

## DAFTAR PUSTAKA

- Aggarwal, M., Alkhayyat, M., Saleh, M.A., Sarmini, M.T., Singh, A., Garg, R., et al. 2023. Alzheimer disease occurs more frequently in patients with Inflammatory Bowel Disease: insight from a nationwide study. *Journal of Clinical Gastroenterology* 57(5):501-507.
- Ahmadpour, S., Behrad, A., Vega, I. 2019. Dark Neurons: A protective mechanism or a mode of death. *Journal of Medical Histology* 3(2): 125-131.
- Ajilore, O., Lamar, M., Medina, J., Watari, K., Elderkin-Thompson, V., Kumar, A. 2015. Disassociation of verbal learning and hippocampal volume in type 2 diabetes and major depression. *International Journal of Geriatric Psychiatry* 30(4): 393–399. <https://doi.org/10.1002/gps.4149>
- Albadawi E. A. 2025. Structural and functional changes in the hippocampus induced by environmental exposures. *Neurosciences (Riyadh, Saudi Arabia)* 30(1):5–19. <https://doi.org/10.17712/nsj.2025.1.20240052>
- Alonso Bellido, I.M., Posada-Pérez, M., Hernández-Rasco, F., Vázquez-Reyes, S., Cabanillas, M., Herrera, A.J., et al. 2023. Microglial Caspase-3 is essential for modulating hippocampal neurogenesis. *Brain, Behavior, and Immunity* 112:206–219.
- Alper, J., Feng, R., Verma, G., Rutter, S., Huang, K.H., Xie, L., et al. 2023. Stress-related reduction of hippocampal subfield volumes in major depressive disorder: A 7-Tesla study. *Frontiers in Psychiatry* 14:1060770.
- Altunkaynak, B.Z., Altunkaynak, E., Unal, D., Unal, B. 2009. A novel application for the cavalieri principle: a stereological and methodological study. *The Eurasian Journal of Medicine* 41(2):99–101.
- Amaral, D.G., Scharfman, H.E., Lavenex, P. 2007. The dentate gyrus: fundamental neuroanatomical organization (dentate gyrus for dummies). *Progress in Brain Research* 163: 3–22. [https://doi.org/10.1016/S0079-6123\(07\)63001-5](https://doi.org/10.1016/S0079-6123(07)63001-5)
- Amlerova, Z., Chmelova, M., Anderova, M., Vargova, L. 2024. Reactive gliosis in traumatic brain injury: a comprehensive review. *Frontiers in Cellular Neuroscience* 18: 1335849. <https://doi.org/10.3389/fncel.2024.1335849>
- Anderova, M., Vorisek, I., Pivonkova, H., Benesova, J., Vargova, L., Cicanic, M., et al. 2011. Cell death/proliferation and alterations in glial morphology contribute to changes in diffusivity in the rat hippocampus after hypoxia-ischemia. *Journal of Cerebral Blood Flow and Metabolism: Official Journal of the International Society of Cerebral Blood Flow and Metabolism* 31(3): 894–907. <https://doi.org/10.1038/jcbfm.2010.168>
- Aniol, V., Manolova, A., Gulyaeva, N. 2022. Early life events and maturation of the dentate gyrus: implications for neurons and glial cells. *International Journal of Molecular Science* 23:4261.
- Aniwan, S., Santiago, P., Loftus, E.V., Jr., Park, S.H. 2022. The epidemiology of inflammatory bowel disease in Asia and Asian immigrants to Western countries. *United European Gastroenterology Journal* 10(10): 1063–1076. <https://doi.org/10.1002/ueg2.12350>

- Antonini Cencicchio, M., Montini, F., Palmieri, V., Massimino, L., Lo Conte, M., Finardi, A., et al. 2025. Microbiota-produced immune regulatory bile acid metabolites control central nervous system autoimmunity. *Cell Reports Medicine* 6(4):102028. <https://doi.org/10.1016/j.xcrm.2025.102028>
- Bal, N., Roshchin, M., Salozhin, S., Balaban, P. 2017. Nitric oxide upregulates proteasomal protein degradation in neurons. *Cellular and Molecular Neurobiology* 37(5):763–769. <https://doi.org/10.1007/s10571-016-0413-9>
- Baracskaý, P., Szepesi, Z., Orbán, G., Juhász, G., Czurkó, A. 2008. Generalization of seizures parallels the formation of "dark" neurons in the hippocampus and pontine reticular formation after focal-cortical application of 4-aminopyridine (4-AP) in the rat. *Brain Research* 1228: 217–228. <https://doi.org/10.1016/j.brainres.2008.06.044>
- Barnes, S.E., Zera, K.A., Ivison, G.T., Buckwalter, M.S., Engleman, E.G. 2021. Brain profiling in murine colitis and human epilepsy reveals neutrophils and TNF $\alpha$  as mediators of neuronal hyperexcitability. *Journal of Neuroinflammation* 18(1):199.
- Bartsch, T., Döhring, J., Reuter, S., Finke, C., Rohr, A., Brauer, H., Deuschl, G., Jansen, O. 2015. Selective neuronal vulnerability of human hippocampal CA1 neurons: lesion evolution, temporal course, and pattern of hippocampal damage in diffusion-weighted MR imaging. *Journal of Cerebral Blood Flow and Metabolism: Official Journal of the International Society of Cerebral Blood Flow and Metabolism* 35(11):1836–1845.
- Beauquis, J., Vinuesa, A., Pomilio, C., Pavía, P., Galván, V., Saravia, F. 2014. Neuronal and glial alterations, increased anxiety, and cognitive impairment before hippocampal amyloid deposition in PDAPP mice, model of Alzheimer's disease. *Hippocampus* 24(3):257–269.
- Bolon B. 2023. Toxicologic pathology forum opinion: interpretation of gliosis in the brain and spinal cord observed during nonclinical safety studies. *Toxicologic Pathology* 51(1-2): 68–76. <https://doi.org/10.1177/01926233231164557>
- Bonhomme, B., Nandi, N., Berera, S., Lee, H., Leung, G., Tse, C. S., Weiss, A., Nessel, L., Ren, Y., Li, H., Aberra, F. N., & Lewis, J. D. (2024). Greater fatigue and reduced neurocognitive speed with symptomatic crohn's disease. *Crohn's & Colitis* 360 7(1):otae069.
- Borzello, M., Ramirez, S., Treves, A., Lee, I., Scharfman, H., Stark, C., et al. 2023. Assessments of dentate gyrus function: discoveries and debates. *Nature Reviews. Neuroscience* 24(8): 502–517. <https://doi.org/10.1038/s41583-023-00710-z>
- Boyce, R.W., Dorph-Petersen, K.A., Lyck, L., Gundersen, H.J. 2010. Design-based stereology: introduction to basic concepts and practical approaches for estimation of cell number. *Toxicologic Pathology* 38(7):1011–1025.
- Brown D.L. 2017. Practical stereology applications for the pathologist. *Veterinary Pathology* 54(3): 358–368. <https://doi.org/10.1177/0300985817695781>

