Title

Gut-Brain Axis Deregulation and Its Possible Contribution to Neurodegenerative Disorders

Abstract

The gut-brain axis is an essential communication pathway between the central nervous system (CNS) and the gastrointestinal tract. The human microbiota is composed of a diverse and abundant microbial community that compasses more than 100 trillion microorganisms that participate in relevant physiological functions such as host nutrient metabolism, structural integrity, maintenance of the gut mucosal barrier, and immunomodulation. Recent evidence in animal models has been instrumental in demonstrating the possible role of the microbiota in neurodevelopment, neuroinflammation, and behavior. Furthermore, clinical studies suggested that adverse changes in the microbiota can be considered a susceptibility factor for neurological disorders (NDs), such as Alzheimer's disease (AD), Parkinson's disease (PD), Huntington's disease (HD), and amyotrophic lateral sclerosis (ALS). In this review, we will discuss evidence describing the role of gut microbes in health and disease as a relevant risk factor in the pathogenesis of neurodegenerative disorders, including AD, PD, HD, and ALS.

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Index Keywords

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References

Aas J.A., Paster B.J., Stokes L.N., Olsen I., Dewhirst F.E., Defining the normal bacterial flora of the oral cavity, J Clin Microbiol, 43, pp. 5721-5732, (2005); Aggarwal N., Kitano S., Puah G.R.Y., Kittelmann S., Hwang I.Y., Chang M.W.,

Microbiome and Human Health: Current Understanding, Engineering, and Enabling Technologies, Chem Rev, 123, pp. 31-72, (2023); Agnello L., Ciaccio M., Neurodegenerative diseases: from molecular basis to therapy, Int J Mol Sci, 23, (2022); Ahn E.H., Kang S.S., Liu X., Chen G., Zhang Z., Chandrasekharan B., Et al., Initiation of Parkinson's disease from gut to brain by δ-secretase, Cell Res, 30, pp. 70-87, (2020); Aizawa E., Tsuji H., Asahara T., Takahashi T., Teraishi T., Yoshida S., Et al., Possible association of Bifidobacterium and Lactobacillus in the gut microbiota of patients with major depressive disorder, J Affect Disord, 202, pp. 254-257, (2016); Akbari E., Asemi Z., Daneshvar Kakhaki R., Bahmani F., Kouchaki E., Tamtaji O.R., Et al., Effect of probiotic supplementation on cognitive function and metabolic status in Alzheimer's disease: a randomized, double-blind and controlled trial, Front Aging Neurosci, 8, (2016); Alexander G.E., Biology of Parkinson's disease: pathogenesis and pathophysiology of a multisystem neurodegenerative disorder, Dialogues Clin Neurosci, 6, pp. 259-280, (2004); Alonso R., Pisa D., Carrasco L., Brain microbiota in Huntington's disease patients, Front Microbiol, 10, (2019); Arumugam M., Raes J., Pelletier E., Le Paslier D., Yamada T., Et al., MetaHIT Consortium (Additional members), Enterotypes of the human gut microbiome, Nature, 473, pp. 174-180, (2011); Backhed F., Ding H., Wang T., Hooper L.V., Koh G.Y., Nagy A., Et al., The gut microbiota as an environmental factor that regulates fat storage, Proc Natl Acad Sci, 101, pp. 15718-15723, (2004); Backhed F., Roswall J., Peng Y., Feng Q., Jia H., Kovatcheva-Datchary P., Et al., Dynamics and Stabilization of the Human Gut Microbiome during the First Year of Life, Cell Host Microbe, 17, (2015); Benros M.E., Eaton W.W., Mortensen P.B., The epidemiologic evidence linking autoimmune diseases and psychosis, Biol Psychiatry, 75, pp. 300-306, (2014); Beqollari D., Romberg C.F., Dobrowolny G., Martini M., Voss A.A., Musaro A., Et al., Progressive impairment of CaV1.1 function in the skeletal muscle of mice expressing a mutant type 1 Cu/Zn superoxide dismutase (G93A) linked to amyotrophic lateral sclerosis, Skelet Muscle, 6, (2016); Bercik P., Denou E., Collins J., Jackson W., Lu J., Jury J., Et

