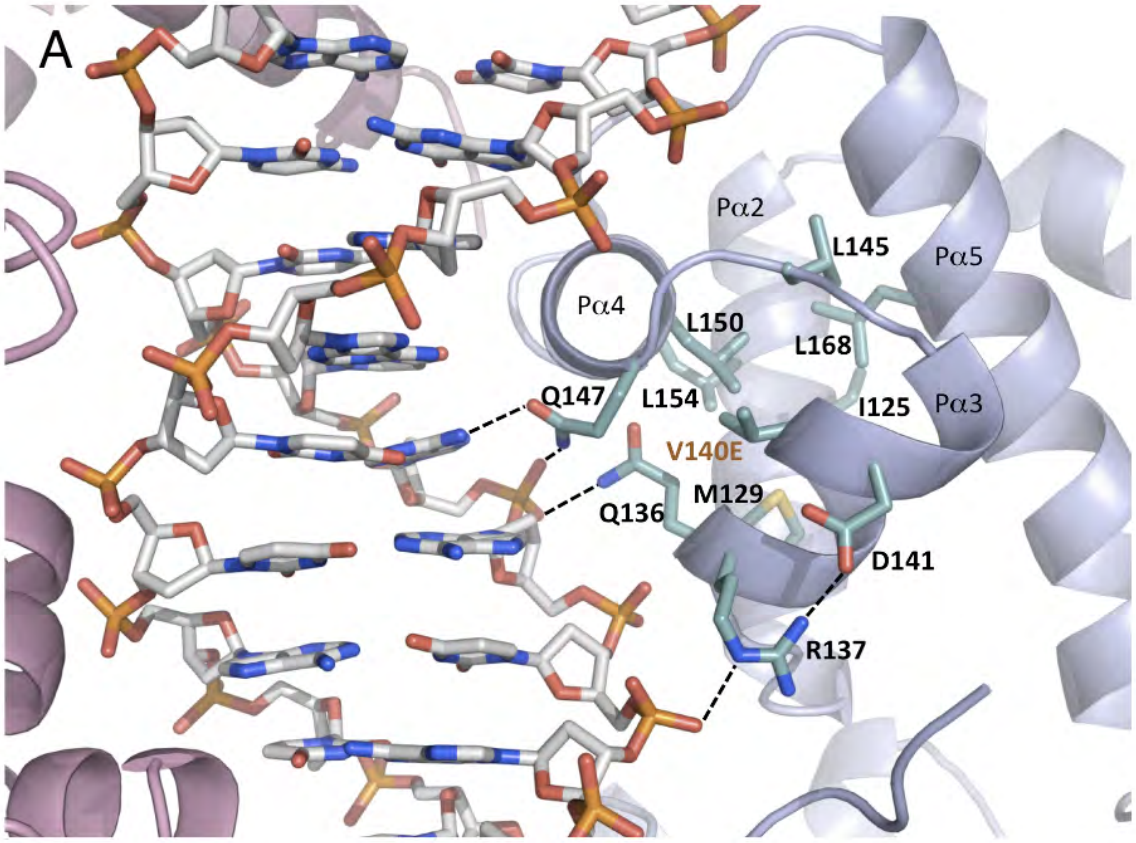


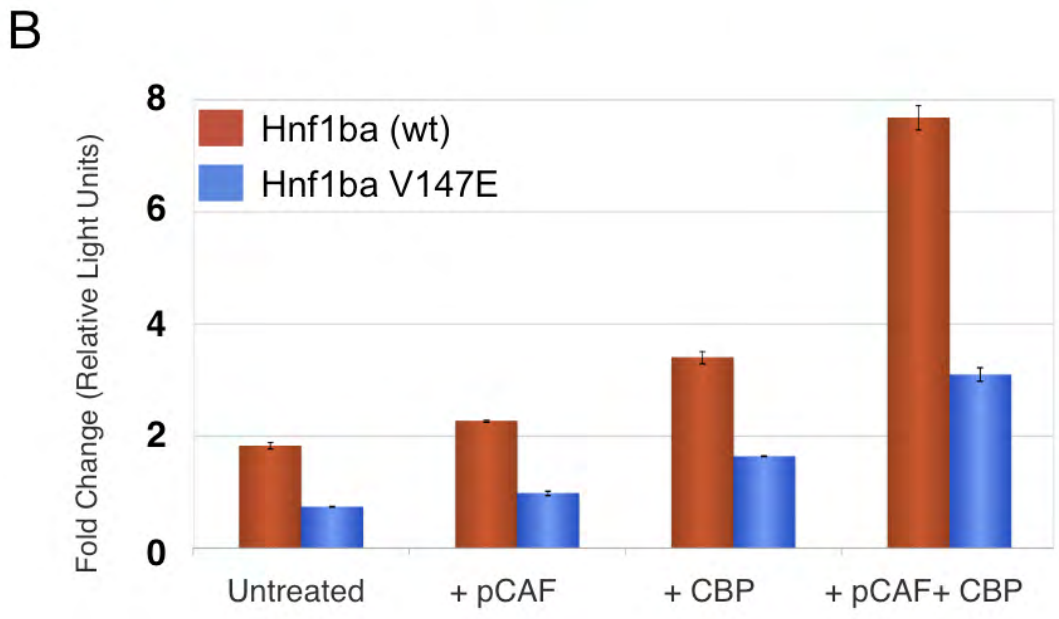


**Fig. S1. The *hnf1ba*$^{s430}$ mutation attenuates protein function.** (**A**) A detailed structural view of V140 and the surrounding residues of human HNF1B (PDB access code 2H8R). The functional/structural key residues and the target sequence-containing DNA are shown as a ball and stick model. Broken lines indicate hydrogen bonds or ionic interactions. HNF1B is made of two DNA-binding domains, POU-homeo and POU-specific with V140 found in the POU-specific domain. Substitution of a highly charged group at this analogous position, as occurs in the zebrafish *hnf1ba*$^{s430-/-}$ mutant (V147E), is predicted to perturb the hydrophobic core leading to structural and functional defects. (**B**) Summary of luciferase transactivation assay using Min6 cells transfected with a multimerized HNF1 reporter B28-Luc (300 ng) in the presence of pcDNA3-Myc-Hnf1ba (wild type) or V147E Hnf1ba (75 ng), along with control or vectors coding pCMV-PCAF or RSV-CBP (50 ng each), as indicated. Each