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AMP-ACTIVATED PROTEIN KINASE IN THE KIDNEY CELLS

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BACKGORUND/AIMS

AMP-activated protein kinase (AMPK) was recognized as a fuel gauge in mammalian cells because it responds to increased cellular energy demands by activating adenosine triphosphate-generating pathways while inhibiting energy-consuming anabolic pathways. The role of AMPK in the kidney was not well understood. This study focused on the role of AMPK in high glucose-induced TGF-β secretion in the mesangial cell and podocyte line.

METHODS

Immortalized podocyte cell line and MES-13 cell line were cultured under either 5.5 mM or 25mM glucose medium. AICAR (5-aminoimidazole-4-carboxamide ribonucleoside) was used to activate AMPK catalytic activity. ELISA was used for measuring TGF-β level. AKT and AMPKα levels were measured by Western blot.

RESULTS

AMPKα was expressed in both cell lines. AMPKα phosphorylation and phosphorylated AKT (Ser 473) level increased with decreased total AKT after AICAR treatment, while no change was observed in the phosphorylated AKT (Thr 308) level. High glucose incubation had no significant effects on the level of AMPK. Increased TGF-β1 level was noted in the MES-13 cell after high-glucose incubation. Similar elevation of TGF-β2 was found but not TGF-β1 upon high glucose exposure in the podocyte. AICAR treatment significant abolished the increase in TGF-β secretion in both cell lines.

DISCUSSION/CONCLUSIONS

This was the first report of an inhibitory effect of AICAR on TGF-β production. The mechanism of this inhibitory effect is unknown but may involve the AMPK-mTOR pathway, AKT pathway, or a direct AICAR effect. Further studies will be performed to elucidate the relationship of AMPK and TGF in these cell lines.

Key Words: glucose, amp-activated kinase, tumor growth factor