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Increased AQP2 Targeting in Primary Cultured IMCD Cells in Response to Angiotensin II through AT1 Receptor

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Vasopressin and angiotensin II (AngII) play a major role in the renal water and sodium reabsorption. We demonstrated that AngII AT1 receptor blockade decreases dDAVP-induced water reabsorption and AQP2 levels in rats, suggesting cross-talk between these two peptide hormones (Am J Physiol Renal Physiol, 2005). To directly address this, primary cultured IMCD cells from male Sprague-Dawley rats were treated with 1) vehicle, 2) AngII, 3) AngII+AT1 receptor blocker (candesartan), 4) dDAVP, 5) AngII+dDAVP, or 6) AngII+dDAVP+candesartan for 15 min with two different concentrations of AngII and dDAVP (protocol 1 and 2). Immunofluorescence microscopy revealed that AngII 10^{-8}M or dDAVP 10^{-11}M treatment for 15 min (protocol 1) was associated with increased AQP2 labeling of the plasma membrane and decreased cytoplasmic labeling, respectively. cAMP level was significantly increased in response to AngII 10^{-8}M treatment and it was potentiated by co-treatment of dDAVP 10^{-11}M+AngII 10^{-8}M. Consistent with this, immunoblotting revealed that p-AQP2 (AQP2 phosphorylated in the PKA-phosphorylation consensus site Ser-256) expression was significantly increased by the co-treatment. The AngII-induced AQP2 targeting was blocked by candesartan (10^{-5}M) co-treatment. In protocol 2, treatment with lower concentration of dDAVP (10^{-12}M) or AngII (10^{-9}M) for 15 min was associated with unchanged subcellular AQP2 redistribution, whereas co-treatment of dDAVP (10^{-12}M)+AngII (10^{-9}M) caused AQP2 targeting to the plasma membrane. The synergetic effect was blunted by candesartan (10^{-5}M) co treatment. In addition, AQP2-transfected MDCK cells exhibited an increased AQP2 targeting in response to either dDAVP (10^{-8}M) or AngII (10^{-7}M) treatment for 15 min. The AngII (10^{-8}M)-induced cAMP accumulation and AQP2 targeting to the plasma membrane of the primary cultured IMCD cells were inhibited by the co-treatment of PKC inhibitor. In conclusion, AngII may play a role in the regulation of AQP2 targeting to the plasma membrane in IMCD cells through AT1 receptor activation and potentiates the effect of dDAVP on AQP2 plasma membrane targeting.