

## Reference Library

The following selections may be of interest to review for Oskar Fischer Prize entries:

Adaikkan, C., Middleton, S. J., Marco, A., Pao, P. C., Mathys, H., Kim, D. N., Gao, F., Young, J. Z., Suk, H. J., Boyden, E. S., McHugh, T. J., & Tsai, L. H. (2019). Gamma Entrainment Binds Higher-Order Brain Regions and Offers Neuroprotection. *Neuron*, 102(5), 929–943.e8. <https://doi.org/10.1016/j.neuron.2019.04.011>

Aguayo, S., Schuh, C. M. A. P., Vicente, B., & Aguayo, L. G. (2018). Association between Alzheimer's Disease and Oral and Gut Microbiota: Are Pore Forming Proteins the Missing Link? *Journal of Alzheimer's Disease*, 65(1), 29–46. <https://doi.org/10.3233/JAD-180319>

Altuna, M., Urdánoz-Casado, A., Sánchez-Ruiz de Gordo, J., Zelaya, M. V., Labarga, A., Lepesant, J. M. J., ... Mendioroz, M. (2019). DNA methylation signature of human hippocampus in Alzheimer's disease is linked to neurogenesis. *Clinical Epigenetics*, 11(1), 91. <https://doi.org/10.1186/s13148-019-0672-7>

Alves de Lima, K., Rustenhoven, J., & Kipnis, J. (2020). Meningeal Immunity and Its Function in Maintenance of the Central Nervous System in Health and Disease. *Annual Review of Immunology*, 38(1), 597–620. <https://doi.org/10.1146/annurev-immunol-102319-103410>

Alzheimer's Disease is a 'Double-Prion Disorder,' Study Shows | UC San Francisco. (n.d.). Retrieved June 18, 2020, from <https://www.ucsf.edu/news/2019/05/414326/alzheimers-disease-double-prion-disorder-study-shows>

Area-Gomez, E., Larrea, D., Pera, M., Agrawal, R. R., Guilfoyle, D. N., Pirhaji, L., ... Nuriel, T. (2020). APOE4 is Associated with Differential Regional Vulnerability to Bioenergetic Deficits in Aged APOE Mice. *Scientific Reports*, 10(1), 4277. <https://doi.org/10.1038/s41598-020-61142-8>

Armiento, V., Hille, K., Naltsas, D., Lin, J. S., Barron, A. E., & Kapurniotu, A. (2020). The Human Host-Defense Peptide Cathelicidin LL-37 is a Nanomolar Inhibitor of Amyloid Self-Assembly of Islet Amyloid Polypeptide (IAPP). *Angewandte Chemie International Edition*, anie.202000148. <https://doi.org/10.1002/anie.202000148>

Askarova, S., Umbayev, B., Masoud, A.-R., Kaiyrykyzy, A., Safarova, Y., Tsoy, A., ... Kushugulova, A. (2020). The Links Between the Gut Microbiome, Aging, Modern Lifestyle and Alzheimer's Disease. *Frontiers in Cellular and Infection Microbiology*, 10(March), 1–12. <https://doi.org/10.3389/fcimb.2020.00104>

Baek H., Ye M., Kang G., Lee C., Lee G., Choi D., Jung J., Kim H., Lee S., Kim J., Lee H., Shim I., Lee J., et al (2016). Neuroprotective effects of CD4<sup>+</sup>CD25<sup>+</sup>Foxp3<sup>+</sup> regulatory T

- cells in a 3xTg-AD Alzheimer's disease model. *Oncotarget*, 7, 69347-69357. <https://doi.org/10.18632/oncotarget.12469>
- Baek, H., Ye, M., Kang, G., Lee, C., Lee, G., Choi, D. Bin, ... Bae, H. (2016). Neuroprotective effects of CD4+CD25+Foxp3+ regulatory T cells in a 3xTg-AD Alzheimer's disease model. *Oncotarget*, 7(43), 69347-69357. <https://doi.org/10.18632/oncotarget.12469>
- Bandea, C. I. (2013). A $\beta$ , tau,  $\alpha$ -synuclein, huntingtin, TDP-43, PrP and AA are members of the innate immune system: a unifying hypothesis on the etiology of AD, PD, HD, ALS, CJD and RSA as innate immunity disorders. *BioRxiv*, (i), 1-10. <https://doi.org/10.1101/000604>
- Baruch, K., Deczkowska, A., David, E., Castellano, J. M., Miller, O., Kertser, A., ... Schwartz, M. (2014). Aging-induced type I interferon response at the choroid plexus negatively affects brain function. *Science*, 346(6205), 89-93. <https://doi.org/10.1126/science.1252945>
- Blusztajn, J. K., Slack, B. E., & Mellott, T. J. (2017). Neuroprotective Actions of Dietary Choline. *Nutrients*, 9(8), 815. <https://doi.org/10.3390/nu9080815>
- Brandenburg, L.-O., Varoga, D., Nicolaeva, N., Leib, S. L., Wilms, H., Podschun, R., ... Lucius, R. (2008). Role of Glial Cells in the Functional Expression of LL-37/Rat Cathelin-Related Antimicrobial Peptide in Meningitis. *Journal of Neuropathology & Experimental Neurology*, 67(11), 1041-1054. <https://doi.org/10.1097/NEN.0b013e31818b4801>
- Bredesen, D. E., John, V., & Galvan, V. (2010). Importance of the Caspase Cleavage Site in Amyloid- $\beta$  Protein Precursor. *Journal of Alzheimer's Disease*, 22(1), 57-63. <https://doi.org/10.3233/JAD-2010-100537>
- Bruch, J., Xu, H., De Andrade, A., & Höglinger, G. (2014). Mitochondrial Complex 1 Inhibition Increases 4-Repeat Isoform Tau by SRSF2 Upregulation. *PLoS ONE*, 9(11), e113070. <https://doi.org/10.1371/journal.pone.0113070>
- Camacho-Pereira, J., Tarragó, M. G., Chini, C. C. S., Nin, V., Escande, C., Warner, G. M., ... Chini, E. N. (2016). CD38 Dictates Age-Related NAD Decline and Mitochondrial Dysfunction through an SIRT3-Dependent Mechanism. *Cell Metabolism*, 23(6), 1127-1139. <https://doi.org/10.1016/j.cmet.2016.05.006>
- Carter, C. J., France, J., Crean, S., & Singhrao, S. K. (2017). The Porphyromonas gingivalis/Host Interactome Shows Enrichment in GWASdb Genes Related to Alzheimer's Disease, Diabetes and Cardiovascular Diseases. *Frontiers in Aging Neuroscience*, 9(DEC), 1-15. <https://doi.org/10.3389/fnagi.2017.00408>
- Cassan, C., Piaggio, E., Zappulla, J. P., Mars, L. T., Couturier, N., Bucciarelli, F., ... Liblau, R. S. (2006). Pertussis Toxin Reduces the Number of Splenic Foxp3 + Regulatory T Cells. *The Journal of Immunology*, 177(3), 1552-1560. <https://doi.org/10.4049/jimmunol.177.3.1552>

