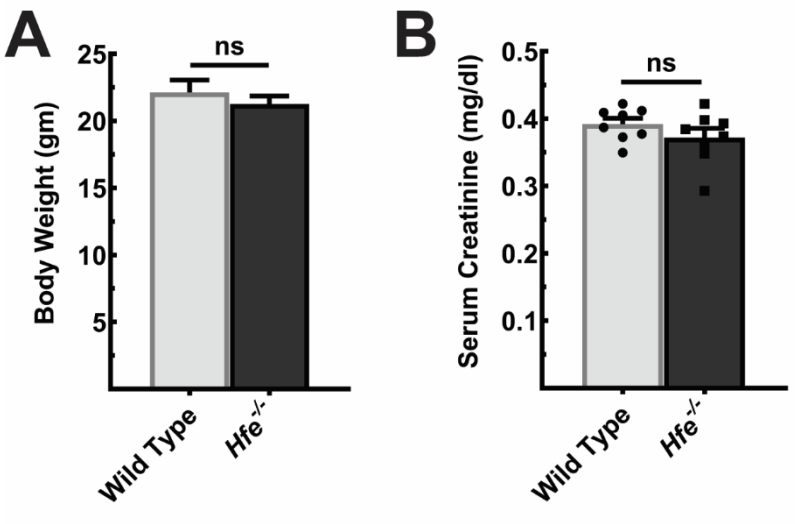
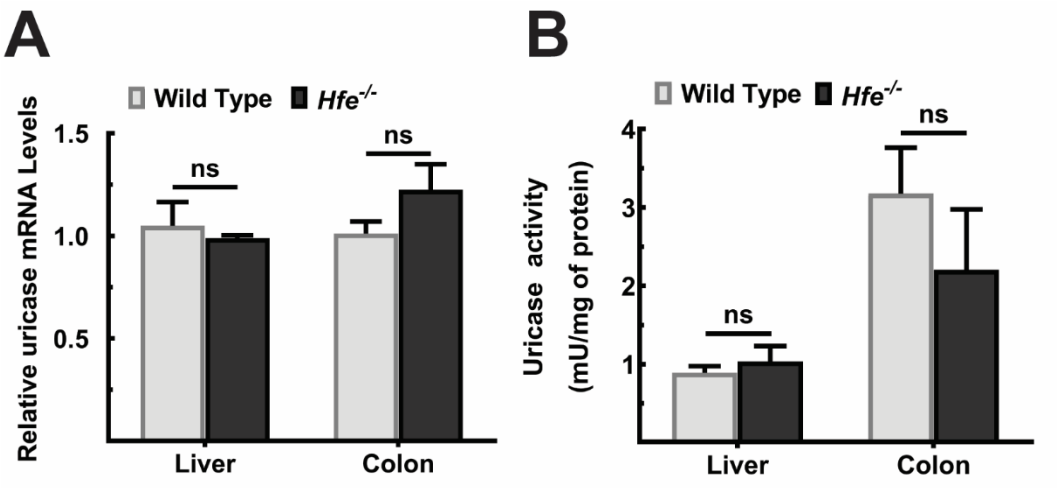
Supplementary Information

Supplementary Table S1. Sequences of PCR Primers used in this study.

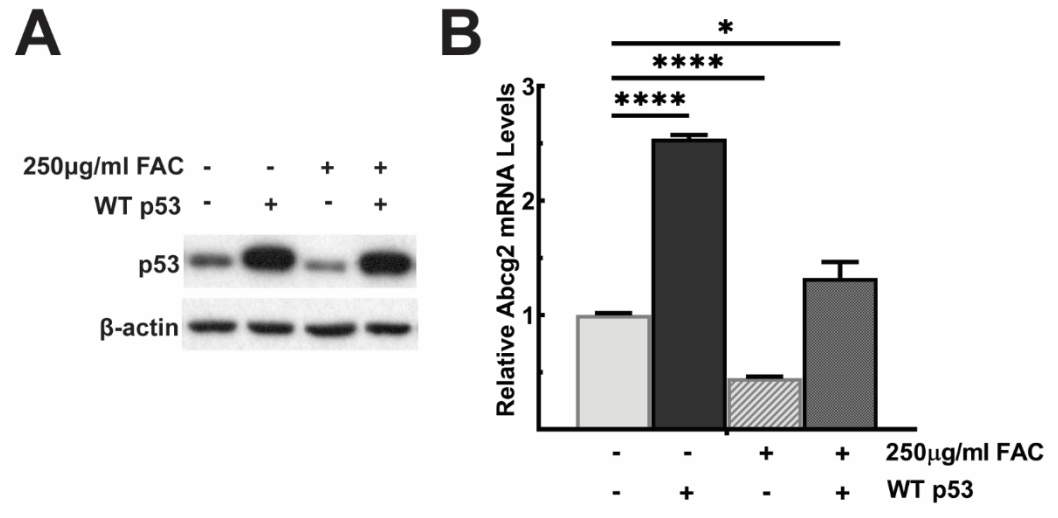
Target	Primer Sequence (5'-3')
mXO	ATG GCA AAA AGG TGG TGG AGA
	GCA ACA TGA TGC AAG GAG CA
mGlut9	TGC ATT GGC GTG TTT TCT GG
	AAA GAG AAG GTA GCG TGG GC
mMrp4	TCT GCG AGC CAA GAA GGA CT
	TCG TCG GGG TCA TAC TTC TCA
mAbcg2	ATA GCC ACA GGC CAA AGT GT
	ACT GCA AAG CTG TGA AGC CA
***hABCG2* ChIP primer**	GAG CAG CGC TTG TGA CTG G
	ACA CGC AGG GAC AAG CCA AA
***hP21* ChIP primer**	CCC ACA GCA GAG GAG AAA GAA
	CTG GAA ATC TCT GCC CAG ACA
***hGADD45A* ChIP Primer**	TCC GAC TAG AGT GTG GCT GG
	ATG AGG GGT GAG CCA GGA AT
***hGAPDH* ChIP Primer**	TAC TAG CGG TTT TAC GGG CG
	TCG AAC AGG AGG AGC AGA GAG CGA
mUrate Oxidase	GTG AGC ACT TCC TCT CTT CTT T
	GGA CGT GTT TGA TCC CAT TCT
m/hHPRT	GCG TCG TGA TTA GCG ATG ATG AAC
	CCT CCC ATC TCC TTC ATG ACA TCT
mGAPDH	TGT AGA CCA TGT AGT TGA GGT CA
	AGG TCG GTG TGA ACG GAT TTG
hABCG2	TCA GAT GGG TTT CCA AGC GT
	AAC CCC AGC TCT GTT CTG GA



Supplementary Figure S1. Serum creatinine levels as a surrogate for glomerular filtration rate in *Hfe*$^{-/-}$ mouse. (**A**) Body weight for *Hfe*$^{-/-}$ mice and wild type control mice at the time of serum collection. Data show mean ± SEM for 4 mice (all males) per group. ns, not significant. (**B**) Serum creatinine levels were measured in *Hfe*$^{-/-}$ mice and wild type counterparts using Creatinine Assay Kit. Data show mean ± SEM for 4 mice per group. ns, not significant.