- Brown, G.C., Heneka, M.T. 2024. The endotoxin hypothesis of Alzheimer's disease. *Molecular Neurodegeneration* 19(1):30. <https://doi.org/10.1186/s13024-024-00722-y>
- Cai, J., Sun, L., Gonzalez, F.J. 2022. Gut microbiota-derived bile acids in intestinal immunity, inflammation, and tumorigenesis. *Cell Host & Microbe* 30(3):289–300. <https://doi.org/10.1016/j.chom.2022.02.004>
- Casini, A., Vivacqua, G., Ceci, L., Leone, S., Vaccaro, R., Tagliaferro, M. 2025. TNBS colitis induces architectural changes and alpha-synuclein overexpression in mouse distal colon: A morphological study. *Cell and Tissue Research* 399(2): 247–265. <https://doi.org/10.1007/s00441-024-03932-4>
- Chapelet, G., Béguin, N., Castellano, B., Grit, I., de Coppet, P., Oullier, T., et al. 2023. Tau expression and phosphorylation in enteroendocrine cells. *Frontiers of Neuroscience* 17:1166848.
- Chen, C., Ahn, E. H., Kang, S.S., Liu, X., Alam, A., Ye, K. 2020a. Gut dysbiosis contributes to amyloid pathology, associated with C/EBP $\beta$ /AEP signaling activation in Alzheimer's disease mouse model. *Science Advances* 6(31): eaba0466. <https://doi.org/10.1126/sciadv.aba0466>
- Chen, F., Bertelsen, A. B., Holm, I. E., Nyengaard, J. R., Rosenberg, R., Dorph-Petersen, K. A. 2020b. Hippocampal volume and cell number in depression, schizophrenia, and suicide subjects. *Brain Research* 1727:146546.
- Chen, L.M., Bao, C.H., Wu, Y., Liang, S. H., Wang, D., Wu, L.Y., et al. 2021. Tryptophan-kynurenine metabolism: a link between the gut and brain for depression in inflammatory bowel disease. *Journal of Neuroinflammation* 18(1): 135. <https://doi.org/10.1186/s12974-021-02175-2>
- Chen, Y., Yu, Y., Kou, J., Qi, H., Zhang, C., Wang, F., et al. 2025. Astrocytic AEG-1 drives neuroinflammation and enhances seizure susceptibility. *Neurobiology of Disease* 212:106957. <https://doi.org/10.1016/j.nbd.2025.106957>
- Childers, R.E., Eluri, S., Vazquez, C., Weise, R.M., Bayless, T. M., Hutfless, S. 2014. Family history of inflammatory bowel disease among patients with ulcerative colitis: a systematic review and meta-analysis. *Journal of Crohn's & Colitis* 8(11): 1480–1497. <https://doi.org/10.1016/j.crohns.2014.05.008>
- Clarke, G., Kennedy, P.J., Groeger, J.A., Quigley, E.M., Shanahan, F., et al. 2020. Impaired cognitive function in Crohn's disease: Relationship to disease activity. *Brain, Behavior, & Immunity - Health* 5:100093.
- Counts, S. E., Alldred, M. J., Che, S., Ginsberg, S. D., & Mufson, E. J. 2014. Synaptic gene dysregulation within hippocampal CA1 pyramidal neurons in mild cognitive impairment. *Neuropharmacology* 79: 172–179. <https://doi.org/10.1016/j.neuropharm.2013.10.018>
- Craig, C.F., Filippone, R.T., Stavely, R. Bornstein J.C., Apostolopoulos, V., Nurgali, K. 2022. Neuroinflammation as an etiological trigger for

