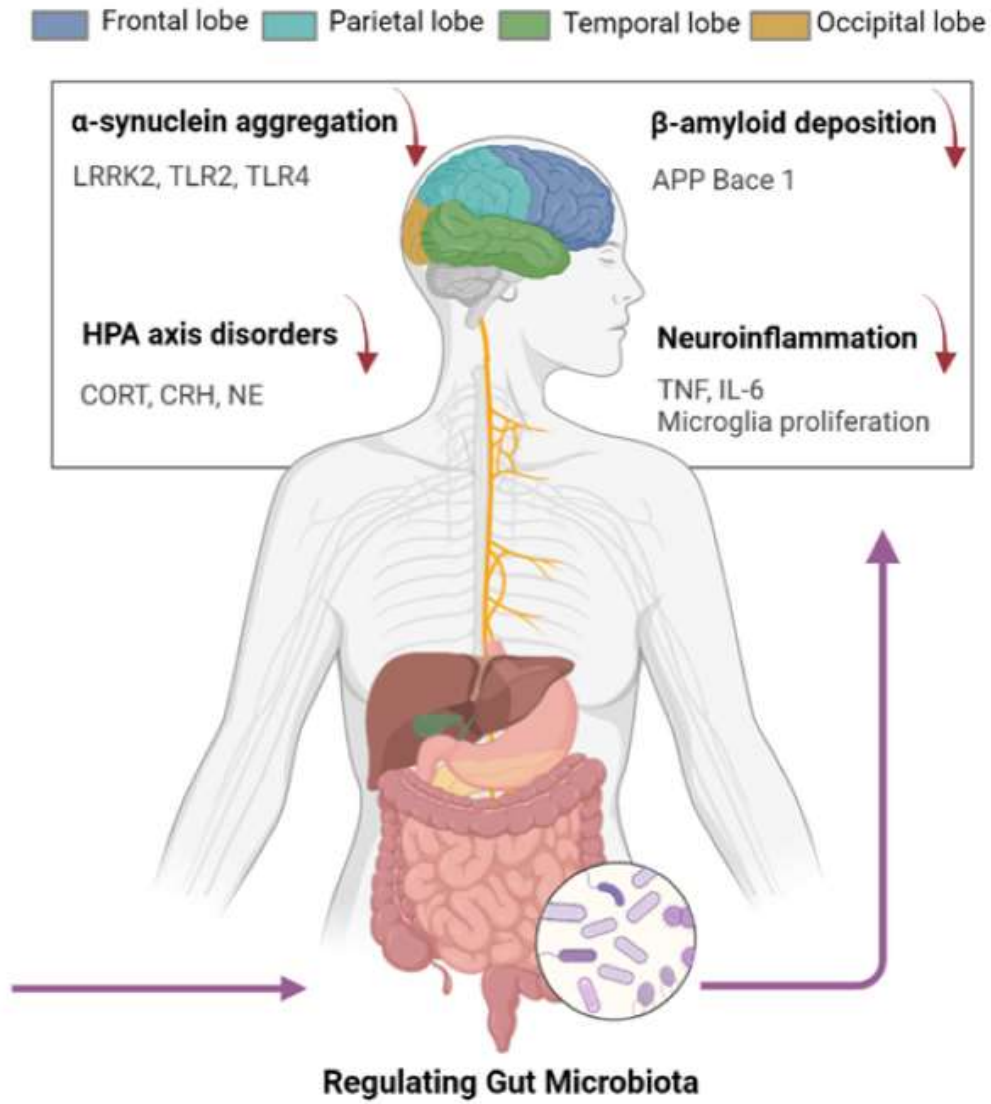


Peki, Durumu Düzeltebilirmiyim? Düzenleyebilirmiyim?