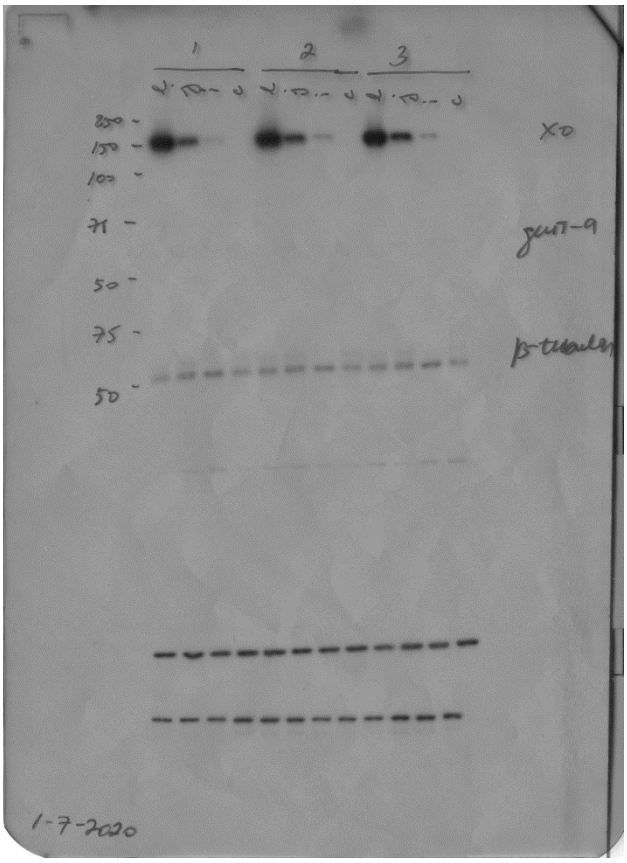


Supplementary Figure S2. Expression and activity of uricase in wild type and *Hfe*$^{-/-}$ mouse liver and colon. (**A**) Quantitative PCR analysis of uricase mRNA in liver and colon of *Hfe*$^{-/-}$ and wild type mice. Data show mean ± SEM for 3 mice per group. ns, not significant. (**B**) Uricase activity in wild type and *Hfe*$^{-/-}$ mice as assessed by the Amplex® Red Uric Acid/Uricase Assay Kit. Data show the mean ± SEM for 3 mice per group. ns, not significant.

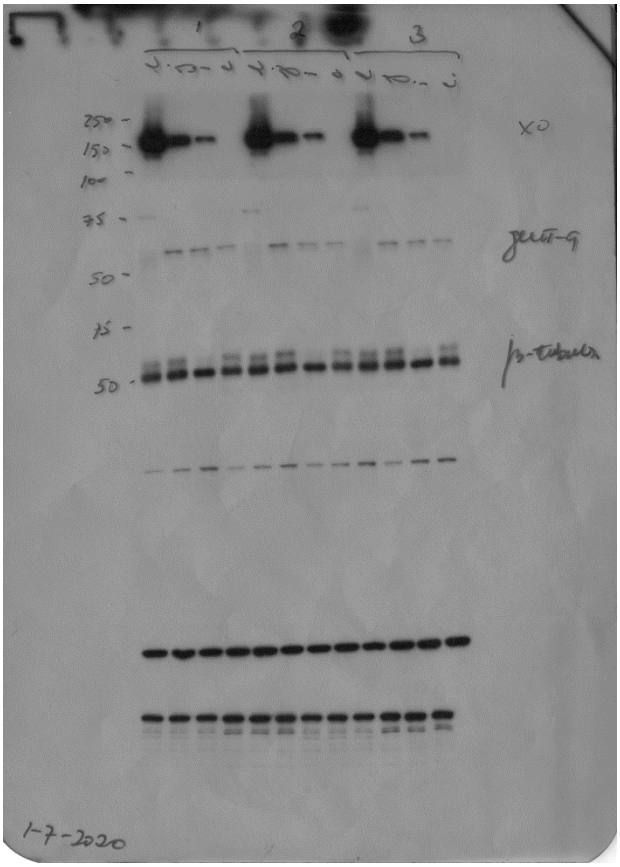


Supplementary Figure S3. ABCG2 expression levels upon iron-induced p53 degradation and subsequent ectopic overexpression of p53. HEK293FT cells were chronically treated with 250 µg/ml FAC for three passages to mimic the environment of the chronic exposure to excess iron. Cells then underwent transfection with pcDNA3-p53 or empty pcDNA3 plasmid constructs. FAC was omitted during transfection. Cells were then used for preparation of protein lysates and total RNA. (**A**) Western blot for p53 protein levels. (**B**) Quantitative PCR analysis to assess ABCG2 mRNA levels. Data show mean ± SEM for 3 independent experiments. *$P < 0.05$; ****$P < 0.0001$.