- depression comorbid with inflammatory bowel disease. *J Neuroinflammation* 19:4.
- Dempsey, E., Abautret-Daly, Á., Docherty, N.G., Medina, C., Harkin, A. 2019. Persistent central inflammation and region specific cellular activation accompany depression- and anxiety-like behaviours during the resolution phase of experimental colitis. *Brain, Behavior, and Immunity* 80:616–632. <https://doi.org/10.1016/j.bbi.2019.05.007>
- Dias, D., Portugal, C. C., Relvas, J., Socodato, R. 2025. From genetics to neuroinflammation: The impact of apoe4 on microglial function in Alzheimer's disease. *Cells* 14(4): 243. <https://doi.org/10.3390/cells14040243>
- Dudek, S.M., Alexander, G.M., Farris, S. 2016. Rediscovering area CA2: unique properties and functions. *Nature Reviews. Neuroscience* 17(2): 89–102. <https://doi.org/10.1038/nrn.2015.22>
- Einenkel, A.M., Salameh A. 2024. Selective vulnerability of hippocampal CA1 and CA2/3 pyramidal cells: What are possible pathomechanisms and should more attention be paid to the CA2/3 region in future studies?. *Journal of Neuroscience Research* 102(1):e25276.
- Escartin, C., Galea, E., Lakatos, A., O'Callaghan, J.P., Petzold, G.C., Serrano-Pozo, A., et al. 2021. Reactive astrocyte nomenclature, definitions, and future directions. *Nature Neuroscience* 24(3):312–325. <https://doi.org/10.1038/s41593-020-00783-4>
- Feng, L., Zhou, N., Li, Z., Fu, D., Guo, Y., et al. 2022. Co-occurrence of gut microbiota dysbiosis and bile acid metabolism alteration is associated with psychological disorders in Crohn's disease. *FASEB Journal: Official Publication of the Federation of American Societies for Experimental Biology*, 36(1):e22100. <https://doi.org/10.1096/fj.202101088RRR>
- Freeman H.J. (2008). Colorectal cancer risk in Crohn's disease. *World Journal of Gastroenterology* 14(12): 1810–1811. <https://doi.org/10.3748/wjg.14.1810>
- Fukuda, A.M., Badaut, J. 2012. Aquaporin 4: a player in cerebral edema and neuroinflammation. *Journal of Neuroinflammation* 9: 279. <https://doi.org/10.1186/1742-2094-9-279>
- Gampierakis, I.A., Koutmani, Y., Semitekolou, M., Morianos, I., Polissidis, A., Katsouda, A., et al. 2021. Hippocampal neural stem cells and microglia response to experimental inflammatory bowel disease (IBD). *Molecular Psychiatry* 26(4):1248-1263.
- Gerstner, E.R., Duda, D.G., di Tomaso, E., Ryg, P.A., Loeffler, J.S., Sorensen, A.G., et al. 2009. VEGF inhibitors in the treatment of cerebral edema in patients with brain cancer. *Nature reviews. Clinical Oncology* 6(4): 229–236. <https://doi.org/10.1038/nrclinonc.2009.14>
- Grathwohl, S., Quansah, E., Maroof, N., Steiner, J. A., Spycher, L., Benmansour, F., et al. 2021. Specific immune modulation of experimental colitis drives enteric alpha-synuclein accumulation and triggers age-related Parkinson-like brain pathology. *Free Neuropathology* 2: 13. <https://doi.org/10.17879/freeneuropathology-2021-3326>

- Guidi, S., Bonasoni, P., Ceccarelli, C., Santini, D., Gualtieri, F., Ciani, E., Bartesaghi, R. 2008. Neurogenesis impairment and increased cell death reduce total neuron number in the hippocampal region of fetuses with Down syndrome. *Brain Pathology (Zurich, Switzerland)* 18(2):180–197. <https://doi.org/10.1111/j.1750-3639.2007.00113.x>
- Gundersen, H.J., Jensen, E.B., Kiêu, K., Nielsen J. 1999. The efficiency of systematic sampling in stereology--reconsidered. *Journal of Microscopy* 193(Pt 3):199–211.
- Gofron, K.K., Wasilewski, A., Małgorzewicz, S. 2025. Effects of GLP-1 analogues and agonists on the gut microbiota: A systematic review. *Nutrients* 17(8): 1303. <https://doi.org/10.3390/nu17081303>
- Halstead, M.R., Geocadin, R.G. 2019. The medical management of cerebral edema: past, present, and future therapies. *Neurotherapeutics: The Journal of the American Society for Experimental NeuroTherapeutics* 16(4):1133–1148. <https://doi.org/10.1007/s13311-019-00779-4>
- Han, C.J., Saligan, L., Crouch, A., Kalady, M.F., Noonan, A.M., Lee, L.J., et al. 2023. Latent class symptom profiles of colorectal cancer survivors with cancer-related cognitive impairment. *Support Care Cancer* 31(10):559.
- Hanscom, M., Loane, D.J., Aubretch, T., Leser, J., Molesworth, K., HeGDekar, N., et al. 2021. Acute colitis during chronic experimental traumatic brain injury in mice induces dysautonomia and persistent extraintestinal, systemic, and CNS inflammation with exacerbated neurological deficits. *Journal Neuroinflammation* 18(1):24.
- Hara, Y., Morrison, J.H. 2014. Chapter Ten - Synaptic Correlates of Aging and Cognitive Decline. In: V. Pickel, M. Segal, (Eds.): *The Synapse*. p. 301-342. Academic Press.
- He, L., Zhang, R., Yang, M., Lu, M. 2024. The role of astrocyte in neuroinflammation in traumatic brain injury. *Biochimica et Biophysica Acta. Molecular Basis of Disease* 1870(3): 166992. <https://doi.org/10.1016/j.bbadis.2023.166992>
- He, X.F., Li, L.L., Xian, W.B., Li, M.Y., Zhang, L.Y., Xu, J.H., et al. 2021. Chronic colitis exacerbates NLRP3-dependent neuroinflammation and cognitive impairment in middle-aged brain. *Journal Neuroinflammation* 18(1):153. Erratum in: *Journal Neuroinflammation* 2022. 15;19(1):18.
- Hernández-Frausto, M., Vivar, C. 2024. Entorhinal cortex-hippocampal circuit connectivity in health and disease. *Frontiers in Human Neuroscience* 20(18):1448791.
- Honoré, E., Khlaifia, A., Bosson, A., Lacaille, J. C. 2021. Hippocampal somatostatin interneurons, long-term synaptic plasticity and memory. *Frontiers in Neural Circuits* 15: 687558. <https://doi.org/10.3389/fncir.2021.687558>
- Houser, M.C., Tansey, M.G. 2017. The gut-brain axis: is intestinal inflammation a silent driver of Parkinson's disease pathogenesis? *NPJ Parkinson's Disease* 11(3):3.
- Howard, C.V., Reed, M.G. 2005. *Unbiased Stereology, Second Edition*. Taylor & Francis, USA.

