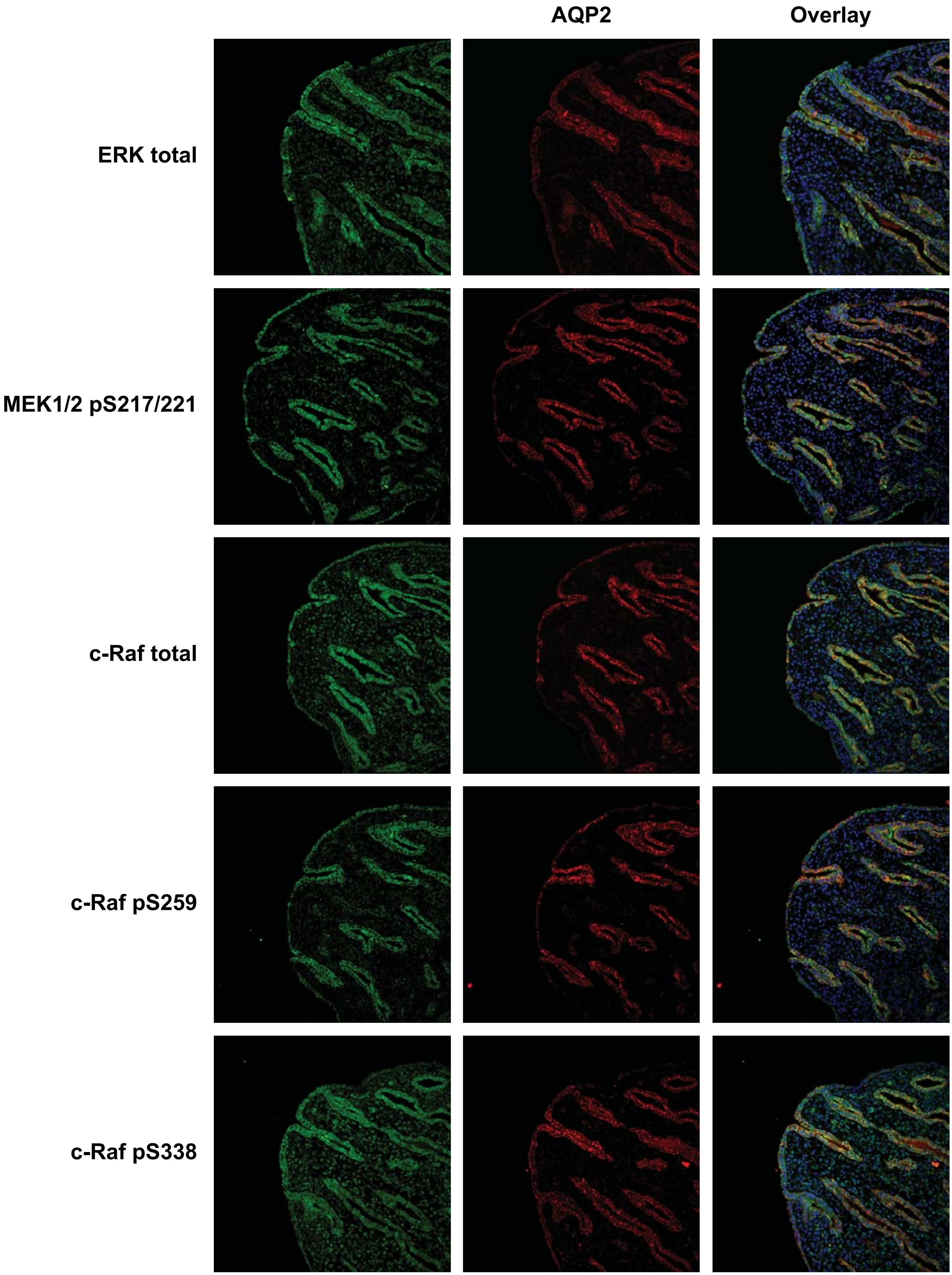
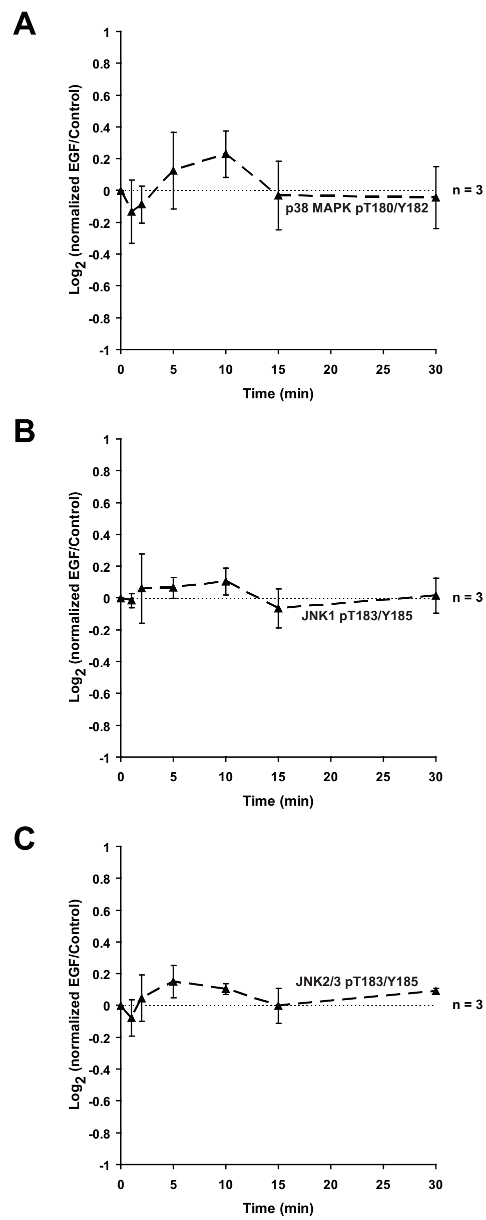
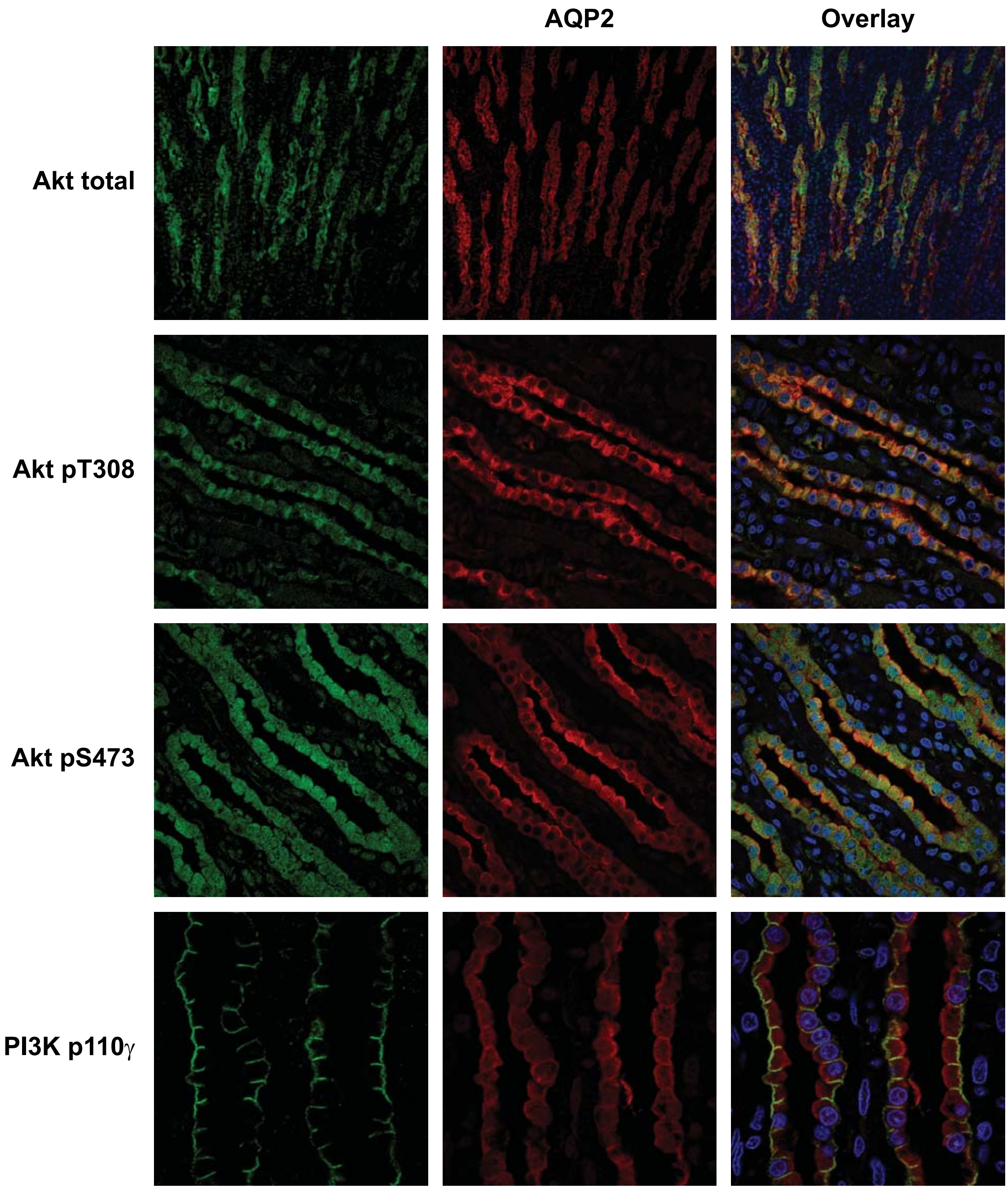
Supplementary Figure 1. Immunofluorescence staining on rat inner medullas using antibodies against the ERK1/2 MAP kinase pathway components and AQP2. See a list of antibodies used in Supplementary Table 1.