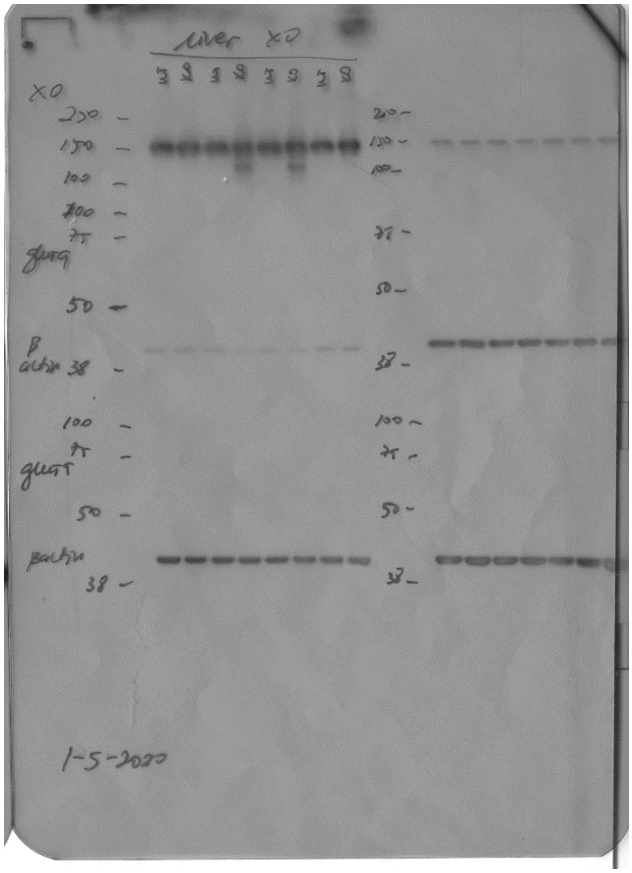
Raw Western Blots



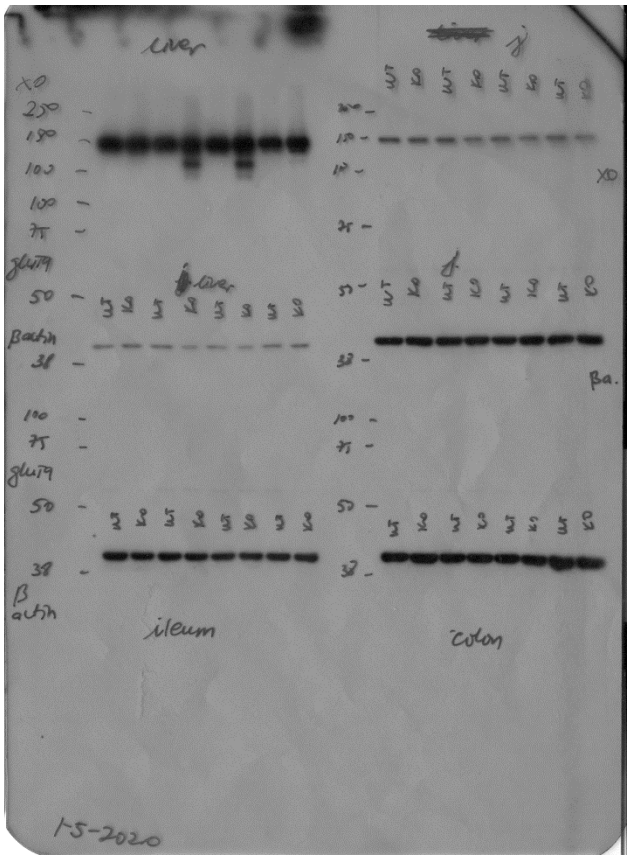
Supplementary Figure S4. Rows from the top: (**1**) XO in WT Liver, Jejunum, Ileum and Colon. Used in Figure 2B. The rest not used. Please disregard.



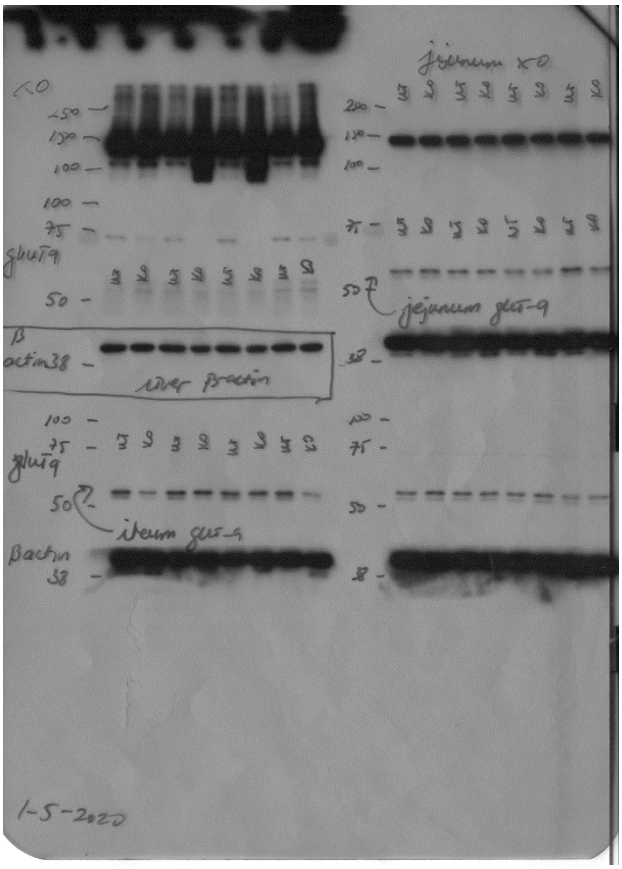
Supplementary Figure S5. Rows from the top: (**1**) XO in WT Liver, Jejunum, Ileum and Colon, longer exposure; (**2**) Not used. Please disregard; (**3**) β-tubulin in WT Liver, Jejunum, Ileum and Colon. Used in Figures 2B and 3B. The rest not used. Please disregard.



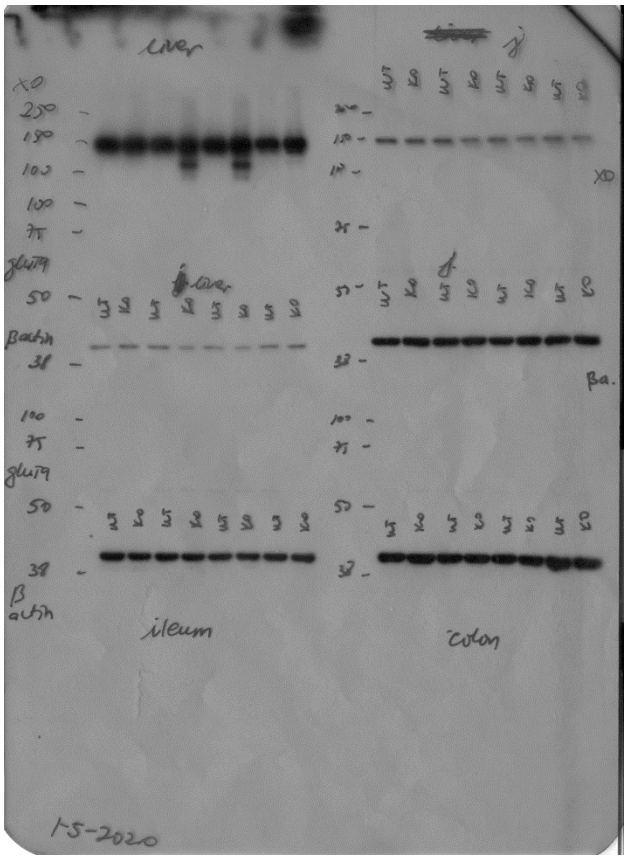
Supplementary Figure S6. Top left row: XO in WT (lanes 1,3,5,7) and *Hfe*$^{-/-}$ (lanes 2,4,6,8) liver. Used in Figure 2D. The rest not used. Please disregard.



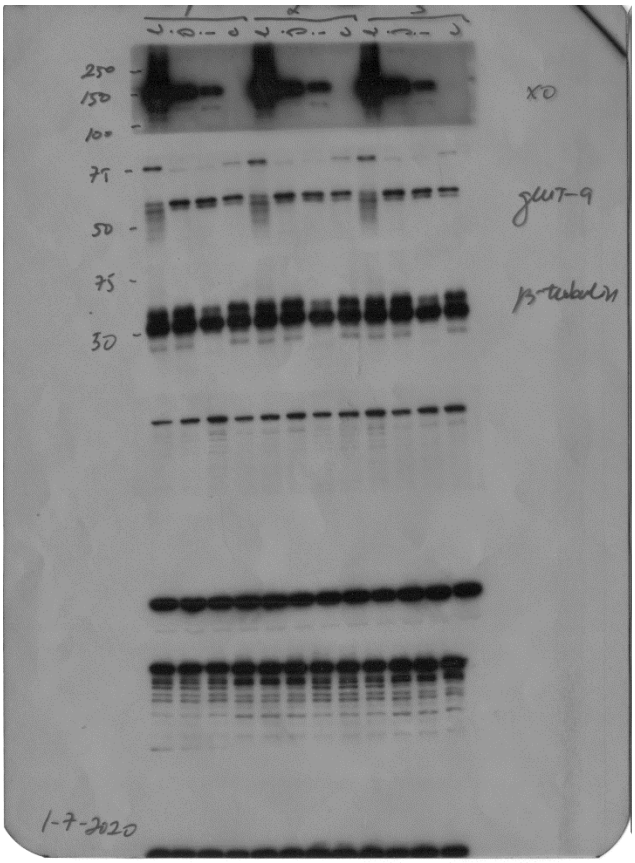
Supplementary Figure S7. Top right row: XO in WT (lanes 1,3,5,7) and *Hfe*$^{-/-}$ (lanes 2,4,6,8) jejunum. Used in Figure 2D. The rest not used. Please disregard.