- Huynh, V.A., Takala, T.M., Murros, K.E., Diwedi, B., Saris, P.E.J. 2023. *Desulfovibrio* bacteria enhance alpha-synuclein aggregation in a *Caenorhabditis elegans* model of Parkinson's disease. *Frontiers in Cellular and Infection Microbiology* 13: 1181315. <https://doi.org/10.3389/fcimb.2023.1181315>
- Igarashi, K.M., Lu, L., Colgin, L.L., Moser, M.B., Moser, E.I. 2014. Coordination of entorhinal-hippocampal ensemble activity during associative learning. *Nature* 510(7503): 143–147. <https://doi.org/10.1038/nature13162>
- Inaba, H., Kishimoto, T., Oishi, S., Nagata, K., Hasegawa, S., Watanabe, T., et al. 2016. Vitamin B1-deficient mice show impairment of hippocampus-dependent memory formation and loss of hippocampal neurons and dendritic spines: potential microendophenotypes of Wernicke-Korsakoff syndrome. *Bioscience, Biotechnology, and Biochemistry* 80(12):2425–2436.
- Jang, S. E., Lim, S.M., Jeong, J.J., Jang, H.M., Lee, H.J., Han, M.J., et al. (2018). Gastrointestinal inflammation by gut microbiota disturbance induces memory impairment in mice. *Mucosal Immunology* 11(2):369–379. <https://doi.org/10.1038/mi.2017.49>
- Jha, M.K., Jo, M., Kim, J.H., Suk, K. 2019. Microglia-Astrocyte Crosstalk: An Intimate Molecular Conversation. *The Neuroscientist : A Review Journal Bringing Neurobiology, Neurology And Psychiatry* 25(3): 227–240. <https://doi.org/10.1177/1073858418783959>
- Jin, J., Xu, Z., Zhang, L., Zhang, C., Zhao, X., Mao, Y., et al. 2023. Gut-derived  $\beta$ -amyloid: Likely a centerpiece of the gut-brain axis contributing to Alzheimer's pathogenesis. *Gut Microbes* 15(1):2167172.
- Jing, R., Cai, Q., Li, W., Zhang, X. 2022. Neural circuits and some new factors involved in hippocampal memory. hippocampus - cytoarchitecture and diseases. In: X. Zhang (Ed.). IntechOpen, UK.
- Jridi, I., Canté-Barrett, K., Pike-Overzet, K., Staal, F.J.T. 2021. Inflammation and Wnt Signaling: Target for Immunomodulatory Therapy?. *Frontiers in Cell and Developmental Biology* 4(8):615131.
- Karademir, M., Gumus, E., Ergul, Y.T.M., Ergul, M., Karabulut, S., Akkaya, R., et al. 2019. Neuroprotective effect of astaxanthin (ATX) against cognitive impairment on PTZ-induced epileptic seizures in rats and against PTZ-induced neurotoxicity in SH-SY5Y human neuroblastoma cell culture. *Cumhuriyet Medical Journal* 41(1): 2121-222.
- Kearns R. 2024. Gut-brain axis and neuroinflammation: the role of gut permeability and the kynurenine pathway in neurological disorders. *Cellular and Molecular Neurobiology* 44(1):64. <https://doi.org/10.1007/s10571-024-01496-z>
- Kherani, Z.S., Auer, R.N. 2008. Pharmacologic analysis of the mechanism of dark neuron production in cerebral cortex. *Acta Neuropathologica* 116(4): 447–452. <https://doi.org/10.1007/s00401-008-0386-y>

- Kim, J.S., Chen, M.H., Wang, H.E., Lu, C.L., Wang, Y.P., Zhang, B. 2023. Inflammatory bowel disease and neurodegenerative diseases. *Gut Liver* 17(4):495-504.
- Knierim J.J. 2015. The hippocampus. *Current Biology: CB* 25(23): R1116–R1121. <https://doi.org/10.1016/j.cub.2015.10.049>
- Knox, E.G., Aburto, M.R., Clarke, G., Cryan, J.F., O'Driscoll, C.M. 2022. The blood-brain barrier in aging and neurodegeneration. *Molecular Psychiatry* 27(6): 2659–2673. <https://doi.org/10.1038/s41380-022-01511-z>
- Kristiansen, S.L., & Nyengaard, J.R. 2012. Digital stereology in neuropathology. *APMIS: Acta Pathologica, Microbiologica, et Immunologica Scandinavica* 120(4):327–340.
- Lanfranco, M.F., Sepulveda, J., Kopetsky, G., Rebeck, G.W. 2021. Expression and secretion of apoE isoforms in astrocytes and microglia during inflammation. *Glia* 69(6): 1478–1493. <https://doi.org/10.1002/glia.23974>
- Lee, K., Kumazoe, M., Marugame, Y., Fujimura Y, Tachibana, H. 2023. Dextran sulfate sodium-induced mild chronic colitis induced cognitive impairment accompanied by inhibition of neuronal maturation in adolescent mice. *Biochemical and Biophysical Research Communications* 669:46-53.
- Lewis S. (2017). Learning and memory: Memories take the sub-way. *Nature Reviews Neuroscience* 18(10): 571. <https://doi.org/10.1038/nrn.2017.117>
- Lewis, J.D., Parlett, L.E., Jonsson Funk, M.L., Brensinger, C., Pate, V., Wu, Q., Dawwas, G. K., Weiss, A., Constant, B.D., McCauley, M., Haynes, K., Yang, J.Y., Schaubel, D. E., Hurtado-Lorenzo, A., Kappelman, M.D. 2023. Incidence, prevalence, and racial and ethnic distribution of inflammatory bowel disease in the United States. *Gastroenterology* 165(5): 1197–1205.e2. <https://doi.org/10.1053/j.gastro.2023.07.003>
- Li, J., Ji, Y., Chen, N., Dai, L., Deng, H. 2023. Colitis-associated carcinogenesis: crosstalk between tumors, immune cells and gut microbiota. *Cell Bioscience* 13(1):194.
- Li, M., Xu, J., Li, L., Zhang, L., Zuo, Z., Feng, Y., et al. 2024. Voluntary wheel exercise improves glymphatic clearance and ameliorates colitis-associated cognitive impairment in aged mice by inhibiting TRPV4-induced astrocytic calcium activity. *Experimental Neurology* 376:114770. <https://doi.org/10.1016/j.expneurol.2024.114770>
- Liang, J., Yang, C., Li, P., Zhang, M., Xie, X., Xie, X., et al. 2023. Astragaloside IV inhibits AOM/DSS-induced colitis-associated tumorigenesis via activation of PPAR $\gamma$  signaling in mice. *Phytomedicine: International Journal of Phytotherapy And Phytopharmacology* 121:155116.
- Lin, R., Chen, F., Wen, S. *et al.* 2018. Interleukin-10 attenuates impairment of the blood-brain barrier in a severe acute pancreatitis rat model. *Journal of Inflammation* 15:4. <https://doi.org/10.1186/s12950-018-0180-0>
- LinGDren, L., Bergdahl, J., Nyberg, L. 2016. Longitudinal Evidence for Smaller Hippocampus Volume as a Vulnerability Factor for Perceived Stress. *Cerebral Cortex (New York, N.Y. : 1991)* 26(8):3527–3533.

