Glucagon and Insulin Stimulate Fibroblast Growth Factor 21 Gene Transcription by Increasing the Expression of Activating Transcription Factor 4

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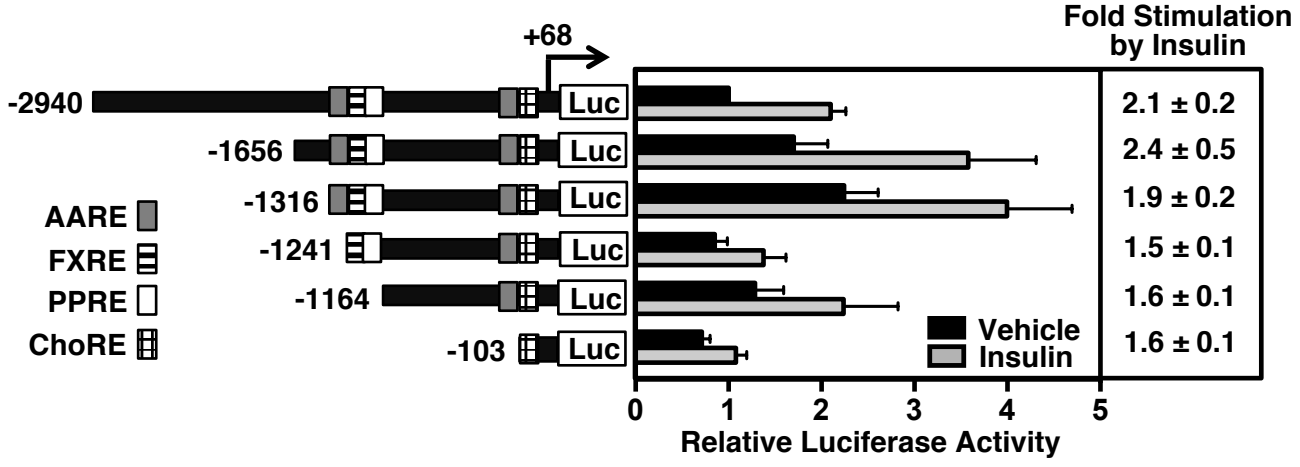

Figure S1: Effects of deletions of the 5-flanking region of the rat FGF21 gene on transcriptional activity in the absence and presence of insulin. Primary rat hepatocytes were transiently transfected with a series of plasmids containing fragments of the rat FGF21 gene linked to the luciferase (Luc) gene as described under "Experimental Procedures." After transfection, cells were treated with 50 nM insulin for 24 h. Cells were harvested, extracts were prepared, and luciferase assays were performed. *Left*, the constructs used in these experiments. The number at the left of each construct is the 5'-end of FGF21 DNA in nucleotides relative to the transcription initiation site. The 3'-end of each construct is +68 bp. The location of a previously identified FXRE (-1222 to -1210 bp), PPRE (-1215 to -1203 bp), ChoRE (-72 to -56 bp), and AARE (-1282 to -1274 bp and -140 to -132 bp) are indicated by boxes with different fills or patterns. *Right,* luciferase activity of cells transfected with the -2949 to +68 bp FGF21 construct and treated with vehicle was set at 1, and all other activities were adjusted proportionately. The -fold stimulation by insulin was calculated by dividing the luciferase activity for cells treated with insulin by that for cells treated with vehicle. The -fold responses were calculated for individual experiments and then averaged. The results are the means ± S.E. of five experiments.