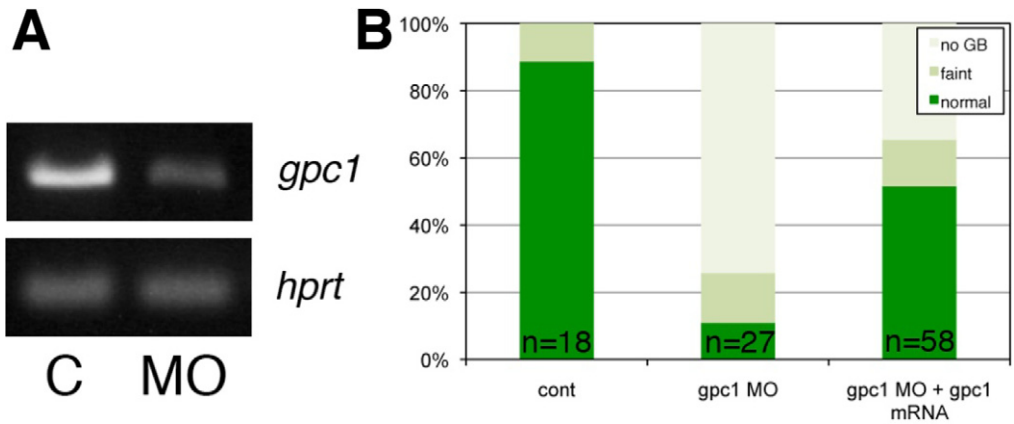
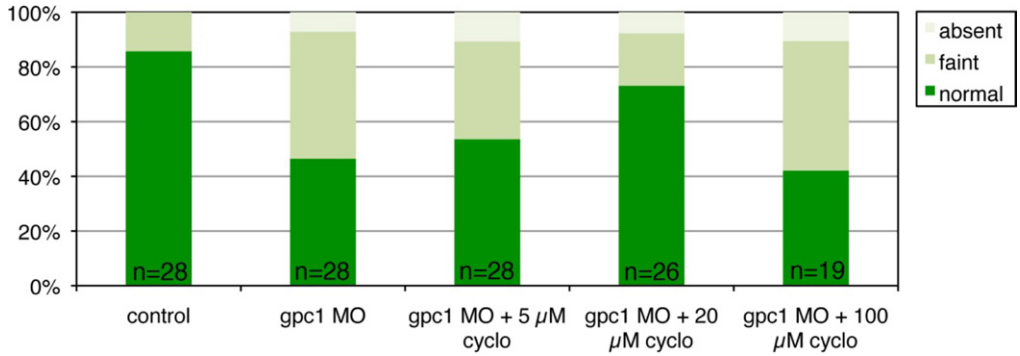
Supplementary Table 1. Summary of CNV Associations With BA.

CNV region deletions	# SNPs	Cases	Controls	Two-tailed	Odds ratio
chr2:241035025-241051687	4	6	4	4.40E-10	138.6545
chr7:87702685-87705881	2	4	0	1.79E-08	NA
chr5:45990384-45996650	2	7	23	3.82E-08	28.5467
chr7:7623829-7625463	2	3	0	1.58E-06	NA
chr3:84779229-84785701	3	3	0	1.58E-06	NA
chr4:38135015-38142051	3	3	4	5.36E-05	65.74138
chr12:123451202-123456184	2	2	0	0.00013813	NA

NOTE. Listed are the top 7 regions noted in our genetic study. The table shows the copy number variation region (CNVR) deletions based on human genome v18 coordinates, the number of SNPs in the regions (# SNPs), number of cases and controls, the *P* value and the odds ratio for the copy number loss in the region of case vs control. Note that the odds ratio cannot be calculated for regions with no copy number loss in controls.



