

GUT-BRAIN AXIS

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NOTE: This poster conveys a general overview and should be considered neither comprehensive nor definitive. The details of this information are understood to be subject to interpretation.

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The blood-brain barrier (BBB) is comprised of endothelial cells, pericytes, astrocytes, neurons, and extracellular matrix components that together function in the maintenance of CNS homeostasis. The BBB of GF mice is more permeable, with decreased tight junction protein expression and disorganized tight junctions. Colonization of GF mice with pathogen-free microbiota increases the expression of tight junction proteins such as transmembrane claudin-5 and occludin, and cytoplasmic zonula occludens-1 (ZO-1), stabilizing the BBB. Additionally, microbiota-derived SCFAs, specifically butyrate, restore BBB stability in GF mice. The vasculature and pericyte coverage are unaffected by changes in microbiota. GF mice also show increased myelination and myelin production in the prefrontal cortex, with alterations in the corpus callosum and other regions. These changes are associated with increased transcription of oligodendrocyte myelin-associated genes as indicated, and unrelated to oligodendrocyte number.

Impact of the Microbiome on Neurodegenerative Diseases.



Alzheimer's disease (AD)- GF and antibiotic-treated AD animal models, such as APP/PS1 mice, have reduced cerebral amyloid, decreased microgliosis (indicated through Iba1 abundance) and overall changes in pro-inflammatory cytokine profile compared to control mice. Recolonization with microbiota derived from conventionally raised APP transgenic mice increases cerebral amyloid pathology. Parkinson's disease (PD)- GF PD animal models, such as mice overexpressing α-synuclein, have reduced α-synuclein inclusions, neuroinflammatory markers (including Iba1), and motor dysfunction compared to controls. Treatment of mice with LPS or particular microbes enhances susceptibility to PD-inducing toxins, including MPTP, leading to rapid loss of tyrosine hydroxylase in the GI tract and CNS. Amyotrophic lateral sclerosis (ALS)- GF or antibiotic-treated SOD1 mice, show exacerbated ALS pathology with increased motor symptoms, and substantially increased mortality.

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GUT-BRAIN AXIS POSTER

ABBREVIATIONS

ENTEROENDOCRINE CELLS (EEC) FACILITATE GUT-TO-BRAIN SIGNALING	
5-HT (R)	5-hydroxytryptamine (receptor)
α7nAChR	Alpha-7 nicotinic receptor
Adrα2A	Alpha-2A-adrenergic receptor
CCK(A/B)-R	Cholecystokinin (A/B) receptor
DRG	Dorsal root ganglia
EEC	Enteroendocrine cell
ENS	Enteric nervous system
FFAR1/2/3/4	Free fatty acid receptor 1/2/3/4
GI	Gastrointestinal
GLP-1(R)	Glucagon-like peptide 1 (receptor)
GPBAR1	G protein-coupled bile acid receptor 1
GPR40	G-protein-coupled receptor 40
iGluRs	lonotropic glutamate receptors
IPAN	Intrinsic primary afferent neuron
LI	Large intestine
mGluRs	Metabotropic glutamate receptors
NPY (2R)	Neuropeptide Y (receptor Y2)
NTS	Nucleus tractus solitarius
PAMPs	Pathogen-associated molecular patterns
PYY	Peptide YY
SCFA	Short chain fatty acid
SGLT1	Sodium-glucose cotransporter 1
SI	Small intestine
T1R1/2/3	Taste receptor type 1, member 1/2/3
TLR1/2/4/5/9	Toll-like receptor 1/2/4/5/9
Y2-R - PYY	Y receptor type 2 - Peptide YY

MICROBIOME-DERIVED SIGNALS DRIVE MICROGLIA MATURATION		
Bre	Brain and reproductive organ-expressed	
Ccl2	Chemokine (C-C motif) ligand 2	
Ccl7	Chemokine (C-C motif) ligand 7	
Csf1	Colony stimulating factor 1	
CsfR1	Colony stimulating factor 1 receptor	
CD31	Platelet endothelial cell adhesion molecule-1 (PECAM-1)	
Cst7	Cystatin F	
Cxcl10	C-X-C motif chemokine ligand 10	
DDIT	DNA-damage inducible transcript	
DDIT4	DNA-damage inducible transcript 4	
F4/80	EGF-like module-containing mucin-like hormone receptor-like 1 (EMR1)	
FFAR2	Free fatty acid receptor 2	
FosB	FBJ murine osteosarcoma viral oncogene homolog B	
GF	Germ-free	
IL-1β	Interleukin 1 beta	
IL-6	Interleukin 6	
IL-12β	Interleukin 12 beta	
LPS	Lipopolysaccharide	
Marco	Macrophage receptor with collagenous structure	
Neurl3	Neuralized E3 ubiquitin protein ligase 3	
Nox2	NADPH oxidase 2	
Relb	V-rel reticuloendotheliosis viral oncogene homolog B	
SPF	Specific pathogen-free	
TGFβ1	Transforming growth factor beta 1	
TNF	Tumor necrosis factor	

BRAIN STRUCTURE IS MODIFIED BY THE MICROBIOME	
BBB	Blood-brain barrier
CNS	Central nervous system
Egr1	Early growth response 1
GF	Germ-free
Mag	Myelin-associated glycoprotein
Мbp	Myelin basic protein
Mobp	Myelin-associated oligodendrocyte basic protein
Mog	Myelin oligodendrocyte glycoprotein
Olig1	Oligodendrocyte transcription factor 1
Plp1	Proteolipid protein 1
SCFA	Short-chain fatty acid
Sox10	SRY-related HMG-box 10
ZO-1	Zonula occludens-1

AβBeta-amyloid peptideADAlzheimer's diseaseALSAmyotrophic lateral sclerosisAPPAmyloid precursor proteinCCKCholecystokininCNSCentral nervous systemGFGerm-freeGFAPGlial fibrillary acidic proteinGIGastrointestinalGLP-1Glucagon-like peptide 1Iba1Ionized calcium binding adapter molecule 1IL-17aInterleukin 17ALCN2Lipocalin-2LPSLipopolysaccharideMPTP1-methyl-4-phenyl-1,2,3,6-tetrahydropy- ridineNoxNADPH oxidasePDParkinson's diseasePS1Presenilin 1ROSReactive oxygen speciesSCFAShort-chain fatty acidSOD1Superoxide dismutase 1TLR2Toll-like receptor 2TLR4Toll-like receptor 4TNFTumor necrosis factor	IMPACT OF THE MICROBIOME ON NEURODEGENERATIVE DISEASES	
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TLR4 Toll-like receptor 4 TNF Tumor necrosis factor	TLR2	Toll-like receptor 2
TNF Tumor necrosis factor	TLR4	Toll-like receptor 4
	TNF	Tumor necrosis factor

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