

Supplementary Table 1 – Characteristics of the primary antibodies, immunohistochemistry conditions and expression of the staining

Antigen (human)	Company	Host	Pre-treatment	Dilution	Predominant neuropathological features / cell type stained	Immune functions
Amyloid (A)β	Covance	Mouse, clone 4G8	80% formic acid and citrate buffer	1/2000	Diffuse and neuritic plaques, cerebral amyloid angiopathy	
Phosphorylated Tau (pS202+pT205)	Fisher Scientific	Mouse, clone AT8	Citrate buffer	1/500	Tangles, dystrophic neurites, neuropil threads	
Iba1	Wako	Rabbit	Citrate buffer	1/1000	Microglia, perivascular macrophages	Cytoplasmic protein involved in cytoskeletal reorganization, membrane ruffling of the microglial processes and actin cross-linking needed for cell migration [51], reflecting microglial motility and migration properties. Higher expression of Iba1 is associated with good MMSE and absence of dementia [44].
CD68	Abcam	Mouse (clone PG-M1)	0.5% pronase	1/50	Microglia, perivascular macrophages	CD68 labels lysosomal and endosomal transmembrane glycoprotein of microglia, indicating phagocytic activity [57]. CD68 is associated with worse MMSE, dementia and ptau [44].
HLA-DP,DQ,DR	Dako	Mouse, clone CR3/43	Citrate buffer	1/200	Microglia, perivascular macrophages	HLA-DR is a Major Histocompatibility Class (MHC) II cell surface receptor which presents antigens to cells of the immune system eliciting an immune response, involved in the non-self recognition and upregulated in inflammation [63]. HLA was identified as a genetic risk factor for Alzheimer's disease [33].
CD64 (FcγRI)	R&D Systems	Goat	EDTA buffer	1/100	Microglia, perivascular macrophages	

CD32a (FcγRIIa)	Abcam	Mouse (clone 13D7)	EDTA buffer	1/2000	Microglia, perivascular macrophages and in some neurons	Fcγ receptors are central effectors of immunoglobulins (IgG) mediated immune response [48].
CD32b (FcγRIIb)	Abcam	Rabbit (clone EP888Y)	EDTA buffer	1/4000	Neurons	CD64 has high affinity for the Fc portion of IgG, triggering a monocyte/macrophage response [67]. CD64 expression reflects the presence of IgG in the brain and thus the involvement of systemic immunity [41]. CD32a/b and CD16 are low/medium affinity receptors for immune complex [48]. CD32b, the only inhibitory receptor, is usually co-expressed with activating FcγR on the majority of innate immune cells [8, 28].
CD16 (FcγRIII)	R&D Systems	Goat	EDTA buffer	1/150	Microglia, perivascular macrophages, some monocytes and neurons	
CHI3L1	R&D Systems	Goat	Citrate buffer, PC	1/100	Microglia, some neurons	CHI3L1 (or YKL40), a highly evolutionary conserved secreted protein contains the conserved chitinase-like enzyme domain but lacks chitinolytic enzymatic activity. CHI3L1 is expressed by various cells [37], implicated in inflammatory disorders involving macrophage activation shown to be involved in promoting inflammation via regulation of M2/Th2-like immune reactions, leading to an immunosuppressive environment [11]. It is a potential neuroinflammatory biomarker for preclinical Alzheimer's disease [26].
IL4R	Sigma	Rabbit	EDTA buffer	1/100	Occasional healthy neurons in Ctrl, tangles and neuropil threads in Alzheimer's disease	IL4/IL4R are anti-inflammatory molecules participating to the alternative activation of macrophages [8, 24].
CCR2	Abcam	Rabbit, clone	EDTA buffer	1/500	Microglia, perivascular macrophages, monocytes	CC-chemokine receptor 2 is required for mononuclear phagocyte recruitment [22] and upregulated in Alzheimer's disease brains [32], but not expressed by microglia in mouse brain [23].
CD3	Dako	Mouse (clone F7.2.38)	None	1/200	T lymphocytes	CD3 is a T-cell co-receptor necessary to activate both CD8 ⁺ and CD4 ⁺ T cells [9], and thus considered as a pan-T cell marker.

Supplementary Table 2 - Primers and probes used for TaqMan qPCR (human sequences)

	Gene	Accession No.	Assay/Probe ID (Thermo Fisher Scientific)	Amplicon Length (bp)
Cytokines/cytokine receptors	<i>IL1β</i>	NM_000576.2	Hs01555410_m1	91
	<i>IL6</i>	NM_000600.4	Hs00985639_m1	66
	<i>TNF</i>	NM_000594.3	Hs99999043_m1	85
	<i>IFN γ</i>	NM_000619.2	Hs00989291_m1	73
	<i>TGF β</i>	NM_000660.5	Hs00998133_m1	57
	<i>IL10</i>	NM_000572.2	Hs00961622_m1	74
	<i>IL4R</i>	NM_000418.3, NM_001257406.1, NM_001257407.1, NM_001257997.1	Hs00166237_m1	70
Enzymes	<i>PTGS2 (COX2)</i>	NM_000963.3	Hs00153133_m1	75
	<i>NOS2</i>	NM_000625.4	Hs01075529_m1	67
	<i>ARG1</i>	NM_000045.3, NM_001244438.1	Hs00968979_m1	78
Receptors	<i>CD206 (MRC1)</i>	NM_002438.3	Hs00267207_m1	82
	<i>CD86</i>	NM_001206924.1, NM_001206925.1, NM_006889.4, NM_175862.4, NM_176892.1	Hs01567026_m1	104
	<i>TREM2</i>	NM_001271821.1, NM_018965.3	Hs00219132_m1	73
	<i>CD163</i>	NM_004244.5, NM_203416.3	Hs00174705_m1	72
Others	<i>CHI3LI</i>	NM_001276.2	Hs00609691_m1	77
	<i>GAPDH</i>	NM_001256799.2, NM_001289745.1, NM_001289746.1, NM_002046.5	Hs02758991_g1	157

Supplementary Table 3 - Comparison of vascular proteins in Alzheimer's cases detected by V-PLEX Meso Scale Discovery Multiplex Assays

Vascular injury panel 2 (pg/ml)	AD-	AD+	P value
CRP	53626.44 (13019.64, 85228.62)	55061.38 (27578.42, 90583.96)	0.461
ICAM-1	65379.43 (41726.25, 89186.55)	60035.26 (43099.03, 96183.34)	0.722
SAA	199894.72 (73367.75, 509940.34)	397225.57 (102854.00, 549630.35)	0.409
VCAM-1	3458.52 (3038.75, 4607.98)	3081.83 (2396.07, 4348.85)	0.158

Values are median with IQR; p value by Mann-Whitney test.

AD, Alzheimer's disease cases; -, without systemic infection; +, with systemic infection; IQR, interquartile range