- Celik, S., Russell, J. C., Pestana, C. R., Lee, T.-I., Mukherjee, S., Crane, P. K., ... Lee, S.-I. (2018). DECODER: A probabilistic approach to integrate big data reveals mitochondrial Complex I as a potential therapeutic target for Alzheimer's disease. *BioRxiv*, 302737. <https://doi.org/10.1101/302737>
- Cheng, Y., & Bai, F. (2018). The Association of Tau with Mitochondrial Dysfunction in Alzheimer's Disease. *Frontiers in Neuroscience*, 12(MAR), 2014–2019. <https://doi.org/10.3389/fnins.2018.00163>
- Chung, C., Silwal, P., Kim, I., Modlin, R. L., & Jo, E.-K. (2020). Vitamin D-Cathelicidin Axis: at the Crossroads between Protective Immunity and Pathological Inflammation during Infection. *Immune Network*, 20(2), 1–26. <https://doi.org/10.4110/in.2020.20.e12>
- Cook, E. K., Sell, G. L., Schaffer, T. B., & Margolis, S. S. (2019). The emergence of Ephexin5 as a therapeutic target in Alzheimer's disease. *Expert Opinion on Therapeutic Targets*, 23(4), 263–265. <https://doi.org/10.1080/14728222.2019.1586884>
- Corsetti, V., Florenzano, F., Atlante, A., Bobba, A., Ciotti, M. T., Natale, F., Della Valle, F., Borreca, A., Manca, A., Meli, G., Ferraina, C., Feligioni, M., D'Aguanno, S., Bussani, R., Ammassari-Teule, M., Nicolin, V., Calissano, P., & Amadoro, G. (2015). NH2-truncated human tau induces deregulated mitophagy in neurons by aberrant recruitment of Parkin and UCHL-1: implications in Alzheimer's disease. *Human molecular genetics*, 24(11), 3058–3081. <https://doi.org/10.1093/hmg/ddv059>
- Cox, P. A., Davis, D. A., Mash, D. C., Metcalf, J. S., & Banack, S. A. (2016). Dietary exposure to an environmental toxin triggers neurofibrillary tangles and amyloid deposits in the brain. *Proceedings of the Royal Society B: Biological Sciences*, 283(1823), 20152397. <https://doi.org/10.1098/rspb.2015.2397>
- Currais, A., Huang, L., Goldberg, J., Petrascheck, M., Ates, G., Pinto-Duarte, A., ... Maher, P. (2019). Elevating acetyl-CoA levels reduces aspects of brain aging. *eLife*, 8, 1–21. <https://doi.org/10.7554/eLife.47866>
- Czubowicz, K., Jęsko, H., Wencel, P., Lukiw, W. J., & Strosznajder, R. P. (2019). The Role of Ceramide and Sphingosine-1-Phosphate in Alzheimer's Disease and Other Neurodegenerative Disorders. *Molecular Neurobiology*, 56(8), 5436–5455. <https://doi.org/10.1007/s12035-018-1448-3>
- Da Costa, K.-A., Niculescu, M. D., Craciunescu, C. N., Fischer, L. M., & Zeisel, S. H. (2006). Choline deficiency increases lymphocyte apoptosis and DNA damage in humans. *The American Journal of Clinical Nutrition*, 84(1), 88–94. <https://doi.org/10.1093/ajcn/84.1.88>
- Da Mesquita, S., Fu, Z., & Kipnis, J. (2018). The Meningeal Lymphatic System: A New Player in Neurophysiology. *Neuron*, 100(2), 375–388. <https://doi.org/10.1016/j.neuron.2018.09.022>

