Cell Reports, Volume *41*

Supplemental information

Pan-claudin family interactome analysis reveals shared and specific interactions

Lorena Suarez-Artiles, Tilman Breiderhoff, Rossana Girardello, Hannes Gonschior, Sophie Rodius, Antoine Lesur, Ulf Reimer, Evelyn Ramberger, Daniel Perez-Hernandez, Dominik Müller, Philipp Mertins, and Gunnar Dittmar

Supplemental information

Pan-claudin family interactome analysis reveals shared and specific interactions

Lorena Suarez-Artiles, Tilman Breiderhoff, Rossana Girardello, Hannes Gonschior, Sophie Rodius, Antoine Lesur, Ulf Reimer, Evelyn Ramberger, Daniel Perez-Hernandez, Dominik Müller, Philipp Mertins, and Gunnar Dittmar

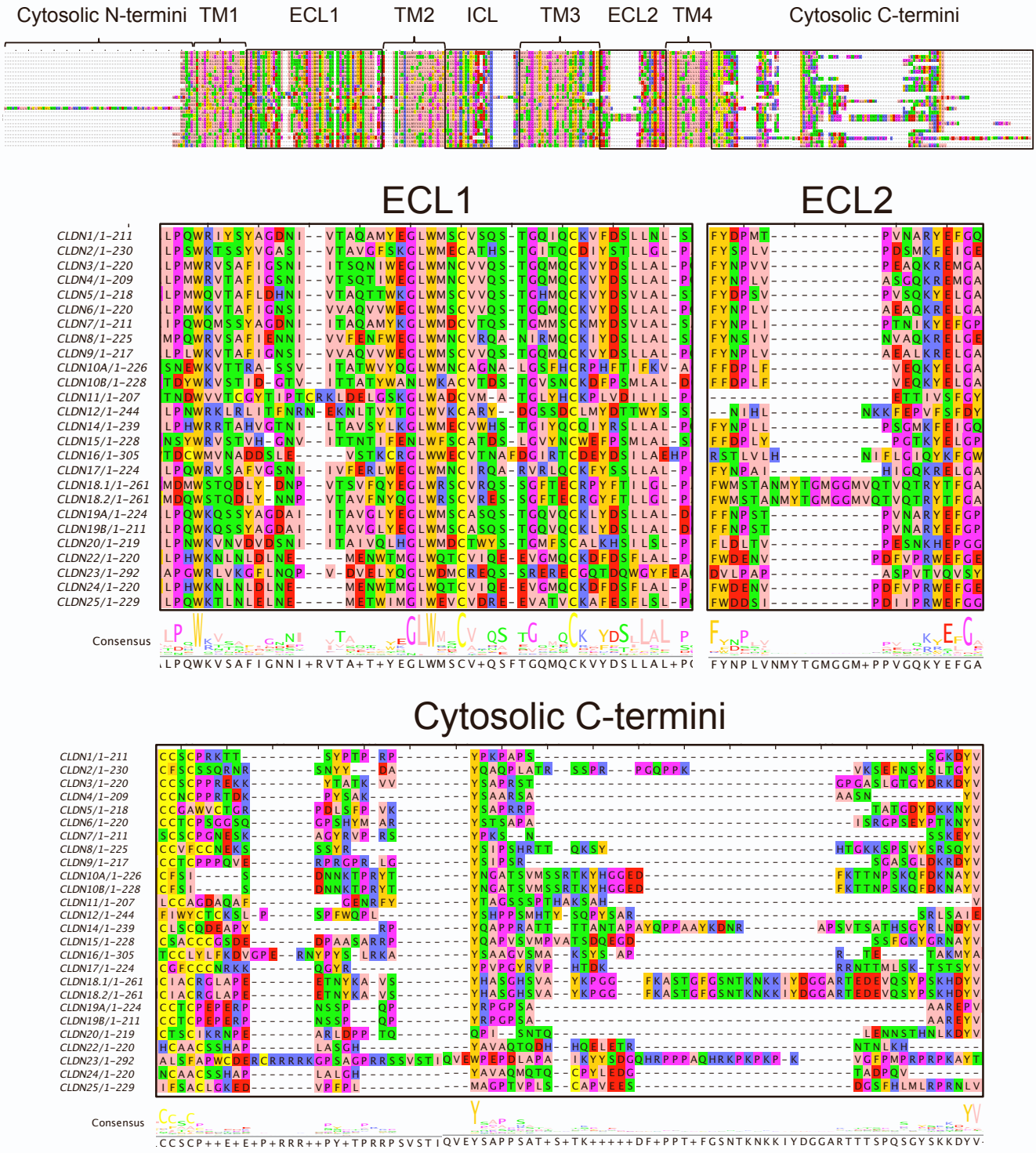
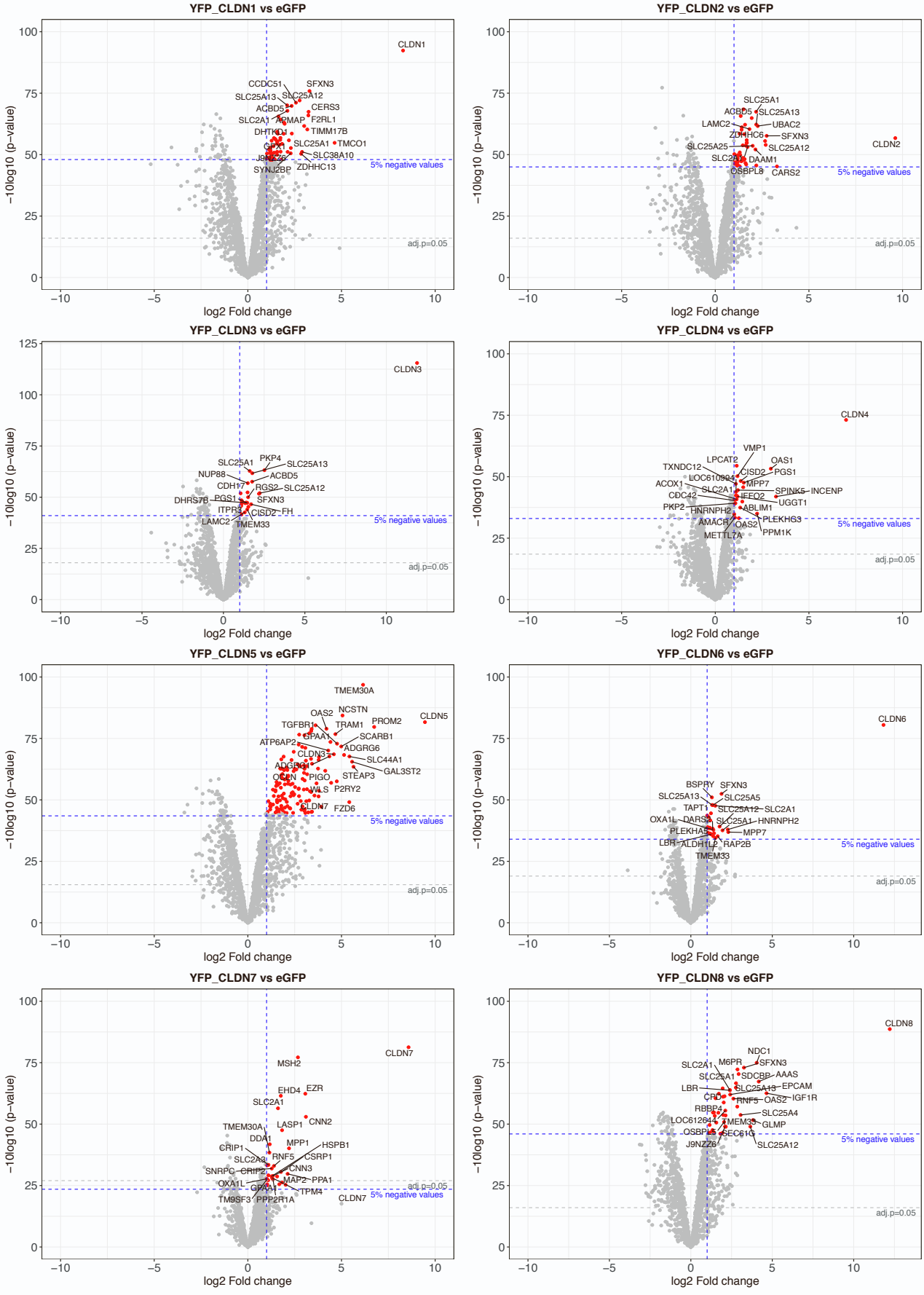
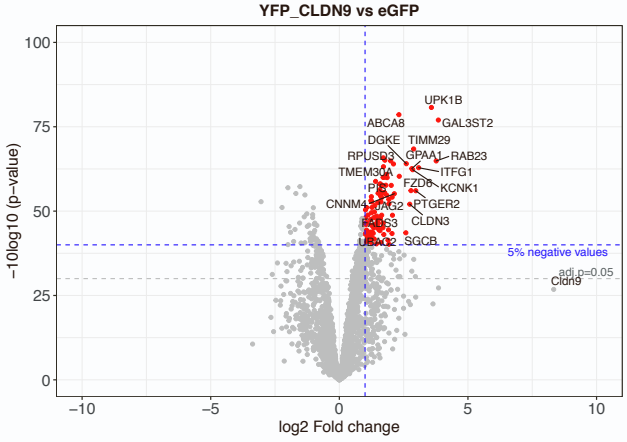
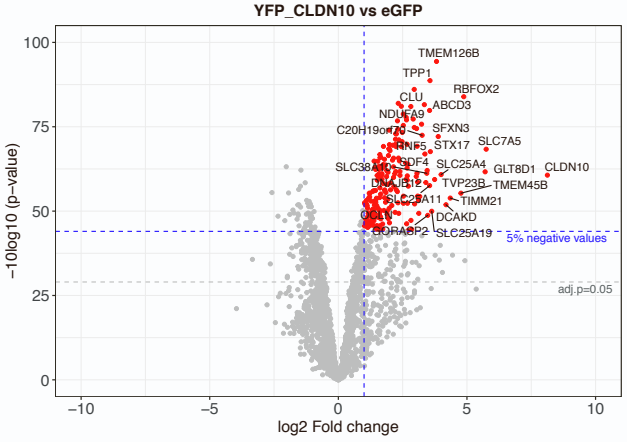
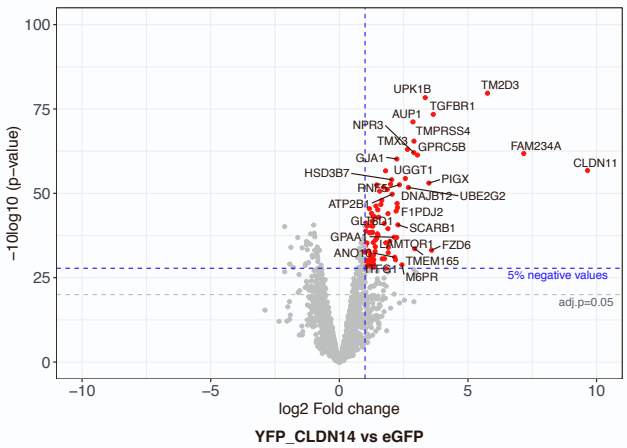