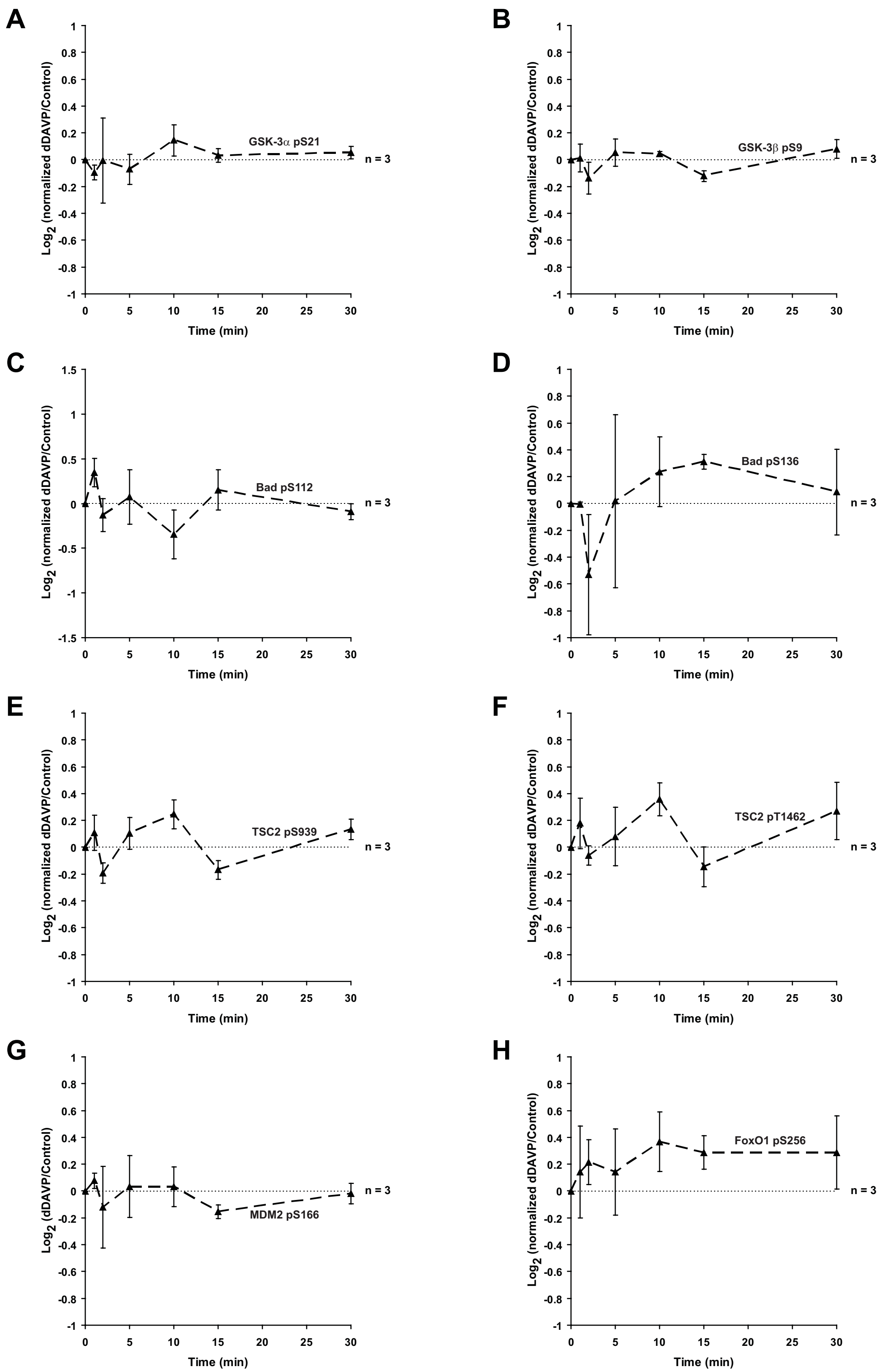
Supplementary Figure 2. EGF effects on p38 MAPK and JNK activation.
0.1 μM EGF did not alter p38 MAPK phosphorylation at T180 and Y182 **(A)**,
JNK1 phosphorylation at T183 and Y185 **(B)**, or JNK2/3 phosphorylation at T183 and Y185 **(C)**.