- Dansokho, C., Ait Ahmed, D., Aid, S., Toly-Ndour, C., Chaigneau, T., Calle, V., ... Dorothée, G. (2016). Regulatory T cells delay disease progression in Alzheimer-like pathology. *Brain*, 139(4), 1237–1251. <https://doi.org/10.1093/brain/awv408>
- De la Rosa, A., Olaso-Gonzalez, G., Arc-Chagnaud, C., Millan, F., Salvador-Pascual, A., García-Lucerga, C., ... Gomez-Cabrera, M. C. (2020). Physical exercise in the prevention and treatment of Alzheimer's disease. *Journal of Sport and Health Science*, 00. <https://doi.org/10.1016/j.jshs.2020.01.004>
- De Lorenzi, E., Chiari, M., Colombo, R., Cretich, M., Sola, L., Vanna, R., ... Barron, A. E. (2017). Evidence that the Human Innate Immune Peptide LL-37 may be a Binding Partner of Amyloid- $\beta$  and Inhibitor of Fibril Assembly. *Journal of Alzheimer's Disease*, 59(4), 1213–1226. <https://doi.org/10.3233/JAD-170223>
- Devi, L. (2006). Accumulation of Amyloid Precursor Protein in the Mitochondrial Import Channels of Human Alzheimer's Disease Brain Is Associated with Mitochondrial Dysfunction. *Journal of Neuroscience*, 26(35), 9057–9068. <https://doi.org/10.1523/JNEUROSCI.1469-06.2006>
- Dief, A. E., Samy, D. M., & Dowedar, F. I. (2015). Impact of exercise and vitamin B1 intake on hippocampal brain-derived neurotrophic factor and spatial memory performance in a rat model of stress. *Journal of Nutritional Science and Vitaminology*, 61(1), 1–7. <https://doi.org/10.3177/jnsv.61.1>
- Dolejší, E., Liraz, O., Rudajev, V., Zimčík, P., Doležal, V., & Michaelson, D. M. (2016). Apolipoprotein E4 reduces evoked hippocampal acetylcholine release in adult mice. *Journal of Neurochemistry*, 136(3), 503–509. <https://doi.org/10.1111/jnc.13417>
- Dominy, S. S., Lynch, C., Ermini, F., Benedyk, M., Marczyk, A., Konradi, A., ... Potempa, J. (2019). Porphyromonas gingivalis in Alzheimer's disease brains: Evidence for disease causation and treatment with small-molecule inhibitors. *Science Advances*, 5(1), eaau3333. <https://doi.org/10.1126/sciadv.aau3333>
- Eckert, A., Schmitt, K., & Götz, J. (2011). Mitochondrial dysfunction - the beginning of the end in Alzheimer's disease? Separate and synergistic modes of tau and amyloid- $\beta$  toxicity. *Alzheimer's Research & Therapy*, 3(2), 15. <https://doi.org/10.1186/alzrt74>
- Eimer, W. A., Vijaya Kumar, D. K., Navalpur Shanmugam, N. K., Rodriguez, A. S., Mitchell, T., Washicosky, K. J., ... Moir, R. D. (2018). Alzheimer's Disease-Associated  $\beta$ -Amyloid Is Rapidly Seeded by Herpesviridae to Protect against Brain Infection. *Neuron*, 99(1), 56–63.e3. <https://doi.org/10.1016/j.neuron.2018.06.030>
- Escobar-Khondiker, M., Hollerhage, M., Muriel, M.-P., Champy, P., Bach, A., Depienne, C., ... Hoglinger, G. U. (2007). Annonacin, a Natural Mitochondrial Complex I Inhibitor, Causes Tau Pathology in Cultured Neurons. *Journal of Neuroscience*, 27(29), 7827–7837. <https://doi.org/10.1523/JNEUROSCI.1644-07.2007>

- Fang, E. F., Hou, Y., Palikaras, K., Adriaanse, B. A., Kerr, J. S., Yang, B., Lautrup, S., Hasan-Olive, M. M., Caponio, D., Dan, X., Rocktäschel, P., Croteau, D. L., Akbari, M., Greig, N. H., Fladby, T., Nilsen, H., Cader, M. Z., Mattson, M. P., Tavernarakis, N., & Bohr, V. A. (2019). Mitophagy inhibits amyloid- $\beta$  and tau pathology and reverses cognitive deficits in models of Alzheimer's disease. *Nature neuroscience*, 22(3), 401–412. <https://doi.org/10.1038/s41593-018-0332-9>
- Fazal, N. (2012). T Cell Suppression in Burn and Septic Injuries. In *Immunosuppression - Role in Health and Diseases*. InTech. <https://doi.org/10.5772/26523>
- Fetahu, I. S., Ma, D., Rabidou, K., Argueta, C., Smith, M., Liu, H., Wu, F., & Shi, Y. G. (2019). Epigenetic signatures of methylated DNA cytosine in Alzheimer's disease. *Science advances*, 5(8), eaaw2880. <https://doi.org/10.1126/sciadv.aaw2880>
- Fick, D. M., Kolanowski, A., Beattie, E., & McCrow, J. (2009). Delirium in Early-Stage Alzheimer's Disease. *Journal of Gerontological Nursing*, 35(3), 30–38. <https://doi.org/10.3928/00989134-20090301-06>
- Fong TG, Jones RN, Shi P, et al. Delirium accelerates cognitive decline in Alzheimer disease. *Neurology*. 2009;72(18):1570-1575. <https://doi.org/10.1212/wnl.0b013e3181a4129a>
- Fong, T. G., Vasunilashorn, S. M., Libermann, T., Marcantonio, E. R., & Inouye, S. K. (2019). Delirium and Alzheimer disease: A proposed model for shared pathophysiology. *International Journal of Geriatric Psychiatry*, 34(6), 781–789. <https://doi.org/10.1002/gps.5088>
- Frost, B. (2016). Alzheimer's disease: An acquired neurodegenerative laminopathy. *Nucleus*, 7(3), 275–283. <https://doi.org/10.1080/19491034.2016.1183859>
- Frost, B., Bardai, F. H., & Feany, M. B. (2016). Lamin Dysfunction Mediates Neurodegeneration in Tauopathies. *Current Biology*, 26(1), 129–136. <https://doi.org/10.1016/j.cub.2015.11.039>
- Gao, J., Wang, L., Liu, J., Xie, F., Su, B., & Wang, X. (2017). Abnormalities of Mitochondrial Dynamics in Neurodegenerative Diseases. *Antioxidants*, 6(2), 25. <https://doi.org/10.3390/antiox6020025>
- Gao, Ju & Wang, Luwen & Gao, Chao & Arakawa, Hiroyuki & Perry, George & Wang, Xinglong. (2019). TDP-43 inhibitory peptide alleviates neurodegeneration and memory loss in an APP transgenic mouse model for Alzheimer's disease. *Biochimica et Biophysica Acta (BBA) - Molecular Basis of Disease*. 1866(1) <https://doi.org/10.1016/j.bbadis.2019.165580>
- Gate, D., Saligrama, N., Leventhal, O. *et al.* Clonally expanded CD8 T cells patrol the cerebrospinal fluid in Alzheimer's disease. *Nature* 577, 399–404 (2020). <https://doi.org/10.1038/s41586-019-1895-7>

