A

	Score Category			
	1	2	3	4
Looping	Heart looping normal	Atrium overlaps ventricle by less than 50% of ventricle	Atrium and ventricle do not overlap	Heart is taut and string-like
Atrial Contraction	Atrium contracts normally	Atrial contraction slow or paristaltic	Atrium near asystolic	Atrium asystolic
Atrial Morphogenesis	Atrium normally shaped	Atrium is bulbous or decreased in size	Atrium is noticeably large and round or small and taut	Atrium appears collapsed
Ventricular Contraction	Ventricle contracts normally	Ventricular contraction slow or paristaltic	Ventricle near asystolic	Ventricle asystolic
Ventricular Morphogenesis	Ventricle normally shaped	Ventricle is bulbous or decreased in size	Ventricle is noticeably large and round or small and taut	Ventricle appears collapsed

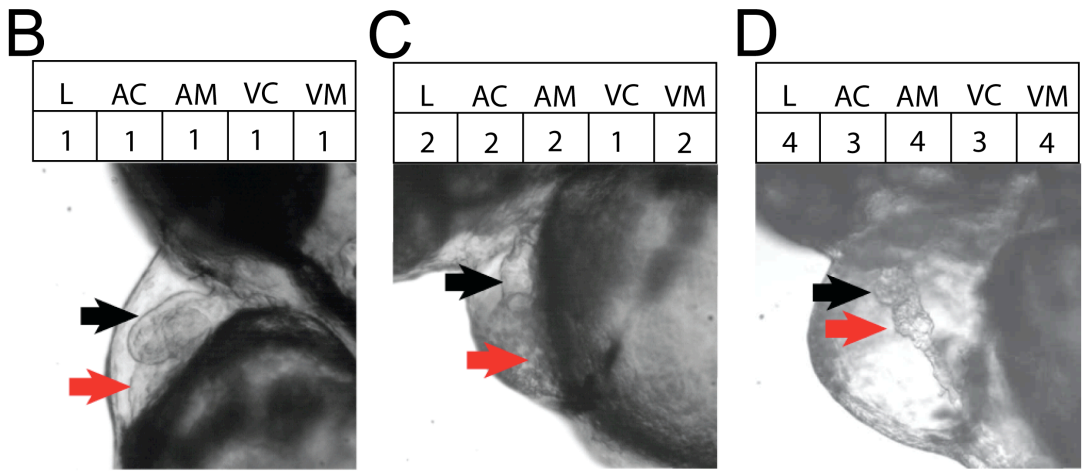


Figure S1 – The five-category score of heart function used to identify differences in morphology and heart conduction. Numerical scores ranging from 1-4 (with 1 being nearest wild type) were assigned to 5 parameters of cardiovascular function from anonymized heart videos. Criteria for assigning these scores are outlined in **A**. Frames from analyzed video files depict hearts scoring progressively higher for all 5 parameters (**B-D**). Specifically: **B** is phenotypically normal, while **C** shows abnormal looping and a minor defect in both atrial and ventricular morphogenesis, and **D** depicts severe abnormalities in looping, conduction, and morphology. Red and black arrows show atria and ventricles, respectively.

