CSF1R

CSF1R (Colony Stimulating Factor 1 Receptor) is a Protein Coding gene. Diseases associated with CSF1R include Leukoencephalopathy, Hereditary Diffuse, With Spheroids and Pigmented Villonodular Synovitis. Among its related pathways are GPCR Pathway and Nanog in Mammalian ESC Pluripotency. Gene Ontology (GO) annotations related to this gene include protein homodimerization activity and protein kinase activity. An important paralog of this gene is KIT.

Dementia associated with brain calcification may occur in Down syndrome and some cases of Fahr's disease (bilateral striatopallidodentate calcinosis). Basal ganglia calcification may occur in Nasu–Hakola disease resulting from TREM2 mutations, and punctate calcification of subcortical and deep white matter may occur in adult-onset leukodystrophy with axonal spheroids and pigmented glia resulting from CSF1R mutations. Brain calcification in hypoparathyroidism or pseudohypoparathyroidism may occasionally be associated with cognitive impairment. All these diagnostic possibilities were excluded by the clinical and investigation findings.

Chance concurrence of two separate disorders (dual pathology), FTD and idiopathic brain calcification, might explain this case. However, a plausible unifying diagnosis for this phenotype is Kosaka–Shibayama disease, or diffuse neurofibrillary tangles with calcification (DNTC). This rare disorder of unknown aetiology is reported almost exclusively from Japan [1)].

Unclassified

1: Lynch DS, Houlden H. Stem cell transplant arrests decline in case of CSF1R leukoencephalopathy. J Neurol Neurosurg Psychiatry. 2019 Aug 10. pii: jnnp-2019-321021. doi: 10.1136/jnnp-2019-321021. [Epub ahead of print] PubMed PMID: 31401565.

2: Lynch DS, Wade C, Paiva ARB, John N, Kinsella JA, Merwick Á, Ahmed RM, Warren JD, Mummery CJ, Schott JM, Fox NC, Houlden H, Adams ME, Davagnanam I, Murphy E, Chataway J. Practical approach to the diagnosis of adult-onset leukodystrophies: an updated guide in the genomic era. J Neurol Neurosurg Psychiatry. 2019 May;90(5):543-554. doi: 10.1136/jnnp-2018-319481. Epub 2018 Nov 22. Review. PubMed PMID: 30467211; PubMed Central PMCID: PMC6581077.

3: Cho HR, Jeon H, Park CK, Park SH, Choi SH. Radiogenomics Profiling for Glioblastoma-related Immune Cells Reveals CD49d Expression Correlation with MRI parameters and Prognosis. Sci Rep. 2018 Oct 30;8(1):16022. doi: 10.1038/s41598-018-34242-9. PubMed PMID: 30375429; PubMed Central PMCID: PMC6207678.

4: Vanlandewijck M, He L, Mäe MA, Andrae J, Ando K, Del Gaudio F, Nahar K, Lebouvier T, Laviña B, Gouveia L, Sun Y, Raschperger E, Räsänen M, Zarb Y, Mochizuki N, Keller A, Lendahl U, Betsholtz C. Author Correction: A molecular atlas of cell types and zonation in the brain vasculature. Nature. 2018 Aug;560(7716):E3. doi: 10.1038/s41586-018-0232-x. PubMed PMID: 29925939.

5: Kazantseva M, Eiholzer RA, Mehta S, Taha A, Bowie S, Roth I, Zhou J, Joruiz SM, Royds JA, Hung NA, Slatter TL, Braithwaite AW. Elevation of the TP53 isoform Δ133p53β in glioblastomas: an alternative to mutant p53 in promoting tumor development. J Pathol. 2018 Sep;246(1):77-88. doi:

10.1002/path.5111. Epub 2018 Jul 31. PubMed PMID: 29888503; PubMed Central PMCID: PMC6120556.

6: Bennett FC, Bennett ML, Yaqoob F, Mulinyawe SB, Grant GA, Hayden Gephart M, Plowey ED, Barres BA. A Combination of Ontogeny and CNS Environment Establishes Microglial Identity. Neuron. 2018 Jun 27;98(6):1170-1183.e8. doi: 10.1016/j.neuron.2018.05.014. Epub 2018 May 31. PubMed PMID: 29861285; PubMed Central PMCID: PMC6023731.