- Ghavami, S., Shojaei, S., Yeganeh, B., Ande, S. R., Jangamreddy, J. R., Mehrpour, M., Christoffersson, J., Chaabane, W., Moghadam, A. R., Kashani, H. H., Hashemi, M., Owji, A. A., & Łos, M. J. (2014). Autophagy and apoptosis dysfunction in neurodegenerative disorders. *Progress in neurobiology*, 112, 24–49.  
<https://doi.org/10.1016/j.pneurobio.2013.10.004>
- Glowczyk, I., Wong, A., Potempa, B., Babyak, O., Lech, M., Lamont, R. J., ... Koziel, J. (2017). Inactive Gingipains from *P. gingivalis* Selectively Skews T Cells toward a Th17 Phenotype in an IL-6 Dependent Manner. *Frontiers in Cellular and Infection Microbiology*, 7(APR), 1–16. <https://doi.org/10.3389/fcimb.2017.00140>
- Goldberg, J., Currais, A., Prior, M., Fischer, W., Chiruta, C., Ratliff, E., ... Schubert, D. (2018). The mitochondrial ATP synthase is a shared drug target for aging and dementia. *Aging Cell*, 17(2), e12715. <https://doi.org/10.1111/acer.12715>
- Gomes, A. P., Price, N. L., Ling, A. J. Y., Moslehi, J. J., Montgomery, M. K., Rajman, L., ... Sinclair, D. A. (2013). Declining NAD<sup>+</sup> induces a pseudohypoxic state disrupting nuclear-mitochondrial communication during aging. *Cell*, 155(7), 1624–1638.  
<https://doi.org/10.1016/j.cell.2013.11.037>
- Haditsch, U., Roth, T., Rodriguez, L., Hancock, S., Cecere, T., Nguyen, M., ... Ermini, F. (2020). Alzheimer's Disease-Like Neurodegeneration in Porphyromonas gingivalis Infected Neurons with Persistent Expression of Active Gingipains. *Journal of Alzheimer's Disease*, 75(4), 1361–1376. <https://doi.org/10.3233/JAD-200393>
- Haileselassie, B., Joshi, A.U., Minhas, P.S., Mukherjee, R., Andreasson, K.I., Mochly-Rosen, D. (2020). Mitochondrial dysfunction mediated through dynamin-related protein 1 (Drp1) propagates impairment in blood brain barrier in septic encephalopathy. *J Neuroinflammation* 17, 36. <https://doi.org/10.1186/s12974-019-1689-8>
- Harach, T., Marungruang, N., Duthilleul, N., Cheatham, V., Mc Coy, K. D., Frisoni, G., ... Bolmont, T. (2017). Reduction of Aβ amyloid pathology in APPS1 transgenic mice in the absence of gut microbiota. *Scientific Reports*, 7(1), 41802.  
<https://doi.org/10.1038/srep41802>
- Harach, T., Marungruang, N., Duthilleul, N., Cheatham, V., Coy, K. D. M., Neher, J. J., ... Bolmont, T. (2015). Reduction of Alzheimer's disease beta-amyloid pathology in the absence of gut microbiota. *Вестник КазНМУ, №3*, с.30. Retrieved from <http://arxiv.org/abs/1509.02273>
- Haran, J. P., Bhattarai, S. K., Foley, S. E., Dutta, P., Ward, D. V., Bucci, V., & McCormick, B. A. (2019). Alzheimer's Disease Microbiome Is Associated with Dysregulation of the Anti-Inflammatory P-Glycoprotein Pathway. *MBio*, 10(3), 1–14.  
<https://doi.org/10.1128/mBio.00632-19>

- Hershenhouse, K. S., Shauly, O., Gould, D. J., & Patel, K. M. (2019). Meningeal Lymphatics: A Review and Future Directions From a Clinical Perspective. *Neuroscience Insights*, 14, 117906951988902. <https://doi.org/10.1177/1179069519889027>
- Hildre, A. S., Solvang, S.-E. H., Aarsland, D., Midtun, Ø., McCann, A., Ervik, A. O., ... Giil, L. M. (2020). Components of the choline oxidation pathway modify the association between the apolipoprotein  $\epsilon 4$  gene variant and cognitive decline in patients with dementia. *Brain Research*, 1726(October 2019), 146519. <https://doi.org/10.1016/j.brainres.2019.146519>
- Hoglinger, G. U., Lannuzel, A., Khondiker, M. E., Michel, P. P., Duyckaerts, C., Feger, J., ... Hirsch, E. C. (2005). The mitochondrial complex I inhibitor rotenone triggers a cerebral tauopathy. *Journal of Neurochemistry*, 95(4), 930–939. <https://doi.org/10.1111/j.1471-4159.2005.03493.x>
- Holth, J.K., Fritschi, S.K., Wang, C., Pedersen, N.P., Cirrito, J.R., Mahan, T.E., Finn, M.B., Manis, M., Geerling, J.C., Fuller, P.M., Lucey, B.P., Holtzman, D.M. (2019). The sleep-wake cycle regulates brain interstitial fluid tau in mice and CSF tau in humans. *Science*, 363(6429), 880-884. DOI: [10.1126/science.aav2546](https://doi.org/10.1126/science.aav2546)
- Huang W, Zhou Y, Tu L, Ba Z, Huang J, Huang N and Luo Y (2020) TDP-43: From Alzheimer's Disease to Limbic-Predominant Age-Related TDP-43 Encephalopathy. *Front. Mol. Neurosci.* 13:26. doi: [10.3389/fnmol.2020.00026](https://doi.org/10.3389/fnmol.2020.00026)  
<https://www.frontiersin.org/articles/10.3389/fnmol.2020.00026/full>
- Jagger, A., Shimojima, Y., Goronzy, J. J., & Weyand, C. M. (2014). Regulatory T Cells and the Immune Aging Process: A Mini-Review. *Gerontology*, 60(2), 130–137. <https://doi.org/10.1159/000355303>
- Jazvinščak Jembrek, M., Babić, M., Pivac, N., Hof, P., & Šimić, G. (2013). Hyperphosphorylation of tau by GSK-3 $\beta$  in Alzheimer's disease: The interaction of A $\beta$  and sphingolipid mediators as a therapeutic target. *Translational Neuroscience*, 4(4), 466–476. <https://doi.org/10.2478/s13380-013-0144-z>
- Jazvinščak Jembrek, M., Hof, P. R., & Šimić, G. (2015). Ceramides in Alzheimer's Disease: Key Mediators of Neuronal Apoptosis Induced by Oxidative Stress and A  $\beta$  Accumulation. *Oxidative Medicine and Cellular Longevity*, 2015, 1–17. <https://doi.org/10.1155/2015/346783>
- Joshi, A.U., Minhas, P.S., Liddelw, S.A., Haileselassie, B., Andreasson, K.I., Dorn II, G.W., Mochly-Rosen, D. (2019). Fragmented mitochondria released from microglia trigger A1 astrocytic response and propagate inflammatory neurodegeneration. *Nat Neurosci* 22, 1635–1648. <https://doi.org/10.1038/s41593-019-0486-0>
- Kahlenberg, J. M., & Kaplan, M. J. (2013). Little Peptide, Big Effects: The Role of LL-37 in Inflammation and Autoimmune Disease. *The Journal of Immunology*, 191(10), 4895–4901. <https://doi.org/10.4049/jimmunol.1302005>