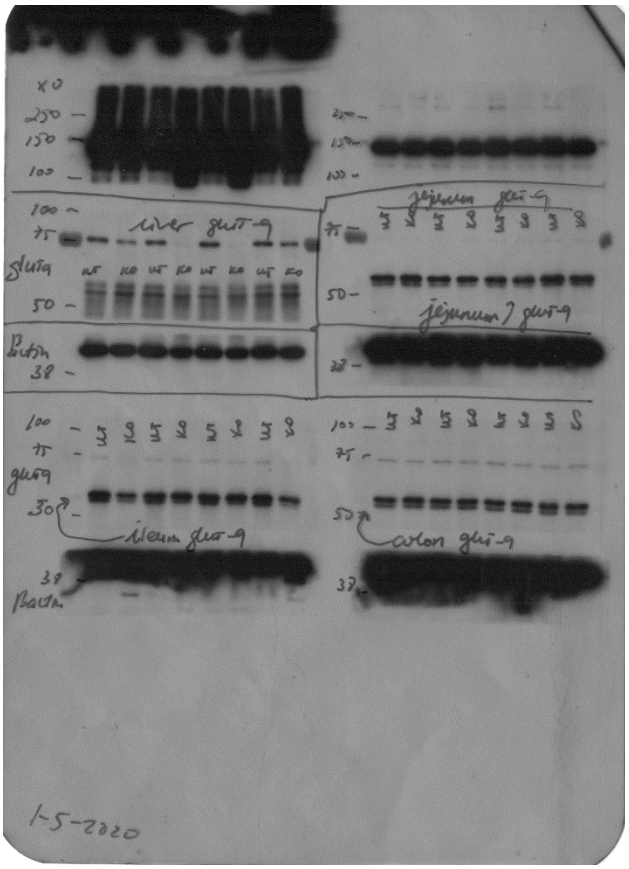
Supplementary Figure S8. Middle right row: β-actin in WT (lanes 1,3,5,7) and *Hfe*$^{-/-}$ (lanes 2,4,6,8) liver. Used in Figures 2D and 3D. The rest not used. Please disregard.



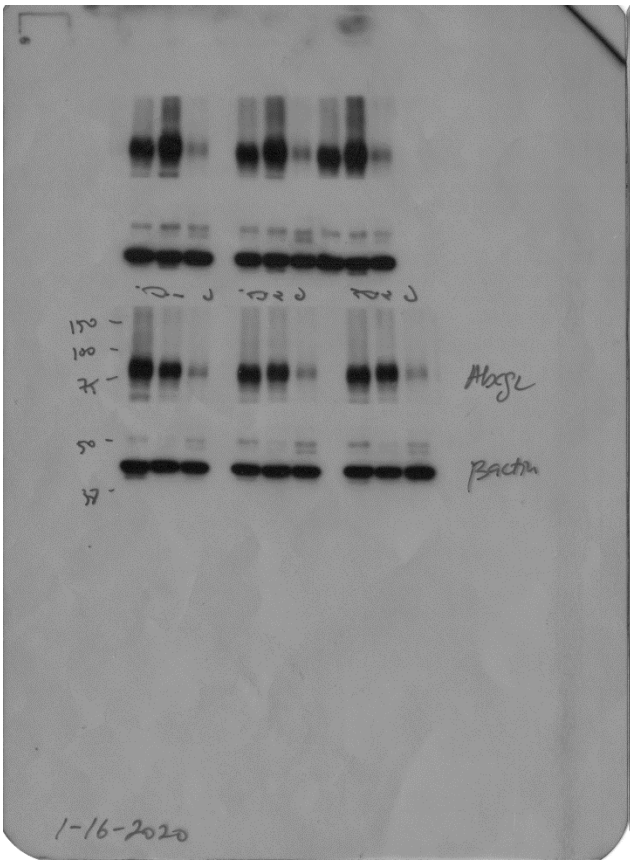
Supplementary Figure S9. Left side, rows from the top: (**1**) XO in WT (lanes 1,3,5,7) and *Hfe*$^{-/-}$ (lanes 2,4,6,8) liver. Higher exposure. (**2**) β-actin in WT (lanes 1,3,5,7) and *Hfe*$^{-/-}$ (lanes 2,4,6,8) liver. Lower exposure; (**3**) β-actin in WT (lanes 1,3,5,7) and *Hfe*$^{-/-}$ (lanes 2,4,6,8) ileum. Used in Figure 3D. Right side, rows from the top: (**1**) XO in WT (lanes 1,3,5,7) and *Hfe*$^{-/-}$ (lanes 2,4,6,8) jejunum; (**2**) β-actin in WT (lanes 1,3,5,7) and *Hfe*$^{-/-}$ (lanes 2,4,6,8) jejunum. Used in Figures 2D and 3D; (**3**) β-actin in WT (lanes 1,3,5,7) and *Hfe*$^{-/-}$ (lanes 2,4,6,8) colon. Used in Figure 3D.



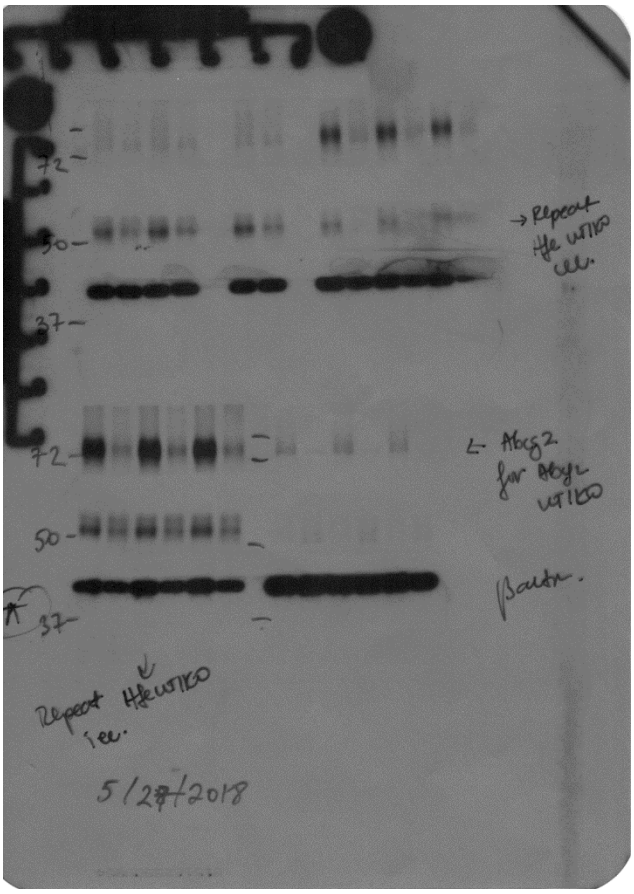
Supplementary Figure S10. Rows from the top: (**1**) XO in WT Liver, Jejunum, Ileum and Colon. Not used. (**2**) Glut9 in WT Liver, Jejunum, Ileum and Colon. Used in Figure 3B. The rest not used. Please disregard.



