

R1- MCB01004-12

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## SUPPLEMENTAL FIGURE LEGENDS

### **Supplemental Figure 1. FXR activation inhibits the glucose-dependent induction of *L-PK* gene expression in HepaRG cells.**

*L-PK* mRNA expression in HepaRG at low (0.5mM) or high (25mM) glucose concentrations and vehicle (DMSO) or GW4064 (5 $\mu$ M) for 24h. *L-PK* and control *36B4* mRNA levels were measured by real-time quantitative PCR. The values were expressed relative to those at low glucose concentration with vehicle, arbitrarily set to 1.

### **Supplemental Figure 2. Both the p300 and CBP coactivators are necessary for glucose-induced *L-PK* gene expression in IHH cells.**

Effect of CBP and/or p300 gene silencing on *L-PK* gene expression in IHH transfected with specific siRNA and incubated at low (1mM) or high (11mM) glucose concentration and vehicle (DMSO) or GW4064 (5 $\mu$ M) for 24h. *L-PK* and control *36B4* mRNA levels were measured by real-time quantitative PCR. Values were expressed relative to those measured at low glucose concentration with vehicle, arbitrarily set to 1.

**Supplemental Figure 3. Several genes regulated both by ChREBP and FXR and identified by microarray analysis in IHH code for enzymes involved in the glycolysis pathway.**

The name and initials of the genes identified using a microarray analysis of IHH mRNAs as up-regulated by glucose and downregulated by activated FXR are respectively underlined and surrounded.

**Supplemental Figure 4. Glucose-induced expression of genes identified using microarray analysis is dependent on ChREBP in IHH.**

Effect of ChREBP gene silencing on the expression of genes from the glycolytic pathway. IHH cells were transfected with specific siRNA and incubated in a medium containing low (1mM) or high (11mM) glucose concentrations and vehicle (DMSO) or GW4064 (5 $\mu$ M) for 24h. Gene and control *36B4* mRNA levels were measured by real-time quantitative PCR. Values were expressed relative to those measured at low glucose concentration with vehicle, arbitrarily set to 1.

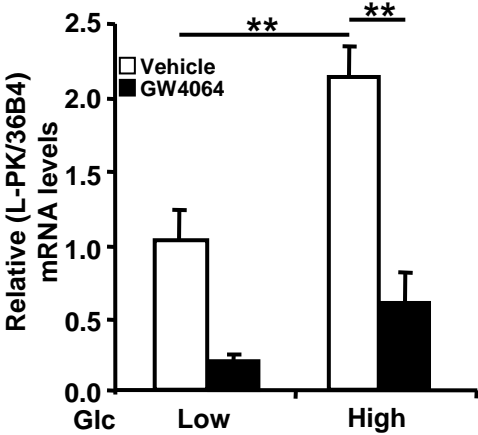
**Supplemental Figure 5. The glucose-induction expression of PNPLA3 and other genes identified by microarray analysis is dependent on HNF4 $\alpha$  in IHH.**

Effect of HNF4 $\alpha$  silencing on PNPLA3, HK3, PGM1, TPI1, PGAM1 and ACSS1 mRNA expression in IHH incubated in a medium containing low (1mM) or high (11mM) glucose concentrations for 24h. mRNA levels were measured by real-time quantitative PCR. Values were expressed relative to those at low glucose concentration with vehicle, arbitrarily set to 1.

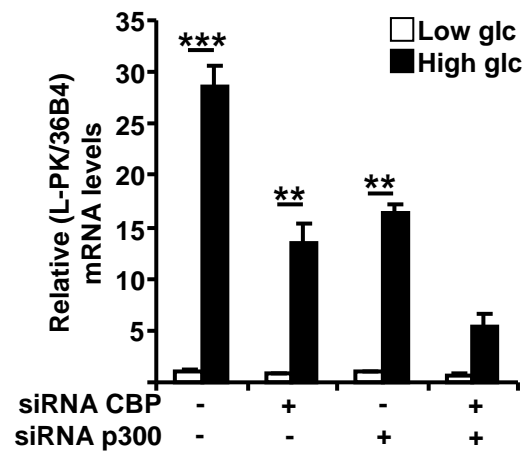
**Supplemental Table 1. Approximately half of the FXR-enriched sites on the promoter of the glucose-regulated genes do not harbor FXR response elements.**

FXR enrichment peaks were searched on the promoter of glucose-regulated genes using ChIP-seq data from mouse liver available on UCSC Genome Bioinformatics group website. Chromosomal coordinates of FXR peaks are indicated, as well as the presence or not of potential FXRE and ChORE on promoter, 30kb before and 30kb after every FXR enrichment peak, as determined by the MathInspector software (Genomatix, Gmbh).