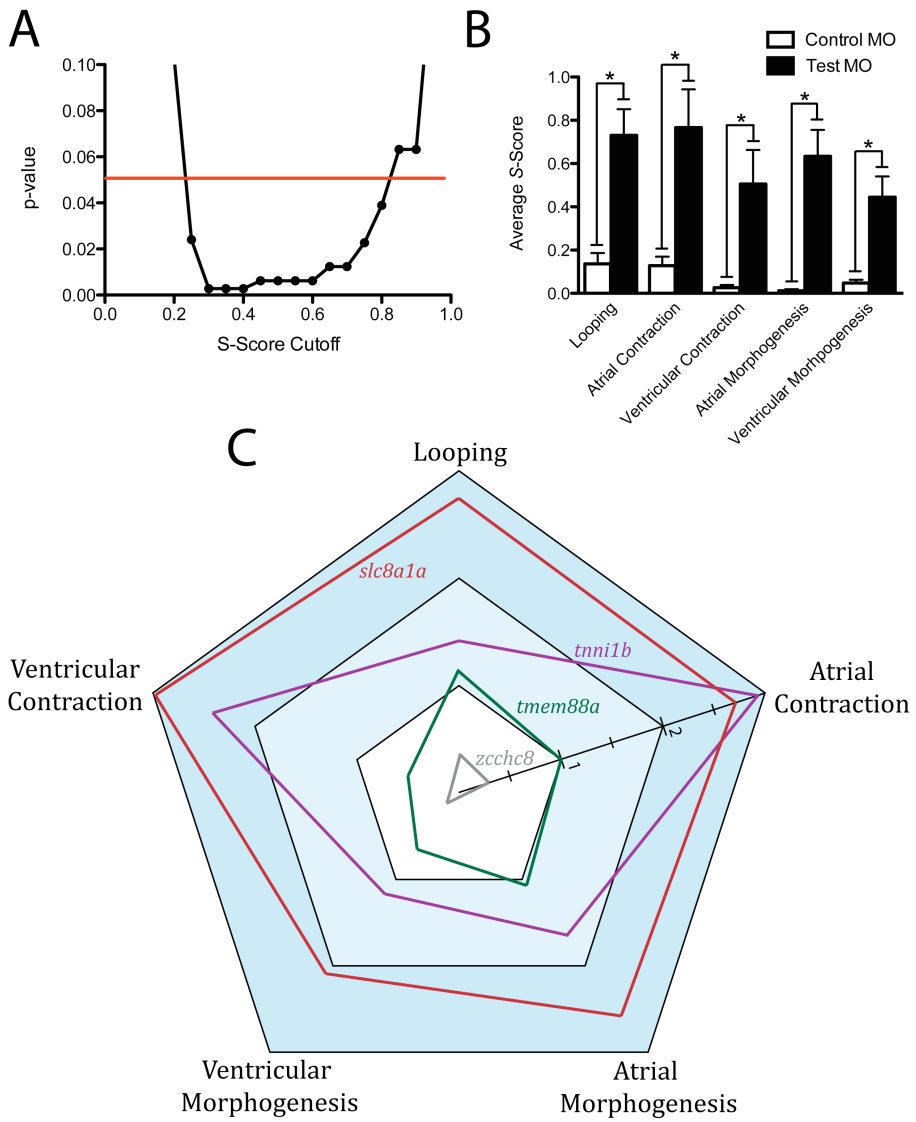


Figure S2 – Categorical scores differentiate test genes from controls. Phenotypes scored following injection of morpholinos targeting high-scoring (test) genes are significantly differentiated from negative control morpholino injections across a wide range of score cutoffs (**A**, red line indicates the p = 0.05 threshold), with scores for all 5 parameters significantly higher for test morpholinos than for controls (**B**). Differences in the 5-parameter scores assigned to each gene become obvious when displayed graphically (**C**; grade of blue coloring indicates severity of defect). The outermost (red) line represents a positive control morpholino targeting *slc8a1a*, which substantially affected all 5 quantified parameters of cardiovascular function. Alternately, *zcchc8* (grey), the highest-scoring negative control gene, showed no substantial phenotypic defects in any parameter upon knockdown. Test gene *tmem88a* (green) showed consistently more moderate defects in looping, atrial morphogenesis, and atrial contraction upon knockdown, while *tnni1b* (purple) resulted in near-complete atrial and ventricular asystole as well as frequent looping defects and consequent alterations in morphology.

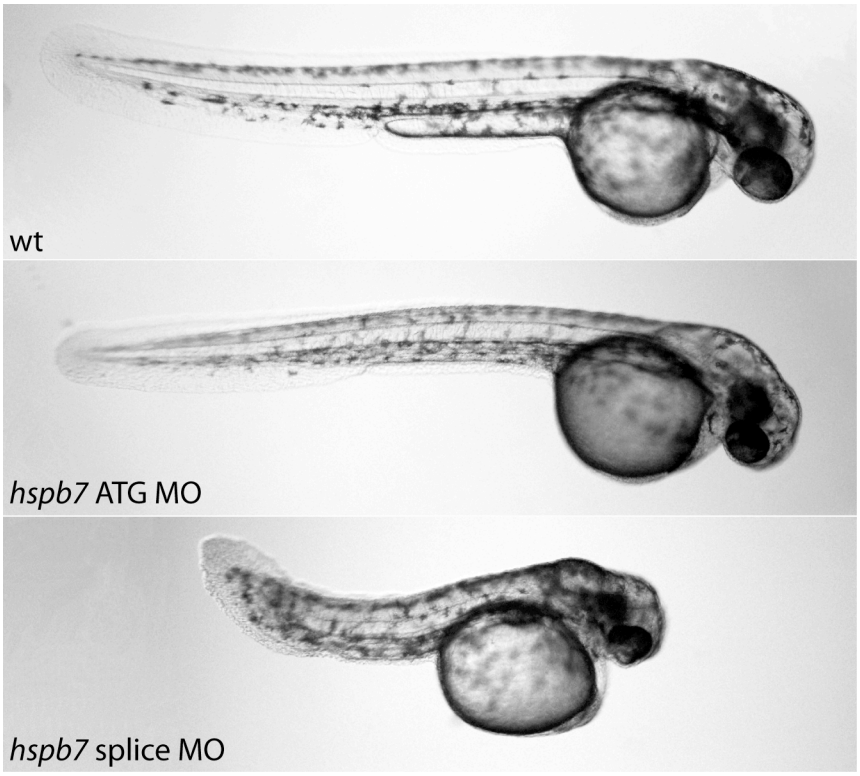


Figure S3 – *hspb7* morpholino injection causes cardiac and tail truncation phenotypes. Compared to wild-type controls at 48hpf (top panel), *hpsb7* ATG (middle panel) and splice blocking (lower panel) morpholinos caused a reduction in cardiac output. In addition to the cardiac phenotype, the ATG morpholino caused an apparent thinning of the musculature in the tail, while the splice morpholino caused tail truncation.