al., The Intestinal microbiota affect central levels of brain-derived neurotropic factor and behavior in mice, Gastroenterology, 141, pp. 599-609.e3, (2011); Berk M., Kapczinski F., Andreazza A.C., Dean O.M., Giorlando F., Maes M., Et al., Pathways underlying neuroprogression in bipolar disorder: focus on inflammation, oxidative stress and neurotrophic factors, Neurosci Biobehav Rev, 35, pp. 804-817, (2011); Bik E.M., Eckburg P.B., Gill S.R., Nelson K.E., Purdom E.A., Francois F., Et al., Molecular analysis of the bacterial microbiota in the human stomach, Proc Natl Acad Sci, 103, pp. 732-737, (2006); Bioque M., Gonzalez-Rodriguez A., Garcia-Rizo C., Cobo J., Monreal J.A., Usall J., Et al., Targeting the microbiome-gut-brain axis for improving cognition in schizophrenia and major mood disorders: A narrative review, Prog Neuropsychopharmacol Biol Psychiatry, 105, (2021); Blacher E., Bashiardes S., Shapiro H., Rothschild D., Mor U., Dori-Bachash M., Et al., Potential roles of gut microbiome and metabolites in modulating ALS in mice, Nature, 572, pp. 474-480, (2019); Blumenstock S., Rodrigues E.F., Peters F., Blazquez-Llorca L., Schmidt F., Giese A., Et al., Seeding and transgenic overexpression of alpha-synuclein triggers dendritic spine pathology in the neocortex, EMBO Mol Med, 9, pp. 716-731, (2017); Boddy S.L., Giovannelli I., Sassani M., Cooper-Knock J., Snyder M.P., Segal E., Et al., The gut microbiome: a key player in the complexity of amyotrophic lateral sclerosis (ALS), BMC Med, 19, (2021); Bolognini D., Tobin A.B., Milligan G., Moss C.E., The pharmacology and function of receptors for short-chain fatty acids, Mol Pharmacol, 89, pp. 388-398, (2016); Bonfili L., Cecarini V., Gogoi O., Gong C., Cuccioloni M., Angeletti M., Et al., Microbiota modulation as preventative and therapeutic approach in Alzheimer’s disease, FEBS J, 288, pp. 2836-2855, (2021); Boullier S., Nougayrede J.P., Marches O., Tasca C., Boury M., Oswald E., Et al., Genetically engineered enteropathogenic Escherichia coli strain elicits a specific immune response and protects against a virulent challenge, Microbes Infect, 5, pp. 857-867, (2003); Bourassa M.W., Alim I., Bultman S.J., Ratan R.R., Butyrate, neuroepigenetics and the gut microbiome: can a high fiber diet improve brain health?, Neurosci Lett, 625, pp.

56-63, (2016); Braak H., Rub U., Gai W.P., Del Tredici K., Idiopathic Parkinson's disease: possible routes by which vulnerable neuronal types may be subject to neuroinvasion by an unknown pathogen, J Neural Transm, 110, pp. 517-536, (2003); Braak H., de Vos R.A.I., Bohl J., Del Tredici K., Gastric α-synuclein immunoreactive inclusions in Meissner's and Auerbach's plexuses in cases staged for Parkinson's disease-related brain pathology, Neurosci Lett, 396, pp. 67-72, (2006); Brandscheid C., Schuck F., Reinhardt S., Schafer K.H., Pietrzik C.U., Grimm M., Et al., Altered gut microbiome composition and tryptic activity of the 5xFAD Alzheimer's mouse model, J Alzheimers Dis, 56, pp. 775-788, (2017); Bruggemann N., Hagenah J., Stanley K., Klein C., Wang C., Raymond D., Et al., Substantia nigra hyperechogenicity with LRRK2 G2019S mutations, Mov Disord, 26, pp. 885-888, (2011); Bunton-Stasyshyn R.K.A., Saccon R.A., Fratta P., Fisher E.M.C., SOD1 Function and its implications for amyotrophic lateral sclerosis pathology: new and renascent themes, Neuroscientist, 21, pp. 519-529, (2015); Burberry A., Wells M.F., Limone F., Couto A., Smith K.S., Keaney J., Et al., C9orf72 suppresses systemic and neural inflammation induced by gut bacteria, Nature, 582, pp. 89-94, (2020); Cabanas M., Piquemal M., Pistono C., Arnaud S., Rakesh D., Poinama E., Et al., Correlations between mutant huntingtin aggregates and behavioral changes in R6/1 mice, J Huntingt Dis, 9, pp. 33-45, (2020); Calvani R., Picca A., Lo Monaco M.R., Landi F., Bernabei R., Marzetti E., Of microbes and minds: a narrative review on the second brain aging, Front Med, 5, (2018); Caminiti S.P., Presotto L., Baroncini D., Garibotto V., Moresco R.M., Gianolli L., Et al., Axonal damage and loss of connectivity in nigrostriatal and mesolimbic dopamine pathways in early Parkinson's disease, NeuroImage Clin, 14, pp. 734-740, (2017); Cani P.D., Human gut microbiome: hopes, threats and promises, Gut, 67, pp. 1716-1725, (2018); Casoli T., Di Stefano G., Fattoretti P., Giorgetti B., Balietti M., Lattanzio F., Et al., Dynamin binding protein gene expression and memory performance in aged rats, Neurobiol Aging, 33, pp. 618.e15-618.e19, (2012); Cattaneo A., Cattane N., Galluzzi S., Provasi S., Lopizzo N., Festari C., Et al.,

