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**Supplemental Figure 3. Effects of pharmacological activation of FXR on *βKL and Fgfr4* mRNA levels.** Hepatocytes were isolated from WT or FXR-KO mice, were treated with 500 nM GW4064, and then, βKL and Fgfr4 mRNA levels were measured by q-RTPCR. SEM, n=6.

**Supplemental Figure 4. Potential FXR binding sites as detected** by the nuclear receptor binding motif search engine **NUBIScan in the 700 bp genomic fragment of *βKL* containing a FXR binding site identified in ChIP-seq studies.**

**Supplemental Figure 5. Adenoviral-mediated FXR compensation experiments in FXR-KO mice.** C57BL/6 wild-type (WT) and FXR knockout (FXR-KO) mice were tail-vein injected with either control Ad-Empty or Ad-FXR. One week later, livers were collected, and mRNA levels of *βKL and Fgfr4* were measured by q-RTPCR.

**Supplemental Figure 6. Effects of GW4064 treatment for different times on hepatic βKL protein levels.** WT mice were injected with GW4064 for the times indicated. βKL protein levels in the liver were detected by IHC. Representative images of hepatic βKL from 3 independent IHC studies are shown.

**Supplemental Figure 7. Pre-treatment with GW4064 enhances responsiveness to FGF19 signaling in primary human hepatocytes.** Primary human hepatocytes (PHH) were pre-treated with GW4064 for 2 h, and then treated with FGF19 for 30 min. Protein levels of total (T-Erk) and phosphorylated (P-Erk) ERK were measured by IB (shown in duplicate).

# Supplemental Figures

**Sequences for the primers used in ChIP and q-RTPCR analyses.**

| **Chip qPCR primers** | |
|---|---|
| Grb2 qChip-f1 | AAGAGCACCCGTGCAAATAC |
| Grb2 qChip-r1 | GAAGGATTTTTCCCCCATGT |
| Sos2 qChip-f1 | ATGAGTCTTTGGGCAAGAGG |
| Sos2 qChip-r1 | TCACAGTAGACAGGCCAGAATG |
| Ras qChip-f1 | TTCACGACACAAAGCCACTC |
| Ras qChip-r1 | AGGAGGTGGAGGTAGGGATG |
| Raf qChip-f1 | CCGGGTCCTTTGTGAAGTAG |
| Raf qChip-r1 | TGTGTTGCTGGGACTTGAAC |
| Map2k1 (Mek1) qChip-f1 | GACATGTTTCAGAGGCAGCA |
| Map2k1 (Mek1) qChip-r1 | TAGGTTTCAGCAGGCAGAGG |
| Ppp2cb qChip-f1 | TCCCTGTTTTCTTCCACCTG |
| Ppp2cb qChip-r1 | GATACTTCCCACCCAGCAGA |
| Map2k6 (Mek6) qChip-f1 | TGCTAGGTGCCTTCCTGTCT |
| Map2k6 (Mek6) qChip-r1 | GCTCAGTGGGTGGAGTGTTT |
| Mapk3 (Erk1) qChip-f1 | TGAGGCAGGTCTTCAAAGGT |
| Mapk3 (Erk1) qChip-r1 | CGCCTAGTTACGCTGTTCCT |
| βKL qChip-f1 | GGCTCTGCAAAAAGGAACAG |
| βKL qChip-r1 | CAGGTAAACCCCTTTGTCCA |

