

Gene screening identified early growth response 1 as a regulator of tubulogenesis in diabetic renal embryopathy

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Background: Maternal hyperglycemia can inhibit morphogenesis of ureteric bud branching, with glial cell line-derived neurotrophic factor (GDNF) as a key regulator of its initiation. Early growth response gene-1 (EGR-1) is one immediate early gene. Our preliminary study found EGR-1 consisting of expression with GDNF in hyperglycemic environment.

Methods: To evaluate the potential relationship of hyperglycemia-GDNF-EGR-1 pathway, *in vitro* human renal proximal tubular epithelial (HRPTE) cells as target and *in vivo* streptozotocin-induced mouse model were used.

Results: *In vivo* microarray, real time-PCR and confocal morphological observation confirmed apoptosis in hyperglycemia-induced fetal nephropathy via activation of the GDNF/MAPK/EGR-1 pathway. *In vitro* evidence indicated high glucose suppressing HRPTE cell migration, and enhanced GDNF-EGR-1 pathway induced apoptosis. Knockdown of EGR-1 by siRNA negated hyperglycemic suppressed GDNF-induced HRPTE cell migration. Also, EGR-1 siRNA alleviated GDNF/EGR-1-induced cRaf/MEK/ERK phosphorylation by 80%.

Conclusion: Our findings demonstrated EGR-1's crucial role in HRPTE cell apoptosis and fetal hyperglycemic nephropathy.