Association of brain amyloidosis with pro-inflammatory gut bacterial taxa and peripheral inflammation markers in cognitively impaired elderly, Neurobiol Aging, 49, pp. 60-68, (2017); Ceppa F.A., Izzo L., Sardelli L., Raimondi I., Tunesi M., Albani D., Et al., Human gut-microbiota interaction in neurodegenerative disorders and current engineered tools for its modeling, Front Cell Infect Microbiol, 10, (2020); Chand K.K., Lee K.M., Lee J.D., Qiu H., Willis E.F., Lavidis N.A., Et al., Defects in synaptic transmission at the neuromuscular junction precede motor deficits in a TDP-43 ^{Q331K} transgenic mouse model of amyotrophic lateral sclerosis, FASEB J, 32, pp. 2676-2689, (2018); Chang C.H., Lin C.H., Lane H.Y., d-glutamate and gut microbiota in Alzheimer’s disease, Int J Mol Sci, 21, (2020); Chen Q.Q., Haikal C., Li W., Li M.T., Wang Z.Y., Li J.Y., Age-dependent alpha-synuclein accumulation and aggregation in the colon of a transgenic mouse model of Parkinson’s disease, Transl Neurodegener, 7, (2018); Coello K., Hansen T.H., Sorensen N., Munkholm K., Kessing L.V., Pedersen O., Et al., Gut microbiota composition in patients with newly diagnosed bipolar disorder and their unaffected first-degree relatives, Brain Behav Immun, 75, pp. 112-118, (2019); Collier T.J., Kanaan N.M., Kordower J.H., Ageing as a primary risk factor for Parkinson’s disease: evidence from studies of non-human primates, Nat Rev Neurosci, 12, pp. 359-366, (2011); Collins S.M., Surette M., Bercik P., The interplay between the intestinal microbiota and the brain, Nat Rev Microbiol, 10, pp. 735-742, (2012); Conley M.N., Wong C.P., Duyck K.M., Hord N., Ho E., Sharpton T.J., Aging and serum MCP-1 are associated with gut microbiome composition in a murine model, PeerJ, 4, (2016); Cryan J.F., O'Riordan K.J., Sandhu K., Peterson V., Dinan T.G., The gut microbiome in neurological disorders, Lancet Neurol, 19, pp. 179-194, (2020); Cussotto S., Sandhu K.V., Dinan T.G., Cryan J.F., The Neuroendocrinology of the microbiota-gut-brain axis: a behavioural perspective, Front Neuroendocrinol, 51, pp. 80-101, (2018); Das B., Nair G.B., Homeostasis and dysbiosis of the gut microbiome in health and disease, J Biosci, 44, (2019); Dash S., Syed Y.A., Khan M.R., Understanding the role

of the gut microbiome in brain development and its association with neurodevelopmental psychiatric disorders, Front Cell Dev Biol, 10, (2022); David L.A., Materna A.C., Friedman J., Campos-Baptista M.I., Blackburn M.C., Perrotta A., Et al., Host lifestyle affects human microbiota on daily timescales, Genome Biol, 15, (2014); Desbonnet L., Clarke G., Traplin A., O'Sullivan O., Crispie F., Moloney R.D., Et al., Gut microbiota depletion from early adolescence in mice: implications for brain and behaviour, Brain Behav Immun, 48, pp. 165-173, (2015); DeTure M.A., Dickson D.W., The neuropathological diagnosis of Alzheimer’s disease, Mol Neurodegener, 14, (2019); Di Gioia D., Bozzi Cionci N., Baffoni L., Amoruso A., Pane M., Mogna L., Et al., A prospective longitudinal study on themicrobiota composition in amyotrophic lateral sclerosis, BMC Med, 18, (2020); Di Pardo A., Amico E., Scalabri F., Pepe G., Castaldo S., Elifani F., Et al., Impairment of blood-brain barrier is an early event in R6/2 mouse model of Huntington Disease, Sci Rep, 7, (2017); Dinan T.G., Cryan J.F., The microbiome-gut-brain axis in health and disease, Gastroenterol Clin North Am, 46, pp. 77-89, (2017); Djousse L., Knowlton B., Cupples L.A., Marder K., Shoulson I., Myers R.H., Weight loss in early stage of Huntington’s disease, Neurology, 59, pp. 1325-1330, (2002); Dorsey E.R., Bloem B.R., The Parkinson pandemic—a call to action, JAMA Neurol, 75, pp. 9-10, (2018); Du G., Dong W., Yang Q., Yu X., Ma J., Gu W., Et al., Altered gut microbiota related to inflammatory responses in patients with Huntington’s disease, Front Immunol, 11, (2021); Eckburg P.B., Bik E.M., Bernstein C.N., Purdom E., Dethlefsen L., Sargent M., Et al., Diversity of the human intestinal microbial flora, Science, 308, pp. 1635-1638, (2005); Endres K., Schafer K.H., Influence of commensal microbiota on the enteric nervous system and its role in neurodegenerative diseases, J Innate Immun, 10, pp. 172-180, (2018); Erkkinen M.G., Kim M.O., Geschwind M.D., Clinical neurology and epidemiology of the major neurodegenerative diseases, Cold Spring Harb Perspect Biol, 10, (2018); Esposito E., Di Matteo V., Di Giovanni G., Death in the substantia nigra: a motor tragedy, Expert Rev Neurother, 7, pp. 677-697, (2007); Fan Y., Pedersen O., Gut microbiota in