- Kallarackal, A. J., Kvarata, M. D., Cammarata, E., Jaberli, L., Cai, X., Bailey, A. M., & Thompson, S. M. (2013). Chronic Stress Induces a Selective Decrease in AMPA Receptor-Mediated Synaptic Excitation at Hippocampal Temporoammonic-CA1 Synapses. *Journal of Neuroscience*, 33(40), 15669–15674. <https://doi.org/10.1523/JNEUROSCI.2588-13.2013>
- Kanekiyo, T., & Bu, G. (2014). The low-density lipoprotein receptor-related protein 1 and amyloid- $\beta^2$  clearance in Alzheimer's disease. *Frontiers in Aging Neuroscience*, 6(MAY), 1–12. <https://doi.org/10.3389/fnagi.2014.00093>
- Khayrullin, A., Krishnan, P., Martinez-Nater, L., Mendhe, B., Fulzele, S., Liu, Y., ... Hamrick, M. (2019). Very Long-Chain C24:1 Ceramide Is Increased in Serum Extracellular Vesicles with Aging and Can Induce Senescence in Bone-Derived Mesenchymal Stem Cells. *Cells*, 8(1), 37. <https://doi.org/10.3390/cells8010037>
- Kim, M., Nevado-Holgado, A., Whiley, L., Snowden, S. G., Soininen, H., Kloszewska, I., ... Legido-Quigley, C. (2017). Association between Plasma Ceramides and Phosphatidylcholines and Hippocampal Brain Volume in Late Onset Alzheimer's Disease. *Journal of Alzheimer's Disease*, 60(3), 809–817. <https://doi.org/10.3233/JAD-160645>
- Kliem, C., Merling, A., Giaisi, M., Köhler, R., Krammer, P. H., & Li-Weber, M. (2012). Curcumin Suppresses T Cell Activation by Blocking Ca<sup>2+</sup> Mobilization and Nuclear Factor of Activated T Cells (NFAT) Activation. *Journal of Biological Chemistry*, 287(13), 10200–10209. <https://doi.org/10.1074/jbc.M111.318733>
- Kriebel, M., Ebel, J., Battke, F., Griesbach, S., & Volkmer, H. (2020). Interference With Complex IV as a Model of Age-Related Decline in Synaptic Connectivity. *Frontiers in Molecular Neuroscience*, 13(March), 1–14. <https://doi.org/10.3389/fnmol.2020.00043>
- Kudo, W., Lee, H.-P., Zou, W.-Q., Wang, X., Perry, G., Zhu, X., ... Lee, H. -g. (2012). Cellular prion protein is essential for oligomeric amyloid- $\beta$ -induced neuronal cell death. *Human Molecular Genetics*, 21(5), 1138–1144. <https://doi.org/10.1093/hmg/ddr542>
- Le Stunff, H., Véret, J., Kassis, N., Denom, J., Meneyrol, K., Paul, J.-L., ... Janel, N. (2019). Deciphering the Link Between Hyperhomocysteinemia and Ceramide Metabolism in Alzheimer-Type Neurodegeneration. *Frontiers in Neurology*, 10(JUL), 1–11. <https://doi.org/10.3389/fneur.2019.00807>
- Lee, J. H., Yu, W. H., Kumar, A., Lee, S., Mohan, P. S., Peterhoff, C. M., Wolfe, D. M., Martinez-Vicente, M., Massey, A. C., Sovak, G., Uchiyama, Y., Westaway, D., Cuervo, A. M., & Nixon, R. A. (2010). Lysosomal proteolysis and autophagy require presenilin 1 and are disrupted by Alzheimer-related PS1 mutations. *Cell*, 141(7), 1146–1158. <https://doi.org/10.1016/j.cell.2010.05.008>
- Lehallier, B., Gate, D., Schaum, N., Nanasi, T., Lee, S. E., Yousef, H., ... Wyss-Coray, T. (2019). Undulating changes in human plasma proteome profiles across the lifespan. *Nature Medicine*, 25(12), 1843–1850. <https://doi.org/10.1038/s41591-019-0673-2>



