

Identification of altered genes in CCM models with various validations.

| Important genes with documented roles in ccm Disease [2] | Differentially expressed genes (DEGs) in human [2] | DEGs in mouse BMEC Ccm3/Krit1ECKO [2] | DEGs in mouse BMEC Ccm3/Pcd10ECKO [2] | DEGs common across mouse BMECs and C.elegans only in Ccm3/Krit1 mutant models [2] | DEGs common across mouse BMECs and C.elegans only in Ccm3/Pcd10 mutant models [2] | CCM1 delimits relationship of PTB/Ph domains [1] | proteomic analysis of cerebral cavernous malformation in HUVECs [2] | Biomechanics of endothelial tubule formation differentially modulated by cerebral cavernous malformation proteins [4] | Target: (H.sapiens ) FROM zebrafish. De pick target proteins [5] | Target: (H.sapiens ) FROM C.elegans. De pick target proteins [5] | Proteomic identification of the CSC [8]                                         | Proteomic analysis of Krit1 Loss-of-Function [3] | CCM3 Gene Network [6]                | ccm1 proteomics in HBMVECs [9] | CCM3 PROTEOMICS in HBMVECs [9] | CCM3 PROTEOMICS in HBMVECs [9] | ccm1 RNA in zebrafish [9] | CCM2 RNA in zebrafish [9] | CCM3 RNA in zebrafish [9] |
|----------------------------------------------------------|----------------------------------------------------|---------------------------------------|---------------------------------------|-----------------------------------------------------------------------------------|-----------------------------------------------------------------------------------|--------------------------------------------------|---------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------|------------------------------------------------------------------|---------------------------------------------------------------------------------|--------------------------------------------------|--------------------------------------|--------------------------------|--------------------------------|--------------------------------|---------------------------|---------------------------|---------------------------|
| CALM1                                                    | A2ML1                                              | 119002N15RIK                          | 1110065P20RIK                         | AAMP                                                                              | ABC81                                                                             | DAB2                                             | SEPT7                                                               | ADD1                                                                                                                  | ABC81                                                            | AKT3                                                             |                                                                                 | Actb                                             | APP                                  | CDH5                           | CDH5                           | STK24                          | APBA2                     | CCM2                      | HMOX2                     |
| CALM3                                                    | AADACL3                                            | 2210013021RIK                         | 2210013021RIK                         | AARS                                                                              | ALDH4A1                                                                           | DOK4                                             | 1433B                                                               | COL8A1                                                                                                                | CSF1R                                                            | APP                                                              | Proteins Identified from SDS-PAGE Gel and ESI-MS                                | Ckb                                              | APLP1                                | CAPN2                          | SUN1                           | SUN1                           | IL1A                      | TRIM44                    |                           |
| CLDN5                                                    | ABCA2                                              | 2310022A10RIK                         | 2610008E11RIK                         | ABCA3                                                                             | COL4A3BP                                                                          | NUMB                                             | 1433E                                                               | FN1                                                                                                                   | CYP24A1                                                          | BCL2                                                             | Proteins that selectively interact with FLAG-OSM                                | Tpm4                                             | CDC25A                               | ECSCR                          | MCM3                           | PLOD2                          | MSN                       | ITGB4                     |                           |
| DLI4                                                     | ABCA4                                              | 2310022B05RIK                         | 5430416009RIK                         | ACY1                                                                              | DNM1L                                                                             | PLEK                                             | 1433F                                                               | ITGA2                                                                                                                 | CYP27A1                                                          | BCL2L1                                                           |                                                                                 | Tubb4b                                           | CDC25B                               | MCM3                           | SFPQ                           | PRKCSH                         | EGR1                      | SULT1A3                   |                           |
| HEG1                                                     | ABCC1                                              | 2610008E11RIK                         | 9330182L06RIK                         | ARK1                                                                              | NOPS8                                                                             | RGS12                                            | 1433G                                                               | ITGB4                                                                                                                 | CYP2R1                                                           | BCL2L2                                                           |                                                                                 | Vim                                              | CDC25C                               | SUN1                           | PA2G4                          | CAV1                           | ITGB4                     | TJP1                      |                           |
| ICAM1                                                    | ABCC3                                              | 3110043021RIK                         | A43010519RIK                          | AMD1                                                                              | NPRL3                                                                             | TBC1D4                                           | 1433T                                                               | LAMA5                                                                                                                 | DYRK1A                                                           | BRSK1                                                            |                                                                                 | Calr                                             | CDC42                                | GLOD4                          | CNN3                           | DOB1                           | EXOC5                     | U2AF1                     |                           |
| KLF2                                                     | ABCC8                                              | 4930402H24RIK                         | AAED1                                 | ATP8B2                                                                            | PDCD10                                                                            | TIN2                                             | 1433Z                                                               | MYO18                                                                                                                 | FLT1                                                             | CAMK1D                                                           |                                                                                 | Eno1                                             | ARHGEF5                              | GAPDH                          | PSME1                          | GLOD4                          | TJP1                      |                           |                           |
| KLF4                                                     | ABHD15                                             | 4930427A07RIK                         | ABCB1A                                | C16orf13                                                                          | RPL21                                                                             | TNS2                                             | 1859                                                                | PLEC                                                                                                                  | KIT                                                              | CAMK2A                                                           |                                                                                 | Gapdh                                            | ARHGEF15                             | CNN3                           | NOS3                           | PSME1                          |                           |                           |                           |
| KRT12                                                    | ABI3                                               | 4930452B06RIK                         | ABCB1B                                | C1GALT1                                                                           | RPS18                                                                             | AGAP2                                            | 1856                                                                | SPTAN1                                                                                                                | LCK                                                              | CAMK2B                                                           |                                                                                 | Hspd1                                            | ARHGEF26                             | CTSB                           | TALDO1                         |                                | PRPF8                     |                           |                           |