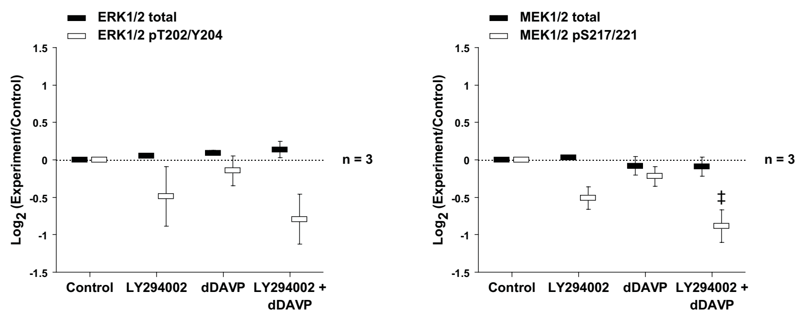
Supplementary Figure 3. Immunofluorescence staining on rat inner medullas using antibodies against Akt, PI3K p110γ, and AQP2. See a list of antibodies used in Supplementary Table 1.



Supplementary Figure 4. dDAVP effects on known Akt substrates.
1 nM dDAVP did not alter GSK-3α phosphorylation at S21 **(A)**, GSK-3β phosphorylation at S9 **(B)**, Bad phosphorylation at S112 **(C)** and S136 **(D)**, TSC2 phosphorylation at S939 **(E)** and T1462 **(F)**, MDM2 phosphorylation at S166 **(G)**, and FoxO1 phosphorylation at S256 **(H)**.



Supplementary Figure 5. Effects of PI3K inhibition on ERK1/2 and MEK1/2 phosphorylation.
IMCD suspensions were preincubated for 25 min in the absence or presence of 25 μM LY294002 and then incubated with vehicle or 1 nM dDAVP for 5 min. ‡ = statistically significant versus dDAVP alone.



Supplementary Table 1. A list of the antibodies used in the present study.