column represents induced fold-activation of the reporter by wild-type Hnf1ba (red) or V147E Hnf1ba (blue) relative to activity measured under identical conditions using pcDNA3 control. V147E Hnf1ba protein less efficiently activates transcription compared with wild-type Hnf1ba ($P<0.001$), but can still be partially enhanced by co-activators pCAF and CBP, suggesting that the V147E Hnf1ba protein function is reduced but not lost.

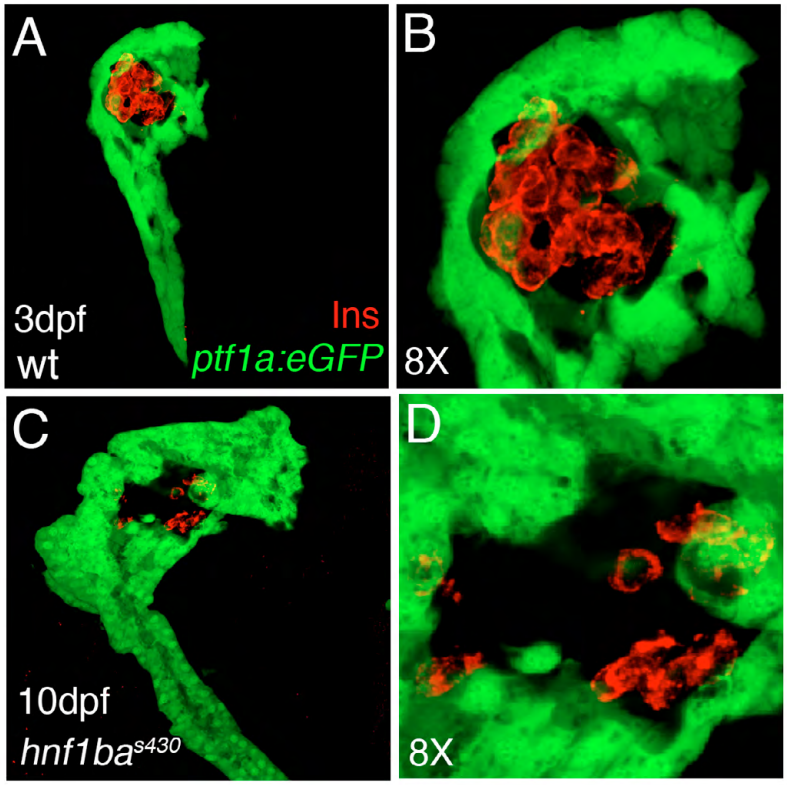


**Fig. S2. Severe example of β-cell number reduction and disorganization in a *hnf1ba*$^{s430}$ mutant with mild exocrine hypoplasia.** (**A-D**) Fluorescent confocal microscopy of *Tg(ptf1a:eGFP)*$^{jh1}$ (green) 3 dpf wild-type (A,B) and 10 dpf *hnf1b*$^{s430}$ mutant (C,D) pancreas stained for insulin to mark β-cells (red). 3D rendering showing an *hnf1ba*$^{s430}$ mutant at 10 dpf with a larger exocrine pancreas (C) than that of a wild type at 3 dpf (A). (B,D) Magnification (8×) of A and C showing that β-cells (red) remain both reduced and disorganized in *hnf1ba*$^{s430}$ mutants at 10 dpf.