| NCAM1                                                    | ABI3BP                                             | 4930453N24RIK                         | ACER3                                 | CAMKK2                                                                            | SCAP                                                                              | APBB1                                            | 1855                                                                | SPTBN2                                                                                                                | NR1I2                                                            | CCR5                                                             |                                                                                 | EEF1A1                                           | NGEF                                 | ERH                            | PRKCSH                         | BCL2A1                         |                           |                           |                           |
| PDCD10                                                   | ABR                                                | 4930523C07RIK                         | ACOT11                                | CD63                                                                              | SNX2                                                                              | APPL1                                            | 1846                                                                | THBS1                                                                                                                 | PDGFRA                                                           | CDC25A                                                           |                                                                                 | Cap2A1                                           | DLI1                                 | NOS3                           | DOB1                           | LMAN1                          |                           |                           |                           |
| PCAM1                                                    | ACSBG1                                             | 4930578C19RIK                         | ADAMTS12                              | CELF2                                                                             | CLF2                                                                              | CAPON                                            | 1815                                                                | CDH5                                                                                                                  | PKI1                                                             | CDC25C                                                           |                                                                                 | RP53                                             | DLI4                                 | PRKCSH                         | HSPA4                          | NOV                            |                           |                           |                           |
| RAP1A                                                    | ACSL3                                              | 5730208B09RIK                         | ADK                                   | CLOC3                                                                             | CPE                                                                               | CCM1                                             | 1853                                                                | CFL1                                                                                                                  | PPP3CA                                                           | CYP24A1                                                          |                                                                                 | PDCD10                                           | JAG2                                 | DOB1                           | HSPB1                          | KLF8                           |                           |                           |                           |
| SLC2A1                                                   | ADAM12                                             | 6430548M08RIK                         | AEBP2                                 |                                                                                   |                                                                                   | DAB1                                             | 1835                                                                | CFL2                                                                                                                  | RARA                                                             | CYP27A1                                                          |                                                                                 | SLC25A4                                          | RORA                                 | CAV1                           | SGTA                           |                                | DHRXK                     |                           |                           |
| SLC3A2                                                   | ADAM19                                             | 9130008F23RIK                         | AFAP1L2                               | CRIM1                                                                             |                                                                                   | DOK1                                             | 1867                                                                | CNN2                                                                                                                  | RARB                                                             | CYP2R1                                                           | Proteins that nonspecifically interact with anti-FLAG antibody-conjugated beads |                                                  | RORC                                 | CAPN9                          |                                |                                |                           |                           |                           |
| TSC2                                                     | ADAM23                                             | 9930111J21RIK1                        | AGFG2                                 | CSRP2                                                                             |                                                                                   | EPS8                                             | 1839                                                                | COL1A2                                                                                                                | RARG                                                             | DNM1                                                             |                                                                                 | FLII                                             | ARHGAP30                             | STRN3                          |                                |                                |                           |                           |                           |
| VIM                                                      | ADAM8                                              | A43010519RIK                          | AGGF1                                 | DHRS7B                                                                            |                                                                                   | EPS8L3                                           | 1838                                                                | COL4A6                                                                                                                | RXRA                                                             | DDP4                                                             |                                                                                 | STK38                                            | ARHGAP31                             |                                |                                |                                |                           |                           |                           |
| ANGPT1                                                   | ADAMTS1                                            | AAGALT                                | AGD2                                  | DPAGT1                                                                            |                                                                                   | FAM43A                                           | 1857                                                                | DAG1                                                                                                                  | RXRB                                                             | DYRK1A                                                           |                                                                                 | ACTG1                                            | SDC1                                 |                                |                                |                                |                           |                           |                           |
| CALM2                                                    | ADAMTS12                                           | AAED1                                 | AHNAK                                 | EFHD2                                                                             |                                                                                   | FRS2                                             | 1C07                                                                | FLNB                                                                                                                  | RXRG                                                             | EPHA2                                                            |                                                                                 | TMOD3                                            | SDC4                                 |                                |                                |                                |                           |                           |                           |
| CCM2                                                     | ADAMTS2                                            | AAMP                                  | AIB37181                              | ENPP6                                                                             |                                                                                   | GULP1                                            | 2A8A                                                                | ITGA10                                                                                                                | SNCA                                                             | FYN                                                              |                                                                                 |                                                  | EXOC8B                               |                                |                                |                                |                           |                           |                           |
| CD58                                                     | ADAMTS5                                            | AARS                                  | AIDA                                  | EXT1                                                                              |                                                                                   | GULP1-t                                          | 4F2                                                                 | LAMB3                                                                                                                 | TUBB4B                                                           | G6PD                                                             | Proteins Identified by MudPIT Analysis That Selectively Interact with FLAG-OSM  |                                                  | STXBP6                               |                                |                                |                                |                           |                           |                           |