- Liu, T., Zhang, L., Joo, D., Sun, S-C. 2017. NF- $\kappa$ B signaling in inflammation. *Signal Transduction and Targeted Therapy* 2:17023.
- Loh, J.S., Mak, W.Q., Tan, L.K.S., Ng, C.X., Chan, H.H., Yeow, S.H., et al. Microbiota-gut-brain axis and its therapeutic applications in neurodegenerative diseases. *Signal Transduction and Targeted Therapy* 9(1):37.
- Lopez-Rojas, J., & Kreutz, M. R. 2016. Mature granule cells of the dentate gyrus-  
-Passive bystanders or principal performers in hippocampal function?. *Neuroscience and Biobehavioral Reviews*, 64, 167–174.
- Lorenzini, L., Zanella, L., Sannia, M., Baldassarro, V.A., Moretti, M., Cescatti, M., et al. 2024. Experimental colitis in young Tg2576 mice accelerates the onset of an Alzheimer's-like clinical phenotype. *Alzheimer's Research & Therapy* 16(1):116.
- Mahbub, N.U., Islam, M.M., Hong, S.T., Chung, H.J. 2024. Dysbiosis of the gut microbiota and its effect on  $\alpha$ -synuclein and prion protein misfolding: consequences for neurodegeneration. *Frontiers in Cellular and Infection Microbiology* 14: 1348279. <https://doi.org/10.3389/fcimb.2024.1348279>
- Marcos, R., Monteiro, R. A., Rocha, E. 2012. The use of design-based stereology to evaluate volumes and numbers in the liver: a review with practical guidelines. *Journal of Anatomy* 220(4): 303–317. <https://doi.org/10.1111/j.1469-7580.2012.01475.x>
- Masanetz, R.K., Mundlos, H., Stolzer, I., Winkler, J., Günther, C., Süß, P. 2025. Absence of microglial activation and maintained hippocampal neurogenesis in a transgenic mouse model of Crohn's Disease. *Cells* 14(11): 841. <https://doi.org/10.3390/cells14110841>
- Mickael M. E., Bhaumik, S., Chakraborti, A., Umfress, A. A., van Groen, T., Macaluso, M., et al. 2022. ROR $\gamma$ t-Expressing Pathogenic CD4<sup>+</sup> T Cells Cause Brain Inflammation during Chronic Colitis. *Journal of Immunology (Baltimore, Md.: 1950)* 208(8):2054–2066. <https://doi.org/10.4049/jimmunol.2100869>.
- Mitchell, J., Kim, S.J., Howe, C., Lee, S., Her, J.Y., Patel, M., et al. 2022. Chronic Intestinal Inflammation Suppresses Brain Activity by Inducing Neuroinflammation in Mice. *The American Journal of Pathology* 192(1): 72–86. <https://doi.org/10.1016/j.ajpath.2021.09.006>
- Namakin, K., Moghaddam, M.H., Sadeghzadeh, S., Mehranpour, M., Vakili, K., Fathi, M., et al. 2023. Elderberry diet improves gut-brain axis dysfunction, neuroinflammation, and cognitive impairment in the rat model of irritable bowel syndrome. *Metabolic Brain Disease* 38(5): 1555–1572. <https://doi.org/10.1007/s11011-023-01187-6>
- Neupsykey. 2017. Pre-Frontal cortex, hippocampus, and the biology of explicit memory storage [online]. <https://neupsykey.com/pre-frontal-cortex-hippocampus-and-the-biology-of-explicit-memory-storage/> [Accessed : 18 June 2025].
- Niekamp, P., Kim, C.H. 2023. Microbial metabolite dysbiosis and colorectal cancer. *Gut and Liver* 17(2):190–203.