- Lieff, J. (2015). The Very Intelligent Choroid Plexus Epithelial Cell. Retrieved June 18, 2020, from <http://jonlieffmd.com/blog/the-very-intelligent-choroid-plexus-epithelial-cell>
- Liu, C.-C., Hu, J., Zhao, N., Wang, J., Wang, N., Cirrito, J. R., ... Bu, G. (2017). Astrocytic LRP1 Mediates Brain A $\beta$  Clearance and Impacts Amyloid Deposition. *The Journal of Neuroscience*, 37(15), 4023–4031. <https://doi.org/10.1523/JNEUROSCI.3442-16.2017>
- Liu, X., Jiao, B., & Shen, L. (2018). The Epigenetics of Alzheimer's Disease: Factors and Therapeutic Implications. *Frontiers in Genetics*, 9(November), 1–10. <https://doi.org/10.3389/fgene.2018.00579>
- Lönn, J., Ljunggren, S., Klarström-Engström, K., Demirel, I., Bengtsson, T., & Karlsson, H. (2018). Lipoprotein modifications by gingipains of *Porphyromonas gingivalis*. *Journal of Periodontal Research*, 53(3), 403–413. <https://doi.org/10.1111/jre.12527>
- Louveau, A., Smirnov, I., Keyes, T. J., Eccles, J. D., Rouhani, S. J., Peske, J. D., ... Kipnis, J. (2015). Structural and functional features of central nervous system lymphatic vessels. *Nature*, 523(7560), 337–341. <https://doi.org/10.1038/nature14432>
- Lu, T., Pan, Y., Kao, S. Y., Li, C., Kohane, I., Chan, J., & Yankner, B. A. (2004). Gene regulation and DNA damage in the ageing human brain. *Nature*, 429(6994), 883–891. <https://doi.org/10.1038/nature02661>
- Martínez-Cué, C., & Rueda, N. (2020). Cellular Senescence in Neurodegenerative Diseases. *Frontiers in cellular neuroscience*, 14, 16. <https://doi.org/10.3389/fncel.2020.00016>
- Mathys, H., Davila-Velderrain, J., Peng, Z., Gao, F., Mohammadi, S., Young, J. Z., Menon, M., He, L., Abdurrob, F., Jiang, X., Martorell, A. J., Ransohoff, R. M., Hafler, B. P., Bennett, D. A., Kellis, M., & Tsai, L. H. (2019). Single-cell transcriptomic analysis of Alzheimer's disease. *Nature*, 570(7761), 332–337. <https://doi.org/10.1038/s41586-019-1195-2>
- McGrath, E. R., Himali, J. J., Xanthakis, V., Duncan, M. S., Schaffer, J. E., Ory, D. S., ... Seshadri, S. (2020). Circulating ceramide ratios and risk of vascular brain aging and dementia. *Annals of Clinical and Translational Neurology*, 7(2), 160–168. <https://doi.org/10.1002/acn3.50973>
- McMahon, L., Schwartz, K., Yilmaz, O., Brown, E., Ryan, L. K., & Diamond, G. (2011). Vitamin D-Mediated Induction of Innate Immunity in Gingival Epithelial Cells. *Infection and Immunity*, 79(6), 2250–2256. <https://doi.org/10.1128/IAI.00099-11>
- Menzies, F. M., Fleming, A., Caricasole, A., Bento, C. F., Andrews, S. P., Ashkenazi, A., Füllgrabe, J., Jackson, A., Jimenez Sanchez, M., Karabiyik, C., Licitra, F., Lopez Ramirez, A., Pavel, M., Puri, C., Renna, M., Ricketts, T., Schlotawa, L., Vicinanza, M., Won, H., Zhu, Y., ... Rubinsztein, D. C. (2017). Autophagy and Neurodegeneration: Pathogenic

- Mechanisms and Therapeutic Opportunities. *Neuron*, 93(5), 1015–1034.  
<https://doi.org/10.1016/j.neuron.2017.01.022>
- Midura-Kiela, M. T., Radhakrishnan, V. M., Larmonier, C. B., Laubitz, D., Ghishan, F. K., & Kiela, P. R. (2012). Curcumin inhibits interferon- $\gamma$  signaling in colonic epithelial cells. *American Journal of Physiology-Gastrointestinal and Liver Physiology*, 302(1), G85–G96.  
<https://doi.org/10.1152/ajpgi.00275.2011>
- Minter, M. R., Zhang, C., Leone, V., Ringus, D. L., Zhang, X., Oyler-Castrillo, P., ... Sisodia, S. S. (2016). Antibiotic-induced perturbations in gut microbial diversity influences neuro-inflammation and amyloidosis in a murine model of Alzheimer's disease. *Scientific Reports*, 6(1), 30028. <https://doi.org/10.1038/srep30028>
- Moir, R. D., Lathe, R., & Tanzi, R. E. (2018). The antimicrobial protection hypothesis of Alzheimer's disease. *Alzheimer's & Dementia*, 14(12), 1602–1614.  
<https://doi.org/10.1016/j.jalz.2018.06.3040>
- Mosconi, L., De Leon, M., Murray, J., E, L., Lu, J., Javier, E., ... Swerdlow, R. H. (2011). Reduced mitochondria cytochrome oxidase activity in adult children of mothers with Alzheimer's disease. *Journal of Alzheimer's Disease*, 27(3), 483–490.  
<https://doi.org/10.3233/JAD-2011-110866>
- Mossmann, D., Vögtle, F.-N., Taskin, A. A., Teixeira, P. F., Ring, J., Burkhart, J. M., ... Meisinger, C. (2014). Amyloid- $\beta$  Peptide Induces Mitochondrial Dysfunction by Inhibition of Preprotein Maturation. *Cell Metabolism*, 20(4), 662–669.  
<https://doi.org/10.1016/j.cmet.2014.07.024>
- Murray, C., Sanderson, D. J., Barkus, C., Deacon, R. M. J., Rawlins, J. N. P., Bannerman, D. M., & Cunningham, C. (2012). Systemic inflammation induces acute working memory deficits in the primed brain: relevance for delirium. *Neurobiology of Aging*, 33(3), 603–616.e3.  
<https://doi.org/10.1016/j.neurobiolaging.2010.04.002>
- Navarro, Ana & Boveris, Alberto. (2007). The mitochondrial energy transduction system and the aging process. *American journal of physiology. Cell physiology*. 292. C670-86.  
<https://doi.org/10.1152/ajpcell.00213.2006>
- Nixon R. A. (2007). Autophagy, amyloidogenesis and Alzheimer disease. *Journal of cell science*, 120(Pt 23), 4081–4091. <https://doi.org/10.1242/jcs.019265>
- Nixon R. A. (2017). Amyloid precursor protein and endosomal-lysosomal dysfunction in Alzheimer's disease: inseparable partners in a multifactorial disease. *FASEB journal : official publication of the Federation of American Societies for Experimental Biology*, 31(7), 2729–2743. <https://doi.org/10.1096/fj.201700359>
- Nixon, R. A., Wegiel, J., Kumar, A., Yu, W. H., Peterhoff, C., Cataldo, A., & Cuervo, A. M. (2005). Extensive involvement of autophagy in Alzheimer disease: an immuno-electron