| CEACAM5                                                  | ADAMTS11                                           | AATK                                  | ALDH4A1                               | FAXC                                                                              |                                                                                   | ICAP1                                            | 5NTD                                                                | MLCP                                                                                                                  | USP1                                                             | LTB4R                                                            | Previously identified CCM complex members                                       |                                                  | FERMT3                               |                                |                                |                                |                           |                           |                           |
| CTTN                                                     | ADAMTS13                                           | ABCA3                                 | ALG10B                                | FGFR3                                                                             |                                                                                   | JIP1                                             | 6PGD                                                                | RAC1                                                                                                                  | WEE1                                                             | MAP2K5                                                           |                                                                                 | MEKK3                                            | CCT2                                 |                                |                                |                                |                           |                           |                           |
| CYP2B6                                                   | ADCY1                                              | ABCA5                                 | ALSZCL                                | GERP3                                                                             |                                                                                   | LDLRAP1                                          | A2MG                                                                |                                                                                                                       | ADORA3                                                           | MAP4K4                                                           |                                                                                 | Bac                                              | ARHGEF16                             |                                |                                |                                |                           |                           |                           |
| EPH82                                                    | ADD1                                               | ABCA7                                 | ANXR2                                 | GABARAPL1                                                                         |                                                                                   | mPID1                                            | AATM                                                                |                                                                                                                       | CACNA1D                                                          | MELK                                                             |                                                                                 | ICAP-1                                           | ARHGEF19                             |                                |                                |                                |                           |                           |                           |
| GLI3                                                     | ADD2                                               | ABCA8B                                | ANXA2                                 | GNAT2                                                                             |                                                                                   | mPID1-t                                          | ACLY                                                                |                                                                                                                       | CACNB2                                                           | MMP14                                                            |                                                                                 | ETF1                                             |                                      |                                |                                |                                |                           |                           |                           |
| IL6                                                      | AEBP1                                              | ABCA9                                 | AP3M1                                 | HLCS                                                                              |                                                                                   | NUMB-L                                           | ACTG                                                                |                                                                                                                       | CCNB2                                                            | MMP2                                                             |                                                                                 | PDCD10                                           | JAG1                                 |                                |                                |                                |                           |                           |                           |
| ITGB1BP1                                                 | AFAP1                                              | ABCR1B                                | APLNR                                 | HMGL1                                                                             |                                                                                   | NUMB-ss                                          | ACTB                                                                |                                                                                                                       | CDK5                                                             | NPC1L1                                                           |                                                                                 |                                                  | Cytoskeletal proteins                |                                |                                |                                |                           |                           |                           |
| MAP3K3                                                   | AGTFBP1                                            | ABCB9                                 | ARF2                                  | IPMK                                                                              |                                                                                   | RABGAP1                                          | ACTBL                                                               |                                                                                                                       | CLK1                                                             | NQO1                                                             |                                                                                 |                                                  | MYH10                                |                                |                                |                                |                           |                           |                           |
| MAPK1                                                    | AHI1                                               | ABCC5                                 | ARHGAP28                              | IQGAP3                                                                            |                                                                                   | SHC1                                             | ACTN1                                                               |                                                                                                                       | CRABP1                                                           | NR1H4                                                            |                                                                                 |                                                  | TUBB6                                |                                |                                |                                |                           |                           |                           |
| MAPK3                                                    | AHNAK2                                             | ABCD1                                 | ARNTL                                 | ITGB8                                                                             |                                                                                   | SNX17                                            | ACTN4                                                               |                                                                                                                       | CRABP2                                                           | NR1I2                                                            |                                                                                 |                                                  | TUBB4A                               |                                |                                |                                |                           |                           |                           |
| MSH2                                                     | AIM1                                               | ABCG1                                 | ASAP1                                 | KIF3A                                                                             |                                                                                   | TBC1D1                                           | ACT2                                                                |                                                                                                                       | CYP27B1                                                          | PBK                                                              |                                                                                 |                                                  | TUBB4B                               |                                |                                |                                |                           |                           |                           |