human metabolic health and disease, Nat Rev Microbiol, 19, pp. 55-71, (2021); Fang P., Kazmi S.A., Jameson K.G., Hsiao E.Y., The microbiome as a modifier of neurodegenerative disease risk, Cell Host Microbe, 28, pp. 201-222, (2020); Fasano A., Bove F., Gabrielli M., Petracca M., Zocco M.A., Ragazzoni E., Et al., The role of small intestinal bacterial overgrowth in Parkinson's disease, Mov Disord, 28, pp. 1241-1249, (2013); Feeney S.J., McKelvie P.A., Austin L., Jean-Francois M.J.B., Kapsa R., Tombs S.M., Et al., Presymptomatic motor neuron loss and reactive astrocytosis in the SOD1 mouse model of amyotrophic lateral sclerosis, Muscle Nerve, 24, pp. 1510-1519, (2001); Feigin V.L., Nichols E., Alam T., Bannick M.S., Beghi E., Blake N., Et al., Global, regional, and national burden of neurological disorders, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016, Lancet Neurol, 18, pp. 459-480, (2019); Fernandez-Real J.M., Serino M., Blasco G., Puig J., Daunis-i-Estadella J., Ricart W., Et al., Gut microbiota interacts with brain microstructure and function, J Clin Endocrinol Metab, 100, pp. 4505-4513, (2015); Figueroa-Romero C., Guo K., Murdock B.J., Paez-Colasante X., Bassis C.M., Mikhail K.A., Et al., Temporal evolution of the microbiome, immune system, and epigenome with disease progression in ALS mice, Dis Model Mech Dmm, (2019); Fischer M., Sipe B., Cheng Y.W., Phelps E., Rogers N., Sagi S., Et al., Fecal microbiota transplant in severe and severe-complicated Clostridium difficile: a promising treatment approach, Gut Microbes, 8, pp. 289-302, (2017); Fitzgerald E., Murphy S., Martinson H.A., Alpha-Synuclein Pathology and the role of the microbiota in Parkinson's disease, Front Neurosci, 13, (2019); Forsyth C.B., Shannon K.M., Kordower J.H., Voigt R.M., Shaikh M., Jaglin J.A., Et al., Increased intestinal permeability correlates with sigmoid mucosa alpha-synuclein staining and endotoxin exposure markers in early Parkinson's disease, PLoS ONE, 6, (2011); Foster J.A., McVey Neufeld K.A., Gut–brain axis: how the microbiome influences anxiety and depression, Trends Neurosci, 36, pp. 305-312, (2013); Frohlich E.E., Farzi A., Mayerhofer R., Reichmann F., Jacan A., Wagner B., Et al., Cognitive impairment by antibiotic-induced gut dysbiosis: analysis

of gut microbiota-brain communication, Brain Behav Immun, 56, pp. 140-155, (2016); Fujiwara H., Hasegawa M., Dohmae N., Kawashima A., Masliah E., Goldberg M.S., Et al., α-Synuclein is phosphorylated in synucleinopathy lesions, Nat Cell Biol, 4, pp. 160-164, (2002); Fulling C., Dinan T.G., Cryan J.F., Gut microbe to brain signaling: what happens in vagus..., Neuron, 101, pp. 998-1002, (2019); Gammon K., Neurodegenerative disease: brain windfall, Nature, 515, pp. 299-300, (2014); Garcia-Redondo A., Dols-Icardo O., Rojas-Garcia R., Esteban-Perez J., Cordero-Vazquez P., Munoz-Blanco J.L., Et al., Analysis of the C9orf72 gene in patients with amyotrophic lateral sclerosis in Spain and different populations worldwide, Hum Mutat, 34, pp. 79-82, (2013); Gareau M.G., Wine E., Rodrigues D.M., Cho J.H., Whary M.T., Philpott D.J., Et al., Bacterial infection causes stress-induced memory dysfunction in mice, Gut, 60, pp. 307-317, (2011); Ghezzi L., Cantoni C., Rotondo E., Galimberti D., The gut microbiome–brain crosstalk in neurodegenerative diseases, Biomedicines, 10, (2022); Giau V., Wu S., Jamerlan A., An S., Kim S., Hulme J., Gut microbiota and their neuroinflammatory implications in Alzheimer's disease, Nutrients, 10, (2018); Gill S.R., Pop M., DeBoy R.T., Eckburg P.B., Turnbaugh P.J., Samuel B.S., Et al., Metagenomic analysis of the human distal gut microbiome, Science, 312, pp. 1355-1359, (2006); Giovannoni S.J., Britschgi T.B., Moyer C.L., Field K.G., Genetic diversity in Sargasso Sea bacterioplankton, Nature, 345, pp. 60-63, (1990); Goedert M., Alzheimer's and Parkinson's diseases: the prion concept in relation to assembled Aβ, tau, and α-synuclein, Science, 349, (2015); Gomez de Aguero M., Ganal-Vonarburg S.C., Fuhrer T., Rupp S., Uchimura Y., Li H., Et al., The maternal microbiota drives early postnatal innate immune development, Science, 351, pp. 1296-1302, (2016); Gomez-Isla T., Hollister R., West H., Mui S., Growdon J.H., Petersen R.C., Et al., Neuronal loss correlates with but exceeds neurofibrillary tangles in Alzheimer's disease: neuronal Loss in the Superior Temporal Sulcus in Alzheimer's Disease, Ann Neurol, 41, pp. 17-24, (1997); Gong Z., Ba L., Tang J., Yang Y., Li Z., Liu M., Et al., Gut microbiota links with cognitive impairment in amyotrophic