- microscopy study. *Journal of neuropathology and experimental neurology*, 64(2), 113–122. <https://doi.org/10.1093/jnen/64.2.113>
- Noé, F. M., & Marchi, N. (2019). Central nervous system lymphatic unit, immunity, and epilepsy: Is there a link? *Epilepsia Open*, 4(1), 30–39. <https://doi.org/10.1002/epi4.12302>
- Olsen, I., Singhrao, S. K., & Potempa, J. (2018). Citrullination as a plausible link to periodontitis, rheumatoid arthritis, atherosclerosis and Alzheimer's disease. *Journal of Oral Microbiology*, 10(1), 1487742. <https://doi.org/10.1080/20002297.2018.1487742>
- Olsen, I., Taubman, M. A., & Singhrao, S. K. (2016). Porphyromonas gingivalis suppresses adaptive immunity in periodontitis, atherosclerosis, and Alzheimer's disease. *Journal of Oral Microbiology*, 8(1), 33029. <https://doi.org/10.3402/jom.v8.33029>
- Piacentini, R., De Chiara, G., Li Puma, D. D., Ripoli, C., Marcocci, M. E., Garaci, E., ... Grassi, C. (2014). HSV-1 and Alzheimer's disease: more than a hypothesis. *Frontiers in Pharmacology*, 5(May), 1–9. <https://doi.org/10.3389/fphar.2014.00097>
- Picone, P., Nuzzo, D., Caruana, L., Scafidi, V., & Di Carlo, M. (2014). Mitochondrial Dysfunction: Different Routes to Alzheimer's Disease Therapy. *Oxidative Medicine and Cellular Longevity*, 2014, 1–11. <https://doi.org/10.1155/2014/780179>
- Poirier, J. (1994). Apolipoprotein E: a pharmacogenetic target for the treatment of Alzheimer's disease. *Mol Diagn*. 4(4), 335–341. [https://doi.org/10.1016/s1084-8592\(99\)80010-1](https://doi.org/10.1016/s1084-8592(99)80010-1)
- Poirier, J., Delisle, M. C., Quirion, R., Aubert, I., Farlow, M., Lahiri, D., ... Gilfix, B. M. (1995). Apolipoprotein E4 allele as a predictor of cholinergic deficits and treatment outcome in Alzheimer disease. *Proceedings of the National Academy of Sciences*, 92(26), 12260–12264. <https://doi.org/10.1073/pnas.92.26.12260>
- Raposo, C., Graubardt, N., Cohen, M., Eitan, C., London, A., Berkutzki, T., & Schwartz, M. (2014). CNS Repair Requires Both Effector and Regulatory T Cells with Distinct Temporal and Spatial Profiles. *Journal of Neuroscience*, 34(31), 10141–10155. <https://doi.org/10.1523/JNEUROSCI.0076-14.2014>
- Richert-Spuhler, L. E., & Lund, J. M. (2015). The Immune Fulcrum. *Progress in Molecular Biology and Translational Science*, 136, 217–243. <https://doi.org/10.1016/bs.pmbts.2015.07.015>
- Rottscholl, R., Haegele, M., Jainsch, B., Xu, H., Respondek, G., Höllerhage, M., ... Höglinger, G. U. (2016). Chronic consumption of Annona muricata juice triggers and aggravates cerebral tau phosphorylation in wild-type and MAPT transgenic mice. *Journal of Neurochemistry*, 139(4), 624–639. <https://doi.org/10.1111/jnc.13835>
- Ryazansky, S., Radion, E., Mironova, A., Akulenko, N., Abramov, Y., Morgunova, V., ... Kalmykova, A. (2017). Natural variation of piRNA expression affects immunity to

- transposable elements. *PLOS Genetics*, 13(4), e1006731. <https://doi.org/10.1371/journal.pgen.1006731>
- Safieh, M., Korczyn, A. D., & Michaelson, D. M. (2019). ApoE4: an emerging therapeutic target for Alzheimer's disease. *BMC Medicine*, 17(1), 64. <https://doi.org/10.1186/s12916-019-1299-4>
- Sahu, P. S., & Ter, E. (2018). Interactions between neurotropic pathogens, neuroinflammatory pathways, and autophagic neural cell death. *Neuroimmunology and Neuroinflammation*, 5(1), 2. <https://doi.org/10.20517/2347-8659.2017.43>
- Sanchez-Mut, J. V., & Gräff, J. (2015). Epigenetic Alterations in Alzheimer's Disease. *Frontiers in Behavioral Neuroscience*, 9(DEC), 1–17. <https://doi.org/10.3389/fnbeh.2015.00347>
- Santos, R. X., Correia, S. C., Wang, X., Perry, G., Smith, M. A., Moreira, P. I., & Zhu, X. (2010). A Synergistic Dysfunction of Mitochondrial Fission/Fusion Dynamics and Mitophagy in Alzheimer's Disease. *Journal of Alzheimer's Disease*, 20(s2), S401–S412. <https://doi.org/10.3233/JAD-2010-100666>
- Sell, G. L., Schaffer, T. B., & Margolis, S. S. (2017). Reducing expression of synapse-restricting protein Ephexin5 ameliorates Alzheimer's-like impairment in mice. *Journal of Clinical Investigation*, 127(5), 1646–1650. <https://doi.org/10.1172/JCI85504>
- Seo, D., Boros, B. D., & Holtzman, D. M. (2019). The microbiome: A target for Alzheimer disease? *Cell Research*, 29(10), 779–780. <https://doi.org/10.1038/s41422-019-0227-7>
- Shafiani, S., Tucker-Heard, G., Kariyone, A., Takatsu, K., & Urdahl, K. B. (2010). Pathogen-specific regulatory T cells delay the arrival of effector T cells in the lung during early tuberculosis. *The Journal of Experimental Medicine*, 207(7), 1409–1420. <https://doi.org/10.1084/jem.20091885>
- Singh, A., Dey, A. B., Mohan, A., Sharma, P. K., & Mitra, D. K. (2012). Foxp3+ Regulatory T Cells among Tuberculosis Patients: Impact on Prognosis and Restoration of Antigen Specific IFN- $\gamma$  Producing T Cells. *PLoS ONE*, 7(9), e44728. <https://doi.org/10.1371/journal.pone.0044728>
- Singhrao, S. K., Harding, A., Poole, S., Kesavalu, L., & Crean, S. (2015). Porphyromonas gingivalis Periodontal Infection and Its Putative Links with Alzheimer's Disease. *Mediators of Inflammation*, 2015, 1–10. <https://doi.org/10.1155/2015/137357>
- Soscia, S. J., Kirby, J. E., Washicosky, K. J., Tucker, S. M., Ingelsson, M., Hyman, B., ... Moir, R. D. (2010). The Alzheimer's Disease-Associated Amyloid  $\beta$ -Protein Is an Antimicrobial Peptide. *PLoS ONE*, 5(3), e9505. <https://doi.org/10.1371/journal.pone.0009505>
- Strazielle, N., Creidy, R., Malcus, C., Boucraut, J., & Ghersi-Egea, J.-F. (2016). T-Lymphocytes Traffic into the Brain across the Blood-CSF Barrier: Evidence Using a Reconstituted