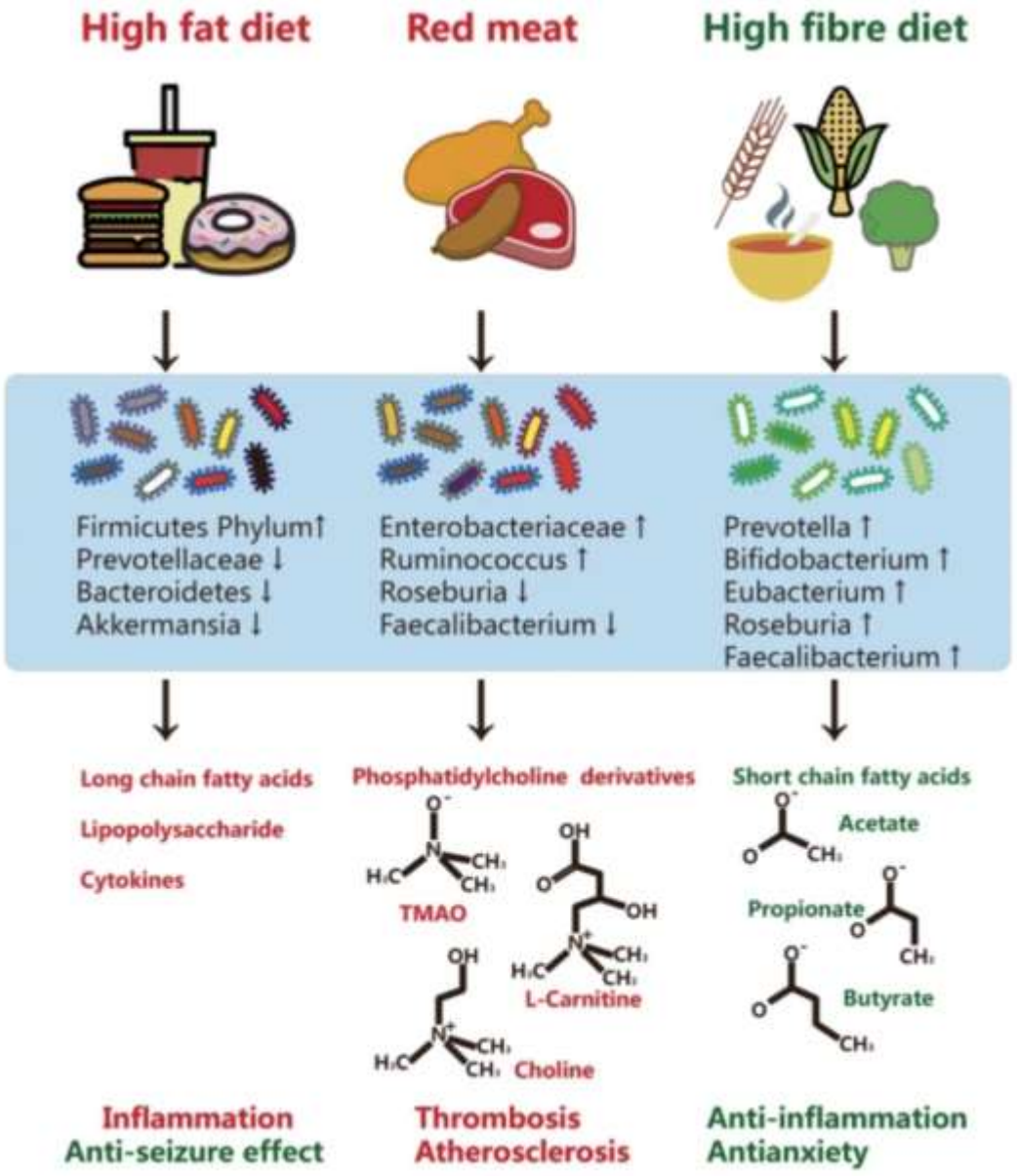
Probiotic Used	Subjects/Samples	Function	Diseases Involved
Lactobacillus plantarum MTCC1325	D-galactose-induced AD albino rats (3 months old)	Reduced formation of Aβ plaques, restored Acetylcholine leve, improved cognitive function	AD
Bifidobacterium breve strain A1	Aβ-injected male ddY mice (10 weeks old)	Produced SCAFs, regulated immune responses and inhibited neural inflammation, improved cognitive function	AD
Lactobacillus fermentum NS9	Ampicillin induced male SD rats	Restored normal composition of gut microbiota, and reversed antibiotics-induced anxiety behavior and spatial memory defects	AD
Lactobacillus helveticus NS8	Adult male SD rats to construct depression-like rat model of chronic restraint stress	Restored level of 5-HT and BDNF in hippocampus body, regulated inflammation responses	AD, anxiety, depression
	Male SD rats to construct rat model of hyperammonemia	Reduced the level of inflammation biomarkers, decreased 5-HT metabolism, restored cognitive function, improved anxiety-like behavior	
Bifidobacterium breve strain A1	Elderly with memory dysfunction	Improvement with cognitive function	AD
Bifidobacterium infantis 35624	SD rats	Modulated HPA stress response, reduced pro-inflammation immune response, increased level of 5-HTP	Depression
Lactobacillus reuteri ATCC 23272	C57BL/6 and BALB/c mice	Inhibited metabolism of tryptophan/kynurenine	Depression
Lactobacillus reuteri ATCC-PTA-6475	ASD mice	Upregulated level of oxytocin in brain, regulated plasticity of neurons	ASD
Bifidobacterium longum NCC3001	AKR mice	Upregulated level of brain-derived neurotrophic factor, regulated plasticity of neurons	Anxiety
Lactobacillus helveticus R0052 and *Bifidobacterium longum* R0175	LPS-induced rats	Reduced level of pro-inflammatory cytokines, reduced the apoptosis of hippocampal cells, improved memory	AD
Lactobacillus rhamnosus GG(L-GG), *Bifidobacterium animalis lactis*(BB-12), and *Lactobacillus acidophilus (LA-5)*	MPTP-induced mice	Butyrate, prevented the loss of dopaminergic neurons by upregulating neurotrophic factors and inhibiting the expression of Mao B	PD
DW2009: a mixture of fermented soybean powder and *L. plantarum* C29 freeze-dried powder.	MCI patients	Increased the abundance of Lactobacilli, increased serum BDNF level, improved cognitive function	AD

AD Alzheimer's disease, PD Parkinson's disease, ASD Autism Spectrum Disorder, SCAFs short-chain fatty acids, 5-HT 5-hydroxytryptamine, 5 hydroxytryptophan, BDNF brain-derived neurotrophic factor, HPA The hypothalamic–pituitary–adrenal axis, LPS lipopolysaccharides, Pyridine,1,2,3,6-tetrahydro-1-methyl-4-phenyl-, Mao B monoamine oxidase B, MCI mild cognitive impairment.





Peki, Durumu Düzeltebilirmiyim? Düzenleyebilirmiyim?



Diyet

Mikrobiyota

Metabolit

Etki

Teşekkürler...