Supplementary Material

# Supplementary Table. Function for the proteins associated to the core signature genes.

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| --- | --- | --- | --- | --- | --- |
| Gene name | Protein name | Protein function | Global roles | Roles in the CNS | References |
| Ank | Ankyrin-1 | Adaptor protein | * Adhesion molecules binding * Serpin binding * CD44 interaction * Participation in cell proliferation, mobility, activation * Membrane proteins attachment | * Production at dendritic spines, modulation of LTD * Expression by microglia in AD * Hypermethylated in AD, PD and HD | (1,2) |
| Anxa5 | Annexin A5 | Lipid-binding protein | * Phospholipids binding * Integrin and heparin binding * Inhibition of phospholipase A * Phagocytosis of apoptotic cells (involved in antigen processing and presentation) * Suppression of proinflammatory cytokine secretion * Inhibition of DCs * Involved in cholesterol metabolism * Possible involvement in membrane repair | * Not expressed in neurons * Increased in AD * Increased in glioma | (3–7) |
| Aplp2 | Amyloid precursor-like protein 2 | Protease inhibitor | * Heparin binding * Modulation of insulin homeostasis and IGF transport * Binding and endocytosis of MHCI molecules | * Presence in proliferative zones in development * Involvement in axonal guidance and synaptic plasticity * Modulation of demyelination/remyelination * Increased in glioblastooma | (8–12) |
| Atp1a3 | Na(+)/K(+) ATPase alpha-3 subunit | Translocase | * ATP-dependent transport of Na+ and K+ across the plasma membrane * Heparan sulfate binding leading to inhibition | * Suposedly restricted to neurons * Association with Aβ, α-synuclein and SOD1 assemblies * Mutations lead to rapid onset dystonia parkinsonism, hemiplegia, cerebellar ataxia, areflexia, pes cavus, optic atrophy, sensorineural hearing loss, early infantile epileptic encephalopathy, autism spectrum disorders, schizophrenia | (13) |
| Clec7a | C-type lectin domain family 7 member | Receptor | * Galectin, zymosan and β-glucan binding * Modulation of cytokine and ROS production by macrophages and DCs * Modulation of innate immune memory, T cell activation and proliferation, and B cell responses * Regulation of autophagy, phagocytosis and the respiratory burst * Anti-tumor properties | * No induction of cytokine production in microglia in response to β-glucan * Detrimental when expressed by microglia in the context of SCI * Promotion of axon regeneration in the optic nerve * Possible involvement in autism spectrum disorders | (14–20) |
| Colec12 | Collectin-12 | Receptor (scavenger) | * Carbohydrates, oxLDL and C-type lectins binding * Regulation of LDL cholesterol in the circulation * Activation of innate immune responses and complement * Involvement in developmental processes | * Facilitation of Aβ clearance by microglia in AD * Increased in AD patients * Increased in myelin-containing phagocytes in MS lesions | (21,22) |
| Csf1 | Colony stimulating factor 1 | Growth factor / Cytokine | * Regulation of survival, proliferation and differentiation of macrophages and monocytes * Modulation of cytokine production in innate immune responses and inflammation * Promotion of reorganization of actin cytoskeleton for cell adhesion and migration * Promotion of lipoprotein clearance | * Expressed by neurons and microglia * Regulates microglia development, particularly in the white matter * Increases DAP12 and decreases antigen presentation in microglia * Decreases macrophage inflammatory phenotype * Promotion of myelin and Aβ clearance by microglia * Induction of IGFBP1 for increased angiogenesis in glioblastoma * Regulation of microglial proliferation in ALS * Increased in glioblastoma | (23–27) |
| Ephx1 | Epoxide hydrolase 1 | Hydrolase | * Converting epoxides in diols for detoxification or bioactivation | * Expression in neurons and astrocytes * Contribution to cerebral metabolism * Increased in glioma * Increased in AD | (28) |
| Fabp5 | Fatty acid binding protein 5 | Lipid-binding protein | * Fatty acid uptake, transport and metabolism * Expression in macrophages for cytokine production and mediation of cellular stress responses * Interaction with PPAR nuclear receptors | * Expression in the perinatal brain * Involvement in motor neuron and astrocyte differentiation * Possible involvement in neurite outgrowth, axon development ad neural cell regeneration * Possible involvement in neurogenesis * Increased in excitotoxic lesions * Increased in peripheral nerve injury * Increased in ischemia | (29–31) |
| Fam20c | Extracellular serine/threonine protein kinase FAM20C | Kinase | * Phosphorylation of fibrinogen * Phosphoryplation of casein * Phosphorylation of osteopontin (SPP1) * Regulation of IGF transport and uptake by IGFBP | * Phosphorylates APP and APOE * Activated by sphingosine and fingolimod | (32–36) |
| Gm1673 | Neuropeptide-like protein C4orf48 homolog | Neuropeptide |  | * Expression in development and adulthood in cortex * Mutation leads to Wolf-Hirschhorn syndrome | (37) |