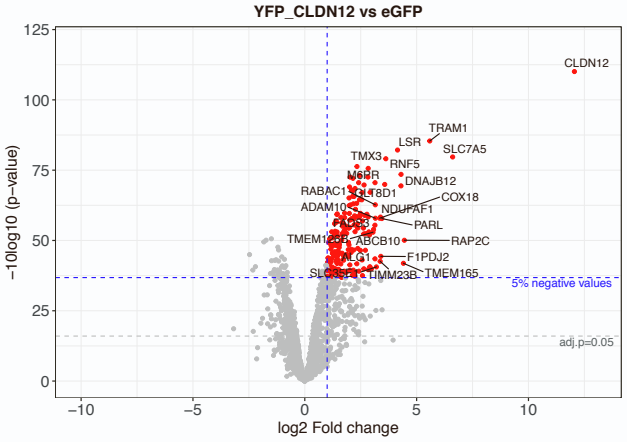
Figure S1 related to the introduction. Sequence alignment of all the claudins expressed in humans. The cytosolic C-termini tail of claudins show higher variability in length and sequence compared to more conserved regions like transmembrane domains (TM1-TM4) or extracellular loops (ECL1 and ECL2). TM: transmembrane. ECL: extracellular loop. ICL: intracellular loop.

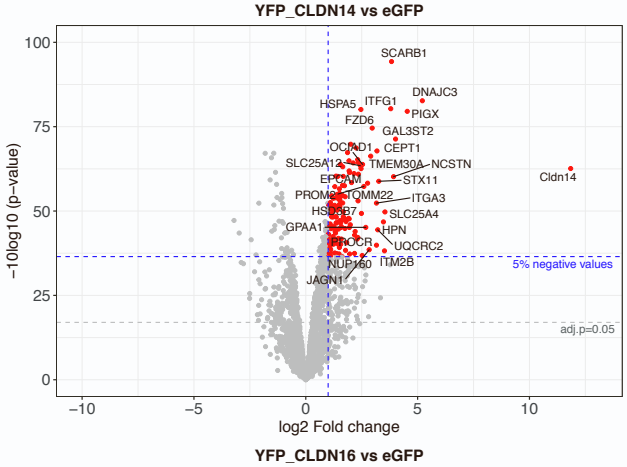

YFP_CLDN1 vs eGFP
CLDN1
CCDC51
SFXN3
SLC25A13
SLC25A12
ACBD5
CERS3
SLC2A1
AGMAP
F2RL1
DHTKD1
TIMM17B
GPX1
SLC25A1
TMCO1
J9NZZ6
SLC38A10
SYNJ2BP
ZDHHC13
5% negative values
adj.p=0.05
−10log10 (p−value)
log2 Fold change
YFP_CLDN2 vs eGFP
CLDN2
SLC25A1
ACBD5
SLC25A13
LAMC2
UBAC2
ZDHHC6
SFXN3
SLC25A25
SLC25A12
SLC2A14
DAAM1
OSBPL8
CARS2
5% negative values
adj.p=0.05
−10log10 (p−value)
log2 Fold change
YFP_CLDN3 vs eGFP
CLDN3
SLC25A1
PKP4
SLC25A13
NUP88
ACBD5
CDH17
RGS2
SLC25A12
DHRS7B
PGS1
SFXN3
ITPR3
CISD2
FH
LAMC2
TMEM33
5% negative values
adj.p=0.05
−10log10 (p−value)
log2 Fold change
YFP_CLDN4 vs eGFP
CLDN4
VMP1
LPCAT2
OAS1
TXNDC12
CISD2
PGS1
LOC610904
ACOX1
MPP7
SLC2A1
SPINK5
INCENP
CDC42
IFEO2
UGGT1
PKP2
ABLIM1
HNRNPH2
PLEKHG3
AMACR
OAS2
PPM1K
METTL7A
5% negative values
adj.p=0.05
−10log10 (p−value)
log2 Fold change
YFP_CLDN5 vs eGFP
TMEM30A
OAS2
NCSTN
CLDN5
TGFBR1
TRAM1
PROM2
GPAA1
SCARB1
ATP6AP2
ADGRG6
CLDN3
SLC44A1
ADGRG4
OCLN
PIGO
STEAP3
GAL3ST2
WLS
P2RY2
CLDN7
FZD6
5% negative values
adj.p=0.05
−10log10 (p−value)
log2 Fold change
YFP_CLDN6 vs eGFP
CLDN6
BSPRY
SFXN3
SLC25A13
SLC25A5
TAPT1
SLC25A12
SLC2A1
OXA1L
DARS2
SLC25A1
HNRNPH2
PLEKHA5
MPP7
LBR
ALDH1L2
RAP2B
TMEM33
5% negative values
adj.p=0.05
−10log10 (p−value)
log2 Fold change
YFP_CLDN7 vs eGFP
CLDN7
MSH2
EHD4
EZR
SLC2A1
TMEM30A
LASP1
CNN2
DDA1
MPP1
HSPB1
CRIP1
RNF5
CSRP1
SLC2A3
CNN3
SNRPC
CRIP2
OXA1L
MAP2
PPA1
GPAA1
TPM4
TM9SF3
PPP2R1A
CLDN7
5% negative values
adj.p=0.05
−10log10 (p−value)
log2 Fold change
YFP_CLDN8 vs eGFP
CLDN8
NDC1
M6PR
SFXN3
SLC2A1
SLC25A1
SDCBP
AAAS
LBR
SLC25A13
EPCAM
CRD
RNF5
OAS2
IGF1R
RBBP4
SLC25A4
LOC612641
TMEM35
GLMP
OSBPL8
SEC61G
J9NZZ6
SLC25A12
5% negative values
adj.p=0.05
−10log10 (p−value)
log2 Fold change

