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| **Supplementary file (3): Validation of the function of the genes identified by AIS tool** | | | | | | |
| **Genes** | **P** | **T** | **Evidence** | **Disease** | **Reference** | **tissue** |
| **CCL20** |  |  | Upregulated | Multiple sclerosis | [1][2] | Endothelial cells |
| **CDC42** |  |  | Upregulated | Cerebral Vascular Malformations | [3] | Endothelial cells |
| **CLDN1** |  |  | upregulated | Stroke, Multiple sclerosis | [4] | Endothelial cells |
| **CTNNB1** |  |  | upregulated | Multiple sclerosis | [5] | Endothelial cells |
| **ERM** |  |  | upregulated | streptococcal Fic | [6][7][8] | Endothelial cells |
| **ITB2** |  |  | Upregulated | ischemia | [9] | Endothelial cells |
| **ICAM1** |  |  | Upregulated | Multiple sclerosis | [10] | CSF |
| **LSP1** |  |  | Upregulated | (CCMs) Cerebral Cavernous Malformations | [11] | Endothelial cells |
| **MADCAM1** |  |  | Upregulated | IFNγ treated | [12] | Endothelial cells |
| **MLCK** |  |  | Upregulated | In vitro model | [13] | Endothelial cells |
| **PNAX1** |  |  | Upregulated | Stroke | [14] | Endothelial cells |
| **RAC1B** |  |  | Upregulated | Hyperglycemia | [15] | Endothelial cells |
| **RHOG** |  |  | Upregulated | In vitro | [16] | Endothelial cells |
| **RHOA** |  |  | Upregulated | Hyperglycemia | [15] | Endothelial cells |
| **SRC** |  |  | Downregulated | In vitro BBB model of MafA | [17] | Endothelial cells |
| **SRF** |  |  | Downregulated | stroke | [18] | Endothelial cells |
| **VASP** |  |  | upregulated | In vitro BBB model of hypoxia | [19] | Endothelial cells |
| **VCAM1** |  |  | Upregulated | Multiple sclerosis | [20] | Endothelial cells |
| **VEGF** |  |  | Upregulated | Brain injury | [21] | Endothelial cells |
| **VWF** |  |  | Upregulated | Single cell mouse brain (homeostasis) | [22] | Endothelial cells |

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| **Cx43** |  |  | downregulated | Familial cerebral cavernous malformations type I | [23] | Endothelial cells |
| **ESAM** |  |  | Association | schizophrenia | [24] | Endothelial cells |
| **IQGAP1** |  |  | Upregulated | In vitro brain injury model | [25] | Endothelial cells |
| **JAMA** |  |  | Downregulated | vivo model of BBB breakdown | [26] | Endothelial cells |
| **JAMB** |  |  | Downregulated | Endothelial cells |
| **JAMC** |  |  | Downregulated | Endothelial cells |
| **JAML** |  |  | upregulated | multiple sclerosis | [27] | Endothelial cells |
| **LCK** |  |  | Unknown | Shown to control PECAM1 function | [28] | Endothelial cells |
| **MMP2** |  |  | Upregulated | Hypertension/stroke/Alzheimer | [29] | Endothelial cells |
| **MMP9** |  |  | Upregulated | Hypertension/stroke/Alzheimer | [29] | Endothelial cells |
| **Occludin** |  |  | Downregulated | multiple sclerosis | [30] | Endothelial cells |
| **PANX1** |  |  | upregulated | ischemic stroke | [14] | Endothelial cells |
| **PECAM1** |  |  | Upregulated | multiple sclerosis | [31] | Endothelial cells |
| **TIAM1** |  |  | Unknown | Shown to be downstream target of VE-CADHERIN | [32] | Endothelial cells |
| **TIMP4** |  |  | Downregulated | In vitro response to Neisseria meningitidis | [17] | Endothelial cells |
| **TIMP1** |  |  | No change in qPCR, but shown to inhibit MMP2 | Focal Cerebral Ischemia | [33] | Endothelial cells |
| **VE-CADHERIN** |  |  | Downregulated | multiple sclerosis | [34] | Endothelial cells |
| **ZO1** |  |  | Downregulated | multiple sclerosis | [30] | Endothelial cells |
| **ZO2** |  |  | Downregulated | CCL2 treatment | [35] | Endothelial cells |
| **ZO3** |  |  | Unknown | Detectd in combination of ZO-1 and ZO-2 | [36] | Endothelial cells |

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| **CAV1** |  |  | Downregulated | chronic traumatic encephalopathy | [37] | Endothelial cells |
| **CAV2** |  |  | Upregulated | Traumatic brain injury | [38][39] | Endothelial cells |
| **CAVIN1** |  |  | Unknown | Shown to be needed for caveolae formation | [40] | Endothelial cells |
| **PLVAP** |  |  | Downregulated | cerebral edema | [41] | Endothelial cells |
| **SNAP23** |  |  | Unknown | Shown to primarily interact with VAMPs | [42] | Endothelial cells |
| **SNAP25** |  |  | Endothelial cells |
| **VAMP1** |  |  | Upregulated in adults | Time point embryo versus adult | [43] | Both left and right lateral ventricular choroid plexuses |
| **VAMP2** |  |  | Unknown | Shown to interact with CAV1 for caveolae formation | [44] | Endothelial cells |
| **VAMP3** |  |  |
| **VAMP8** |  |  | upregulated | Time point; embryo versus adult | [43] | Both left and right lateral ventricular choroid plexuses |

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