Antibody	Catalog #	Species	Type	Source
AQP2 total	LL265	Chicken	Polyclonal	Our laboratory (1)
AQP2 pS256	AN244	Rabbit	Polyclonal	A gift from Søren Nielsen (3)
AQP2 pS261	5231	Rabbit	Polyclonal	Our laboratory (2)
Akt total	9272	Rabbit	Polyclonal	Cell Signaling Technology, Inc., Danvers, MA
Akt total (IF)	4685	Rabbit	Monoclonal	
Akt pT308	9275	Rabbit	Polyclonal	
Akt pT308 (IF)	9266	Rabbit	Monoclonal	
Akt pS473	9271	Rabbit	Polyclonal	
Akt pS473 (IF)	3787	Rabbit	Monoclonal	
Phospho-(Ser/Thr) Akt Substrate	9614	Rabbit	Monoclonal	
ERK1/2 total	9102	Rabbit	Polyclonal	
ERK1/2 pT202/Y204	9106	Mouse	Monoclonal	
MEK1/2 total	4694	Mouse	Monoclonal	
MEK1/2 pS217/221	9121	Rabbit	Polyclonal	
c-Raf total	9422	Rabbit	Polyclonal	
c-Raf pS259	9421	Rabbit	Polyclonal	
c-Raf pS338	9427	Rabbit	Monoclonal	
p38 MAPK total	9228	Mouse	Monoclonal	
p38 MAPK pT180/Y182	9216	Mouse	Monoclonal	
JNK total	9258	Rabbit	Monoclonal	
JNK pT183/Y185	9255	Mouse	Monoclonal	
GSK-3α total	9338	Rabbit	Polyclonal	
GSK-3α pS21	9331	Rabbit	Polyclonal	
GSK-3β total	9315	Rabbit	Monoclonal	
GSK-3β pS9	9331	Rabbit	Polyclonal	
Bad total	9292	Rabbit	Polyclonal	
Bad pS112	9291	Rabbit	Polyclonal	
Bad pS136	9295	Rabbit	Polyclonal	
TSC2 total	3635	Rabbit	Monoclonal	
TSC2 pS939	3615	Rabbit	Polyclonal	
TSC2 pT1462	3617	Rabbit	Monoclonal	
MDM2 pS166	3521	Rabbit	Polyclonal	
FoxO1 total	9462	Rabbit	Polyclonal	
FoxO1 pS256	9461	Rabbit	Polyclonal	
PI3K p110γ	4252	Rabbit	Polyclonal	

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Supplementary Table 2. A list of the interactions between parent nodes and child nodes in the network diagram of vasopressin signaling in the IMCD (Figure 16).

Parent node	Interaction	Child node	Reference
AVP	directly activates	AVPR2	(2)
AVPR2	indirectly activates	RYR1	(9)
AVPR2	directly activates	ARRB1	(25)
AVPR2	directly activates	GNAS	(17)
AVPR2	directly activates	Gβ/Gγ	(17)
RYR1	directly releases	Ca++	(32)
ARRB1	hypothetically activates	PI3K	Present study, (24)
GNAS	directly activates	ADCY3	(26)
GNAS	directly activates	ADCY6	(26)
GNAS	hypothetically activates	PI3K	Present study
Gβ/Gγ	hypothetically activates	PI3K	Present study, (27)
Ca++	directly activates	RYR1	(32)
Ca++	directly activates	CALM	(31)
Ca++	directly inhibits	ADCY6	(4)
Ca++	hypothetically activates	PI3K	Present study, (29)
ADCY3	directly catalyzes the formation of	cAMP	(28)
ADCY6	directly catalyzes the formation of	cAMP	(28)
CALM	directly activates	MYLK	(8)
CALM	directly activates	PDE1	(6)
CALM	directly activates	ADCY3	(14)
CALM	hypothetically activates	PI3K	Present study
cAMP	directly inhibits	PRKAR	(13)
cAMP	directly activates	RAPGEF3	(10)
cAMP	hypothetically activates	PDK2	Present study, (18)
MYLK	directly activates	MRLCB	(23)
PDE1	directly degrades	cAMP	(3)
PDE4	directly degrades	cAMP	(3)
PRKAR	directly inhibits	PRKAC	(13)
PRKAC	directly activates	AQP2	(16)
PRKAC	directly inhibits	c-Raf	Present study, (11)
RAPGEF3	directly activates	RAP1	(10)
RAP1	hypothetically activates	B-Raf	(20)
RAP1	hypothetically inhibits	c-Raf	(21)
MRLCB	directly activates	MYH9	(30)
MRLCB	directly activates	MYH10	(30)
MYH9	indirectly activates the trafficking of	AQP2	(8)
MYH10	indirectly activates the trafficking of	AQP2	(8)
c-Raf	directly activates	MEK1/2	(7)
B-Raf	hypothetically activates	MEK1/2	(7)
MEK1/2	directly activates	ERK1/2	(19)

PI3K	directly activates	PDK1	(1)
PI3K	directly activates	PDK2	(5)
PDK1	directly activates	AKT	(1)
PDK2	directly activates	AKT	(5)
Hyperosmolality	indirectly activates	PI3K	Present study, (15)
Hyperosmolality	indirectly activates	p38 MAPK	Present study, (22)
AQP2	directly activates	Water transport	(12)

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