| PRRT2                                                    | AK5                                                | ABHD17A                               | ATP6B                                 | KRT12                                                                             |                                                                                   | TNS2-t                                           | ADH2                                                                |                                                                                                                       | DHODH                                                            | PPP3R1                                                           |                                                                                 |                                                  | CFL1                                 |                                |                                |                                |                           |                           |                           |
| PTEN                                                     | AKT3                                               | ABHD17B                               | ATP2B4                                | LRRCS7                                                                            |                                                                                   | Tbclt1d4-t                                       | ADT3                                                                |                                                                                                                       | EHADH                                                            | PRKCG                                                            |                                                                                 |                                                  | TUBA4A                               |                                |                                |                                |                           |                           |                           |
| PTGS2                                                    | ALPK2                                              | ABI3                                  | ATP7A                                 | MGAT5                                                                             |                                                                                   |                                                  | ADHNC                                                               |                                                                                                                       | FLT4                                                             | PRKCH                                                            |                                                                                 |                                                  | TUBA1C                               |                                |                                |                                |                           |                           |                           |
| RABGEF1                                                  | ALPL                                               | ABLIM3                                | AZIN1                                 | MOSPD2                                                                            |                                                                                   |                                                  | AKA12                                                               |                                                                                                                       | GPR35                                                            | PSP1                                                             |                                                                                 |                                                  | TUBA1A                               |                                |                                |                                |                           |                           |                           |
| SERPIN1                                                  | AMER3                                              | ABR                                   | B4GALT5                               | MRAS                                                                              |                                                                                   |                                                  | ALBU                                                                |                                                                                                                       | KDR                                                              | PTGES                                                            | Protein translation and folding                                                 |                                                  | HIST1H3E                             |                                |                                |                                |                           |                           |                           |
| SMARCE1                                                  | AMICA1                                             | ACACB                                 | B9D2                                  | NEK7                                                                              |                                                                                   |                                                  | ALDOA                                                               |                                                                                                                       | LRRK2                                                            | PTPN1                                                            |                                                                                 |                                                  | EF1A1                                |                                |                                |                                |                           |                           |                           |
| TERF2IP                                                  | AMPH                                               | ACAD12                                | BAG5                                  | NMT2                                                                              |                                                                                   |                                                  | AMPL                                                                |                                                                                                                       | MST1R                                                            | RARA                                                             |                                                                                 |                                                  | CCT3                                 |                                |                                |                                |                           |                           |                           |
| TP53                                                     | ANK2                                               | ACADSB                                | BAIAP2                                | NTSC2                                                                             |                                                                                   |                                                  | AMPN                                                                |                                                                                                                       | PDGFRB                                                           | RARB                                                             |                                                                                 |                                                  | CCT6A                                |                                |                                |                                |                           |                           |                           |
| ULK1                                                     | ANK3                                               | ACER3                                 | BAIAP2L1                              | NTN1                                                                              |                                                                                   |                                                  | ANR31                                                               |                                                                                                                       | SRC                                                              | RARG                                                             |                                                                                 |                                                  | CCT7                                 |                                |                                |                                |                           |                           |                           |
| VEGFA                                                    | ANKRD36B                                           | ACOT11                                | BCAS3                                 | NUP85                                                                             |                                                                                   |                                                  | ANXA1                                                               |                                                                                                                       | TNNC2                                                            | RBP1                                                             |                                                                                 |                                                  | TCP1                                 |                                |                                |                                |                           |                           |                           |
|                                                          | ANKS18                                             | ACTA2                                 | BCCIP                                 | DNK1T                                                                             |                                                                                   |                                                  | ANXA2                                                               |                                                                                                                       | TUBA1A                                                           | RORA                                                             |                                                                                 |                                                  | DNAB6                                |                                |                                |                                |                           |                           |                           |