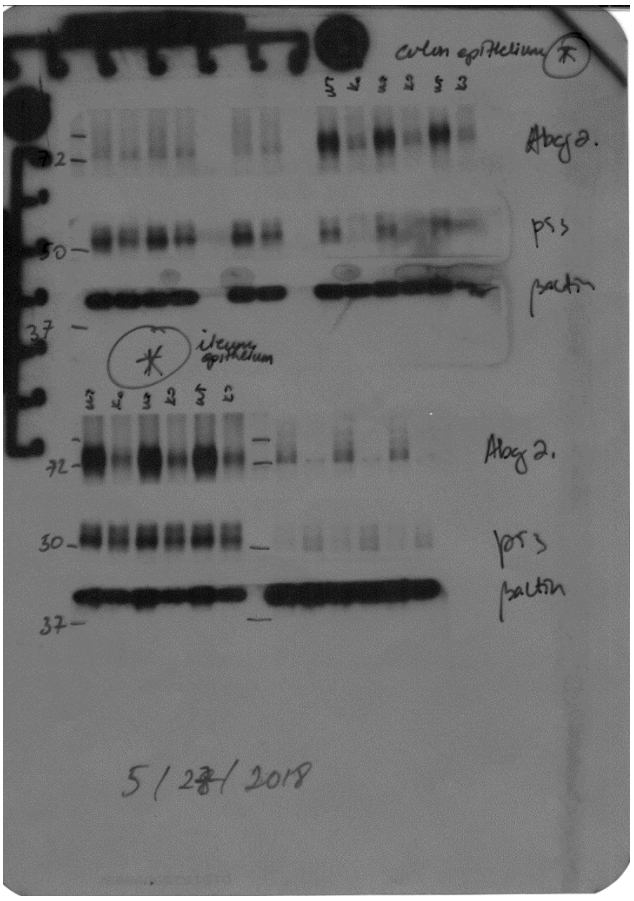
Supplementary Figure S11. Left side, rows from the top: (**1**) Not used, please disregard; (**2**) Glut9 in WT (lanes 1,3,5,7) and *Hfe*$^{-/-}$ (lanes 2,4,6,8) liver. Used in Figure 3D; (**3**) Not used. Please disregard; (**4**) Glut9 in WT (lanes 1,3,5,7) and *Hfe*$^{-/-}$ (lanes 2,4,6,8) ileum. Used in Figure 3D; (**4**) Not used. Please disregard. Right side, rows from the top: (**1**) Not used, please disregard; (**2**) Glut9 in WT (lanes 1,3,5,7) and *Hfe*$^{-/-}$ (lanes 2,4,6,8) jejunum. Used in Figure 3D; (**3**) Not used. Please disregard; (**4**) Glut9 in WT (lanes 1,3,5,7) and *Hfe*$^{-/-}$ (lanes 2,4,6,8) colon. Used in Figure 3D; (**4**) Not used. Please disregard.



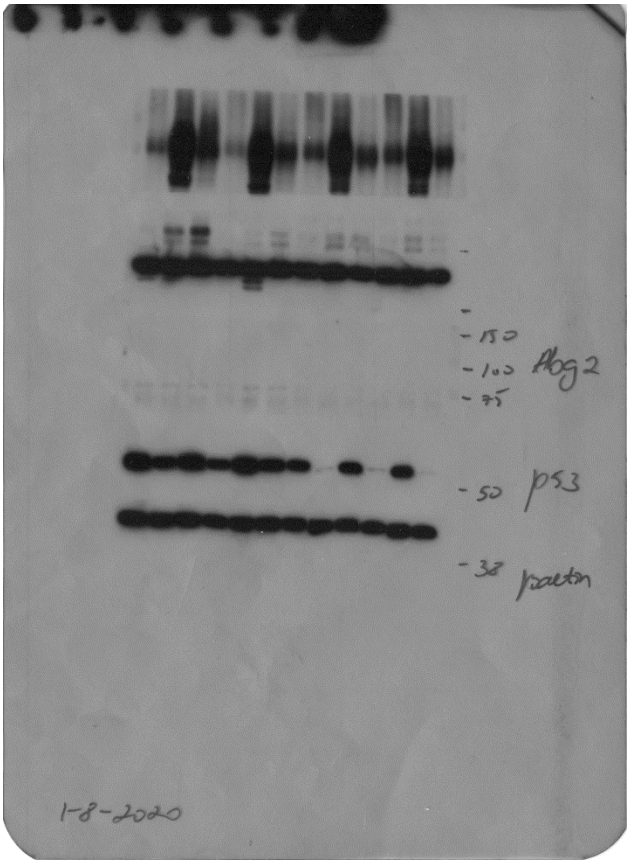
Supplementary Figure S12. Rows from the top: (**1**) and (**2**) Not used. Please disregard; (**3**) Abcg2 in jejunum, ileum and colon epithelium, in triplicates. Used in Figure 4B; (**4**) β-actin in jejunum, ileum and colon epithelium, in triplicates. Used in Figure 4B.