lateral sclerosis: a multi-omics study, J Biomed Res, 37, (2023); Gorecki A.M., Preskey L., Bakeberg M.C., Kenna J.E., Gildenhuys C., MacDougall G., Et al., Altered gut microbiome in Parkinson's disease and the influence of lipopolysaccharide in a human α-synuclein over-expressing mouse model, Front Neurosci, 13, (2019); Gries M., Christmann A., Schulte S., Weyland M., Rommel S., Martin M., Et al., Parkinson mice show functional and molecular changes in the gut long before motoric disease onset, Mol Neurodegener, 16, (2021); Gubert C., Kong G., Renoir T., Hannan A.J., Exercise, diet and stress as modulators of gut microbiota: Implications for neurodegenerative diseases, Neurobiol Dis, 134, (2020); Gubert C., Gasparotto J.H., Morais L., Convergent pathways of the gut microbiota–brain axis and neurodegenerative disorders, Gastroenterol Rep, 10, (2022); Guo T., Zhang D., Zeng Y., Huang T.Y., Xu H., Zhao Y., Molecular and cellular mechanisms underlying the pathogenesis of Alzheimer's disease, Mol Neurodegener, 15, (2020); Hamilton R.L., Lewy bodies in Alzheimer's disease: a neuropathological review of 145 cases using α-synuclein immunohistochemistry, Brain Pathol, 10, pp. 378-384, (2006); Han Y., Wang B., Gao H., He C., Hua R., Liang C., Et al., Vagus nerve and underlying impact on the gut microbiota-brain axis in behavior and neurodegenerative diseases, J Inflamm Res, 15, pp. 6213-6230, (2022); Haran J.P., Bhattarai S.K., Foley S.E., Dutta P., Ward D.V., Bucci V., Et al., Alzheimer's disease microbiome is associated with dysregulation of the anti-inflammatory p-glycoprotein pathway, Mbio, 10, pp. e00632-006319, (2019); Hardiman O., Al-Chalabi A., Chio A., Corr E.M., Logroscino G., Robberecht W., Et al., Amyotrophic lateral sclerosis, Nat Rev Dis Primer, 3, (2017); Harrison I.F., Anis H.K., Dexter D.T., Associated degeneration of ventral tegmental area dopaminergic neurons in the rat nigrostriatal lactacystin model of parkinsonism and their neuroprotection by valproate, Neurosci Lett, 614, pp. 16-23, (2016); Hasan N., Yang H., Factors affecting the composition of the gut microbiota, and its modulation, PeerJ, 7, (2019); Heijtz R.D., Wang S., Anuar F., Qian Y., Bjorkholm B., Samuelsson A., Et al., Normal gut microbiota modulates brain

development and behavior, Proc Natl Acad Sci, 108, pp. 3047-3052, (2011); Hill J.M., Lukiw W.J., Microbial-generated amyloids and Alzheimer's disease (AD), Front Aging Neurosci, 7, (2015); Hoffner G., Island M.L., Djian P., Purification of neuronal inclusions of patients with Huntington's disease reveals a broad range of N-terminal fragments of expanded huntingtin and insoluble polymers: Huntingtin fragments and polymers in inclusions, J Neurochem, 95, pp. 125-136, (2005); Hoffner G., Soues S., Djian P., Aggregation of expanded huntingtin in the brains of patients with Huntington disease, Prion, 1, pp. 26-31, (2007); Holmqvist S., Chutna O., Bousset L., Aldrin-Kirk P., Li W., Bjorklund T., Et al., Direct evidence of Parkinson pathology spread from the gastrointestinal tract to the brain in rats, Acta Neuropathol (berl), 128, pp. 805-820, (2014); Hooper L.V., Littman D.R., Macpherson A.J., Interactions between the microbiota and the immune system, Science, 336, pp. 1268-1273, (2012); Hou K., Wu Z.X., Chen X.Y., Wang J.Q., Zhang D., Xiao C., Et al., Microbiota in health and diseases, Signal Transduct Target Ther, 7, (2022); Hu X., Wang T., Jin F., Alzheimer's disease and gut microbiota, Sci China Life Sci, 59, pp. 1006-1023, (2016); Ivanov I.I., Frutos R De L., Manel N., Yoshinaga K., Rifkin D.B., Sartor R.B., Et al., Specific microbiota direct the differentiation of IL-17-producing T-Helper cells in the mucosa of the small intestine, Cell Host Microbe, 4, pp. 337-349, (2008); Jaarsma D., Haasdijk E.D., Grashorn J.A.C., Hawkins R., van Duijn W., Verspaget H.W., Et al., Human Cu/Zn Superoxide Dismutase (SOD1) Overexpression in mice causes mitochondrial vacuolization, axonal degeneration, and premature motoneuron death and accelerates motoneuron disease in mice expressing a familial amyotrophic lateral sclerosis Mutant SOD1, Neurobiol Dis, 7, pp. 623-643, (2000); Jandhyala S.M., Role of the normal gut microbiota, World J Gastroenterol, 21, (2015); Jiang H., Ling Z., Zhang Y., Mao H., Ma Z., Yin Y., Et al., Altered fecal microbiota composition in patients with major depressive disorder, Brain Behav Immun, 48, pp. 186-194, (2015); Jin Y., Wu S., Zeng Z., Fu Z., Effects of environmental pollutants on gut microbiota, Environ Pollut, 222, pp. 1-9, (2017);

