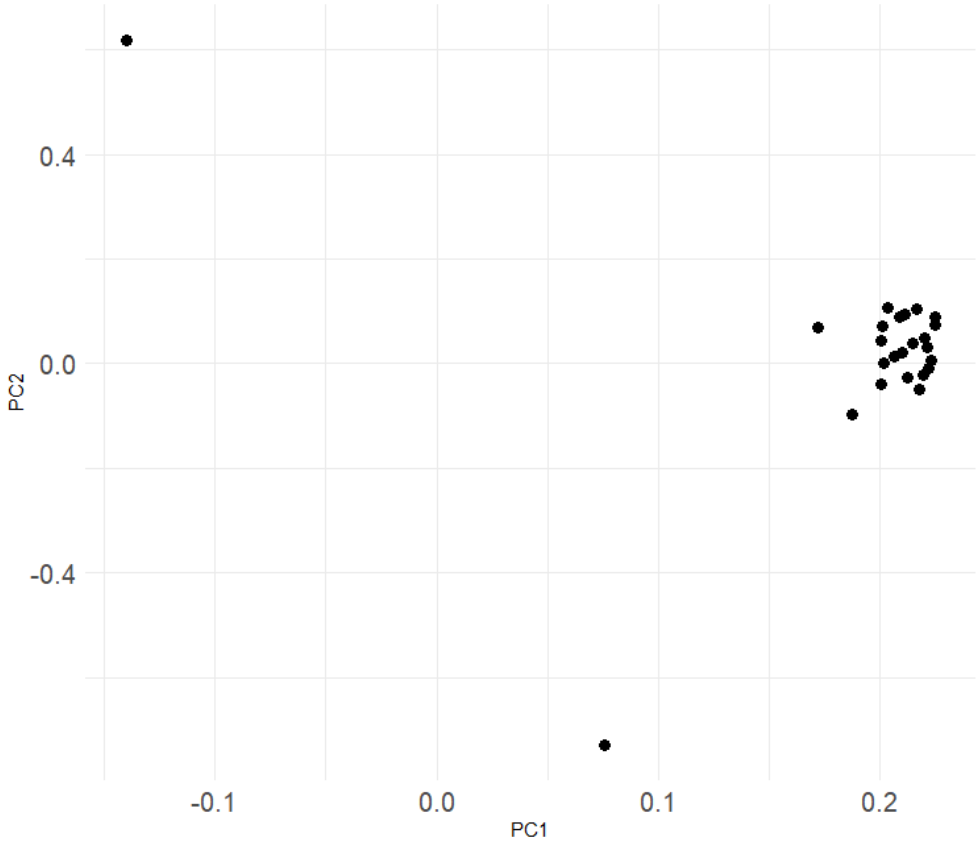
Supplementary Material



Supplementary Figure 1. Principal component analysis (PCA) was applied to the protein expression data of the proteins that were associated with ePVS volume, and the first two principal components (PCs) were inspected for potential outliers. Each dot represents one CADASIL patient. Two patients were separated from the rest of the cohort and were excluded from further analyses.

Abbreviation	Full name
A1BG	alpha-1-B glycoprotein
ABL2	ABL proto-oncogene 2, non-receptor tyrosine kinase
AGT	angiotensinogen
ALOX5	arachidonate 5-lipoxygenase
APOB	apolipoprotein B
ARTN	artemin
BAG4	BAG cochaperone 4
BECN1	beclin 1
BPI	bactericidal permeability increasing protein
C1S	complement C1s
CCL2	C-C motif chemokine ligand 2
CD300C	CD300c molecule
CHST14	carbohydrate sulfotransferase 14
CNTN5	contactin 5
CXCL17	C-X-C motif chemokine ligand 17
CXCL8	C-X-C motif chemokine ligand 8
DAG1	dystroglycan 1
DCN	decorin
DCP1B	decapping mRNA 1B
DEFA3	defensin alpha 3
DNAJC11	DnaJ heat shock protein family (Hsp40) member C11
DTNA	Dystrobrevin alpha
DUSP10	dual specificity phosphatase 10
EBI3	Epstein-Barr virus induced 3
EFNB3	ephrin B3
ELANE	elastase, neutrophil expressed
EREG	epiregulin
EXOC7	exocyst complex component 7
FCN1	ficolin 1
FGF20	fibroblast growth factor 20
FGF9	fibroblast growth factor 9
FLT1	fms related receptor tyrosine kinase 1
FURIN	furin
GPX2	glutathione peroxidase 2
GZMB	granzyme B
GZMK	granzyme K
HCK	hematopoietic cell kinase
ICOSLG	inducible T cell costimulator ligand
IL12A	interleukin 12A
IL1R2	interleukin 1 receptor type 2
IL1RL1	interleukin 1 receptor like 1
IL20RA	interleukin 20 receptor subunit alpha

