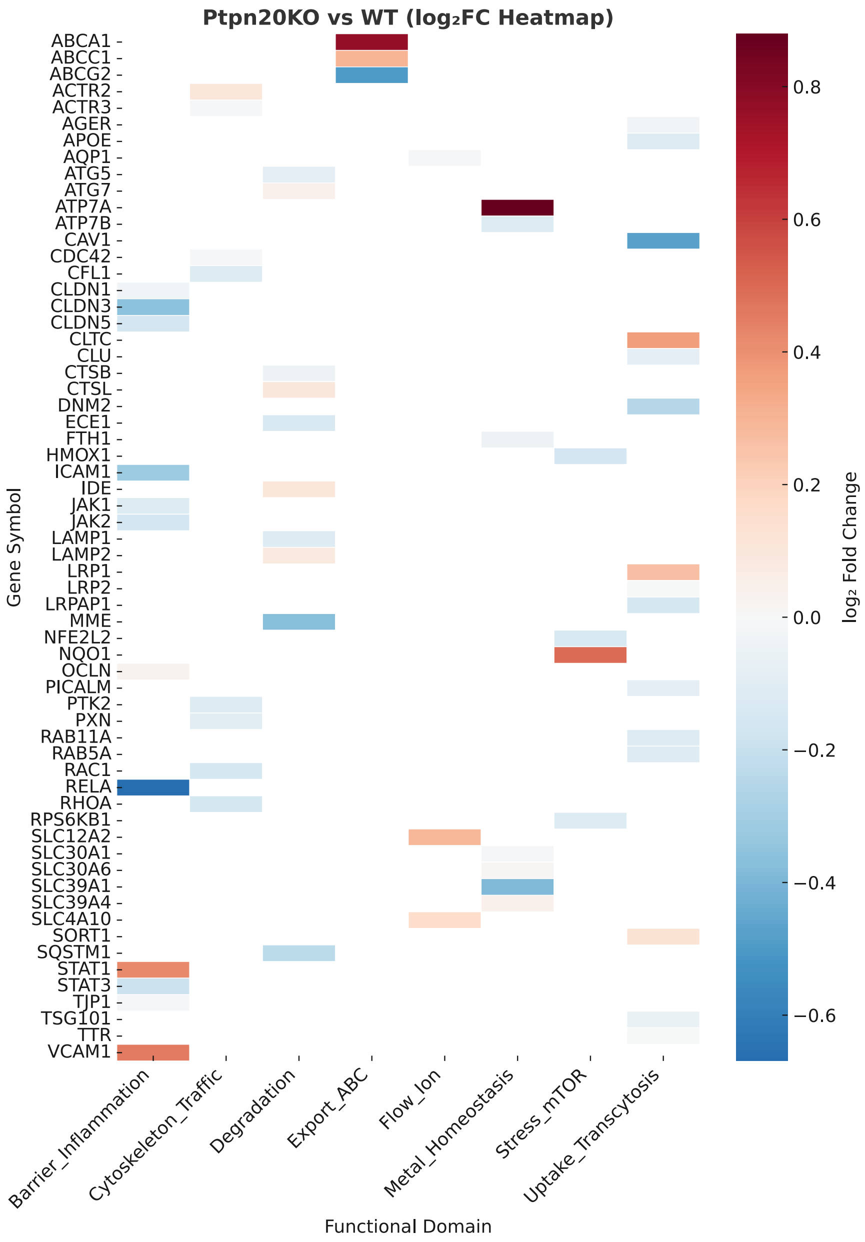