|                                                          | ANTR1                                              | ACTB                                  | BCL10                                 | PACRB                                                                             |                                                                                   |                                                  | ANXA3                                                               |                                                                                                                       | TUBA1B                                                           | RORC                                                             |                                                                                 |                                                  | DNAB2                                |                                |                                |                                |                           |                           |                           |
|                                                          | ANTR2                                              | ACTR3                                 | BCL2                                  | PDGFRA                                                                            |                                                                                   |                                                  | ANXA5                                                               |                                                                                                                       | TUBB                                                             | RORA                                                             |                                                                                 |                                                  | CCT2                                 |                                |                                |                                |                           |                           |                           |
|                                                          | ANXA1                                              | ACVR1L                                | BEND7                                 | PLCD3                                                                             |                                                                                   |                                                  | ANXA6                                                               |                                                                                                                       | TUBB1                                                            | RXRB                                                             |                                                                                 |                                                  | CCT5                                 |                                |                                |                                |                           |                           |                           |
|                                                          | AOAH                                               | ACY1                                  | BICD2                                 | PLK1                                                                              |                                                                                   |                                                  | APMAP                                                               |                                                                                                                       | TUBB4A                                                           | RXRG                                                             |                                                                                 |                                                  | CCT8                                 |                                |                                |                                |                           |                           |                           |
|                                                          | APBA2                                              | ACY3                                  | BMP4                                  | PLXDC2                                                                            |                                                                                   |                                                  | ARF3                                                                |                                                                                                                       |                                                                  | SLK                                                              |                                                                                 |                                                  | CCT4                                 |                                |                                |                                |                           |                           |                           |
|                                                          | APC                                                | ADA                                   | BMP6                                  | POLD1                                                                             |                                                                                   |                                                  | ARF1                                                                |                                                                                                                       |                                                                  | TLR4                                                             |                                                                                 |                                                  | DNAB1                                |                                |                                |                                |                           |                           |                           |
|                                                          | APLN                                               | ADAM11                                | BST1                                  | POLH                                                                              |                                                                                   |                                                  | ARF4                                                                |                                                                                                                       |                                                                  | TOP2B                                                            |                                                                                 |                                                  | HSP90                                |                                |                                |                                |                           |                           |                           |
|                                                          | APLNR                                              | ADAM12                                | BTG                                   | PRPS2                                                                             |                                                                                   |                                                  | ARP3                                                                |                                                                                                                       |                                                                  | AGTR1                                                            |                                                                                 |                                                  | Signaling                            |                                |                                |                                |                           |                           |                           |
|                                                          | APOBR                                              | ADAM15                                | BTG2                                  | RAD51                                                                             |                                                                                   |                                                  | ARPC4                                                               |                                                                                                                       |                                                                  | AKR1B1                                                           |                                                                                 |                                                  | RIN2                                 |                                |                                |                                |                           |                           |                           |
|                                                          | APOL6                                              | ADAM8                                 | C1QTNF1                               | REEP2                                                                             |                                                                                   |                                                  | ATPA                                                                |                                                                                                                       |                                                                  | AKT1                                                             |                                                                                 |                                                  | PPP2R2D                              |                                |                                |                                |                           |                           |                           |
|                                                          | ARHGAP21                                           | ADAMTS10                              | C2CD2L                                | RF2                                                                               |                                                                                   |                                                  | ATPB                                                                |                                                                                                                       |                                                                  | AKT2                                                             |                                                                                 |                                                  | PPP2CA                               |                                |                                |                                |                           |                           |                           |