Kaur S.J., McKeown S.R., Rashid S., Mutant SOD1 mediated pathogenesis of Amyotrophic Lateral Sclerosis, Gene, 577, pp. 109-118, (2016); Kelly J.R., Minuto C., Cryan J.F., Clarke G., Dinan T.G., The role of the gut microbiome in the development of schizophrenia, Schizophr Res, 234, pp. 4-23, (2021); Keshavarzian A., Green S.J., Engen P.A., Voigt R.M., Naqib A., Forsyth C.B., Et al., Colonic bacterial composition in Parkinson's disease: COLONIC MICROBIOTA IN PARKINSON'S DISEASE, Mov Disord, 30, pp. 1351-1360, (2015); Kesika P., Suganthy N., Sivamaruthi B.S., Chaiyasut C., Role of gut-brain axis, gut microbial composition, and probiotic intervention in Alzheimer's disease, Life Sci, 264, (2021); Kim C.H., Control of lymphocyte functions by gut microbiota-derived short-chain fatty acids, Cell Mol Immunol, 18, pp. 1161-1171, (2021); Kim S., Kwon S.H., Kam T.I., Panicker N., Karuppagounder S.S., Lee S., Et al., Transneuronal propagation of pathologic α-synuclein from the gut to the brain models Parkinson's disease, Neuron, 103, pp. 627-641.e7, (2019); King C.H., Desai H., Sylvetsky A.C., Lotempio J., Ayanyan S., Carrie J., Et al., Baseline human gut microbiota profile in healthy people and standard reporting template, (2018); Knuesel T., Mohajeri M.H., The role of the gut microbiota in the development and progression of major depressive and bipolar disorder, Nutrients, 14, (2021); Kong G., Cao K.A.L., Judd L.M., Li S., Renoir T., Hannan A.J., Microbiome profiling reveals gut dysbiosis in a transgenic mouse model of Huntington's disease, Neurobiol Dis, 135, (2020); Yi K.X., Han Y.X., L Juan X., Qing Z.Y., Pingliu Z.L.Y., Et al., Evaluation of fecal microbiota transplantation in Parkinson's disease patients with constipation, Microb Cell Factories, 20, (2021); Langille M.G.I., Zaneveld J., Caporaso J.G., McDonald D., Knights D., Reyes J.A., Et al., Predictive functional profiling of microbial communities using 16S rRNA marker gene sequences, Nat Biotechnol, 31, pp. 814-821, (2013); Lebouvier T., Chaumette T., Paillusson S., Duyckaerts C., Bruley des Varannes S., Neunlist M., Et al., The second brain and Parkinson's disease, Eur J Neurosci, 30, pp. 735-741, (2009); Lee V.M.Y., Goedert M., Trojanowski J.Q., Neurodegenerative Tauopathies, Annu Rev Neurosci, 24, pp.