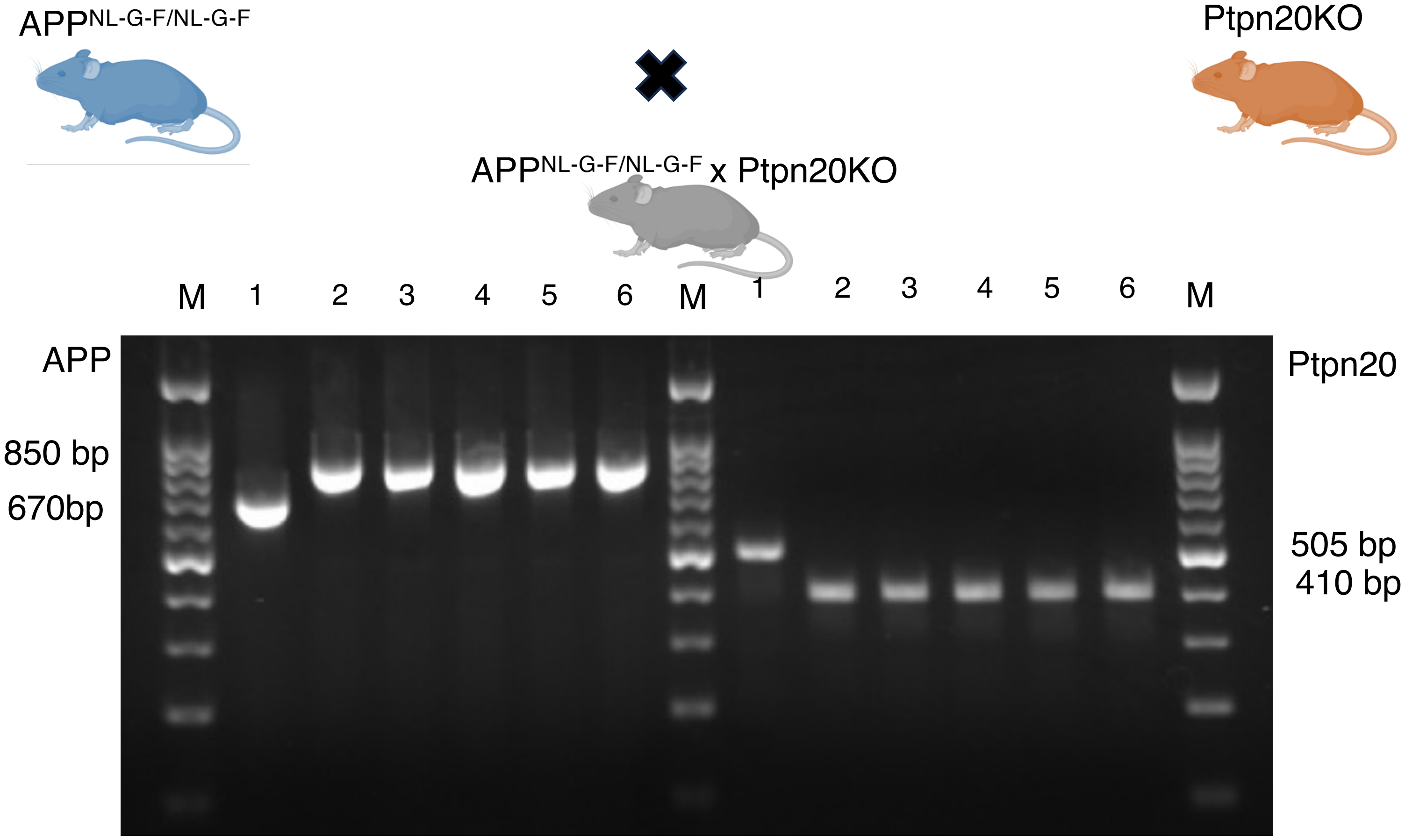
Fig.S1