IL20RB	interleukin 20 receptor subunit beta
IL7R	interleukin 7 receptor
IMPA1	inositol monophosphatase 1
IRF4	interferon regulatory factor 4
KIR2DL3	killer cell immunoglobulin like receptor, two Ig domains and long cytoplasmic tail 3
KLF4	KLF transcription factor 4
LAMP1	lysosomal associated membrane protein 1
LAT	linker for activation of T cells
LMNB1	lamin B1
MAPK9	mitogen-activated protein kinase 9
MBD4	methyl-CpG binding domain 4, DNA glycosylase
MTFR1	mitochondrial fission regulator 1
MTX2	metaxin 2
NFKBIE	NFKB inhibitor epsilon
NR3C1	nuclear receptor subfamily 3 group C member 1
NRXN1	neurexin 1
NTN1	netrin 1
NTRK1	neurotrophic receptor tyrosine kinase 1
PDE7A	phosphodiesterase 7A
PILRA	paired immunoglobin like type 2 receptor alpha
PLA2G1B	phospholipase A2 group IB
PLEKHB1	pleckstrin homology domain containing B1
POLH	DNA polymerase eta
PRC1	protein regulator of cytokinesis 1
PRSS57	serine protease 57
PRTN3	proteinase 3
PSMD7	proteasome 26S subunit, non-ATPase 7
PTK6	protein tyrosine kinase 6
PTPN4	protein tyrosine phosphatase non-receptor type 4
PTPRJ	protein tyrosine phosphatase receptor type J
PTS	6-pyruvoyltetrahydropterin synthase
RGS5	regulator of G protein signaling 5
ROBO3	roundabout guidance receptor 3
RSPO1	R-spondin 1
RSPO4	R-spondin 4
SAMM50	sorting and assembly machinery component 50
SCLY	selenocysteine lyase
SCUBE1	signal peptide, CUB domain and EGF like domain containing 1
SELPLG	selectin P ligand
SLAMF6	Signaling lymphocytic activation molecule family member 6

SLC3A2	solute carrier family 3 member 2
SLITRK2	SLIT and NTRK like family member 2
SPDL1	spindle apparatus coiled-coil protein 1
STATH	statherin
SUN3	Sad1 and UNC84 domain containing 3
TBK1	TANK binding kinase 1
TNFRSF9	TNF receptor superfamily member 9
TNS2	tensin 2
TRIO	trio Rho guanine nucleotide exchange factor
UNC5A	unc-5 netrin receptor A
UNG	uracil DNA glycosylase
VAMP3	vesicle associated membrane protein 3
ZBTB33	zinc finger and BTB domain containing 33

Supplementary Table 1. Members of the protein-protein interaction network of proteins that are positively associated with ePVS volume, presented on Figure 3. Abbreviations are in alphabetical order on the left column and full names on the right column. ePVS = enlarged Perivascular Spaces.

Abbreviation	**Full name**
ALPI	alkaline phosphatase, intestinal
AMY1B	mylase alpha 1B
AMY2B	amylase alpha 2B
APOB	apolipoprotein B
APOC3	apolipoprotein C3
CPB2	carboxypeptidase B2
OPCML	opioid binding protein/cell adhesion molecule like
PCSK2	proprotein convertase subtilisin/kexin type 2
PPY	pancreatic polypeptide
PRSS3	serine protease 3
REG3G	regenerating family member 3 gamma

Supplementary Table 2. Members of the protein-protein interaction network of proteins that are negatively associated with ePVS volume, presented on Figure 4. Abbreviations are in alphabetical order on the left column and full names on the right column. ePVS = enlarged Perivascular Spaces.

Abbreviation	Full name
CABP2	calcium binding protein 2
CCL2	C-C motif chemokine ligand 2
CXCL17	C-X-C motif chemokine ligand 17
CXCL8	C-X-C motif chemokine ligand 8
DEFA3	defensin alpha 3
DPEP2	dipeptidase 2
EBI3	Epstein-Barr virus induced 3
FGF9	fibroblast growth factor 9
HCK	hematopoietic cell kinase
IL12A	interleukin 12A
NTN1	netrin 1
OLIG1	oligodendrocyte transcription factor 1
OPCML	opioid binding protein/cell adhesion molecule like
PLEKHB1	pleckstrin homology domain containing B1
PRSS57	serine protease 57
PSMD7	proteasome 26S subunit, non-ATPase 7
PTER	phosphotriesterase related
PTS	6-pyruvoyltetrahydropterin synthase
SLITRK2	SLIT and NTRK like family member 2
RSPO1	R-spondin 1
RSPO4	R-spondin 4
XAGE2	X antigen family member 2
ZNF263	zinc finger protein 263

Supplementary Table 3. Proteins commonly associated with ePVS and other imaging measures (WMH, BPF), presented on Figure 5. Abbreviations are in alphabetical order on the left column and full names on the right column. BPF = Brain Parenchymal Fraction, ePVS = enlarged Perivascular Spaces, WMH = White Matter Hyperintensities.