Movie 1. Wild-type zebrafish embryo. All videos were taken at 48 hpf using standard light microscopy (see Methods). Videos were originally taken at 250 frames per second (~4 seconds long, 1088 frames total), but are slowed here to 30 frames per second for ease of phenotype visualization. Videos are also compressed and shortened to allow ease of download. Full-length, uncompressed videos are available upon request.
Movie 2. Knockdown of *tnni1b* (ATG morpholino)
Movie 3. Knockdown of *tnni1b* (splice morpholino)
Movie 4. Knockdown of *nppa* (ATG morpholino 1)

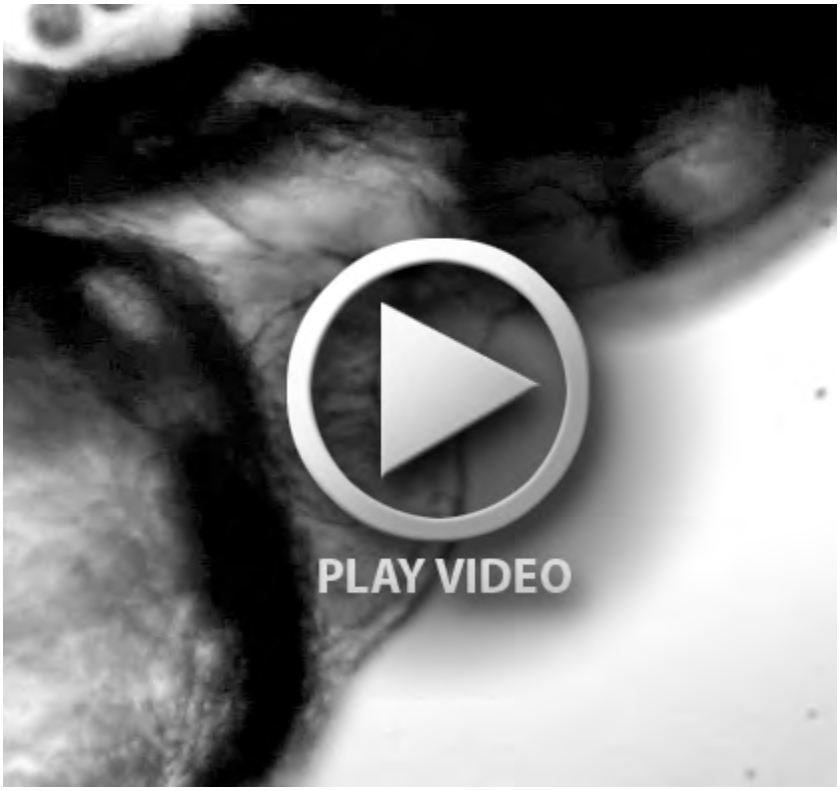
Table S1: List of gene features used for each learner, with feature importance measured as root mean square error (RMSE) introduced by removing the given feature. For GBA, features were binarized based on specific qualifiers. For example, having a Pearson's correlation coefficient of greater than 0.7 in a given expression dataset was included as a single feature for gene pairs. The 'GBA' worksheet lists all features in descending order by RMSE, along with the qualifier used. The 'GBP' worksheet is an anatomical term by feature matrix, with each element of this matrix corresponding to the RMSE for that feature, in that term's prediction.

Table S2: Evaluation of each of the 388 phenotype predictors. Please note that although all terms are included here, highly specific (*i.e.* less than 7 positive training examples), and broadly defined terms were excluded from further analysis due to variability in performance (indicated in the 'Removed' column). Metrics included are area under the receiver operating characteristic curve (ROC-AUC), precision at 20% recall (p@20r), and precision at 20% recall over prior (p@20r over prior).

Table S3: Spreadsheet containing all gene-anatomical term associations scoring above an 80% precision cutoff as estimated independently for each term. Each row indicates an individual gene-phenotype association prediction and the assigned precision score as estimated through cross validation.

Table S4: Description of all morpholino sequences designed for this study. Targeted genes are divided into test (high-scoring), confirmation (second morpholino screened for a given gene), negative control (low-scoring), or positive control (*slc8a1a*). Morpholino target type, whether transcription start site (ATG) or exon/intron or intron/exon boundary (Splice Blocking) is also indicated. Table also indicates gross morphological phenotypes observable at the indicated dose.

Table S5: Cardiac output (CO) for all morpholino injections. These injections were performed as co-injections with a morpholino targeting *p53* and compared against *p53* morpholino injection alone. Red coloring indicates a significant reduction in CO. CO is reported as nL/min.



Movie 1.

Movie 2.

Movie 3.

Movie 4.

Table S1.

Download Table S1

Table S2.

Download Table S2

Table S3.

Download Table S3

Table S4.

Download Table S4

Table S5.

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