The horizontal axis represents functional domains, and the vertical axis represents gene symbols. Red indicates genes upregulated in Ptpn20KO compared with WT, whereas blue indicates downregulated genes

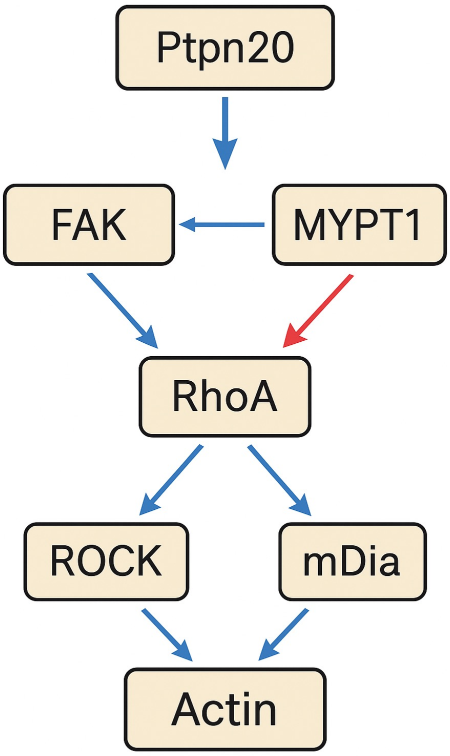
Domain	SYMBOL	$\log_2$FC	Direction
Uptake_Transcytosis	CAV1	-0.4750849	Down
Uptake_Transcytosis	DNM2	-0.2509616	Down
Uptake_Transcytosis	LRPAP1	-0.1505597	Down
Uptake_Transcytosis	APOE	-0.1243281	Down
Uptake_Transcytosis	RAB11A	-0.1243281	Down
Uptake_Transcytosis	RAB5A	-0.1110313	Down
Uptake_Transcytosis	PICALM	-0.0840643	Down
Uptake_Transcytosis	CLU	-0.0840643	Down
Uptake_Transcytosis	TSG101	-0.0565835	Down
Uptake_Transcytosis	AGER	-0.0285692	Down
Uptake_Transcytosis	LRP2	0	NA
Uptake_Transcytosis	TTR	0	NA
Uptake_Transcytosis	SORT1	0.12432814	Up
Uptake_Transcytosis	LRP1	0.26303441	Up
Uptake_Transcytosis	CLTC	0.36737107	Up
Export_ABC	ABCG2	-0.4956952	Down
Export_ABC	ABCC1	0.29865832	Up
Export_ABC	ABCA1	0.77399633	Up
Degradation	MME	-0.3673711	Down
Degradation	SQSTM1	-0.2387869	Down
Degradation	ECE1	-0.1375035	Down
Degradation	LAMP1	-0.1110313	Down
Degradation	ATG5	-0.0840643	Down
Degradation	CTSB	-0.0426443	Down
Degradation	ATG7	0.04264434	Up
Degradation	LAMP2	0.08406426	Up
Degradation	CTSL	0.0976108	Up
Degradation	IDE	0.11103131	Up
Flow_Ion	AQP1	-0.0143553	Down
Flow_Ion	SLC4A10	0.16349873	Up
Flow_Ion	SLC12A2	0.28688115	Up
Barrier_Inflammation	RELA	-0.6690268	Down
Barrier_Inflammation	CLDN3	-0.3561438	Down
Barrier_Inflammation	ICAM1	-0.3219281	Down
Barrier_Inflammation	STAT3	-0.1890338	Down
Barrier_Inflammation	CLDN5	-0.1634987	Down
Barrier_Inflammation	JAK2	-0.1634987	Down
Barrier_Inflammation	JAK1	-0.1243281	Down
Barrier_Inflammation	CLDN1	-0.0285692	Down
Barrier_Inflammation	TJP1	-0.0143553	Down
Barrier_Inflammation	OCLN	0.02856915	Up
Barrier_Inflammation	STAT1	0.422233	Up
Barrier_Inflammation	VCAM1	0.45417589	Up
Metal_Homeostasis	SLC39A1	-0.3895668	Down
Metal_Homeostasis	ATP7B	-0.1243281	Down
Metal_Homeostasis	FTH1	-0.0426443	Down
Metal_Homeostasis	SLC30A1	-0.0143553	Down
Metal_Homeostasis	SLC30A6	0.01435529	Up
Metal_Homeostasis	SLC39A4	0.04264434	Up
Metal_Homeostasis	ATP7A	0.87970577	Up
Stress_mTOR	HMOX1	-0.1634987	Down
Stress_mTOR	NFE2L2	-0.1375035	Down
Stress_mTOR	RPS6KB1	-0.1243281	Down
Stress_mTOR	NQO1	0.49569516	Up
Cytoskeleton_Traffic	RAC1	-0.1505597	Down
Cytoskeleton_Traffic	RHOA	-0.1505597	Down
Cytoskeleton_Traffic	CFL1	-0.1243281	Down
Cytoskeleton_Traffic	PTK2	-0.1110313	Down
Cytoskeleton_Traffic	PXN	-0.0976108	Down
Cytoskeleton_Traffic	CDC42	-0.0143553	Down
Cytoskeleton_Traffic	ACTR3	-0.0143553	Down
Cytoskeleton_Traffic	ACTR2	0.11103131	Up

Fig.S2



Mouse No.1 shows an APP band at 670 bp and a Ptpn20 band at 505 bp, corresponding to the WT genotype. Mice No.2–6 show an APP band at 850 bp and a Ptpn20 band at 410 bp, indicating successful generation of APPKI × Ptpn20KO double mutants. “M” denotes the molecular size marker.