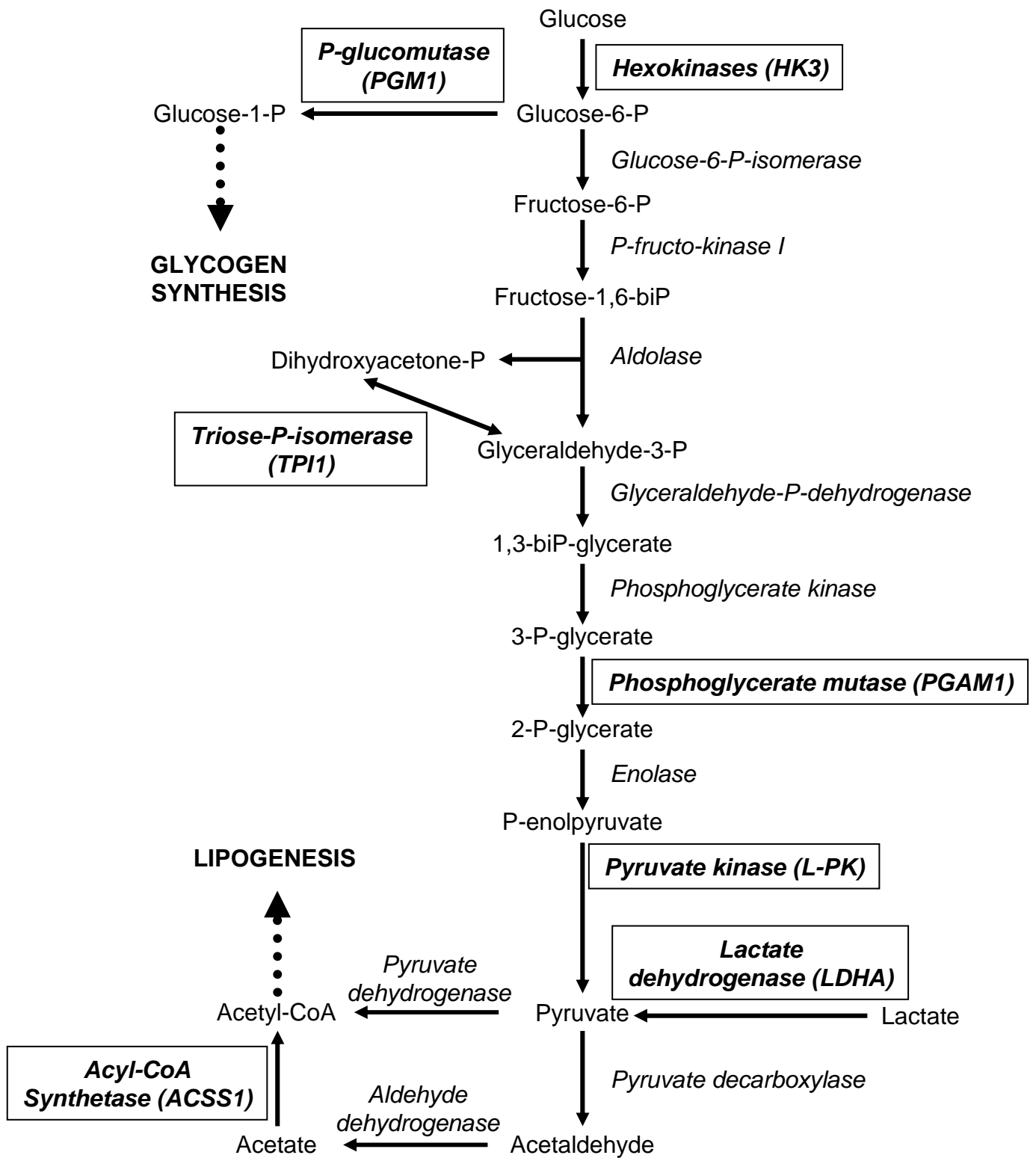
Supplemental Figure 1. Caron S & Huaman Samanez C