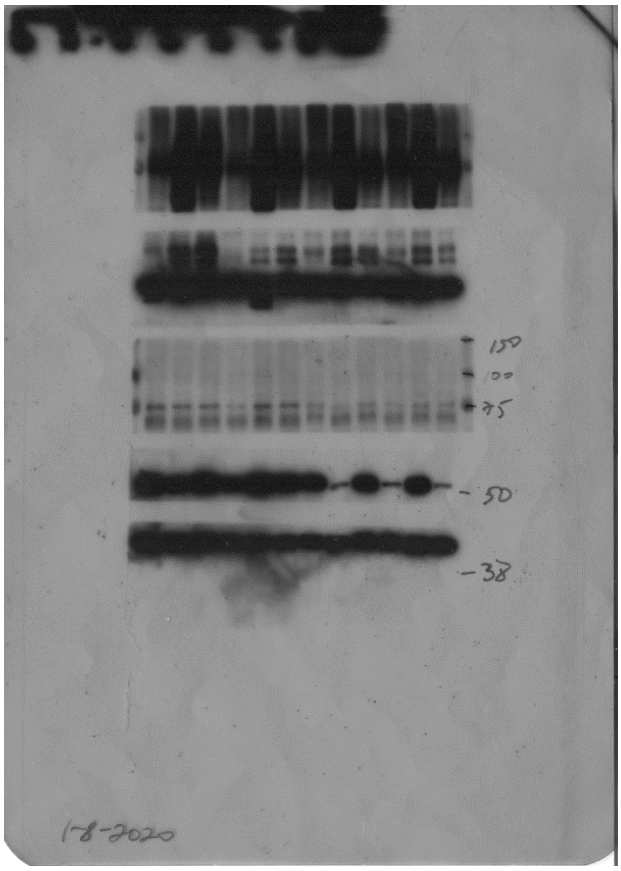
Supplementary Figure S13. Rows from the top: (**1**) Only last 6 lanes used. Abcg2 in WT (lanes 9,11,13) and *Hfe*$^{-/-}$ (lanes 10,12,14) colon epithelium. Used in Figure 5B; (**2**) Only first 7 lanes used (lane 5 is blank). p53 in WT (lanes 1,3,6) and *Hfe*$^{-/-}$ (lanes 2,4,7) colon epithelium. Used in Figure 7C; (**3**) β-actin in WT (lanes 1,3,6,9,11,13) and *Hfe*$^{-/-}$ (lanes 2,4,7,10,12,14) colon epithelium. Used in Figures 5B and 7C; (**4**) Only first 6 lanes used. Abcg2 in WT (lanes 1,3,5) and *Hfe*$^{-/-}$ (lanes 2,4,6) ileum epithelium. Used in Figure 5B; (**5**) Only first 6 lanes used. p53 in WT (lanes 1,3,5) and *Hfe*$^{-/-}$ (lanes 2,4,6) ileum epithelium. Used in Figure 7A; (**6**) Only first 6 lanes used. β-actin in WT (lanes 1,3,5) and *Hfe*$^{-/-}$ (lanes 2,4,6) ileum epithelium. Used in Figures 5B and 7A. Please disregard the rest.



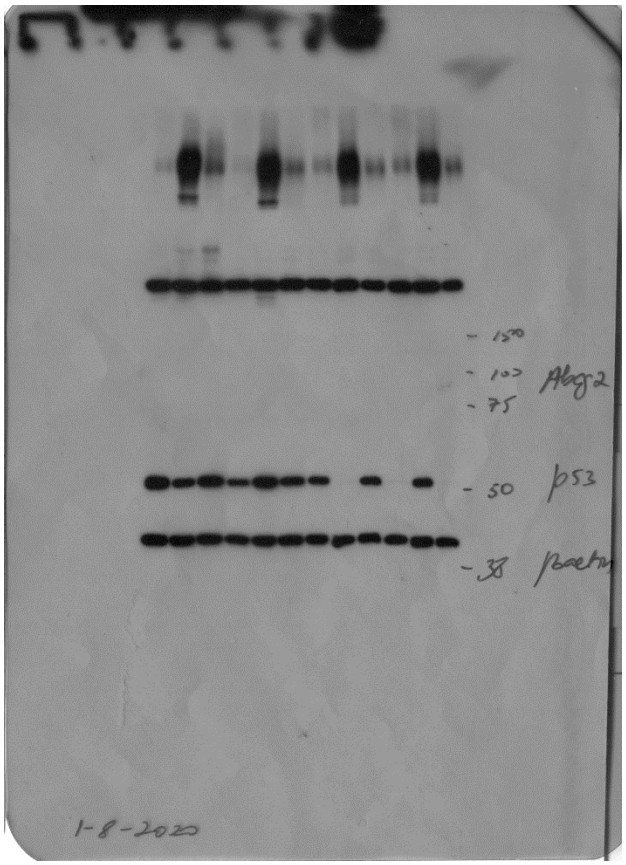
Supplementary Figure S14. Higher exposure of Supplementary Figure S13. Rows from the top: (**1**) Only last 6 lanes used. Abcg2 in WT (lanes 9,11,13) and *Hfe*$^{-/-}$ (lanes 10,12,14) colon epithelium. Used in Figure 5B; (**2**) Only first 7 lanes used (lane 5 is blank). p53 in WT (lanes 1,3,6) and *Hfe*$^{-/-}$ (lanes 2,4,7) colon epithelium. Used in Figure 7C; (**3**) β-actin in WT (lanes 1,3,6,9,11,13) and *Hfe*$^{-/-}$ (lanes 2,4,7,10,12,14) colon epithelium. Used in Figures 5B and 7C; (**4**) Only first 6 lanes used. Abcg2 in WT (lanes 1,3,5) and *Hfe*$^{-/-}$ (lanes 2,4,6) ileum epithelium. Used in Figure 5B; (**5**) Only first 6 lanes used. p53 in WT (lanes 1,3,5) and *Hfe*$^{-/-}$ (lanes 2,4,6) ileum epithelium. Used in Figure 7A; (**6**) Only first 6 lanes used. β-actin in WT (lanes 1,3,5) and *Hfe*$^{-/-}$ (lanes 2,4,6) ileum epithelium. Used in Figures 5B and 7A. Please disregard the rest.