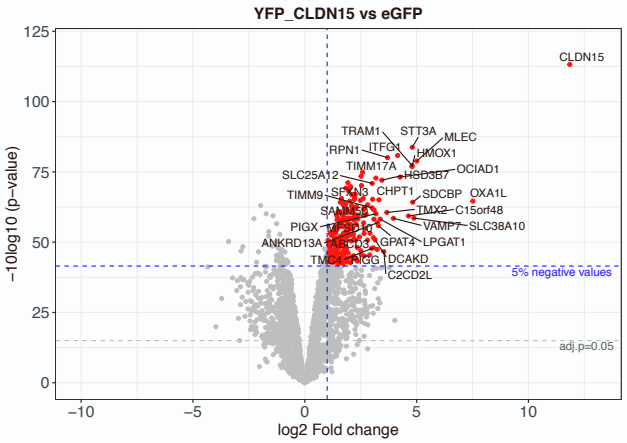

YFP_CLDN9 vs eGFP
−10log10 (p−value)
log2 Fold change
UPK1B
ABCA8
GAL3ST2
DGKE
TIMM29
RPUSD3
GPAA1
RAB23
TMEM30A
ITFG1
FZD6
KCNK1
CNNM4
PTGER2
CLDN3
UBXN2
SGCB
5% negative values
adj.p=0.05
Cldn9

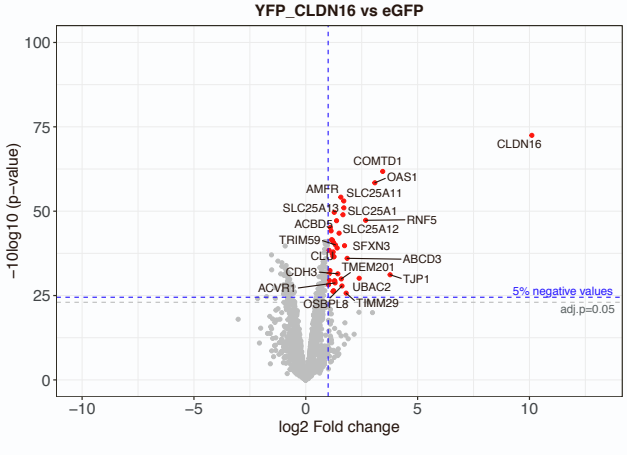

YFP_CLDN10 vs eGFP
−10log10 (p−value)
log2 Fold change
TMEM126B
TPP1
RBFOX2
CLU
ABCD3
NDUFA9
SFXN3
C20H19orf70
RNF5
STX17
SLC7A5
SLC38A10
SDF4
SLC25A4
GLT8D1
CLDN10
DNAJB12
TVP23B
TMEM45B
SLC25A11
TIMM21
OCLN
DCAKD
ARGRAP2
SLC25A19
5% negative values
adj.p=0.05

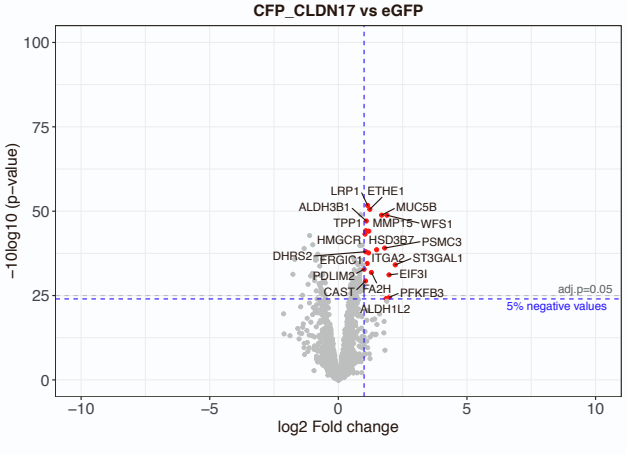

YFP_CLDN11 vs eGFP
−10log10 (p−value)
log2 Fold change
UPK1B
TM2D3
TGFBR1
AUP1
NPR3
TMPRSS4
TMX3
GPRC5B
FAM234A
GJA1
CLDN11
HSD3B7
UGGT1
PIGX
RNF5
DNAJB12
UBE2G2
ATP2B1
F1PDJ2
GLRX1
SCARB1
GPAA1
LAMTOR1
FZD6
ANO10
TMEM165
ITFG1
M6PR
5% negative values
adj.p=0.05

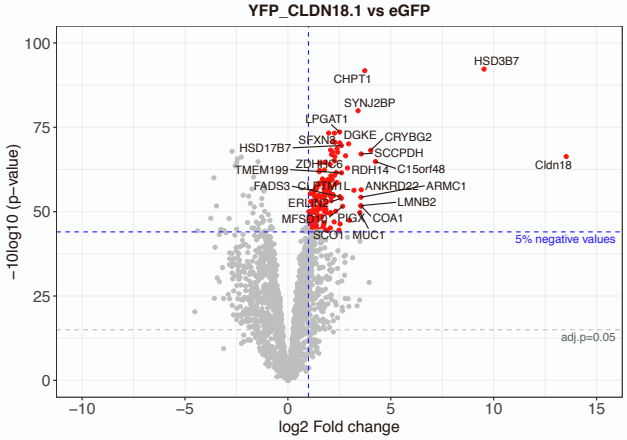

YFP_CLDN12 vs eGFP
−10log10 (p−value)
log2 Fold change
CLDN12
TRAM1
LSR
SLC7A5
TMX3
RNF5
USHR
DNAJB12
RABAC1
GLT8D1
COX18
ADAM10
NDUFAF1
PARL
TMEM126B
ABCB10
RAP2C
MLEC
F1PDJ2
SLC25A11
TIMM23B
TMEM165
5% negative values
adj.p=0.05

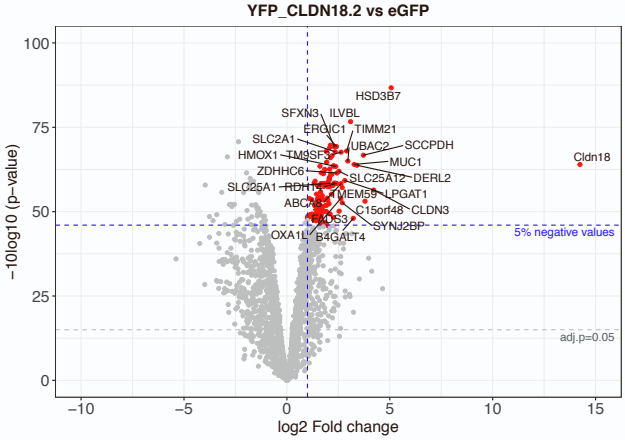

YFP_CLDN14 vs eGFP
−10log10 (p−value)
log2 Fold change
SCARB1
DNAJC3
HSPA5
ITFG1
PIGX
FZD6
GAL3ST2
OCIAD1
CEPT1
SLC25A12
TMEM30A
NCSTN
EPCAM
STX11
Cldn14
PROM2
TOMM22
ITGA3
HSD3B7
SLC25A4
GPAA1
HPN
RPUCR
UQCRC2
NUP160
ITM2B
JAGN1
5% negative values
adj.p=0.05

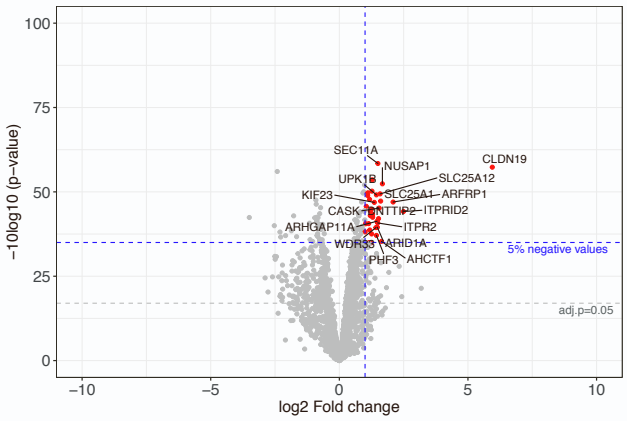

YFP_CLDN15 vs eGFP
−10log10 (p−value)
log2 Fold change
CLDN15
TRAM1
STT3A
MLEC
RPN1
ITFG1
PMOX1
TIMM17A
OCIAD1
SLC25A12
HSD3B7
TIMM9
CHPT1
SDCBP
OXA1L
SAMM50
TMX2
C15orf48
PIGX
VAMP7
SLC38A10
ANKRD13A
GPAT4
LPGAT1
TMC4
DCAKD
C2CD2L
5% negative values
adj.p=0.05