| **Cloning /EMSA primers** | |
|---|---|
| βKL(700bp-wt)-Luc-f1 | TTACTCGAGTATCATGCGCTGAGACATGAACT |
| βKL(700bp-wt)-Luc-r1 | TAGAGATCTCTAGCTGCGTTCTAAGCTGTTCC |
| βKL(552bp-wt)-Luc-f1 | TTGGTACCTACCCCAGCACCCGAATAAAAC |
| βKL(552bp-wt)-Luc-r1 | TTGCTAGCCATCTCGTGGTTCTGGTTTCCC |
| βKL(195bp)-Luc-f1 | TTGGTACCTAGAGTTTGACCCCCAGCAC |
| βKL(195bp)-Luc-r1 | TGCTAGCCTAGTGATGCCTCTGTGTGGATG |
| βKL(700bp-mut)-Luc-f1 | TATATACAGGCCCTTTAATTACATATATTTCACTTGGAC |
| βKL(700bp-mut)-Luc-r1 | GTCCAAGTGAAATATATGTAATTAAAGGGCCTGTATATA |
| βKL IR2 EMSA-f1 | CAGGCCCTTGGGTCAAATGTCTTTCACTTGGA C |
| βKL IR2 EMSA-r1 | GTCCAAGTGAAAGACATTTGACCCAAGGGCCTG |
| Shp IR1 EMSA-f1 | TGGTACAGCCTGAGTTAATGACCTTGTTTATC |
| Shp IR1 EMSA-r1 | GATAAACAAGGTCATTAACTCAGGCTGTACCA |

**Sequences for the primers used in ChIP and q-RTPCR analyses. (Con't)**

| qPCR primers | |
|---|---|
| m36B4-F | CGACATCACAGAGCAGGC |
| m36B4-R | CACCGAGGCAACAGTTGG |
| mβKL-F | CGAGCCCATTGTTACCTTGT |
| mβKL-R | CTCCAAAGGTCTGGAAGCAG |
| mFgfr4-F | GACCAAACCAGCACCGTGGCTGTGAAGATG |
| mFgfr4-R | GTTTCCCTTGGCGGCACATTCCACAATCA C |
| mGrb2-F | TCAATGGGAAAGATGGCTTC |
| mGrb2-R | GAGCATTTCTTCTGCCTTGG |
| mSos2-F | TGTTCGTCCATCAAATCCAA |
| mSos2-R | AGATGCTGTGCTTTCCGTCT |
| mRas-F | GGCTGTGCCTGGAGACTAAG |
| mRas-R | CTTCTGGCTCACCTGCCTAC |
| mRaf-F | TTCAGTGGCTGTCAGTCTGG |
| mRaf-R | ACTGTCCACTTCCCCTTCCT |
| mMek1-F | CTAGTGACCTGGGTGGTCGT |
| mMek1-R | CACAAGGCTCCCTCTCAGAC |
| mPpp2cb-F | GGGGTCTGGTCACTTGAAAA |
| mPpp2cb-R | GATACTTCCCACCCAGCAGA |
| mMek6-F | ACTGGTCGACCCTACTGTGG |
| mMek6-R | CCCCTTTGGAGAGGAAAAAG |
| mErk1-F | TCCTTTTGGATCTGGTCCTG |
| mErk1-R | CCCCAGCAAAGTGAGAGAAG |
| mCyp7a1-F | CATCTCAAGCAAACACCATTCC |
| mCyp7a1-R | TCACTTCTTCAGAGGCTGGTTTC |
| mCyp8b1-F | GAACTCAACCAGGCCATGCT |
| mCyp8b1-R | AGGAGCTGGCACCTAGACT |
| mShp-F | CAAGAAGATTCTGCTGGAGG |
| mShp-R | GGATGTCAACATCTCCAATG |
| h36b4-F | GGTCCTCCTTGGTGAACAC |
| h36b4-R | AAGGCTGTGGTGCTGATG |
| hCyp7a1-F | CAAGGAATCGCTGAGGCTTTC |
| hCyp7a1-R | ACCGTCCTCAAGGTGCAAAGT |
| hCyp8b1-F | AAGCATGGGGATGTGTTCAC |
| hCyp8b1-R | CAAACTTGCGGAACTCCATG |
| mFgf15 premRNA-F | CATGCACACAGCCTCTTGTC |
| mFgf15 premRNA-R | TCCATTTCCTCCCTGAAGGT |
| mβKL premRNA-F | TCGCTGCTTCCTTTTCTCTG |
| mβKL premRNA-R | ATAGGCATCCTGCCACTCAA |
| mFgfr4 premRNA-F | CCTCTCCTTGTCCTGGCTTT |
| mFgfr4 premRNA-R | CACTTTCCATCACCAGGCTC |
| mSHP premRNA-F | CAACTATCCGAAGGCCACAT |
| mSHP premRNA-R | ACCCTCTCTACCCACCCACT |
| mcyp7a1 premRNA-F | TTTGCATCATGGCTTCAGAG |
| mcyp7a1 premRNA-R | TCTTCCAGACACTCCCCAAC |