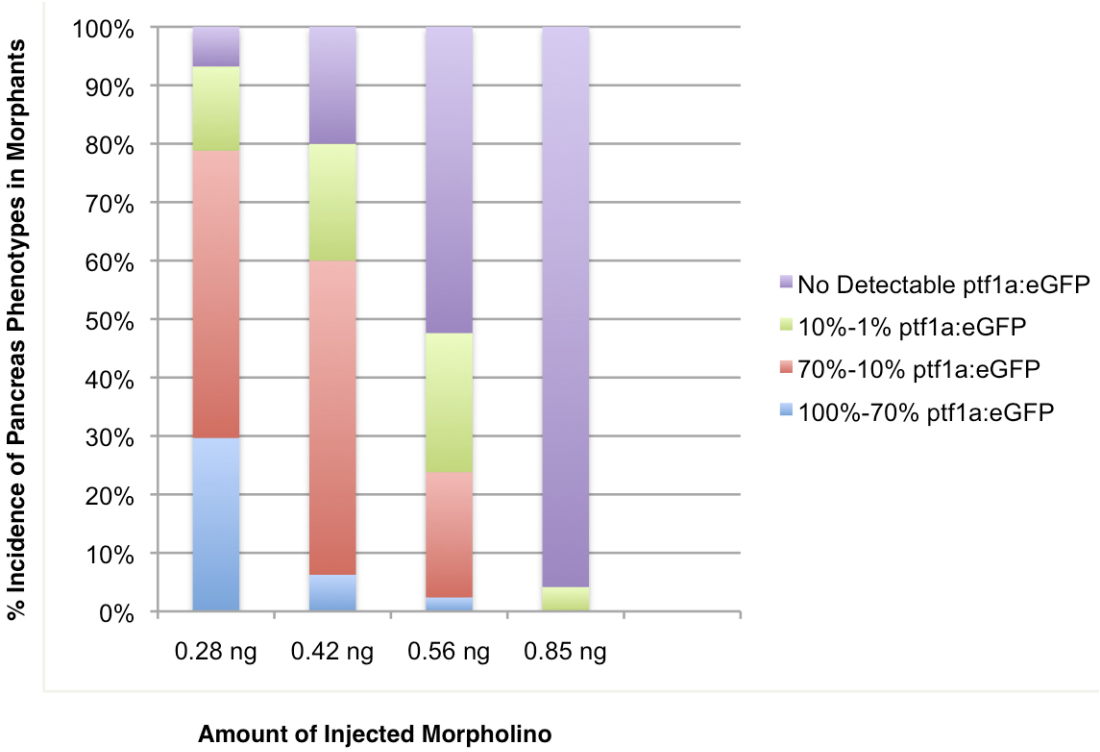


**Fig. S3. Dose-dependent severity of pancreas hypoplasia resulting from *hnf1ba* knock-down via morpholino.** Distribution of pancreas hypoplasia severity caused by antisense morpholino knock-down of Hnf1ba translation, as assessed by pancreatic *ptf1a:*eGFP expression. Injected embryos were scored at 80 hpf based on size of *ptf1a:*eGFP-positive foregut tissue relative to uninjected clutchmates. Higher doses of Hnf1ba morpholino produce a higher incidence of more severe pancreas hypoplasia and agenesis defects (n>48 for each dosage).

**Table S1. Quantification of hepatopancreas phenotypes in *wnt2bb*$^{s404}$ and *hnf1ba*$^{s430}$ mutants**

| Genotype | % with no hepatocytes | | % with no exocrine cells | % with no hepatocytes or exocrine cells | % with no hepatocytes, exocrine cells, or extra hp ducts |
|---|---|---|---|---|---|
| | 80 hpf | 120 hpf | 120 hpf | 80 hpf | 80 hpf |
| *wnt2bb*$^{s404}$ | 11 (46/422) | 0 (n>200) | 0 (>200) | 0 (>200) | 0 (>200) |
| *hnf1ba*$^{s430}$ | 0 (n>200) | 0 (n>200) | 8.4 (34/406) | 0 (>200) | 0 (>200) |
| *wnt2bb*$^{s404}$; *hnf1ba*$^{s430}$ | 80 (44/55) | 54 49/91 | 34 (31/91) | 24 (22/91) | 6 (3/48) |

The incidence of hepatopancreas agenesis phenotypes in *wnt2bb*$^{s404}$, *hnf1ba*$^{s430}$ and *wnt2bb*$^{s404}$*; hnf1ba*$^{s430}$ double mutants at 80 and 120 hours post fertilization (hpf). Presence of hepatocytes based on *lfabp:dsRed* expression; presence of exocrine cells based on *ptf1a:eGFP* expression; presence of duct cells based on 2F11 labeling.