Fig.S3

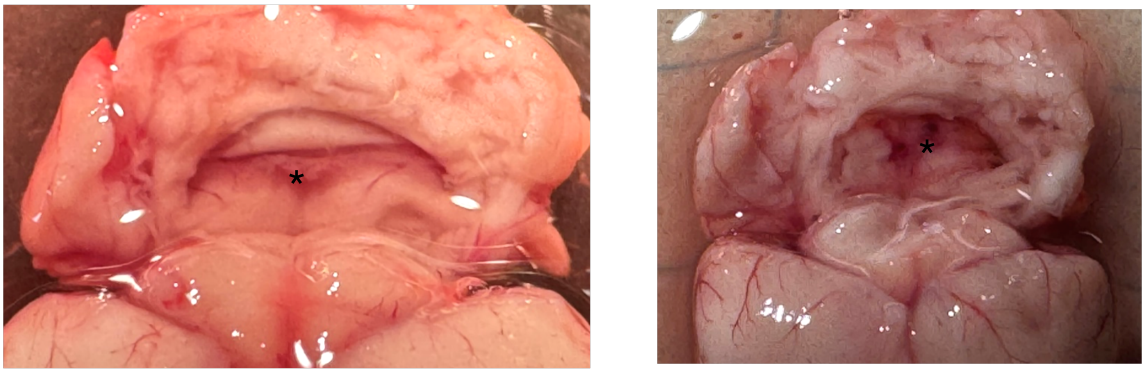


The schematic illustrates a proposed signaling framework linking Ptpn20 to RhoA-dependent regulation of the actin cytoskeleton. Ptpn20 is depicted as potentially interfacing with focal adhesion kinase (FAK) and myosin phosphatase target subunit 1 (MYPT1), both known modulators of RhoA activity. Blue arrows indicate putative positive or permissive regulatory interactions, whereas the red arrow denotes a potential inhibitory influence of MYPT1 on RhoA. RhoA activation feeds into two major downstream effectors—ROCK and mDia—which together regulate actin polymerization, filament stability, and cytoskeletal organization. This diagram summarizes hypothesized relationships based on observed phenotypes in Ptpn20-deficient choroid plexus tissue, while acknowledging that the direct biochemical substrates of Ptpn20 remain to be identified.

Fig.S4

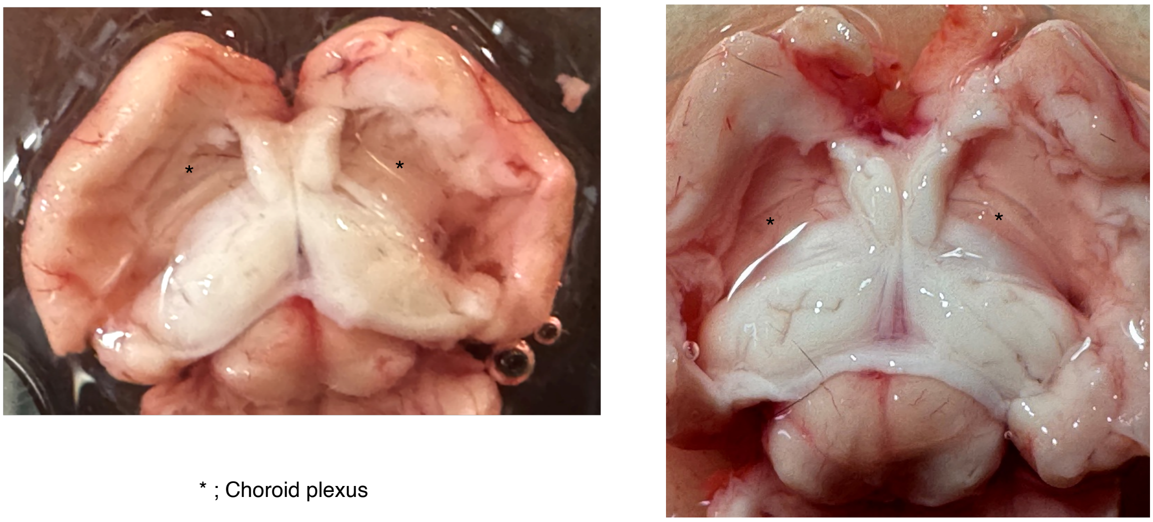
4th ventricle

WT Ptpn20KO



Lateral ventricle

WT Ptpn20KO



* ; Choroid plexus