|                                                          | ARHGAP25                                           | ADAT2                                 | CACNA1A                               | RPS6KA5                                                                           |                                                                                   |                                                  | ATPO                                                                |                                                                                                                       |                                                                  | ALDH1A2                                                          |                                                                                 |                                                  | GNB2L1                               |                                |                                |                                |                           |                           |                           |
|                                                          | ARHGAP26                                           | ADD3                                  | CACNB3                                | RRAS2                                                                             |                                                                                   |                                                  | B2MG                                                                |                                                                                                                       |                                                                  | ALDH1A3                                                          |                                                                                 |                                                  | GNB4                                 |                                |                                |                                |                           |                           |                           |
|                                                          | ARHGAP30                                           | ADGRA3                                | CAMK2N1                               | SLC12A8                                                                           |                                                                                   |                                                  | BASP1                                                               |                                                                                                                       |                                                                  | ALOX12                                                           |                                                                                 |                                                  | PPP2R1A                              |                                |                                |                                |                           |                           |                           |
|                                                          | ARHGAP35                                           | ADGRE5                                | CAND2                                 | SLT2                                                                              |                                                                                   |                                                  | BGAL                                                                |                                                                                                                       |                                                                  | ALOX15                                                           |                                                                                 |                                                  | PPP1CC                               |                                |                                |                                |                           |                           |                           |
|                                                          | ARHGDB                                             | ADGRG1                                | CAPN2                                 | SPARCL1                                                                           |                                                                                   |                                                  | BST2                                                                |                                                                                                                       |                                                                  | ALOX15B                                                          |                                                                                 |                                                  | Vesicular transport proteins         |                                |                                |                                |                           |                           |                           |
|                                                          | ARHGEF9                                            | ADGRG3                                | CAR2                                  | SUSD2                                                                             |                                                                                   |                                                  | C1QB                                                                |                                                                                                                       |                                                                  | ALOX5                                                            |                                                                                 |                                                  | TFRC                                 |                                |                                |                                |                           |                           |                           |
|                                                          | ARL11                                              | ADGRG3                                | CAR5B                                 | TMEM180                                                                           |                                                                                   |                                                  | CALD1                                                               |                                                                                                                       |                                                                  | ALOX5AP                                                          |                                                                                 |                                                  | COPB1                                |                                |                                |                                |                           |                           |                           |
|                                                          | ARNT2                                              | ADGRG4                                | CAR7                                  | TRPC6                                                                             |                                                                                   |                                                  | CALM                                                                |                                                                                                                       |                                                                  | AMY1A                                                            |                                                                                 |                                                  | COPA                                 |                                |                                |                                |                           |                           |                           |
|                                                          | ARSD                                               | ADIPOR2                               | CASP3                                 | TTT38                                                                             |                                                                                   |                                                  | CALR                                                                |                                                                                                                       |                                                                  | APEX1                                                            |                                                                                 |                                                  | ARF1                                 |                                |                                |                                |                           |                           |                           |
|                                                          | ASH1L                                              | ADK                                   | CAS7                                  | TUBB2B                                                                            |                                                                                   |                                                  | CALX                                                                |                                                                                                                       |                                                                  | BACE1                                                            |                                                                                 |                                                  | ARF2                                 |                                |                                |                                |                           |                           |                           |
|                                                          | ASPM                                               | ADAM                                  | CBX6                                  | UBR7                                                                              |                                                                                   |                                                  | CAND1                                                               |                                                                                                                       |                                                                  | BAD                                                              |                                                                                 |                                                  | ARF3                                 |                                |                                |                                |                           |                           |                           |
|                                                          | ASPN                                               | ADORA2A                               | CDC12                                 | UNC13A                                                                            |                                                                                   |                                                  | CAMP1                                                               |                                                                                                                       |                                                                  | CAMK3                                                            |                                                                                 |                                                  | ARF4                                 |                                |                                |                                |                           |                           |                           |