Supplementary Figure 1. Documentation of *gpc1* knockdown. (*A*) PCR showing decrease in the exon 3-4 product in larvae injected with a *gpc1* MO targeting the splice acceptor site of exon 4. Note that expression of *hprt* is equivalent between control (C) and MO conditions. (*B*) Quantification of PED6 uptake in control (cont) larvae, larvae injected with *gpc1* MO, and larvae coinjected with *gpc1* MO and *gpc1* mRNA. Note that injection of *gpc1* mRNA reverses the effect of the *gpc1* MO, demonstrated specificity of the MO. $P < .0001$ for *gpc1* MO alone vs *gpc1* MO and *gpc1* mRNA by chi-square.

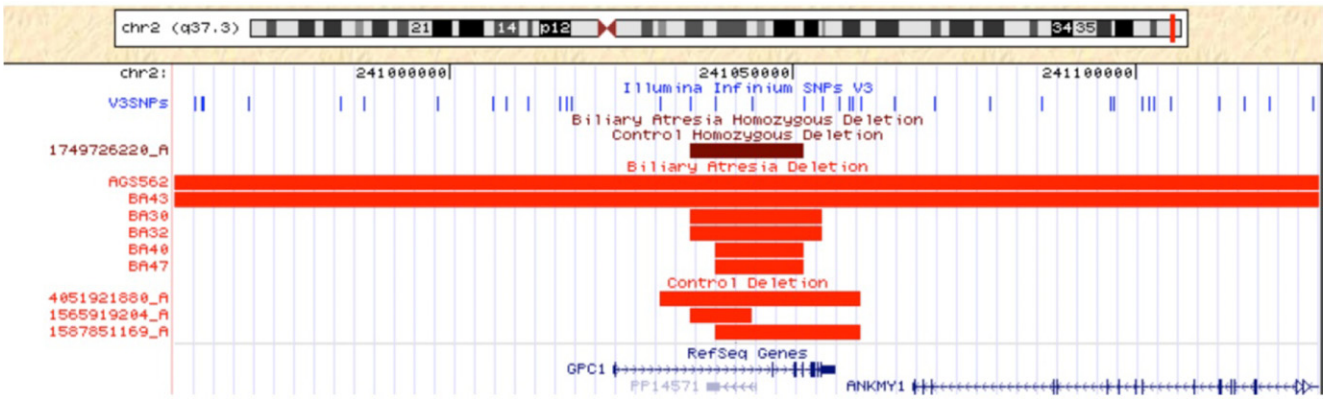


Supplementary Figure 2. Dose response of cyclopamine rescue of *gpc1* knockdown. Gallbladder PED6 uptake, shown as a percentage of the total number in each condition, with the number per condition given at the bottom of the bar. Note that the percentage of larvae with normal gallbladder intensity increases from *gpc1* MO alone through 20 μM, but that this percentage decreases with 100 μM cyclopamine. Note also that the total number of larvae is lower with the highest concentration of cyclopamine, likely representing larval death at this dose.

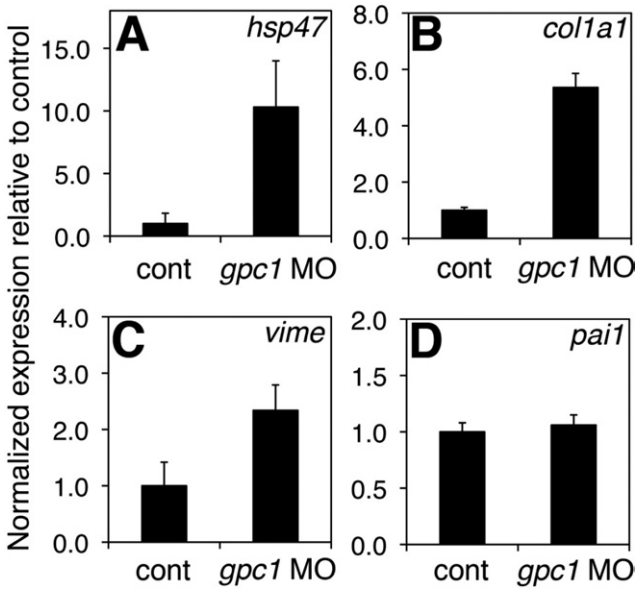
Supplementary Table 2. Primer and Morpholinos Used for In Situ Hybridization, Knockdown, and QPCR

