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Suppression of TASK Channels in Adrenal Cortical Cells by Angiotensin II

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Summary

Angiotensin II (AngII) induces aldosterone secretion through inhibiting K^+ channels in zona glomerulosa (ZG) cells. TASK1 and TASK3 channels in adrenal cortical (AC) cells including ZG have been detected at the mRNA, but not protein, levels. In addition, molecular mechanisms for AngII-induced inhibition of TASK channels remain an open question. We have reported that TASK1 channels in adrenal medullary cells and PC12 cells are internalized in the order of seconds in response to nerve growth factor (NGF). This internalization was triggered by AP-2 binding to a di-leucine motif present in the TASK1 channel. TASK3 channels were not internalized in reponse to NGF because of the lack of the di-leucine motif. If TASK3 forms a heteromer with TASK1 in AC cells, TASK3 is expected to be internalized with TASK1 in response to AngII. The present experiment was aimed to elucidate whether TASK channels are expressed in AC cells at the protein levels and how the intracellular distribution of TASK channels are affected by AngII. For these issues mouse AC cells and the human AC cell line H295R were used. Isolated AC cells were obtained with collagenase treatment of mouse adrenal cortical tissues. TASK1-like immunoreactive material (IR) in AC cells was mainly located in the cytoplasm and minimally at the cell periphery, whereas TASK3-like IR was predominantly at the cell periphery. The majority of TASK1- or TASK3-like IR was abolished by deletion of each gene. Consistent with the distribution of endogenous TASK channels, GFP-TASK1 and GFP-TASK3 channels exogenously expressed in H295R cells were present mainly in the cytoplasm and at the cell periphery, respectively. When H295R cells were stimulated by AngII, practically no GFP-TASK1 was detected at the cell periphery and GFP-TASK3 was trafficked to the cytoplasm from the cell periphery. The trafficking of GFP-TASK3 in H295R cells could be accounted for by heteromer formation of exogenous TASK3 with endogenous TASK1. The present results indicated that TASK1 and TASK3 channels in AC cells are mainly present in the cytoplasm and at the cell periphery, respectively. TASK1 channels at the cell periphery were internalized in response to AngII. In addition, part of TASK3 channels at the cell periphery were also internalized in response to AngII, raising the possibility that TASK3 makes a heteromer channel with TASK1.