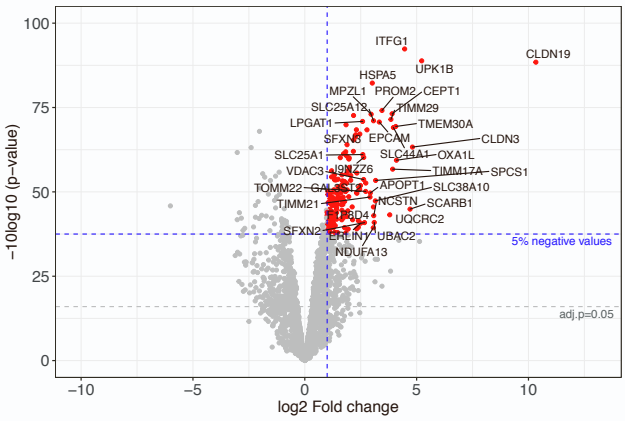

YFP_CLDN16 vs eGFP
−10log10 (p−value)
log2 Fold change
CLDN16
COMTD1
OAS1
AMFR
SLC25A11
SLC25A13
SLC25A1
RNF5
ACBD5
SLC25A12
TRIM59
SFXN3
CLU
ABCD3
TMEM201
CDH3
TJP1
AOVR1
UBAC2
OSBPL8
TIMM29
5% negative values
adj.p=0.05

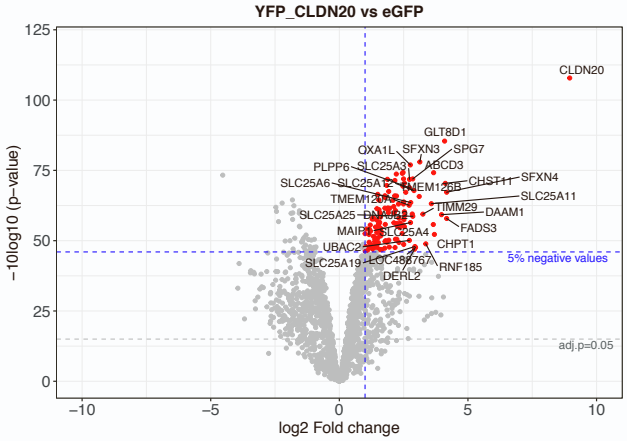

CFP_CLDN17 vs eGFP
−10log10 (p−value)
log2 Fold change
LRP1
ETHE1
ALDH3B1
MUC5B
TPP1
MMP15
WFS1
HMGCR
HSD3B7
PSMC3
DHRS2
ERGIC1
ITGA2
ST3GAL1
PDLIM2
EIF3I
CAST
FA2H
PFKFB3
ALDH1L2
adj.p=0.05
5% negative values

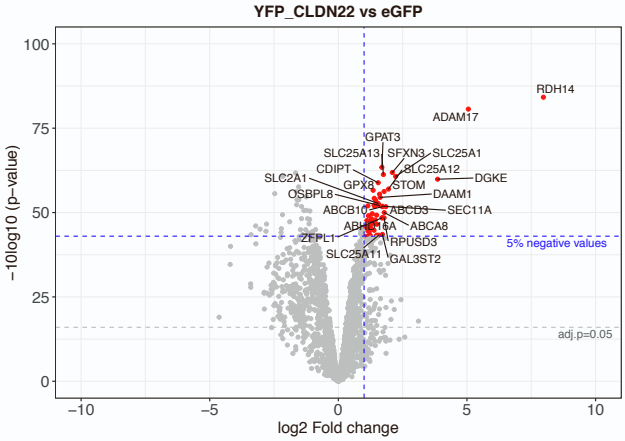

YFP_CLDN18.1 vs eGFP
HSD3B7
CHPT1
SYNJ2BP
LPGAT1
DGKE
CRYBG2
SFXN3
SCCPDH
HSD17B7
ZDHHC6
RDH14
C15orf48
TMEM199
Cldn18
FADS3
CLPTM1L
ANKRD22
ARMC1
ERLIN2
LMNB2
MFSD11
PIGX
COA1
SCO1
MUC1
5% negative values
adj.p=0.05
−10log10 (p−value)
log2 Fold change

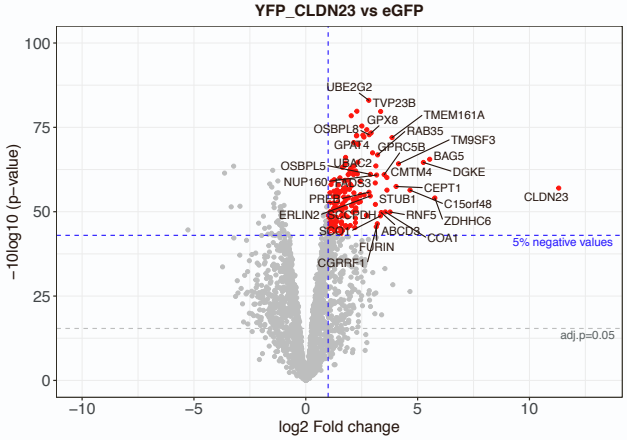

YFP_CLDN18.2 vs eGFP
HSD3B7
SFXN3
ILVBL
ERGIC1
TIMM21
SLC2A1
UBAC2
SCCPDH
HMOX1
TM9SF3
MUC1
Cldn18
ZDHHC6
SLC25A12
DERL2
SLC25A1
RDH14
TMEM59
LPGAT1
ABCA5
C15orf48
CLDN3
FADS3
SYNJ2BP
OXA1L
B4GALT4
5% negative values
adj.p=0.05
−10log10 (p−value)
log2 Fold change


CFP_CLDN19a vs eGFP
SEC11A
NUSAP1
CLDN19
UPK1B
SLC25A12
KIF23
SLC25A1
ARFRP1
CASK
ITPRID2
ITPR2
ARHGAP11A
WDR33
ARID1A
PHF3
AHCTF1
5% negative values
adj.p=0.05
−10log10 (p−value)
log2 Fold change


YFP_CLDN19b vs eGFP
ITFG1
CLDN19
UPK1B
HSPA5
MPZL1
PROM2
CEPT1
SLC25A13
TIMM29
LPGAT1
TMEM30A
SFXN3
EPCAM
CLDN3
SLC25A1
SLC44A1
OXA1L
VDAC3
TIMM17A
SPCS1
TOMM22
APOPT1
SLC38A10
TIMM21
NCSTN
SCARB1
UQCRC2
SFXN2
ERLIN1
UBAC2
NDUFA13
5% negative values
adj.p=0.05
−10log10 (p−value)
log2 Fold change


YFP_CLDN20 vs eGFP
CLDN20
GLT8D1
OXA1L
SFXN3
SPG7
PLPP6
SLC25A3
ABCD3
SLC25A6
SLC25A4
CHST11
SFXN4
TMEM126B
TMEM126A
SLC25A11
SLC25A25
TIMM29
DAAM1
MAIP1
FADS3
UBAC2
CHPT1
SLC25A19
LOC485767
RNF185
DERL2
5% negative values
adj.p=0.05
−10log10 (p−value)
log2 Fold change


YFP_CLDN22 vs eGFP
RDH14
ADAM17
GPAT3
SLC25A13
SFXN3
SLC25A1
CDIPT
SLC25A12
SLC2A1
GPX8
STOM
DGKE
OSBPL8
DAAM1
ABCB10
ABCD3
SEC11A
ABHD16A
ABCA8
ZFPL1
RPUSD3
SLC25A11
GAL3ST2
5% negative values
adj.p=0.05
−10log10 (p−value)
log2 Fold change


YFP_CLDN23 vs eGFP
UBE2G2
TVP23B
GPX8
TMEM161A
OSBPL8
RAB35
TM9SF3
GPAT4
GPRC5B
BAG5
OSBPL5
UBAC2
CMTM4
DGKE
NUP160
FADS3
CEPT1
CLDN23
PREB
STUB1
C15orf48
ERLIN2
SCCPDH
RNF5
ZDHHC6
SCO1
ABCD3
COA1
FURIN
CGRRF1
5% negative values
adj.p=0.05
−10log10 (p−value)
log2 Fold change