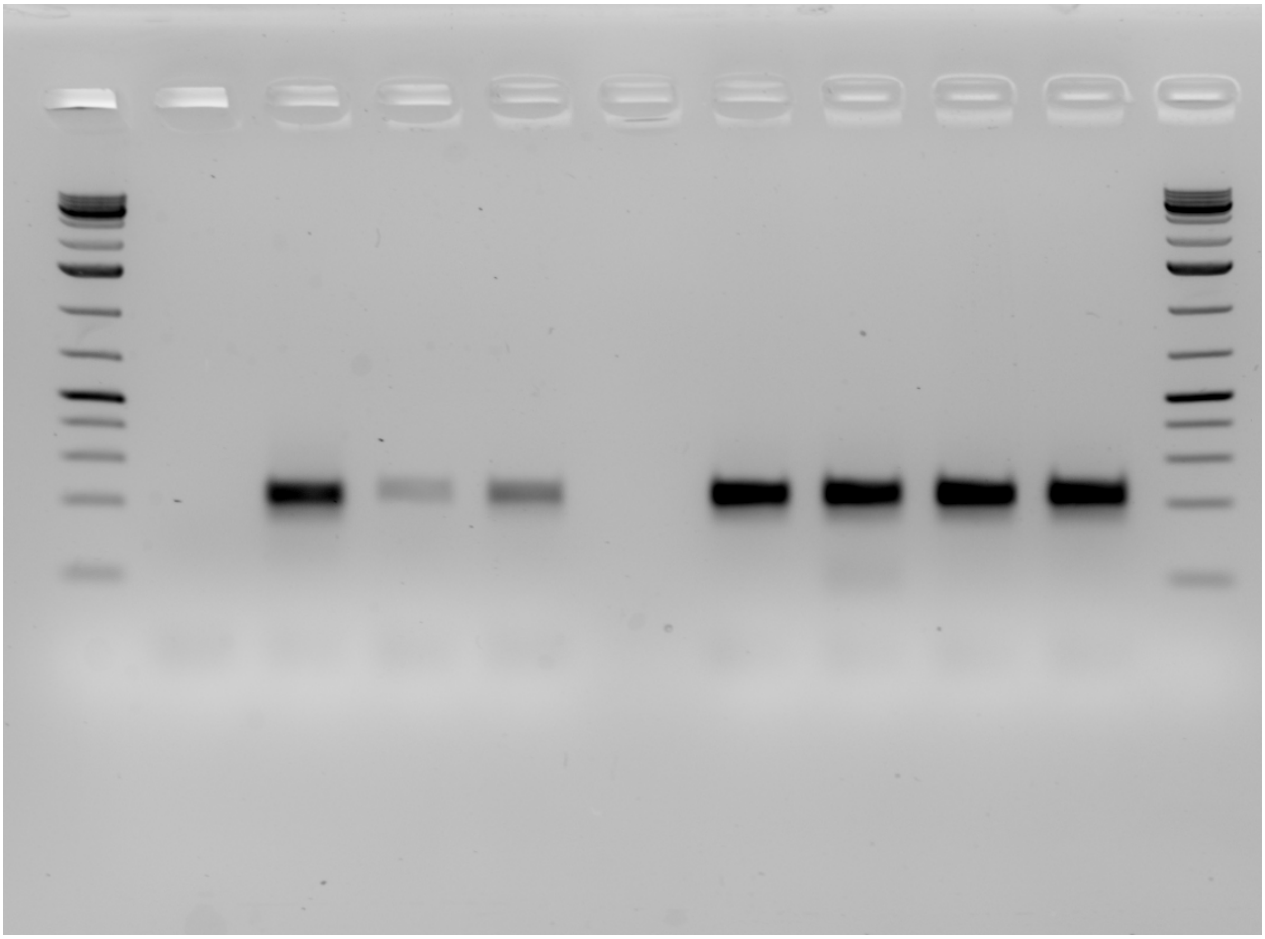
Supplementary Figure S15. Rows from the top: (**1**), (**2**), and (**3**) Not used. Please disregard; (**4**) Only last 6 lanes used. p53 in CCD841 pLKO.1 (lanes 7, 9, and 11) and p53 shRNA (lanes 8, 10, and 12). Used in Figure 6B; (**5**) Not used. Please disregard.



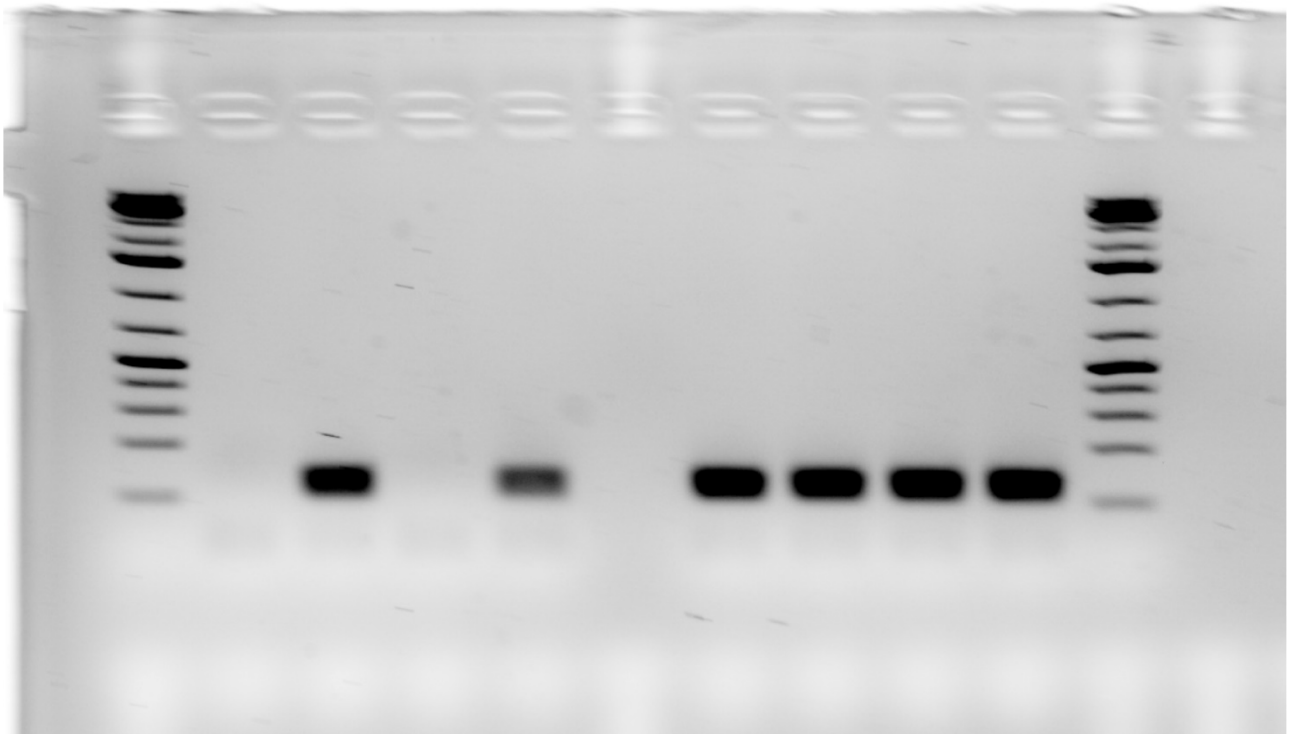
Supplementary Figure S16. Higher exposure of Supplementary Figure S15. Rows from the top: (**1**) and (**2**) Not used. Please disregard; (**3**) Only last 6 lanes used. ABCG2 in CCD841 pLKO.1 (lanes 7, 9, and 11) and p53 shRNA (lanes 8, 10, and 12). Used in Figure 6B; (**4**) and (**5**) Not used. Please disregard.