Name	Sequence
***gpc* riboprobe primers**	
gpc1-F1	CAACCACTGGTGACAAATGC
gpc1T3-B1	ATTGGCATTAACCCTCACTAAAGGGAACGCAACCAAATGAATCACA
gpc2-F1	CTGCTCTGCTCTGCTGTCTG
gpc2T3-B1	GAATTCATTAACCCTCACTAAAGGGAAGCTGTTCCACTCGCTGTTT
gpc3-F1	AGAATGCTGCCCTCTTTCAA
gpc3T3-B1	GAATTCATTAACCCTCACTAAAGGGACAAAGCTTCTCCGAGACCAC
gpc4-F1	GCTGTTGGACAATGCAGAGA
gpc4T3-B1	GAATTCATTAACCCTCACTAAAGGGAGTCAACCTCCACGTCTGGAT
gpc5-F1	TAAACACCAGGGTCCCACAT
gpc5T3-B1	GAATTCATTAACCCTCACTAAAGGGAAGCCCATAAACTCCCGTCTT
gpc6-F1	AGCGAGGAGCTCAGAGACAC
gpc6T3-B1	GAATTCATTAACCCTCACTAAAGGGAGTGCTCGAGGTGTGTGTGTT
***gpc1* morpholinos**	
gpc1-5′	GCGCGACCGCTGTCAGATCCATTGT
gpc1-IE4	TGGGACCTGTGGAAAGAGTGACCAT
***gpc1* MO documentation**	
gpc1ex3-F1	GCAGGAGTGTTTCGTGACCT
gpc1ex4-B1	GGTTTGACTGATCCCAGACC
QPCR primers	
gli2a-F1	AAAAACAGGGCGGGACTACT
gli2a-B1	ATGCTGGGTTGGAGGTACAG
ptch1-F1	GGTTACCATGGATGGCTTTG
ptch1-B1	TCAGCATCAAAAGTGGCTTG
foxl1-F1	CAAAAACCCCCGTACAGCTA
foxl1-B1	GAGAGGTTATGGCGGATTGA
znf697-F1	TCCCAACAAGAGCACTTTGA
znf697-B1	GGGATGCTTTTTGGAGTGAA
ccnd1-F1	CTGTGCGACAGACGTCAACT
ccnd1-B1	CTGACACGATCGCAGACAGT

NOTE. The reverse *gpc* primers contain a T3 sequence for direct synthesis of riboprobe in the antisense direction.



Supplementary Figure 3. *GPC1* deletions in BA and control patients. Map of the region on 2q37.3 from the UCSC genome browser (hg v.18), showing 4 control patients with deletions over *GPC1* (out of 5088) and 6 BA patients out of 61 with deletions in the same region. This is our most significant signal ($P = 4.4 \times 10^{-10}$) with an odds ratio of 138.7.



Supplementary Figure 4. Elevation of fibrogenic genes in *gpc1* morphants. Quantitative PCR of genes important in fibrogenesis and epithelial-mesenchymal transition (EMT) on cDNA derived from livers from control (cont) and *gpc1* morpholino-injected 5 dpf larva (*gpc1* MO). The increases in *hsp47* (*A*), *col1a1* (*B*), and *vime* (*C*) are statistically significant ($P \leq .05$). There is no change in expression of the TGFb target gene *pai1* (*D*). Primer sequences for *hsp47*, *col1a1*, and *vime* have been reported previously (EauClaire et al, 2012).[52] The primer sequences for *pai1* are: pai1-F1 CCA TCT GGA GTG CTG AGT GA, pai1-B1 GTC ATA GTC CAC GCC ATC CT.