Carbohydrate response element binding-protein is activated by elevated glucose levels in the normal murine liver cell line NMuLi

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ABSTRACT
Carbohydrate response element (ChRE) binding protein (ChREBP) is a transcription factor that is regulated by intracellular glucose levels and activates several lipogenic genes including acetyl CoA carboxylase (ACC). Previous studies of the ChREBP system have used both in vivo models as well as isolated primary hepatocytes. Due to the difficulties in isolation and genetic variability of primary cell culture, we propose the use of a normal murine liver cell line (NMuLi) as a convenient alternative to primary isolated hepatocytes. We show that high (25 mM) but not low (0.5 or 5 mM) glucose activates a luciferase reporter driven by 4 repeated ChREs, as well as the murine ACC promoter segment from −220 to +21. Furthermore, using small interfering RNA to knock-down ChREBP, we show that ChREBP is required for this glucose-induced luciferase reporter activation. Finally, using chromatin immunoprecipitation we show that ChREBP directly binds to the ChRE within the promoter region of the ACC gene in the presence of high but not low glucose. Together, these results suggest that NMuLi cells may be used as an alternative to primary isolated hepatocytes for studies of the ChREBP system.