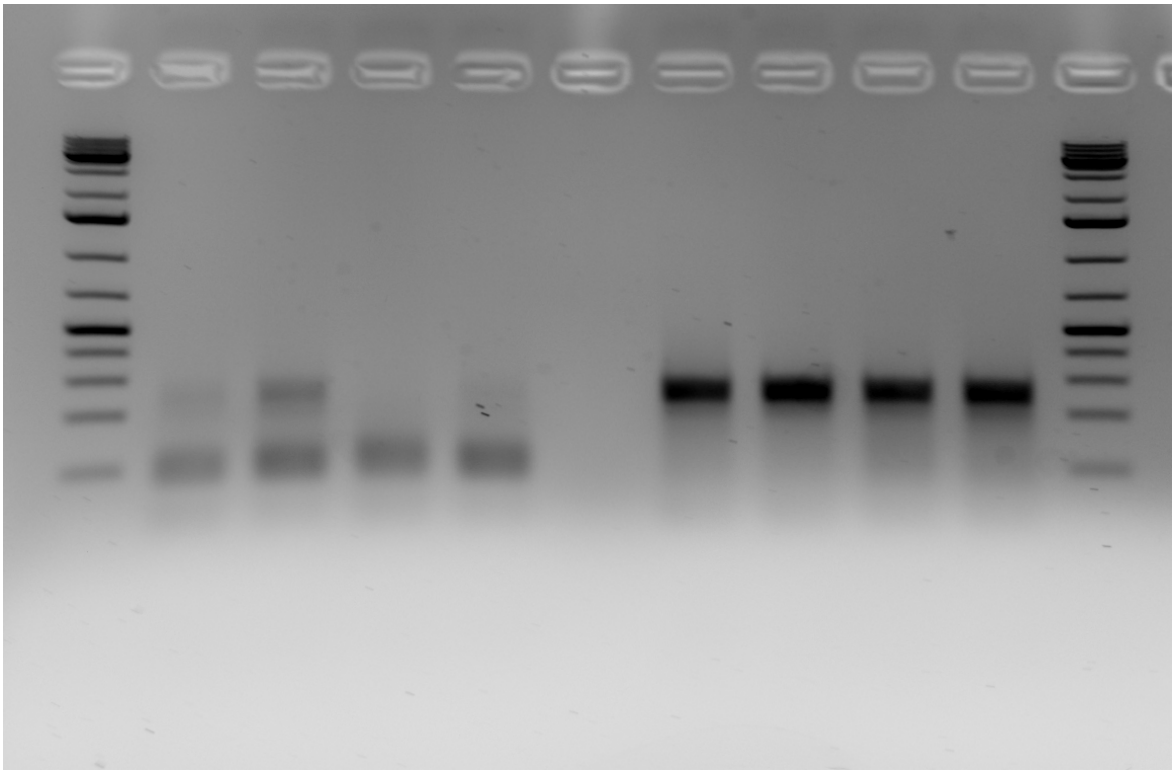
Supplementary Figure S17. Lower exposure of Supplementary Figure S15. Only last row used. Please disregard the rest. (**5**) Only last 6 lanes used. β-actin in CCD841 pLKO.1 (lanes 7, 9, and 11) and p53 shRNA (lanes 8, 10, and 12). Used in Figure 6B.



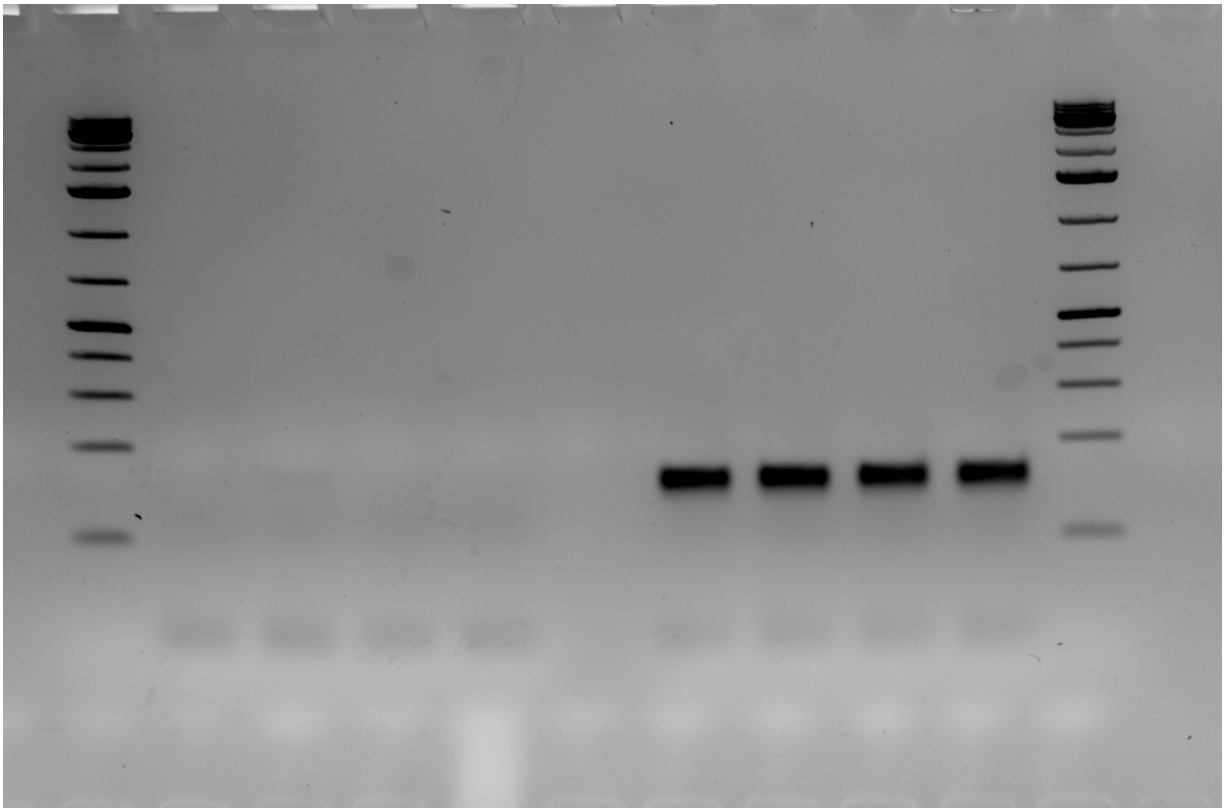
Supplementary Figure S18. Agarose gel for ChIP *ABCG2*. First 4 lanes are pulldown. Last 4 lanes are the input. Lanes 1,3,6,8 are the IgG. Lanes 2,4,7,9 are p53 IP. Lanes 1,2,6,7 are CCD841 pLKO.1. Lanes 3,4,8,9 are CCD841 p53 shRNA. Used in Figure 6B.



Supplementary Figure S19. Agarose gel of ChIP *p21*. First 4 lanes are pulldown. Last 4 lanes are the input. Lanes 1,3,6,8 are the IgG. Lanes 2,4,7,9 are p53 IP. Lanes 1,2,6,7 are CCD841 pLKO.1. Lanes 3,4,8,9 are CCD841 p53 shRNA. Used in Figure 6B.



Supplementary Figure S20. Agarose gel of ChIP *GADD45A*. First 4 lanes are pulldown. Last 4 lanes are the input. Lanes 1,3,6,8 are the IgG. Lanes 2,4,7,9 are p53 IP. Lanes 1,2,6,7 are CCD841 pLKO.1. Lanes 3,4,8,9 are CCD841 p53 shRNA. Used in Figure 6B.



Supplementary Figure S21. Agarose gel of ChIP *GAPDH.* First 4 lanes are pulldown. Last 4 lanes are the input. Lanes 1,3,6,8 are the IgG. Lanes 2,4,7,9 are p53 IP. Lanes 1,2,6,7 are CCD841 pLKO.1. Lanes 3,4,8,9 are CCD841 p53 shRNA. Used in Figure 6B.