1121-1159, (2001); Leng F., Edison P., Neuroinflammation and microglial activation in Alzheimer disease: where do we go from here?, Nat Rev Neurol, 17, pp. 157-172, (2021); Lethbridge L., Johnston G.M., Turnbull G., Co-morbidities of persons dying of Parkinson's disease, Prog Palliat Care, 21, pp. 140-145, (2013); Levy M., Kolodziejczyk A.A., Thaiss C.A., Elinav E., Dysbiosis and the immune system, Nat Rev Immunol, 17, pp. 219-232, (2017); Ley R.E., Peterson D.A., Gordon J.I., Ecological and evolutionary forces shaping microbial diversity in the human intestine, Cell, 124, pp. 837-848, (2006); Li Q., Barres B.A., Microglia and macrophages in brain homeostasis and disease, Nat Rev Immunol, 18, pp. 225-242, (2018); Li W., Wu X., Hu X., Wang T., Liang S., Duan Y., Et al., Structural changes of gut microbiota in Parkinson's disease and its correlation with clinical features, Sci China Life Sci, 60, pp. 1223-1233, (2017); Li S., Zhuo M., Huang X., Huang Y., Zhou J., Xiong D., Et al., Altered gut microbiota associated with symptom severity in schizophrenia, PeerJ, 8, (2020); Li H., Ni J., Qing H., Gut Microbiota: Critical Controller and Intervention Target in Brain Aging and Cognitive Impairment, Front Aging Neurosci, 13, (2021); Liu P., Wu L., Peng G., Han Y., Tang R., Ge J., Et al., Altered microbiomes distinguish Alzheimer's disease from amnestic mild cognitive impairment and health in a Chinese cohort, Brain Behav Immun, 80, pp. 633-643, (2019); Lloyd-Price J., Abu-Ali G., Huttenhower C., The healthy human microbiome, Genome Med, 8, (2016); Longinetti E., Fang F., Epidemiology of amyotrophic lateral sclerosis: an update of recent literature, Curr Opin Neurol, 32, pp. 771-776, (2019); Lu G., Wen Q., Cui B., Li Q., Zhang F., Washed microbiota transplantation stopped the deterioration of amyotrophic lateral sclerosis: the first case report and narrative review, J Biomed Res, 37, (2023); Lundgren S.N., Madan J.C., Emond J.A., Morrison H.G., Christensen B.C., Karagas M.R., Et al., Maternal diet during pregnancy is related with the infant stool microbiome in a delivery mode-dependent manner, Microbiome, 6, (2018); Attitudes to dementia, a global survey: public health: Engaging people in ADRD research, Alzheimers Dement, 2020, (2019); Lynch S.V., Pedersen O., The human

intestinal microbiome in health and disease, N Engl J Med, 375, pp. 2369-2379, (2016); Ma Q., Xing C., Long W., Wang H.Y., Liu Q., Wang R.F., Impact of microbiota on central nervous system and neurological diseases: the gut-brain axis, J Neuroinflammation, 16, (2019); Macdonald M., A novel gene containing a trinucleotide repeat that is expanded and unstable on Huntington's disease chromosomes, Cell, 72, pp. 971-983, (1993); Macpherson A.J., Geuking M.B., McCoy K.D., Immune responses that adapt the intestinal mucosa to commensal intestinal bacteria, Immunology, 115, pp. 153-162, (2005); Magen I., Fleming S.M., Zhu C., Garcia E.C., Cardiff K.M., Dinh D., Et al., Cognitive deficits in a mouse model of pre-manifest Parkinson's disease, Eur J Neurosci, 35, pp. 870-882, (2012); Maqsood R., Stone T.W., The Gut-Brain Axis, BDNF, NMDA and CNS Disorders, Neurochem Res, 41, pp. 2819-2835, (2016); Mayer E.A., Tillisch K., Gupta A., Gut/brain axis and the microbiota, J Clin Invest, 125, pp. 926-938, (2015); Maynard C.L., Elson C.O., Hatton R.D., Weaver C.T., Reciprocal interactions of the intestinal microbiota and immune system, Nature, 489, pp. 231-241, (2012); Mazmanian S.K., Liu C.H., Tzianabos A.O., Kasper D.L., An immunomodulatory molecule of symbiotic bacteria directs maturation of the host immune system, Cell, 122, pp. 107-118, (2005); Mazzini L., Mogna L., De Marchi F., Amoruso A., Pane M., Aloisio I., Et al., Potential role of gut microbiota in ALS pathogenesis and possible novel therapeutic strategies, J Clin Gastroenterol, 52, pp. S68-S70, (2018); Mehrabi N.F., Waldvogel H.J., Tippett L.J., Hogg V.M., Synek B.J., Faull R.L.M., Symptom heterogeneity in Huntington's disease correlates with neuronal degeneration in the cerebral cortex, Neurobiol Dis, 96, pp. 67-74, (2016); Melhem H., Kaya B., Ayata C.K., Hruz P., Niess J.H., Metabolite-sensing G protein-coupled receptors connect the diet-microbiota-metabolites axis to inflammatory bowel disease, Cells, 8, (2019); Miana-Mena F.J., Gonzalez-Mingot C., Larrode P., Munoz M.J., Olivan S., Fuentes-Broto L., Et al., Monitoring systemic oxidative stress in an animal model of amyotrophic lateral sclerosis, J Neurol, 258, pp. 762-769, (2011); Moffitt H., McPhail

