Supporting Information

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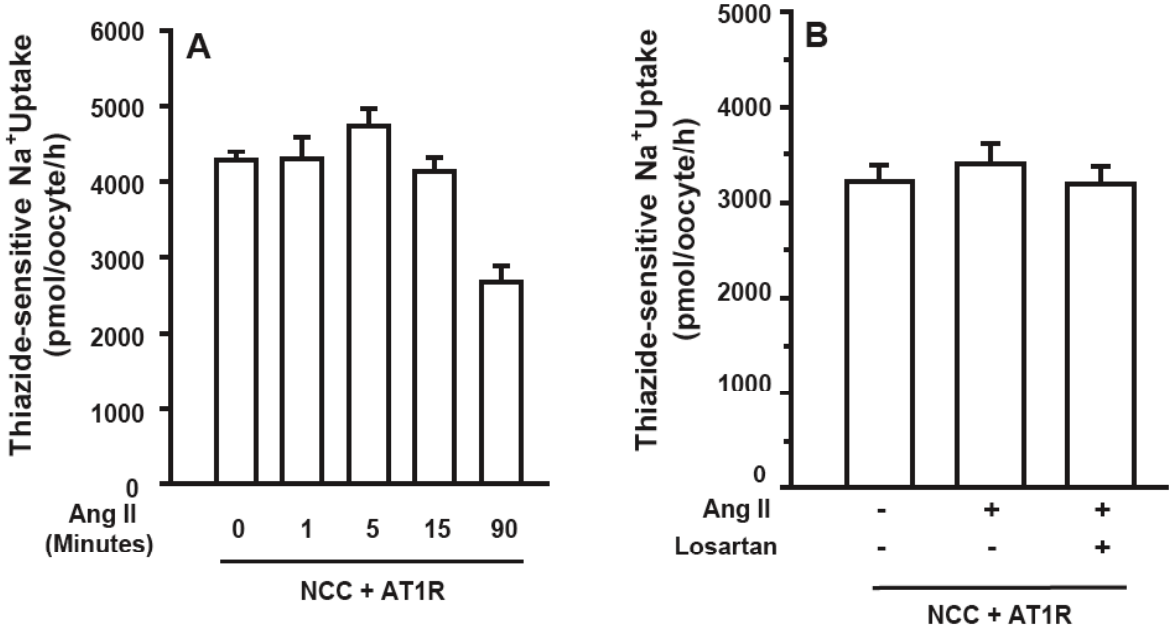

Fig. S1. Absence of effect of AngII signaling without WNK4. NCC and AT1R were expressed in *Xenopus* oocytes and thiazide-sensitive Na^+ uptake was measured as described in *Methods*. (*A*) In the absence of WNK4, addition of AT1R, with or without AngII, had no significant effect on NCC activity. (*B*) Losartan + AngII have no effect on NCC activity in the absence of WNK4.

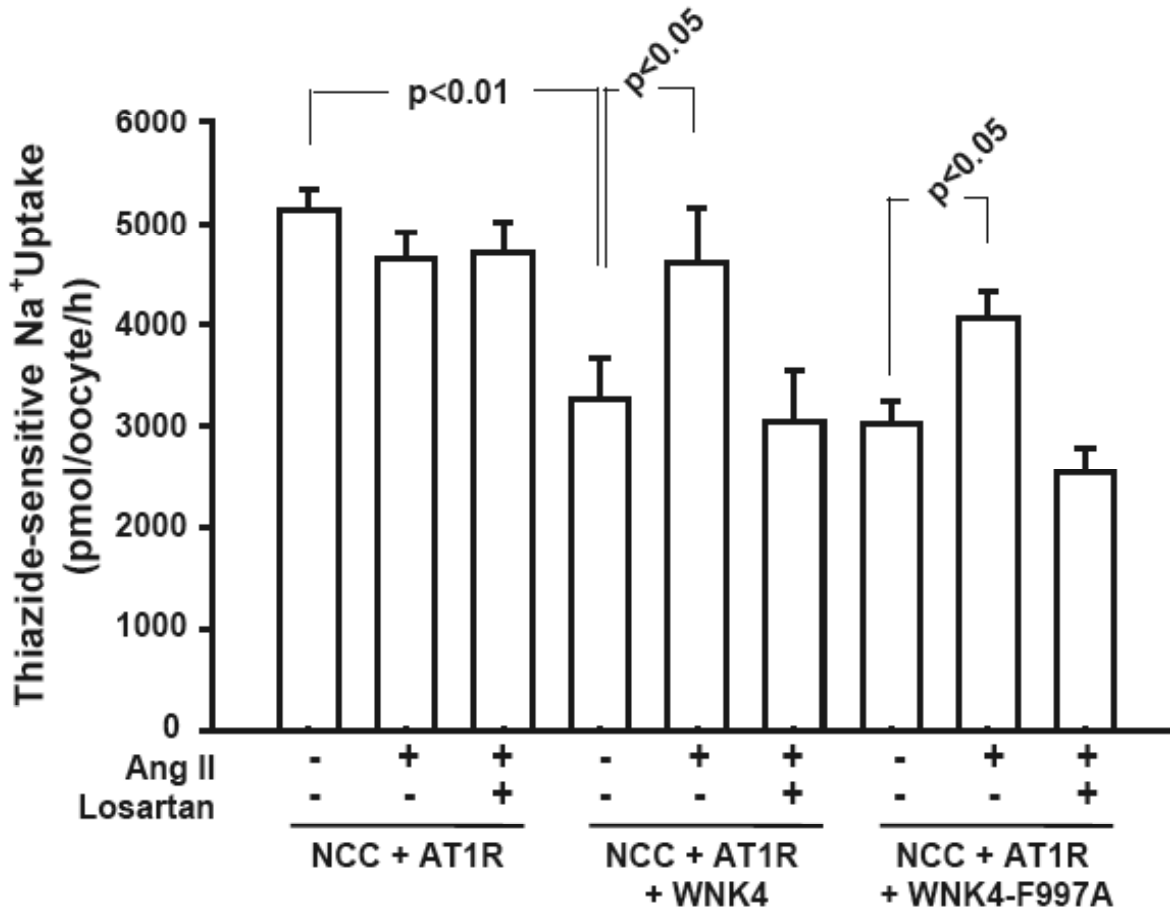

Fig. S2. Disruption of the SPAK binding site in WNK4 has no effect on WNK4's inhibition of NCC or its response to AngII. The SPAK binding site in WNK4 was disrupted by the F997A mutation, and indicated constructs were expressed in *Xenopus* oocytes and thiazide-sensitive Na^+ uptake was measured as described in *Methods*. Like WT WNK4, WNK4-F997A inhibits NCC activity in the absence of AngII signaling; this inhibition is alleviated by AngII signaling, and the effect of AngII is prevented by the AT1R inhibitor losartan.