- Nikolaus, S., Schulte, B., Al-Massad, N., Thieme, F., Schulte, D.M., Bethge, J., et al. 2017. Increased tryptophan metabolism is associated with activity of inflammatory bowel diseases. *Gastroenterology* 153(6):1504–1516.e2. <https://doi.org/10.1053/j.gastro.2017.08.028>
- Nurmasitoh, T., Sari, D.C.R., Susilowati, R. 2023. Moderate-intensity intermittent exercise prevents memory deficit, hippocampal neuron loss, and elevated level of Alzheimer's dementia markers in the hippocampus of trimethyltin-induced rats. *Annals Anatomy* 249:152103.
- Olén, O., Erichsen, R., Sachs, M. C., Pedersen, L., Halfvarson, J., Askling, J., Ekbom, A., Sørensen, H.T., Ludvigsson, J.F. 2020. Colorectal cancer in ulcerative colitis: a Scandinavian population-based cohort study. *Lancet (London, England)* 395(10218):123–131. [https://doi.org/10.1016/S0140-6736\(19\)32545-0](https://doi.org/10.1016/S0140-6736(19)32545-0)
- Oltmer, J., Rosenblum, E.W., Williams, E.M., Roy, J., Llamas-Rodriguez, J., Perosa, V., et al. 2023. Stereology neuron counts correlate with deep learning estimates in the human hippocampal subregions. *Scientific Reports* 13(1): 5884. <https://doi.org/10.1038/s41598-023-32903-y>
- Omandhika, W.A. 2024. Pengaruh pemberian prebiotik beras hitam dan probiotik *Escherichia coli* NISSLE 1917 terhadap ekspresi gen IL-6, TNF- $\alpha$ , dan IL-10 pada hewan model *colitis-associated colorectal cancer* (CA-CRC) [Thesis]. Program Studi Magister Biologi UGM, Yogyakarta
- Omenetti, S., Pizarro, T.T. 2015. The Treg/Th17 Axis: A Dynamic Balance Regulated by the Gut Microbiome. *Frontiers in Immunology* 6:639. <https://doi.org/10.3389/fimmu.2015.00639>
- Osanai, H., Nair, I.R., Kitamura, T. 2023. Dissecting cell-type-specific pathways in medial entorhinal cortical-hippocampal network for episodic memory. *Journal of Neurochemistry* 166(2):172–188.
- Piancone, F., La Rosa, F., Marventano, I., Saresella, M., Clerici, M. 2021. The role of the inflammasome in neurodegenerative diseases. *Molecules* 26:953.
- Popov, J., Caputi, V., Nandeesha, N., Rodriguez, D.A., Pai, N. 2021. Microbiota-Immune Interactions in Ulcerative Colitis and Colitis Associated Cancer and Emerging Microbiota-Based Therapies. *International Journal of Molecular Sciences* 22(21):11365. <https://doi.org/10.3390/ijms222111365>
- Porter, R.J., Arends, M.J., Churchhouse, A.M.D., Din, S. 2021. Inflammatory bowel disease-associated colorectal cancer: translational risks from mechanisms to medicines. *Journal of Crohn's and Colitis* 15(12):2131–2141.
- Prigent, A., Lionnet, A., Durieu, E., Chapelet, G., Bourreille, A., Neunlist, M., et al. 2019. Enteric alpha-synuclein expression is increased in Crohn's disease. *Acta Neuropathologica* 137(2): 359–361. <https://doi.org/10.1007/s00401-018-1943-7>
- Redwine, J.M., Kosofsky, B., Jacobs, R.E., Games, D., Reilly, J.F., Morrison, J.H., et al. 2003. Dentate gyrus volume is reduced before onset of plaque formation in PDAPP mice: a magnetic resonance microscopy and

- stereologic analysis. *Proceedings of the National Academy of Sciences* 100(3):1381-6.
- Rolls E.T. 2018. The storage and recall of memories in the hippocampo-cortical system. *Cell and Tissue Research* 373(3):577–604.
- Rolls, E.T., Treves, A. 2024. A theory of hippocampal function: New developments. *Progress in Neurobiology* 238:102636.
- Rosenberg, G.A., Yang, Y. 2007. Vasogenic edema due to tight junction disruption by matrix metalloproteinases in cerebral ischemia. *Neurosurgical Focus* 22(5): E4.  
<https://doi.org/10.3171/foc.2007.22.5.5>
- Rubin, D.C., Shaker, A., & Levin, M. S. 2012. Chronic intestinal inflammation: inflammatory bowel disease and colitis-associated colon cancer. *Frontiers in Immunology* 3: 107. <https://doi.org/10.3389/fimmu.2012.00107>
- Salguero, M.V., Al-Obaide, M.A.I., Singh, R., Siepmann, T., Vasylyeva, T.L. 2019. Dysbiosis of Gram-negative gut microbiota and the associated serum lipopolysaccharide exacerbates inflammation in type 2 diabetic patients with chronic kidney disease. *Experimental and Therapeutic Medicine* 18(5):3461–3469. <https://doi.org/10.3892/etm.2019.7943>
- Sasabayashi, D., Yoshimura, R., Takahashi, T., Takayanagi, Y., Nishiyama, S., Higuchi, Y., et al. 2021. Reduced hippocampal subfield volume in schizophrenia and clinical high-risk state for psychosis. *Frontiers in Psychiatry* 12: 642048. <https://doi.org/10.3389/fpsy.2021.642048>
- Sato, Y., Tsujinaka, S., Miura, T., Kitamura, Y., Suzuki, H., Shibata, C. 2023. Inflammatory bowel disease and colorectal cancer: Epidemiology, Etiology, Surveillance, and Management. *Cancers*, 15(16), 4154. <https://doi.org/10.3390/cancers15164154>
- Schmitz, C., Hof, P.R. 2000. Recommendations for straightforward and rigorous methods of counting neurons based on a computer simulation approach. *Journal of Chemical Neuroanatomy* 20(1): 93–114. [https://doi.org/10.1016/s0891-0618\(00\)00066-1](https://doi.org/10.1016/s0891-0618(00)00066-1)
- Schoenfeld, T.J., McCausland, H.C., Morris, H.D., Padmanaban, V., Cameron, H.A. 2017. Stress and loss of adult neurogenesis differentially reduce hippocampal volume. *Biological Psychiatry* 82(12):914–923.
- Shah, S.C., Itzkowitz, S.H. 2022. Colorectal cancer in inflammatory bowel disease: mechanisms and management. *Gastroenterology* 162(3):715-730.
- Shahgoli, V.K., Noorolyai, S., Ahmadvour Youshanlui, M., Saeidi, H., Nasiri, H., Mansoori, B., et al. Inflammatory bowel disease, colitis, and cancer: unmasking the chronic inflammation link. *International Journal of Colorectal Disease* 39(1):173.
- Sharma, N., Dhiman, S., Bodh, V., Sharma, D., Sharma, R., Sharma, S., et al. Cognitive dysfunction in ulcerative colitis patients in remission and its comparison with patients with irritable bowel syndrome and healthy controls. *Indian Journal of Gastroenterology* 40(2):169-175.
- Sin, R., Sotogaku, N., Ohnishi, Y.N., Shuto, T., Kuroiwa, M., Kawahara, Y., et al. 2023. Inhibition of STAT-mediated cytokine responses to chemically-induced colitis prevents inflammation-associated neurobehavioral