G.D., Woodman B., Hobbs C., Bates G.P., Formation of polyglutamine inclusions in a wide range of non-CNS tissues in the HdhQ150 knock-in mouse model of Huntington's disease, PLoS ONE, 4, (2009); Mohajeri M.H., Brummer R.J.M., Rastall R.A., Weersma R.K., Harmsen H.J.M., Faas M., Et al., The role of the microbiome for human health: from basic science to clinical applications, Eur J Nutr, 57, pp. 1-14, (2018); Mohammadkhah A.I., Simpson E.B., Patterson S.G., Ferguson J.F., Development of the gut microbiome in children, and lifetime implications for obesity and cardiometabolic disease, Children, 5, (2018); Monda V., Villano I., Messina A., Valenzano A., Esposito T., Moscatelli F., Et al., Exercise modifies the gut microbiota with positive health effects, Oxid Med Cell Longev, 2017, pp. 1-8, (2017); Morton J.T., Marotz C., Washburne A., Silverman J., Zaramela L.S., Edlund A., Et al., Establishing microbial composition measurement standards with reference frames, Nat Commun, 10, (2019); Mulak A., Bonaz B., Brain-gut-microbiota axis in Parkinson's disease, World J Gastroenterol, 21, pp. 10609-10620, (2015); Musser M.A., Michelle S.-S., Balancing on the crest – evidence for disruption of the enteric ganglia via inappropriate lineage segregation and consequences for gastrointestinal function, Dev Biol, 382, pp. 356-364, (2013); Nair A.T., Ramachandran V., Joghee N.M., Antony S., Ramalingam G., Gut Microbiota dysfunction as reliable non-invasive early diagnostic biomarkers in the pathophysiology of Parkinson's disease: a critical review, J Neurogastroenterol Motil, 24, pp. 30-42, (2018); Needham B.D., Kaddurah-Daouk R., Mazmanian S.K., Gut microbial molecules in behavioural and neurodegenerative conditions, Nat Rev Neurosci, 21, pp. 717-731, (2020); Nguyen T.T., Kosciolek T., Daly R.E., Vazquez-Baeza Y., Swafford A., Knight R., Et al., Gut microbiome in Schizophrenia: Altered functional pathways related to immune modulation and atherosclerotic risk, Brain Behav Immun, 91, pp. 245-256, (2021); Niccoli T., Partridge L., Isaacs A.M., Ageing as a risk factor for ALS/FTD, Hum Mol Genet, 26, pp. R105-R113, (2017); Nichols E., Steinmetz J.D., Vollset S.E., Fukutaki K., Chalek J., Abd-Allah F., Et al., Estimation of the global prevalence of dementia in

2019 and forecasted prevalence in 2050: an analysis for the Global Burden of Disease Study 2019, Lancet Public Health, 7, pp. e105-e125, (2022); O'Hara A.M., Shanahan F., The gut flora as a forgotten organ, EMBO Rep, 7, pp. 688-693, (2006); O'Toole P.W., Jeffery I.B., Gut microbiota and aging, Science, 350, pp. 1214-1215, (2015); Oswal A., Cao C., Yeh C.H., Neumann W.J., Gratwicke J., Akram H., Et al., Neural signatures of hyperdirect pathway activity in Parkinson's disease, Nat Commun, 12, (2021); Parhizkar S., Holtzman D.M., APOE mediated neuroinflammation and neurodegeneration in Alzheimer's disease, Semin Immunol, 59, (2022); Pascoal T.A., Benedet A.L., Ashton N.J., Kang M.S., Therriault J., Chamoun M., Et al., Publisher correction: microglial activation and tau propagate jointly across Braak stages, Nat Med, 27, pp. 2048-2049, (2021); Pei Z., Bini E.J., Yang L., Zhou M., Francois F., Blaser M.J., Bacterial biota in the human distal esophagus, Proc Natl Acad Sci, 101, pp. 4250-4255, (2004); Petersen A., Expanded CAG repeats in exon 1 of the Huntington's disease gene stimulate dopamine-mediated striatal neuron autophagy and degeneration, Hum Mol Genet, 10, pp. 1243-1254, (2001); Peterson C.T., Dysfunction of the microbiota-gut-brain axis in neurodegenerative disease: The promise of therapeutic modulation with prebiotics, medicinal herbs, probiotics, and synbiotics, J Evid-Based Integr Med, 25, (2020); Peterson J., Garges S., Giovanni M., McInnes P., Wang L., Et al., The NIH HMP Working Group. The NIH human microbiome project, Genome Res, 19, pp. 2317-2323, (2009); Pringsheim T., Wiltshire K., Day L., Dykeman J., Steeves T., Jette N., The incidence and prevalence of Huntington's disease: a systematic review and meta-analysis, Mov Disord, 27, pp. 1083-1091, (2012); Pringsheim T., Fiest K., Jette N., The international incidence and prevalence of neurologic conditions: How common are they?, Neurology, 83, pp. 1661-1664, (2014); Quintanilla R.A., Orellana D.I., Gonzalez-Billault C., Maccioni R.B., Interleukin-6 induces Alzheimer-type phosphorylation of tau protein by deregulating the cdk5/p35 pathway, Exp Cell Res, 295, pp. 245-257, (2004); Reigstad C.S., Salmonson C.E., Iii J.F.R., Szurszewski J.H., Linden D.R., Sonnenburg

J.L., Et al., Gut microbes promote colonic serotonin production through an effect of short-chain fatty acids on enterochromaffin cells, FASEB J, 29, pp. 1395-1403, (2015); Remy P., Doder M., Lees A., Turjanski N., Brooks D., Depression in Parkinson’s disease: loss of dopamine and noradrenaline innervation in the limbic system, Brain, 128, pp. 1314-1322, (2005)

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