**Fig. S1. Sequences for the primers used in ChIP and q-RTPCR analyses.**

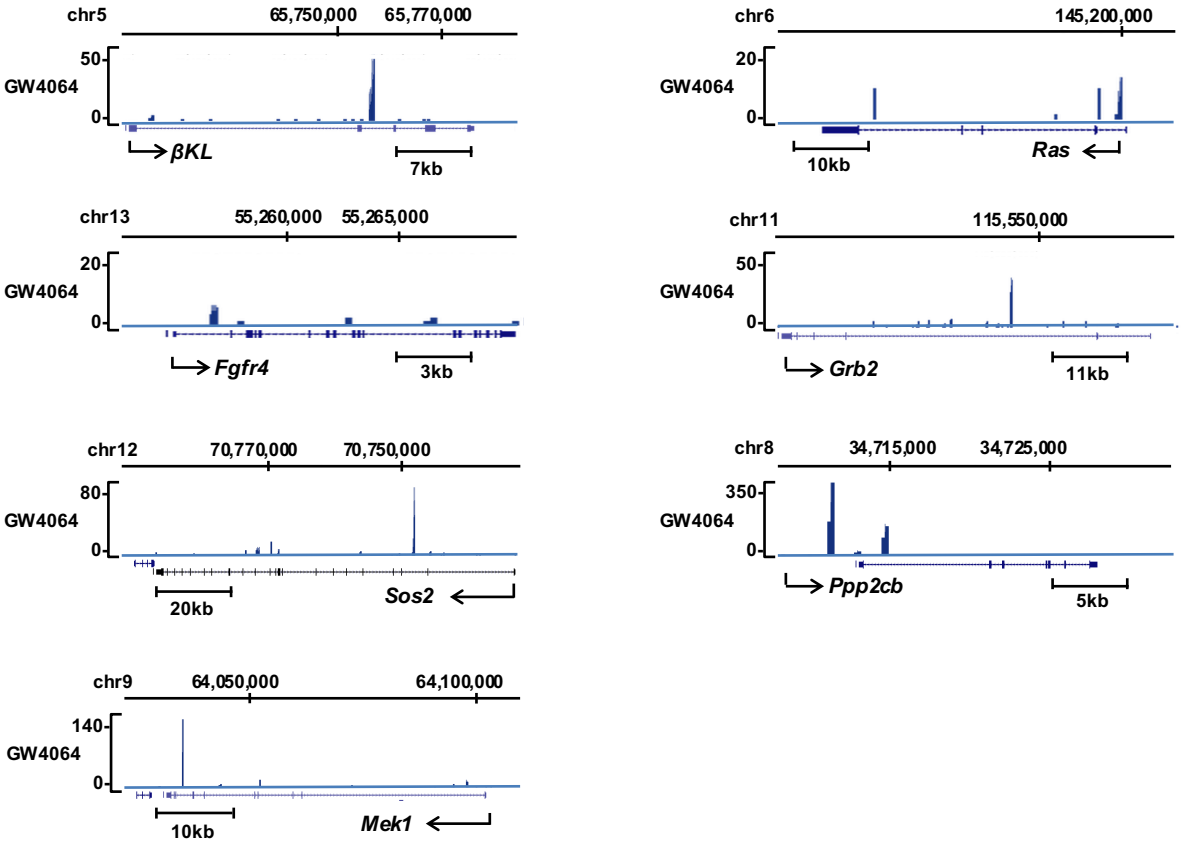


**Fig. S2. FXR binds to key component genes of the FGF19 signaling pathway.** Browser images from liver ChIP-seq data from mice treated with GW4064 for 1 h (Lee et al., Hepatology, 2012) using the UCSC genome browser. The direction of gene transcription is indicated by the arrow and the beginning of the arrow indicates the position of the transcriptional start site (TSS).