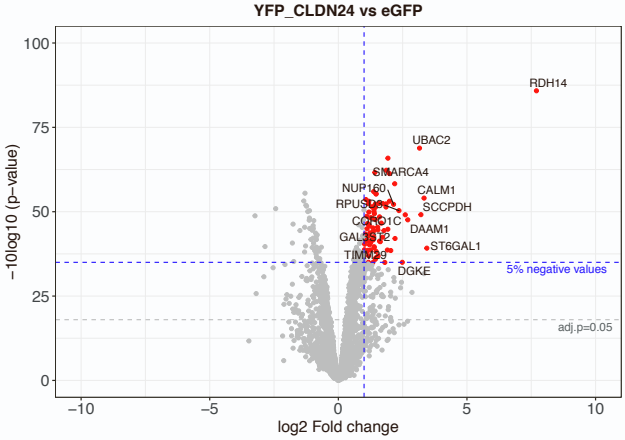
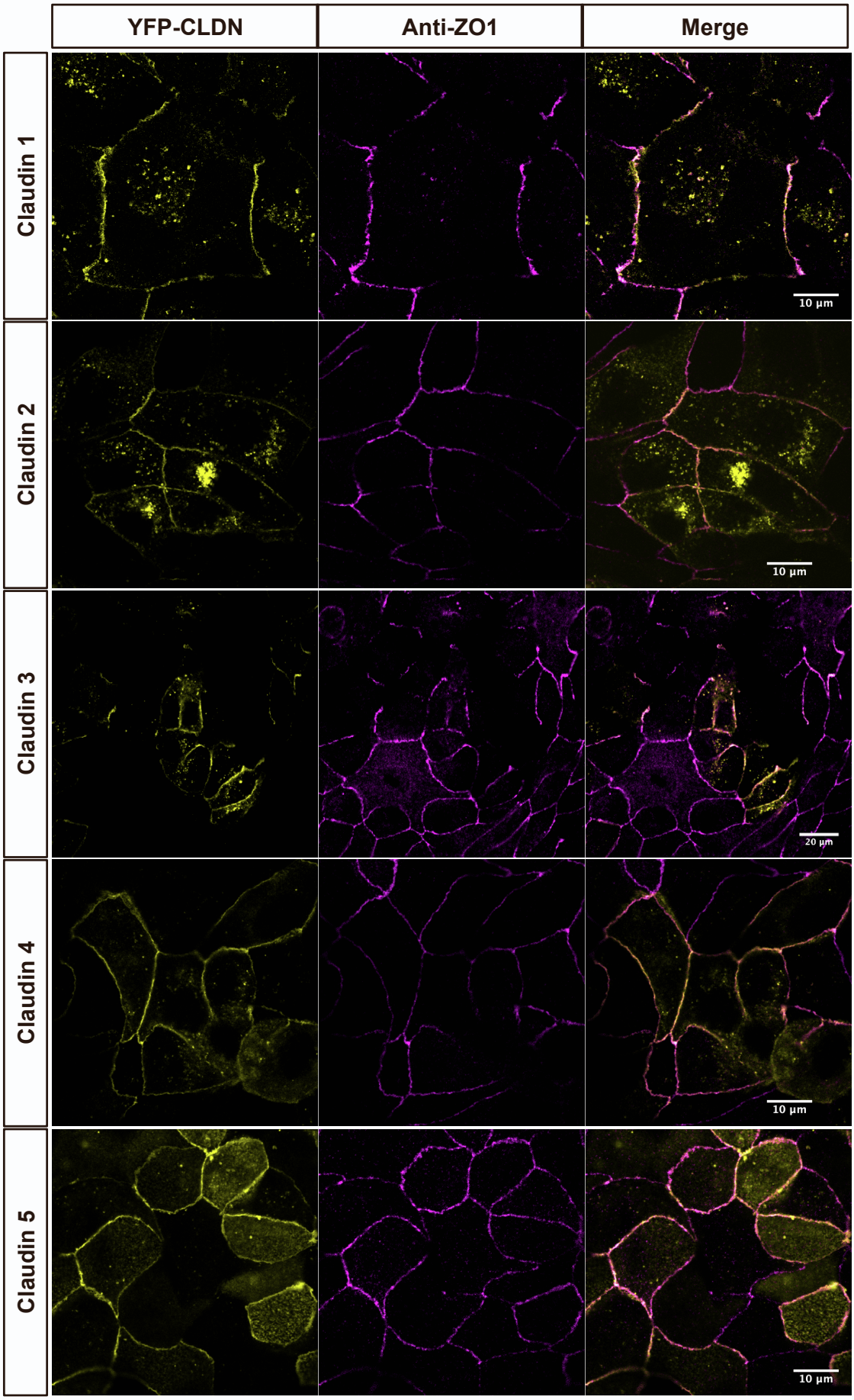
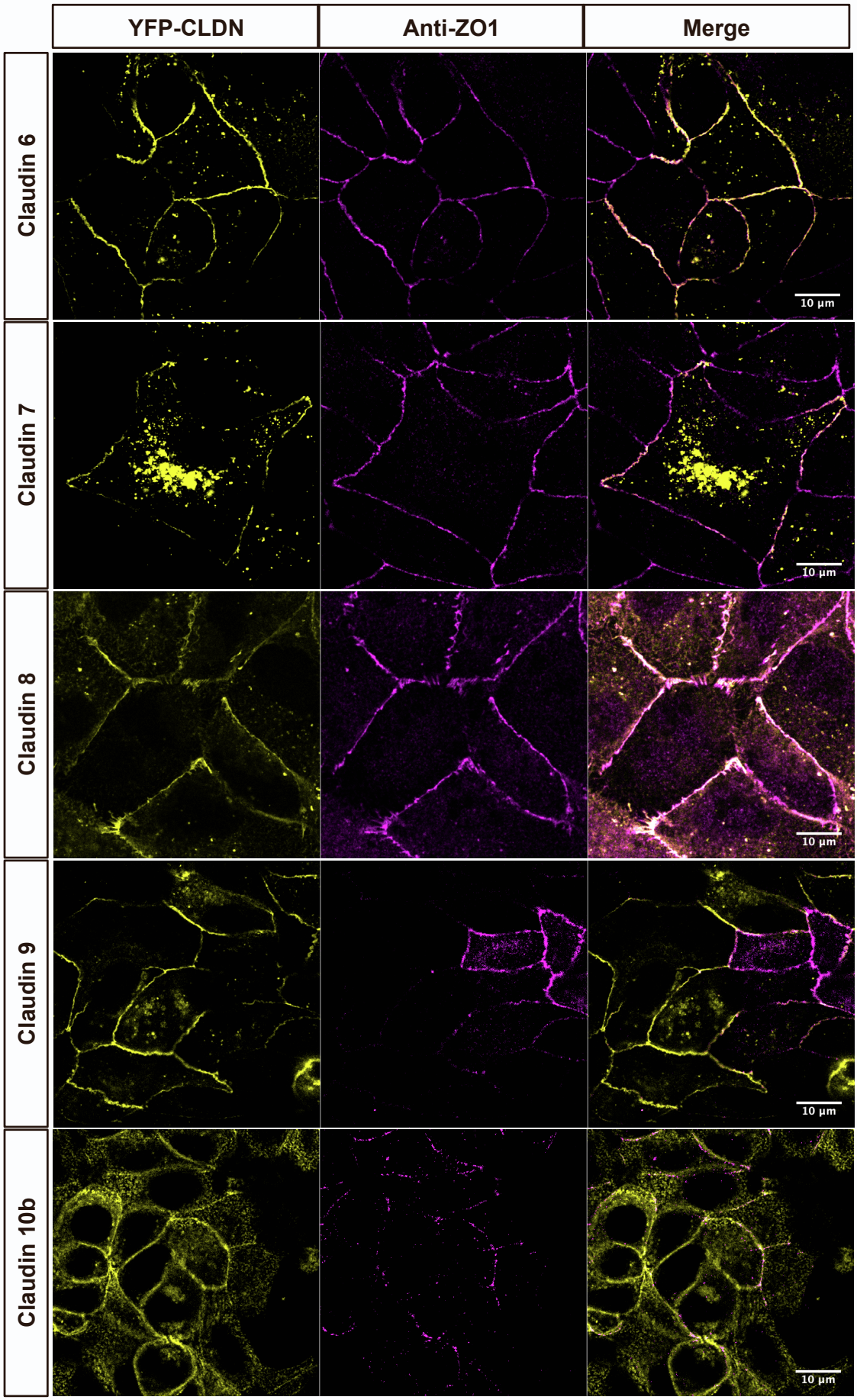