|                                                          | ATCAY                                              | AFAP1L2                               | CCDC88C                               | VEPFI                                                                             |                                                                                   |                                                  | CATB                                                                |                                                                                                                       |                                                                  | CAMK2D                                                           |                                                                                 |                                                  | ARF5B                                |                                |                                |                                |                           |                           |                           |
|                                                          | ATL1                                               | AFF4                                  | CCDC93                                | WARS                                                                              |                                                                                   |                                                  | CATD                                                                |                                                                                                                       |                                                                  | CAMK2G                                                           |                                                                                 |                                                  | COPG1                                |                                |                                |                                |                           |                           |                           |
|                                                          | ATP12A                                             | AGAP1                                 | CCL2                                  | WLS                                                                               |                                                                                   |                                                  | CAV1                                                                |                                                                                                                       |                                                                  | CKAR                                                             |                                                                                 |                                                  | Metabolism and biosynthetic proteins |                                |                                |                                |                           |                           |                           |
|                                                          | ATP1A2                                             | AGMO                                  | CCM2L                                 | XPO4                                                                              |                                                                                   |                                                  | CAZ1                                                                |                                                                                                                       |                                                                  | CDC42BP1                                                         |                                                                                 |                                                  | ENO1                                 |                                |                                |                                |                           |                           |                           |
|                                                          | ATP1A3                                             | AGPAT2                                | CCH1                                  | ZDHHC14                                                                           |                                                                                   |                                                  | CLK3                                                                |                                                                                                                       |                                                                  | CLK3                                                             |                                                                                 |                                                  | CAD                                  |                                |                                |                                |                           |                           |                           |
|                                                          | ATP1B1                                             | AHNAK                                 | CD164                                 |                                                                                   |                                                                                   |                                                  | CH10                                                                |                                                                                                                       |                                                                  | CNR1                                                             |                                                                                 |                                                  | PAICS                                |                                |                                |                                |                           |                           |                           |
|                                                          | ATP2B2                                             | A1467606                              | CD247                                 |                                                                                   |                                                                                   |                                                  | CH60                                                                |                                                                                                                       |                                                                  | CREB1                                                            |                                                                                 |                                                  | Miscellaneous                        |                                |                                |                                |                           |                           |                           |
|                                                          | ATP2B3                                             | A1661453                              | CD38                                  |                                                                                   |                                                                                   |                                                  | CSY                                                                 |                                                                                                                       |                                                                  | CYP1A2                                                           |                                                                                 |                                                  | FAR1                                 |                                |                                |                                |                           |                           |                           |
|                                                          | ATP8A1                                             | AIDA                                  | CD40                                  |                                                                                   |                                                                                   |                                                  | CKAP4                                                               |                                                                                                                       |                                                                  | CYP26A1                                                          |                                                                                 |                                                  | H2-D1                                |                                |                                |                                |                           |                           |                           |







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|  |  | ZFPM1        |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|  |  | ZFX          |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|  |  | ZGRF1        |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|  |  | ZIC3         |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|  |  | ZIK1         |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|  |  | ZKSCAN4      |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|  |  | ZMI21        |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|  |  | <b>ZNRF1</b> |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|  |  | ZRANB3       |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|  |  | ZWINT        |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|  |  | <b>ZYX</b>   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|  |  | ZZEF1        |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |

**Supplemental Table 1A. Identification of altered genes in CCM models with various validations.** A total of 9 CCM studies were analyzed to identify genes that overlapped as perturbed in various CCM models. For Datasets, non-human genes were converted to human homologs before processing and all genes capitalized to ensure overlaps were not misidentified due to case changes. Studies are divided into columns based on detection method, background strain (i.e. mouse BMEC Ccm1/Krit1 ECKO) and organism. Genes that are italicized and bolded are genes duplicated in another column. Overlaps within the same study (EX: First 6 columns) were not considered "validated", only overlaps within two different studies are considered "validated". Abbreviations: Differentially expressed genes (DEG's), human umbilical vein endothelial cells (HUVEC), Human Brain Microvascular Endothelial Cells (HBMVEC). Reference numbering can be found in Supplemental Table 7.