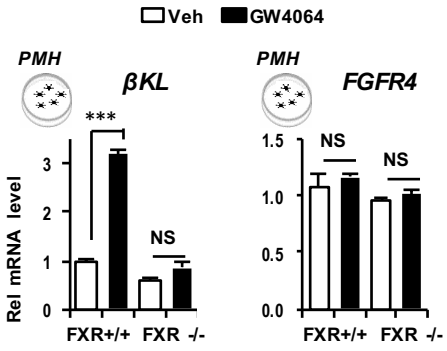


**Fig. S3. Effects of pharmacological activation of FXR on βKL and Fgfr4 mRNA levels.** Hepatocytes were isolated from WT or FXR-KO mice, were treated with 500 nM GW4064, and then, βKL and Fgfr4 mRNA levels were measured by q-RTPCR. SEM, n=6.

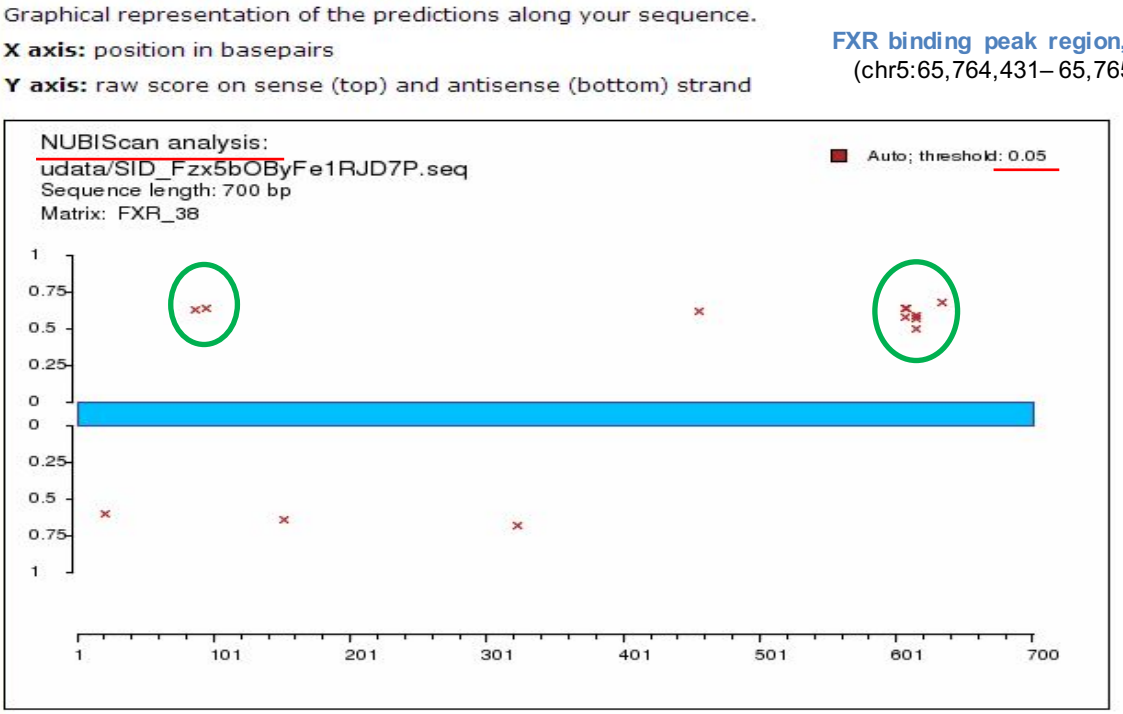


**Fig. S4. Potential FXR binding sites as detected by the nuclear receptor binding motif search engine NUBIScan in the 700 bp genomic fragment of βKL containing a FXR binding site identified in ChIP-seq studies.**

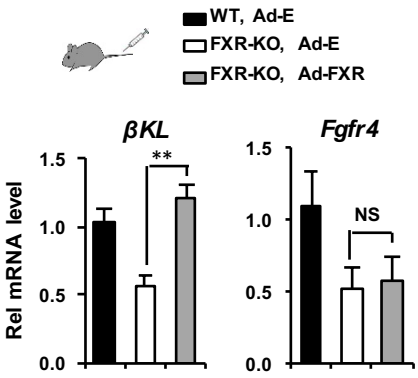


**Fig. S5. Adenoviral-mediated FXR compensation experiments in FXR-KO mice.** C57BL/6 wild-type (WT) and FXR knockout (FXR-KO) mice were tail-vein injected with either control Ad-Empty or Ad-FXR. One week later, livers were collected, and mRNA levels of βKL and Fgfr4 were measured by q-RTPCR.