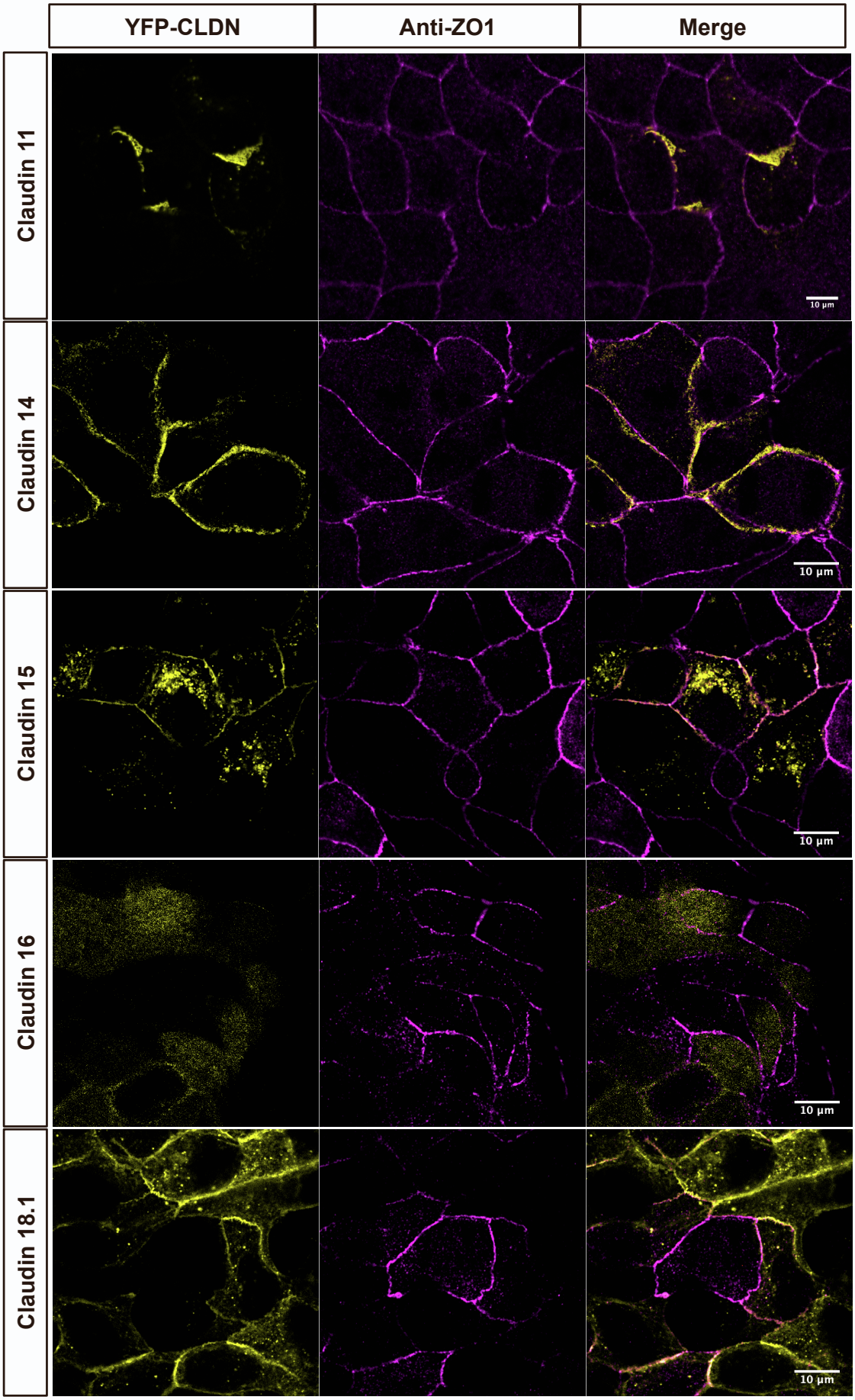
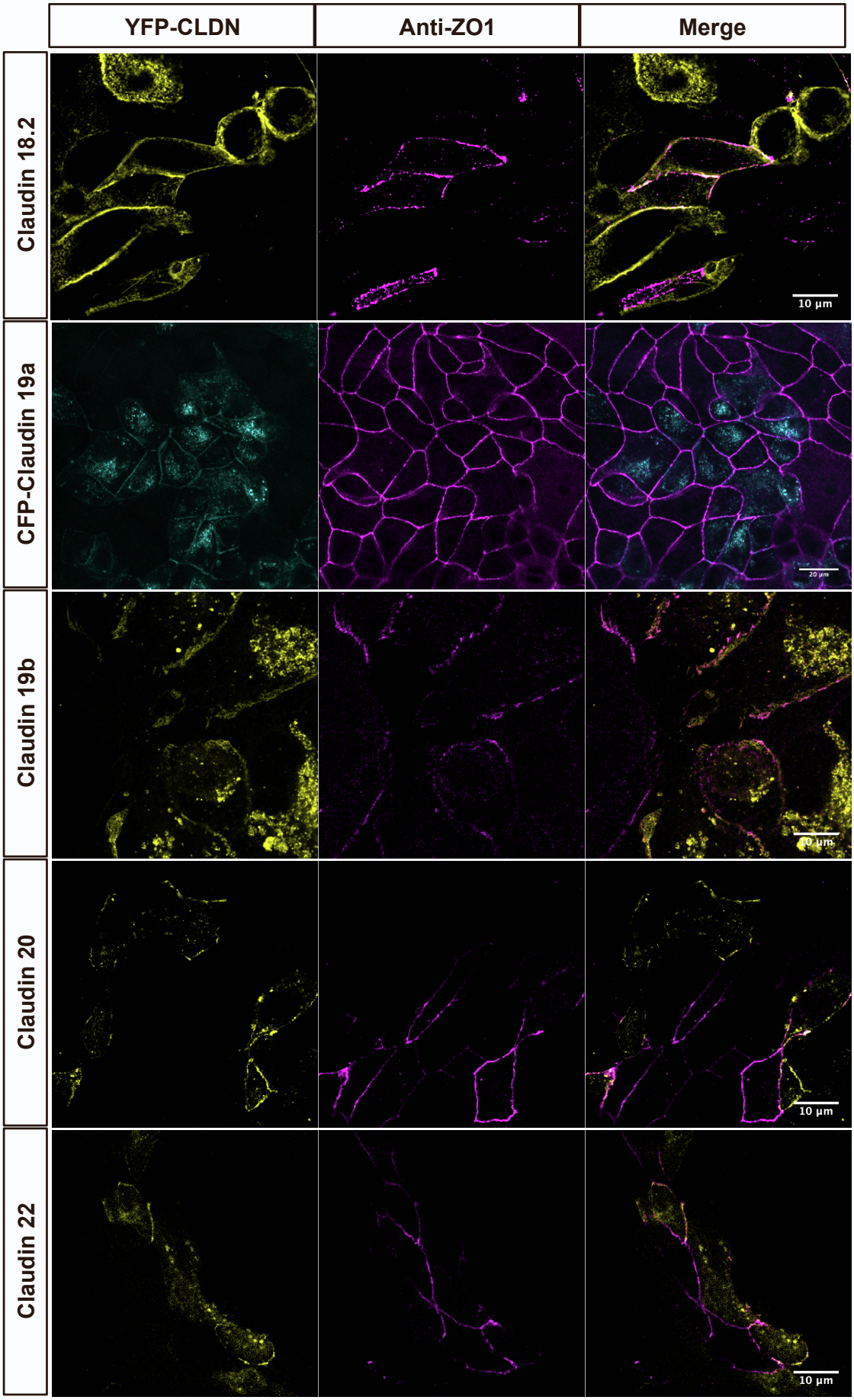