## Supplemental Figure 2. Caron S & Huaman Samanez C

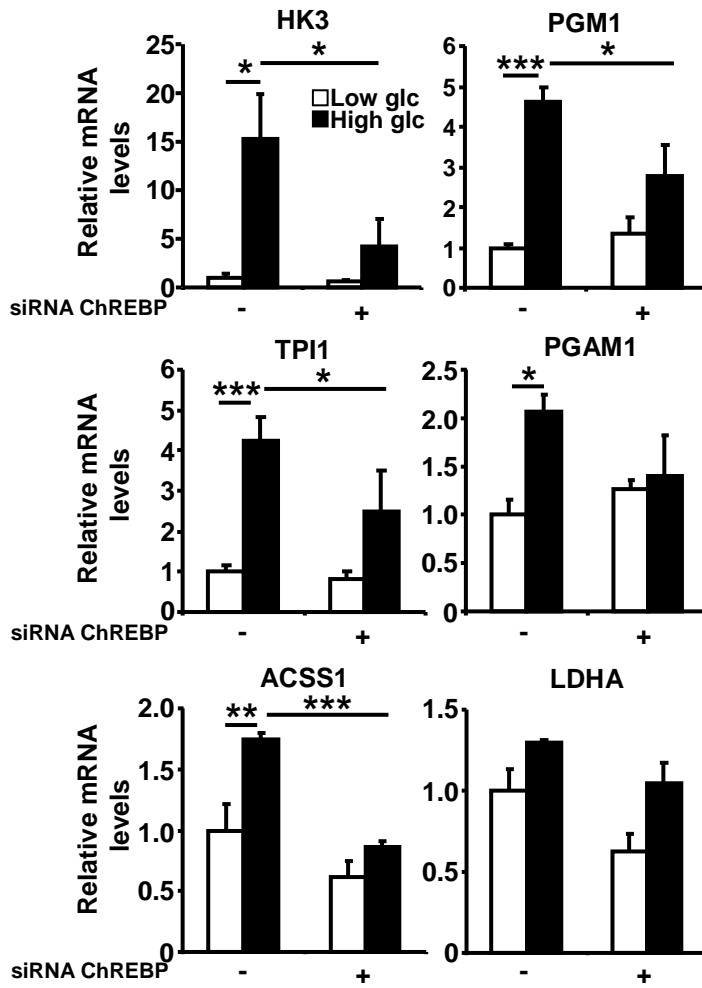


Supplemental Figure 3. Caron S & Huaman Samanez C

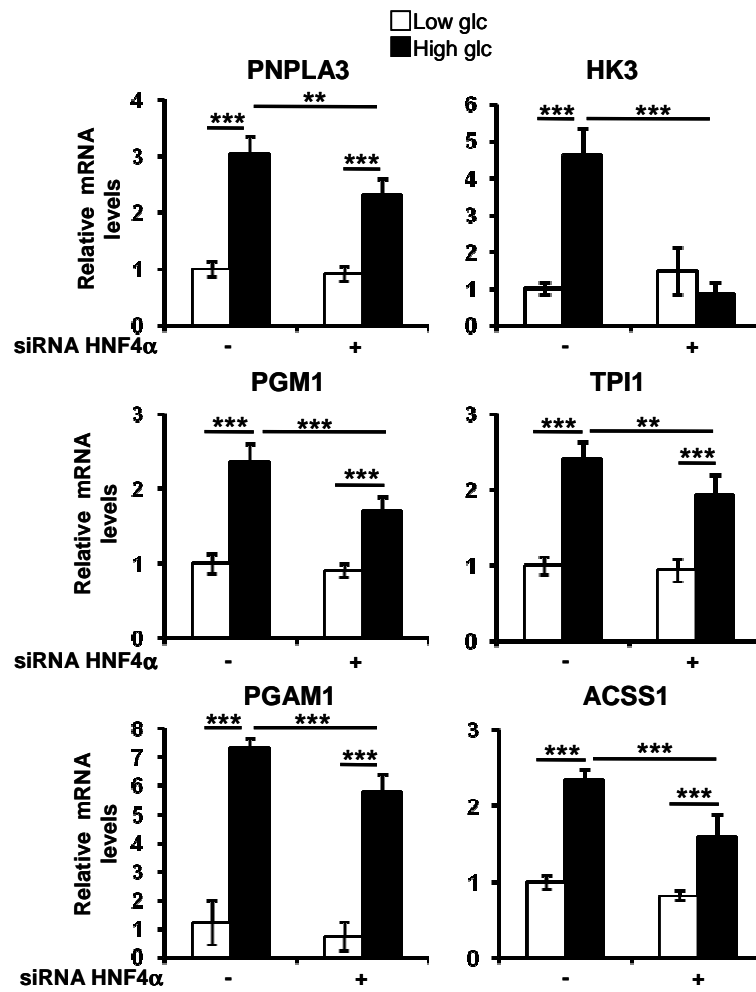


Metabolite	<b>LEGEND</b>
Enzyme	
<b>METABOLIC PATHWAY</b>	
<b>Name (Initials)</b>	Gene whose expression is induced by ChREBP and inhibited by activated FXR

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# Supplemental Figure 5. Caron S & Huaman Samanez C





**Supplemental Table 1. Caron S & Huaman Samanez C**

Gene name	Gene official symbol	FXR enrichment (position)	Potential FXRE	Potential ChORE
Liver Pyruvate Kinase	<b>LPK</b>	Up to 9 (chr3:88940313-88940721)	NO	YES
Fatty Acid Synthase	<b>FAS</b>	Up to 117 (A) (chr11:120685864-120686333)	YES	YES
Patatin-like phospholipase domain-containing protein 3	<b>PNPLA3</b>	Up to 53 (A) (chr15:83986402-83986994)	NO	NO
		Up to 131 (B) (chr15:83998732-83999266)	YES	YES
		Up to 10 (C) (chr15:84022432-84022942)	YES	YES
		Up to 23 (D) (chr15:84023967-84024356)	YES	YES
		Up to 29 (E) (chr15 :84026864-84027306)	YES	YES
		Up to 46 (F) (chr15:84027311-84027631)	YES	YES