7: Lin X, Meng G, Liu X, Yu T, Bai C, Fei X, Deng S, Zhao J, Ren S, Zhang J, Wu Z, Wang S, Zhang J, Zhang L. The Differentially Expressed Genes of Human Sporadic Cerebral Cavernous Malformations. World Neurosurg. 2018 May;113:e247-e270. doi: 10.1016/j.wneu.2018.02.002. Epub 2018 Feb 14. PubMed PMID: 29454117.

8: Hilla AM, Diekmann H, Fischer D. Microglia Are Irrelevant for Neuronal Degeneration and Axon Regeneration after Acute Injury. J Neurosci. 2017 Jun 21;37(25):6113-6124. doi: 10.1523/JNEUROSCI.0584-17.2017. Epub 2017 May 24. PubMed PMID: 28539419; PubMed Central PMCID: PMC6596505.

9: Lynch DS, Rodrigues Brandão de Paiva A, Zhang WJ, Bugiardini E, Freua F, Tavares Lucato L, Macedo-Souza LI, Lakshmanan R, Kinsella JA, Merwick A, Rossor AM, Bajaj N, Herron B, McMonagle P, Morrison PJ, Hughes D, Pittman A, Laurà M, Reilly MM, Warren JD, Mummery CJ, Schott JM, Adams M, Fox NC, Murphy E, Davagnanam I, Kok F, Chataway J, Houlden H. Clinical and genetic characterization of leukoencephalopathies in adults. Brain. 2017 May 1;140(5):1204-1211. doi: 10.1093/brain/awx045. PubMed PMID: 28334938; PubMed Central PMCID: PMC5405235.

10: Lynch DS, Zhang WJ, Lakshmanan R, Kinsella JA, Uzun GA, Karbay M, Tüfekçioglu Z, Hanagasi H, Burke G, Foulds N, Hammans SR, Bhattacharjee A, Wilson H, Adams M, Walker M, Nicoll JA, Chataway J, Fox N, Davagnanam I, Phadke R, Houlden H. Analysis of Mutations in AARS2 in a Series of CSF1R-Negative Patients With Adult-Onset Leukoencephalopathy With Axonal Spheroids and Pigmented Glia. JAMA Neurol. 2016 Dec 1;73(12):1433-1439. doi: 10.1001/jamaneurol.2016.2229. PubMed PMID: 27749956.

11: Guo X, Xue H, Shao Q, Wang J, Guo X, Chen X, Zhang J, Xu S, Li T, Zhang P, Gao X, Qiu W, Liu Q, Li G. Hypoxia promotes glioma-associated macrophage infiltration via periostin and subsequent M2 polarization by upregulating TGF-beta and M-CSFR. Oncotarget. 2016 Dec 6;7(49):80521-80542. doi: 10.18632/oncotarget.11825. PubMed PMID: 27602954; PubMed Central PMCID: PMC5348338.

12: Lynch DS, Jaunmuktane Z, Sheerin UM, Phadke R, Brandner S, Milonas I, Dean A, Bajaj N, McNicholas N, Costello D, Cronin S, McGuigan C, Rossor M, Fox N, Murphy E, Chataway J, Houlden H. Hereditary leukoencephalopathy with axonal spheroids: a spectrum of phenotypes from CNS vasculitis to parkinsonism in an adult onset leukodystrophy series. J Neurol Neurosurg Psychiatry. 2016 May;87(5):512-9. doi: 10.1136/jnnp-2015-310788. Epub 2015 May 2. PubMed PMID: 25935893; PubMed Central PMCID: PMC4853550.

13: Schuberth M, Levin J, Sawalhe D, Schwarzkopf R, von Baumgarten L, Ertl-Wagner B, Rominger A, Arzberger T, Kretzschmar HA, Froböse T, Diehl-Schmid J, Biskup S, Danek A. [Hereditary diffuse leukencephalopathy with spheroids: a microgliopathy due to CSF1 receptor impairment]. Nervenarzt. 2014 Apr;85(4):465-70. doi: 10.1007/s00115-014-4052-4. German. PubMed PMID: 24706185.

1)

Ukai K, Kosaka K. Diffuse neurofibrillary tangles with calcification (Kosaka-Shibayama disease) in Japan. Psychiatry Clin Neurosci 2016; 70: 131–40.