| Gpnmb | Transmembrane glycoprotein NMB | Glycoprotein / Chemoattractant | * Heparin and integrin binding * Interaction with CD44 * Involvement in motility and angiogenesis through Wnt signaling * Negative regulation of T cell activation via syndecan binding * Involvement in lysosome function | * Contribution to memory * Protection following ischemia * Protection in ALS * Participates in glioblastoma growth through Wnt signaling and NA+/K+ ATPase * Increased in glioblastoma, * Increased in AD (in microglia) * Increased in PD * Increased in ALS * Increased in MS lesions (in foamy macrophages) | (38–42) |
| Hpse | Heparanase | Heparanase | * Heparan sulfate cleavage leading to extracellular matrix integrity reduction * Regulation of signaling pathways * Facilitation of cell migration * Involvement in syndecan shedding * Participation in tumor invasion | * Expression in brain development * Involvement in microglial migration * Restriction of microglial inflammatory response * Dual roles in EAE and MS * Dual roles in AD * Delays prion disease onset * Promotes glioma progression * Increased in AD * Increased in glioma * Increased in stroke | (43–47) |
| Igf1 | Insulin-like growth factor 1 | Growth factor / Hormone | * Signaling downstream of growth hormone * Involvement in cell growth and maturation * Activation of anabolic processes * Association with decreased lifespan * Interaction with integrins (including the SPP1 receptor) | * Promotion of neuron survival and primary myelination during development by microglia expression * Presence in neurogenic niches * Involvement in protection against cellular injury, neurogenesis, angiogenesis and amyloid clearance * Dual roles in AD | (48–50) |
| Itgax | Integrin alpha-x | Integrin / Receptor | * Binds to CD18 to make up complement receptor 4 (for iC3b) * Fibrinogen binding * Mediation of cellular interactions during inflammatory responses * Mediation of cell recruitment * Regulation of cytoskeleton rearrangement * Regulation of activation and proliferation of leucocytes | * Reviewed here | (51) |
| Lilrb4 | Leucocyte immunoglobulin-like receptor subfamily B member 4 | Receptor  (Ig superfamily) | * MHCI binding * Induced by IFNβ * Promotion of tolerance by immune response downregulation | * Involvement in immune responsiveness in MS * Increased in aging * Increased in MS lesions | (52–54) |
| Lpl | Lipoprotein lipase | Hydrolase | * Involvement in blood lipoprotein triglyceride catabolism * Activated by Apolipoprotein C * Participation in fatty acid transport * Participation in lipoprotein formation (LDL, VLDL, HDL) * Possible involvement in cellular interactions * Interaction with heparan proteoglycans * Interaction with APOE | * Regulation of neuronal survival and proliferation * Promotion of foam cell formation * Reduction in microglia leads to decreased lipid uptake, shift in mitochondria activity and decreased immune reactivity * Participation in myelin clearance * Increased in AD * Increased in glioma | (55,56) |
| Nceh1 | Neutral cholesterol ester hydrolase 1 | Hydrolase | * Involvement in reverse cholesterol transport * Platelet activating factor biosynthesis * Lipophospholipid signaling * Detoxification * Cholesterol esters lipolysis | * Involved in formation of foam cells | (57–59) |
| Plaur | Urokinase plasminogen activator surface receptor | Receptor  (Ig superfamily) | * Integrin, LRP1, EGR and PDGFRβ binding as coreceptors * Participation in cell migration, proliferation and survival * Induction of actin cytoskeleton reorganization | * High expression during development and disease, contraction in adulthood * Involvement in synaptic repair and axonal recovery * Presence in injury, MS and prion disease * Increased in epilepsy * Increased in AD * Increased in glioma | (60,61) |
| Pld3 | Phospholipase D3 | Hydrolase | * Unclear functions (Possible function in hydrolysis of membrane phospholipids) | * Expressed in brain development * Possible involvement in APP processing * Risk variant for AD | (62,63) |
| Plin2 | Perilipin-2 | Lipid binding protein | * Involvement in formation of lipid droplets * Interaction with PPAR nuclear reveptors | * Increased in injury (in microglia) | (64–66) |
| Spp1 | Osteopontin | Cytokine | * Integrin binding (particularly CD11c/CD18) * CD44 interaction * Involvement in cellular motility, adhesion and survival * Regulation of developmental processes, tissue remodeling and immune function * Possible inhibition of apoptosis * Possible modulation of T cell activation * Regulated by IFNβ | * Involvement in neural precursor proliferation * Involvement in memory and myelination in development * Participation in synaptic plasticity, reinnervation, axonal growth, synapse reorganization and functional recovery following injury * Enhances immunosuppression * Increased in AD * Increased in MS * Increased in glioblastoma * Increased in NMDAR encephalitis * Decreased in PD | (67–70) |

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