Thioredoxin-interacting protein	<b>TXNIP</b>	Up to 27 (A) (chr3:96358905-96359436)	NO	NO
		Up to 20 (B) (chr3:96361487-96362066)	NO	YES
		Up to 20 (C) (chr3:96377921-96378474)	NO	NO
		Up to 39 (D) (chr3:96379407-96379902)	YES	NO
Phosphoglucomutase 1	<b>PGM1</b>	Up to 10 (A) (chr5:64493733-64493973)	YES	NO
		Up to 8 (B) (chr5:64505457-64505905)	NO	NO
Hexokinase 3	<b>HK3</b>	Up to 5 (chr13:55095871-55096022)	NO	YES
Triosephosphate isomerase 1	<b>TPI1</b>	Up to 12 (A) (chr6:124762082-124762542)	NO	YES
		Up to 12 (B) (chr6:124762944-124763323)	NO	NO
		Up to 12 (C) (chr6:124764053-124764522)	NO	NO
Phosphoglycerate mutase 1	<b>PGAM1</b>	Up to 7 (A) (chr19:41979838-41980061)	YES	NO
		Up to 6 (B) (chr19:41986170-41986471)	NO	NO
		Up to 5 (C) (chr19:41987204-41987614)	NO	NO
Lactate deshydrogenase A	<b>LDHA</b>	Up to 45 (A) (chr7:54085144-54085732)	YES	NO
		Up to 20 (B) (chr7:54088699-54089134)	NO	NO
		Up to 105 (C) (chr7:54094273-54094735)	YES	NO
		Up to 80 (D)	YES	NO

		(chr7:54094816-54095277)		
		Up to 30 (E) (chr7:54098471-54098911)	YES	NO
		Up to 30 (F) (chr7:54100669-54101171)	NO	YES
Acyl-CoA synthetase short-chain family member 1	<b>ACSS1</b>	Up to 10 (chr2:150434192-150434512)	NO	NO