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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