8 Abstract

The hormon AVP regulates the water reabsorption in renal collecting duct principal cells. The binding of AVP to the V2R elevates cAMP levels, resulting in activation of the PKA. PKA phosphorylates AQP2, thereby inducing its translocation from intracellular vesicles into the apical membrane, facilitating water reabsorption. Not only the phosphorylation of AQP2 by PKA but also the tethering of PKA to subcellular compartments by AKAPs is a prerequisite for the AQP2-translocation. During the search for AKAPs involved in the AQP2-translocation, a new splice variant of AKAP18, AKAP18δ, was identified. AKAP18δ is expressed in IMCD cells. This was shown by Western blot analyses and by immunoprecipitation with the A18δ3. The *in vitro* AKAP function was shown in an RII overlay experiment. The *in vivo* AKAP function was shown by co-precipitation of AKAP18δ with the RII subunits via cAMP agarose pull down and by FRET experiments in living cells. In FRET experiments it was also possible to show the inhibitory effect of the peptide S-Ht31 for the AKAP18δ-CFP-RIIα-YFP interaction. The introduction of a prolin in to the RII binding site of AKAP18δ-CFP lead to a decrease in FRET ratio, thereby mapping the RII binding site *in vivo*.

Several results lead to the hypothesis that AKAP18δ is involved in the AVP-induced AQP2-translocation. Both, AQP2 and AKAP18δ, are in the kidney mainly expressed in the inner medulla an in the IMCD cells mainly in the HS fraction. In cAMP-agarose precipitates from AVP-stimulated IMCD cells the amount of AKAP18δ was lower than obtained from unstimulated cells. This result indicates the involvement of AKAP18δ in the AVP-induced signal pathway. The data provide evidence for an involvement of AKAP18δ in the AVP-induced AQP2-translocation by anchoring PKA in close proximity to its substrate AQP2.