Choroid Plexus Epithelium. *PLOS ONE*, *11*(3), e0150945.  
<https://doi.org/10.1371/journal.pone.0150945>

Sun, W., Samimi, H., Gamez, M. *et al.* Pathogenic tau-induced piRNA depletion promotes neuronal death through transposable element dysregulation in neurodegenerative tauopathies. *Nat Neurosci* **21**, 1038–1048 (2018). <https://doi.org/10.1038/s41593-018-0194-1>

Swerdlow, R. H., Koppel, S., Weidling, I., Hayley, C., Ji, Y., & Wilkins, H. M. (2017). Mitochondria, Cybrids, Aging, and Alzheimer's Disease. In *Progress in Molecular Biology and Translational Science* (Vol. 146, pp. 259–302).  
<https://doi.org/10.1016/bs.pmbts.2016.12.017>

Tada, H., Shimizu, T., Matsushita, K., & Takada, H. (2017). Porphyromonas gingivalis-induced IL-33 down-regulates hCAP-18/LL-37 production in human gingival epithelial cells. *Biomedical Research*, *38*(3), 167–173. <https://doi.org/10.2220/biomedres.38.167>

Uddin, M. S., Stachowiak, A., Mamun, A. Al, Tzvetkov, N. T., Takeda, S., Atanasov, A. G., ... Stankiewicz, A. M. (2018). Autophagy and Alzheimer's Disease: From Molecular Mechanisms to Therapeutic Implications. *Frontiers in Aging Neuroscience*, *10*(JAN), 1–18.  
<https://doi.org/10.3389/fnagi.2018.00004>

University of Eastern Finland. (2019). Dietary choline associates with reduced risk of dementia. *ScienceDaily*. Retrieved June 18, 2020 from  
[www.sciencedaily.com/releases/2019/08/190806101530.htm](http://www.sciencedaily.com/releases/2019/08/190806101530.htm)

Van der Mast, R. C., van den Broek, W. W., Fekkes, D., Peplinkhuizen, L., & Habbema, J. D. F. (2000). Is Delirium After Cardiac Surgery Related to Plasma Amino Acids and Physical Condition? *The Journal of Neuropsychiatry and Clinical Neurosciences*, *12*(1), 57–63.  
<https://doi.org/10.1176/jnp.12.1.57>

Wong, A. (2019). *Citrullination of LL-37 as a mechanism that selectively controls immunostimulatory potential of DNA*.

Xie, L., Choudhury, G. R., Winters, A., Yang, S. H., & Jin, K. (2015). Cerebral regulatory T cells restrain microglia/macrophage-mediated inflammatory responses via IL-10. *European Journal of Immunology*, *45*(1), 180–191. <https://doi.org/10.1002/eji.201444823>

Yan, T., Liang, J., Gao, J., Wang, L., Fujioka, H., Zhu, X., & Wang, X. (2020). FAM222A encodes a protein which accumulates in plaques in Alzheimer's disease. *Nature Communications*, *11*(1), 411. <https://doi.org/10.1038/s41467-019-13962-0>

Yang, J., Wu, J., Zhang, R., Yao, M., Liu, Y., Miao, L., & Sun, W. (2017). Porphyromonas gingivalis oral infection promote T helper 17/Treg imbalance in the development of atherosclerosis. *Journal of Dental Sciences*, *12*(1), 60–69.  
<https://doi.org/10.1016/j.jds.2016.10.003>

- Yin, C., Ackermann, S., Ma, Z., Mohanta, S. K., Zhang, C., Li, Y., ... Habenicht, A. J. R. (2019). ApoE attenuates unresolvable inflammation by complex formation with activated C1q. *Nature Medicine*, 25(3), 496–506. <https://doi.org/10.1038/s41591-018-0336-8>
- Yousef, H., Czupalla, C.J., Lee, D. *et al.* Aged blood impairs hippocampal neural precursor activity and activates microglia via brain endothelial cell VCAM1. *Nat Med* 25, 988–1000 (2019). <https://doi.org/10.1038/s41591-019-0440-4>
- Yu, W., Geng, S., Suo, Y., Wei, X., Cai, Q., Wu, B., ... Wang, B. (2018). Critical Role of Regulatory T Cells in the Latency and Stress-Induced Reactivation of HSV-1. *Cell Reports*, 25(9), 2379–2389.e3. <https://doi.org/10.1016/j.celrep.2018.10.105>
- Zhang, L., Trushin, S., Christensen, T. A., Tripathi, U., Hong, C., Geroux, R. E., ... Trushina, E. (2018). Differential effect of amyloid beta peptides on mitochondrial axonal trafficking depends on their state of aggregation and binding to the plasma membrane. *Neurobiology of Disease*, 114(March), 1–16. <https://doi.org/10.1016/j.nbd.2018.02.003>
- Zhang, L., Zhang, S., Maezawa, I., Trushin, S., Minhas, P., Pinto, M., ... Trushina, E. (2015). Modulation of Mitochondrial Complex I Activity Averts Cognitive Decline in Multiple Animal Models of Familial Alzheimer's Disease. *EBioMedicine*, 2(4), 294–305. <https://doi.org/10.1016/j.ebiom.2015.03.009>
- Zhang, P., Kishimoto, Y., Grammatikakis, I., Gottimukkala, K., Cutler, R. G., Zhang, S., Abdelmohsen, K., Bohr, V. A., Misra Sen, J., Gorospe, M., & Mattson, M. P. (2019). Senolytic therapy alleviates A $\beta$ -associated oligodendrocyte progenitor cell senescence and cognitive deficits in an Alzheimer's disease model. *Nature neuroscience*, 22(5), 719–728. <https://doi.org/10.1038/s41593-019-0372-9>
- Zott, B., Simon, M. M., Hong, W., Unger, F., Chen-Engerer, H. J., Frosch, M. P., Sakmann, B., Walsh, D. M., & Konnerth, A. (2019). A vicious cycle of  $\beta$  amyloid-dependent neuronal hyperactivation. *Science*, 365(6453), 559–565. <https://doi.org/10.1126/science.aay0198>