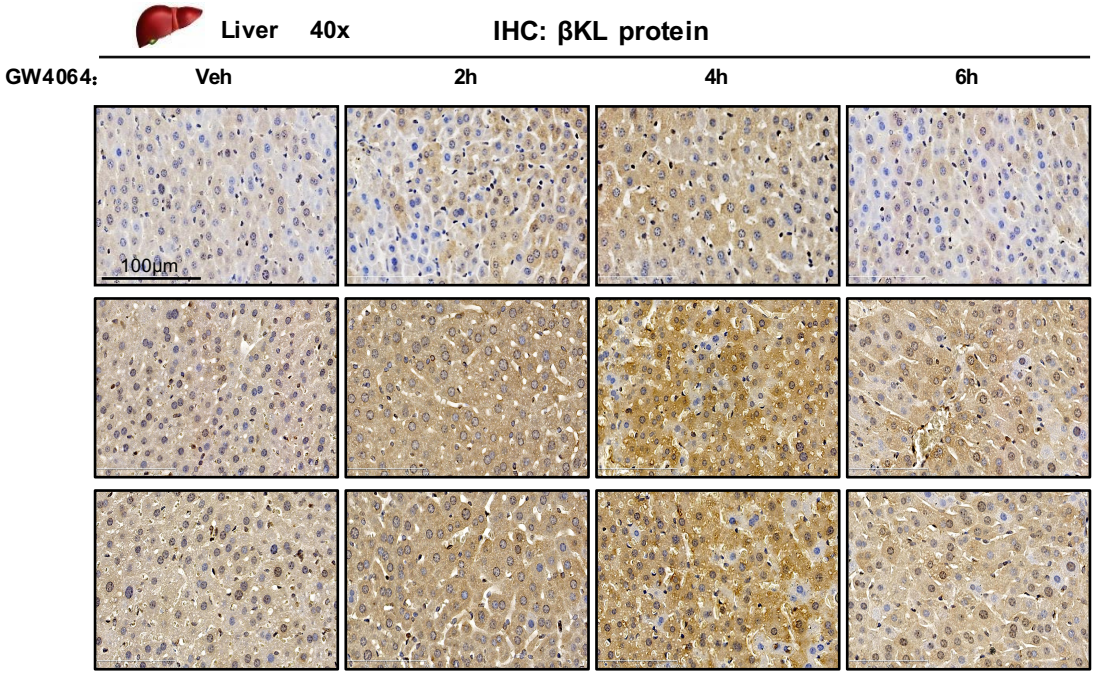


**Fig. S6. Effects of GW4064 treatment for different times on hepatic βKL protein levels.** WT mice were injected with GW4064 for the times indicated. βKL protein levels in the liver were detected by IHC. Representative images of hepatic βKL from 3 independent IHC studies are shown.

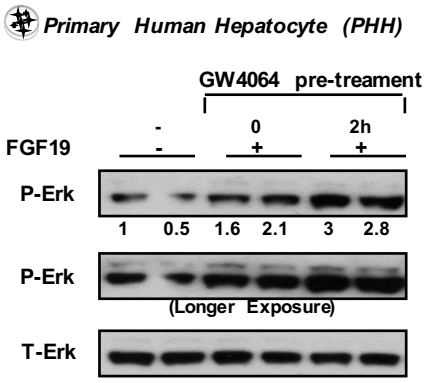


**Fig. S7. Pre-treatment with GW4064 enhances responsiveness to FGF19 signaling in primary human hepatocytes.** Primary human hepatocytes (PHH) were pre-treated with GW4064 for 2 h, and then treated with FGF19 for 30 min. Protein levels of total (T-Erk) and phosphorylated (P-Erk) ERK were measured by IB (shown in duplicate).