- impairments. *Brain, Behavior, and Immunity* 114:173–186.  
<https://doi.org/10.1016/j.bbi.2023.08.019>
- Small, S.A., Schobel, S.A., Buxton, R.B., Witter, M.P., Barnes, C.A. 2011. A pathophysiological framework of hippocampal dysfunction in ageing and disease. *Nature Review Neuroscience* 12(10):585-601.
- Sofroniew M.V. 2014. Astrogliosis. *Cold Spring Harbor Perspectives in Biology* 7(2):a020420. <https://doi.org/10.1101/cshperspect.a020420>
- Solikhah. 2024. Pengaruh pemberian probiotik *Escherichia Coli* Strain Nissle 1917 dan prebiotik sereal beras hitam (*Oryza sativa* L. 'Sembada Hitam') terhadap tingkat kerusakan histologi colon serta distribusi makrofag pada mencit model colitis associated colorectal cancer (CA-CRC) [Tesis]. Program Studi Magister Biologi UGM, Yogyakarta.
- Sonobe, Y., Takeuchi, H., Kataoka, K., Li, H., Jin, S., Mimuro, M., et al. 2016. Interleukin-25 expressed by brain capillary endothelial cells maintains blood-brain barrier function in a protein kinase C $\epsilon$ -dependent manner. *The Journal of Biological Chemistry* 291(24):12573.  
<https://doi.org/10.1074/jbc.A109.025940>
- Sun, Z., Zhao, S., Suo, X., Dou, Y. 2022. Sirt1 protects against hippocampal atrophy and its induced cognitive impairment in middle-aged mice. *BMC Neuroscience* 23(1):33.
- Takahashi, K., Kurokawa, K., Hong, L., Miyagawa, K., Mochida-Saito, A., Takeda, H., et al. Tsuji M. Hippocampal and gut AMPK activation attenuates enterocolitis-like symptoms and co-occurring depressive-like behavior in ulcerative colitis model mice: Involvement of brain-gut autophagy. *Experimental Neurology* 373:114671.
- Talley, S., Valiauga, R., Anderson, L., Cannon, A.R., Choudhry, M.A., Campbell, E.M. 2021. DSS-induced inflammation in the colon drives a proinflammatory signature in the brain that is ameliorated by prophylactic treatment with the S100A9 inhibitor paquinimod. *Journal Neuroinflammation* 18(1):263.
- Tang, C., Wang, J., Ge, M., Fu, L., Huang, J., Yadav, H., et al. 2025. DSS-induced colitis exacerbates Alzheimer's pathology via neutrophil elastase and cathepsin B activation. *International Immunopharmacology* 155: 114666.  
<https://doi.org/10.1016/j.intimp.2025.114666>
- Tang, W., Zhu, H., Feng, Y., Guo, R., Wan, D. 2020. The Impact of Gut Microbiota Disorders on the Blood-Brain Barrier. *Infection and Drug Resistance* 13:3351-3363.
- Torshin, V.I., Kastyro, I.V., Reshetov, I.V., Kostyaeva, M.G., Popadyuk, V.I. 2022. The Relationship between p53-Positive Neurons and Dark Neurons in the Hippocampus of Rats after Surgical Interventions on the Nasal Septum. *Doklady. Biochemistry and Biophysics* 502(1): 30–35.  
<https://doi.org/10.1134/S1607672922010094>
- Trichka, J., Zou, W.Q. 2021. Modulation of Neuroinflammation by the Gut Microbiota in Prion and Prion-Like Diseases. *Pathogens*. 10(7):887.
- Tu, Y., Fu, J., Wang, J., Fu, G., Wang, L., Zhang, Y. 2012. Extracellular matrix metalloproteinase inducer is associated with severity of brain oedema

- following experimental subarachnoid haemorrhage in rats. *The Journal of International Medical Research* 40(3): 1089–1098.  
<https://doi.org/10.1177/147323001204000328>
- Uceda, S., Echeverry-Alzate, V., Reiriz-Rojas, M., Martínez-Miguel, E., Pérez-Curiel, A., Gómez-Senent, S., et al. (2023). Gut Microbial Metabolome and Dysbiosis in Neurodegenerative Diseases: Psychobiotics and Fecal Microbiota Transplantation as a Therapeutic Approach—A Comprehensive Narrative Review. *International Journal of Molecular Sciences* 24(17): 13294. <https://doi.org/10.3390/ijms241713294>
- Valiukas, Z., Tangalakis, K., Apostolopoulos, V., Feehan, J. 2025. Microglial activation states and their implications for Alzheimer's Disease. *The Journal of Prevention of Alzheimer's Disease* 12(1): 100013.  
<https://doi.org/10.1016/j.tjpad.2024.100013>
- Visovatti, M.A., Reuter-Lorenz, P.A., Chang, A.E., Northouse, L., Cimprich, B. (2016). Assessment of cognitive impairment and complaints in individuals with colorectal cancer. *Oncology Nursing Forum* 43(2):169–178.  
<https://doi.org/10.1188/16.ONF.43-02AP>
- Vitali, R., Prioreshi, C., Lorenzo Rebenaque, L., Colantoni, E., Giovannini, D., Frusciante, S., et al. (2022). Gut-brain axis: insights from hippocampal neurogenesis and brain tumor development in a mouse model of experimental colitis induced by dextran sodium sulfate. *International Journal of Molecular Sciences* 23(19): 11495.  
<https://doi.org/10.3390/ijms231911495>
- Vetter, L.E., Merkel, S., Bénard, A., Krautz, C., Brunner, M., Mittelstädt, A., Schlegel, N., Wiegeling, A., Germer, C. T., Weber, K., Grützmann, R., Weber, G.F. 2021. Colorectal cancer in Crohn's colitis is associated with advanced tumor invasion and a poorer survival compared with ulcerative colitis: a retrospective dual-center study. *International Journal of Colorectal Disease* 36(1): 141–150. <https://doi.org/10.1007/s00384-020-03726-4>
- Wang Y, Jin S, Sonobe Y, Cheng Y, Horiuchi H, Parajuli B, et al. 2014. Interleukin-1 $\beta$  induces blood–brain barrier disruption by downregulating sonic hedgehog in astrocytes. *PLoS ONE* 9(10): e110024.
- Wang, H., Song, G., Chuang, H., Chiu, C., Abdelmaksoud, A., Ye, Y., Zhao, L. 2018. Portrait of glial scar in neurological diseases. *International Journal of Immunopathology and Pharmacology* 31: 2058738418801406.  
<https://doi.org/10.1177/2058738418801406>
- Wang, R., Ren, H., Kaznatcheyeva, E., Lu, X., Wang, G. 2023. Association of glial activation and  $\alpha$ -Synuclein pathology in Parkinson's disease. *Neuroscience Bulletin* 39(3): 479–490.  
<https://doi.org/10.1007/s12264-022-00957-z>
- Wang, Z., Zhou, L., An, D., Xu, W., Wu, C., Sha, S., et al. 2019. Author Correction: TRPV4-induced inflammatory response is involved in neuronal death in pilocarpine model of temporal lobe epilepsy in mice. *Cell Death & Disease* 10(7):491. <https://doi.org/10.1038/s41419-019-1691-1>