YFP_CLDN24 vs eGFP
RDH14
UBAC2
SMARCA4
NUP160
CALM1
RPUSD3
SCCPDH
CGRRF1
DAAM1
GAL3ST2
ST6GALNAC2
TIMM29
DGKE
5% negative values
adj.p=0.05
−10log10 (p−value)
log2 Fold change

Figure S2, related to Figure 2. Volcano plots showing the results from all CoIP experiments. LFQ intensity values of YFP/CFP-Claudin pull-downs were compared against the GFP control using moderated t-test. First significance level adj-pval<0.05 (grey line), 2nd level cutoff of adj-pval that leaves only 5% of the interactions identified in the GFP control (blue line).


YFP-CLDN
Anti-ZO1
Merge
Claudin 1
Claudin 2
Claudin 3
Claudin 4
Claudin 5
10 µm
10 µm
20 µm
10 µm
10 µm


YFP-CLDN
Anti-ZO1
Merge
Claudin 6
Claudin 7
Claudin 8
Claudin 9
Claudin 10b
10 µm
10 µm
10 µm
10 µm
10 µm


YFP-CLDN
Anti-ZO1
Merge
Claudin 11
Claudin 14
Claudin 15
Claudin 16
Claudin 18.1
10 µm


YFP-CLDN
Anti-ZO1
Merge
Claudin 18.2
CFP-Claudin 19a
Claudin 19b
Claudin 20
Claudin 22
10 µm
20 µm
10 µm
10 µm
10 µm

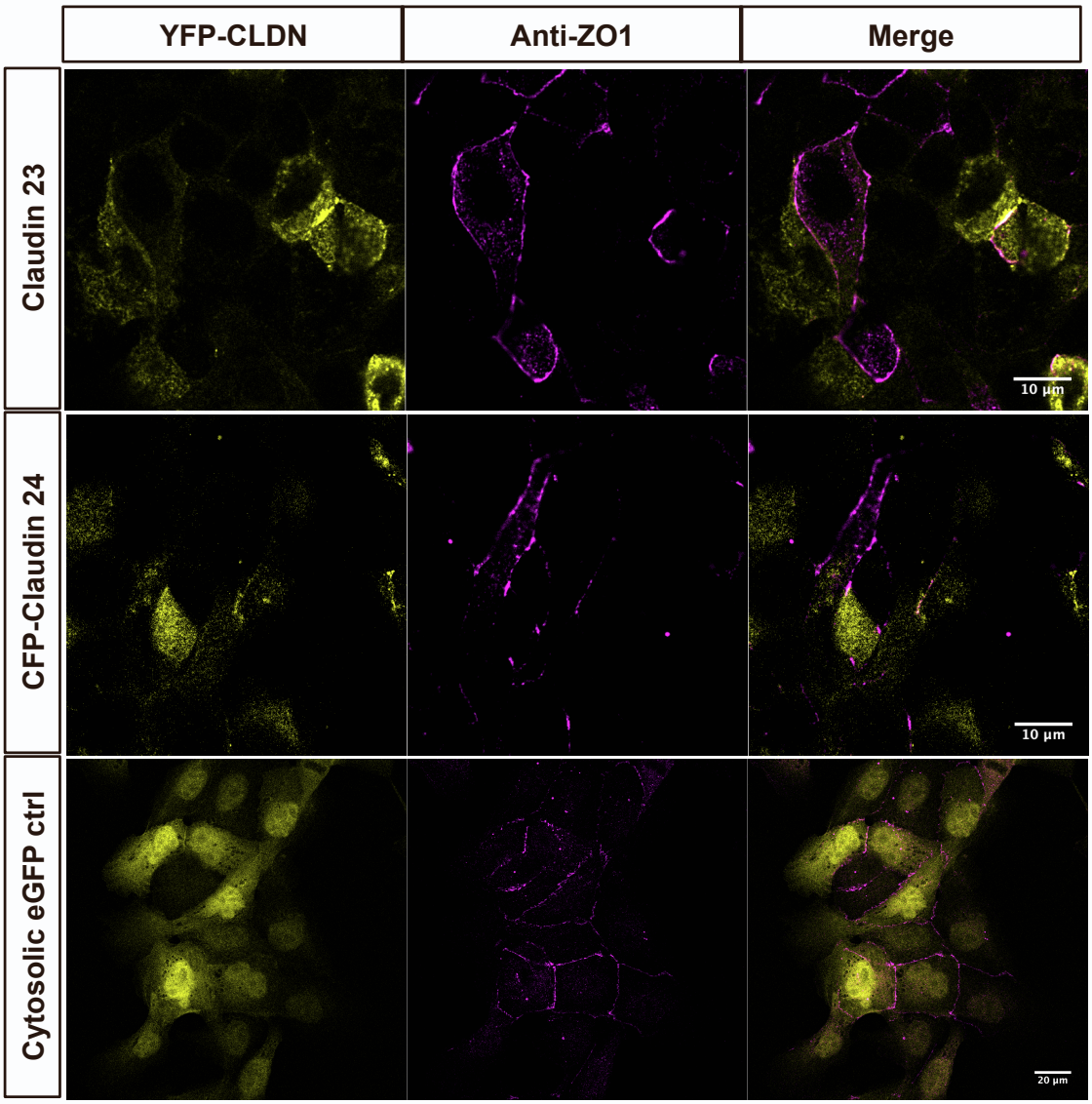


Figure S3, related to Figure 2. Confocal microscopy images of MDCK-C7 stable cell lines overexpressing recombinant YFP-/CFP- claudins. Anti-ZO-1 (61-7300 Invitrogen) and Alexa Fluor® 647 were used for tight junction staining.