- Waxman, E.A., Lynch, D.R. 2005. N-methyl-D-aspartate receptor subtypes: multiple roles in excitotoxicity and neurological disease. *The Neuroscientist : A Review Journal Bringing Neurobiology, Neurology and Psychiatry* 11(1): 37–49. <https://doi.org/10.1177/1073858404269012>
- Wei W, Wang S, Xu C, Zhou X, Lian X, He L, Li K. 2022. Gut microbiota, pathogenic proteins and neurodegenerative diseases. *Frontiers of Microbiology* 13:959856.
- West, M.J., Bach, G., Söderman, A., Jensen, J.L. 2009. Synaptic contact number and size in stratum radiatum CA1 of APP/PS1DeltaE9 transgenic mice. *Neurobiology of Aging* 30(11):1756–1776.
- White, T.A., Miller, S.L., Sutherland, A.E., Allison, B.J., Camm, E.J. 2024. Perinatal compromise affects development, form, and function of the hippocampus part one; clinical studies. *Pediatric Research* 95(7):1698-1708.
- Witter, M.P. 2010. Connectivity of the Hippocampus. In: V. Cutsuridis, B. Graham, S. Cobb, I. Vida (Eds). *Hippocampal Microcircuits. Springer Series in Computational Neuroscience*, Springer, New York, NY.
- Xingi, R., Cheng, J., Yu, J., Li, S., Ma, H., Zhao, Y. 2023. Trifluoperazine reduces apoptosis and inflammatory responses in traumatic brain injury by preventing the accumulation of Aquaporin4 on the surface of brain cells. *International Journal of Medical Sciences* 20(6):797–809. <https://doi.org/10.7150/ijms.82677>
- Yang, R., Gao, G., Yang, H. 2022. The pathological mechanism between the intestine and brain in the early stage of parkinson's disease. *Frontiers in Aging and Neuroscience*. 14:861035.
- Yang, T., Dai, Y., Chen, G., & Cui, S. 2020. Dissecting the Dual Role of the Glial Scar and Scar-Forming Astrocytes in Spinal Cord Injury. *Frontiers in Cellular Neuroscience* 14: 78. <https://doi.org/10.3389/fncel.2020.00078>
- Yokose, J., Marks, W.D., Yamamoto, N., Ogawa, S.K., Kitamura, T. 2021. Entorhinal cortical Island cells regulate temporal association learning with long trace period. *Learning & Memory* 28(9): 319–328. <https://doi.org/10.1101/lm.052589.120>
- Yuan, X., Chen, B., Duan, Z., Xia, Z., Ding, Y., Chen, T., et al. 2021. Depression and anxiety in patients with active ulcerative colitis: crosstalk of gut microbiota, metabolomics and proteomics. *Gut Microbes* 13(1): 1987779. <https://doi.org/10.1080/19490976.2021.1987779>
- Yurt, K.K., Kivrak, E.G., Altun, G., Mohamed, H., Ali, F., Gasmalla, H.E., et al. 2018. A brief update on physical and optical disector applications and sectioning-staining methods in neuroscience. *Journal of Chemical Neuroanatomy* 93:16–29.
- Zhang, W., An, Y., Qin, X., Wu, X., Wang, X., Hou, H., et al. 2021a. Gut microbiota-derived metabolites in colorectal cancer: the bad and the challenges. *Frontiers in Oncology* 11:739648.
- Zhang, H., Wei, W., Zhao, M., Ma, L., Jiang, X., Pei, H., et al. 2021b. Interaction between A $\beta$  and Tau in the Pathogenesis of Alzheimer's

- Disease. *International Journal of Biological Sciences* 17(9): 2181–2192. <https://doi.org/10.7150/ijbs.57078>
- Zhang, W., Xiao, D., Mao, Q., Xia, H. 2023. Role of neuroinflammation in neurodegeneration development. *Signal Transduction and Targeted Therapy* 8(1):267.
- Zhao, L.P., Wu, J., Quan, W., Zhou, Y., Hong, H., Niu, G.Y., et al. 2023a. DSS-induced colitis activates the kynurenine pathway in serum and brain by affecting IDO-1 and gut microbiota. *Frontiers in Immunology* 13:1089200. <https://doi.org/10.3389/fimmu.2022.1089200>
- Zheng, J.Y., Li, X.X., Lin, W.Y., Su, S., Wu, H.C., Hu, R.D., et al. 2023. Huang-Lian-Jie-Du decoction alleviates depressive-like behaviors in dextran sulfate sodium-induced colitis mice via Trem2/Dap12 pathway. *Journal of Ethnopharmacology* 315:116658.
- Zhou, R.W., Harpaz, N., Itzkowitz, S.H. Parsons, R.E. 2023. Molecular mechanisms in colitis-associated colorectal cancer. *Oncogenesis* 12:48.
- Zimatkin, S.M. & Bon, E.I. (2018). Dark Neurons of the Brain. *Neuroscience and Behavioral Physiology* 48: 908.912.