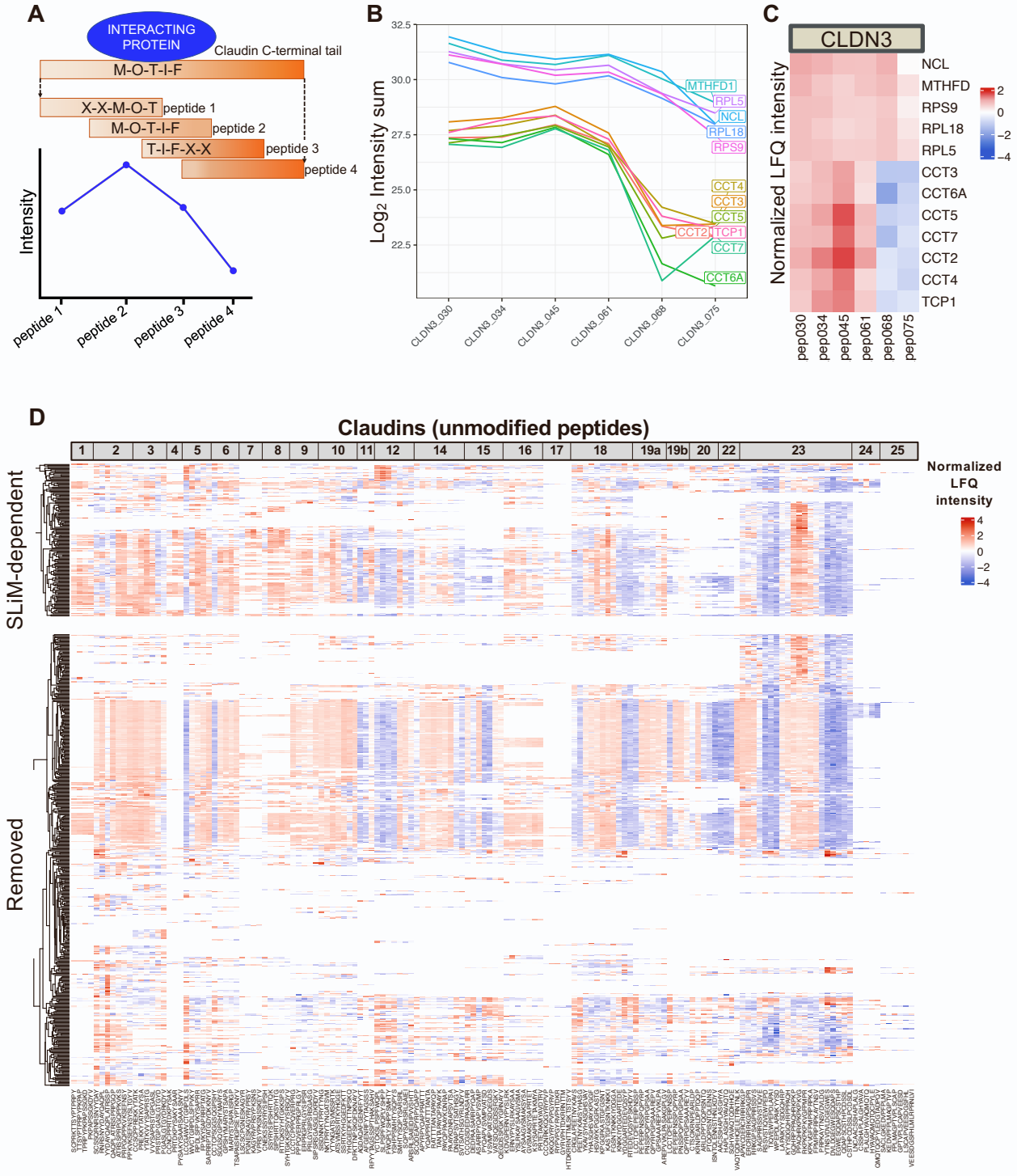


Figure S4, related to Figure 3. Filtering strategy for SLiM-dependent interactors identified by PRISMA. **A.** Schematic representation of the SLiM-based intensity profile pattern used to filter significant PRISMA interactions. **B, C.** Example of the intensity profile of filtered (highly abundant unspecific proteins) and SLiM-dependent (CCT/TriC subunits) significant claudin interactors. **D.** Heatmap showing all the significant interactors identified by PRISMA with the SLiM-dependent interactors on top (based on their intensity profile) and the interactions that were removed after the filtering process.

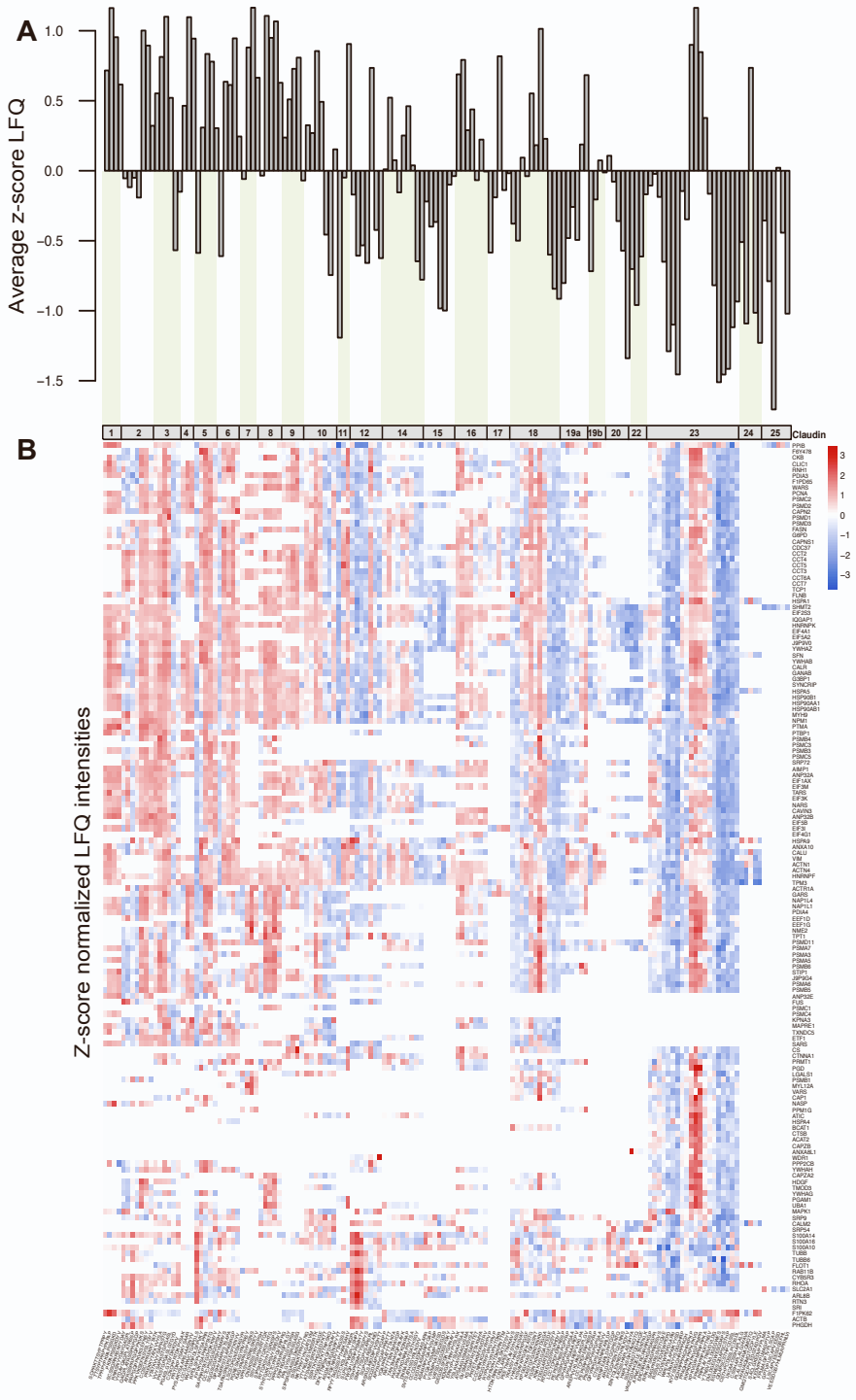


Figure S5, related to Figure 3. Interacting partners of the unstructured C-termini of claudins identified by PRISMA. A. Bar plot corresponding to the normalized intensities of the significant interactions (p-value<0.05 and intensity binding profile) identified per peptide spot. **B.** Heatmap showing the interaction patterns of the significant proteins identified interacting with unmodified peptides derived from the C-terminal region of human claudins.

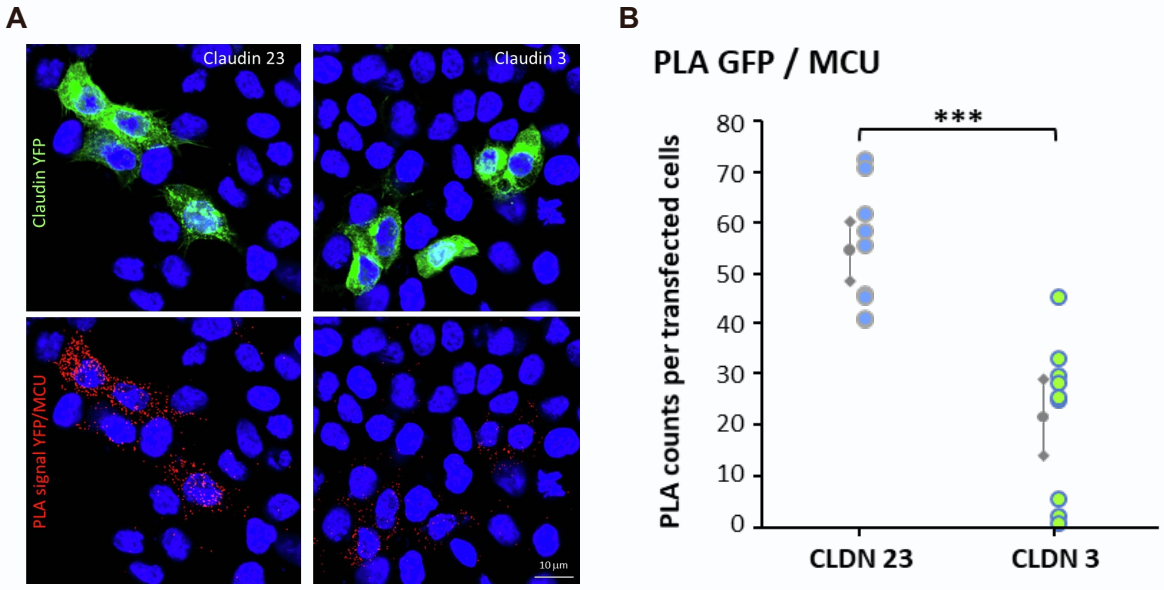


Figure S6, related to Figure 4. Proximity ligation assay confirms interaction between claudin-23 and the mitochondrial protein MCU. A. Immunofluorescence images of PLA between MCU and claudin-23 or claudin-3. Caco2 cells were transiently transfected with YFP-tagged claudin-23 or claudin-3. MCU mitochondrial protein interacts with claudin-23 but not with claudin-3. **B.** Dot plot representing the number of PLA signals per transfected cell. Statistically significant results ($P<0.05$) confirm those of the YFP-tagged claudin-23 CoIP .