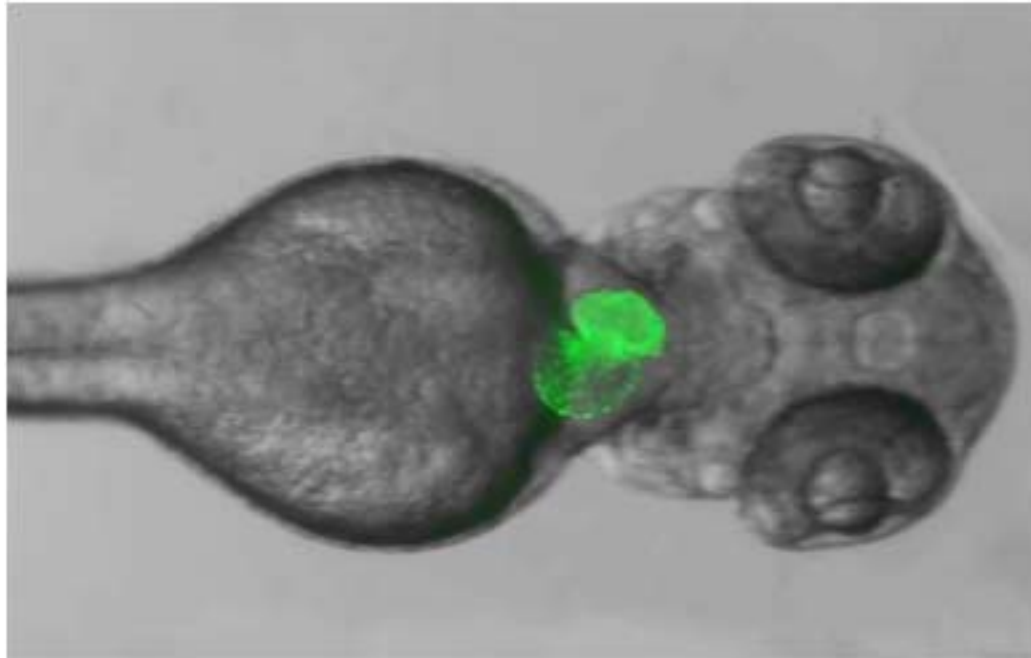


Genome-Wide Discovery Of Human Heart Enhancers



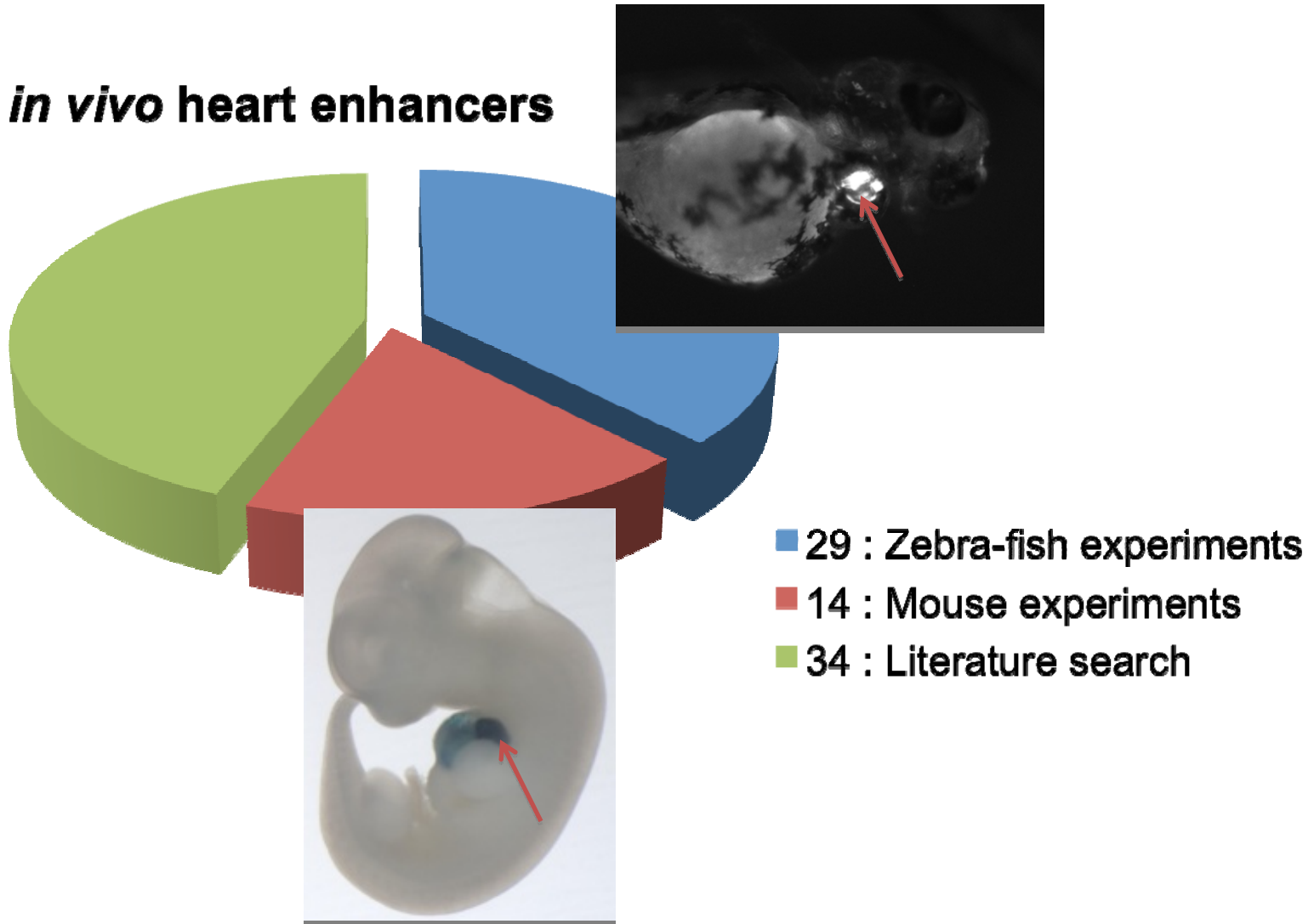
Ivan Ovcharenko



Computational Biology Branch, National Center for Biotechnology Information,
NLM, National Institutes of Health, Bethesda, MD, USA

Large Training Set of *in Vivo* Heart Enhancers

77 *in vivo* heart enhancers



De novo motif discovery

| Name | Logo | Top two matches Motif p-val | fraction of sequences with ≥ 1 match |
|------|------|-----------------------------------|--|
| A | | LMO2 2.6×10^{-8} | |
| | | GATA2 4.7×10^{-8} | |
| B | | MEF2 5.0×10^{-8} | |
| | | aMEF2 8.2×10^{-5} | |
| C | | ETS 1.6×10^{-4} | |
| | | PRDM1 5.9×10^{-4} | |
| D | | ETS 8.3×10^{-7} | |
| | | GATA4 3.2×10^{-4} | |
| E | | SP1 2.8×10^{-7} | |
| | | MAZ 1.1×10^{-5} | |



active in the heart

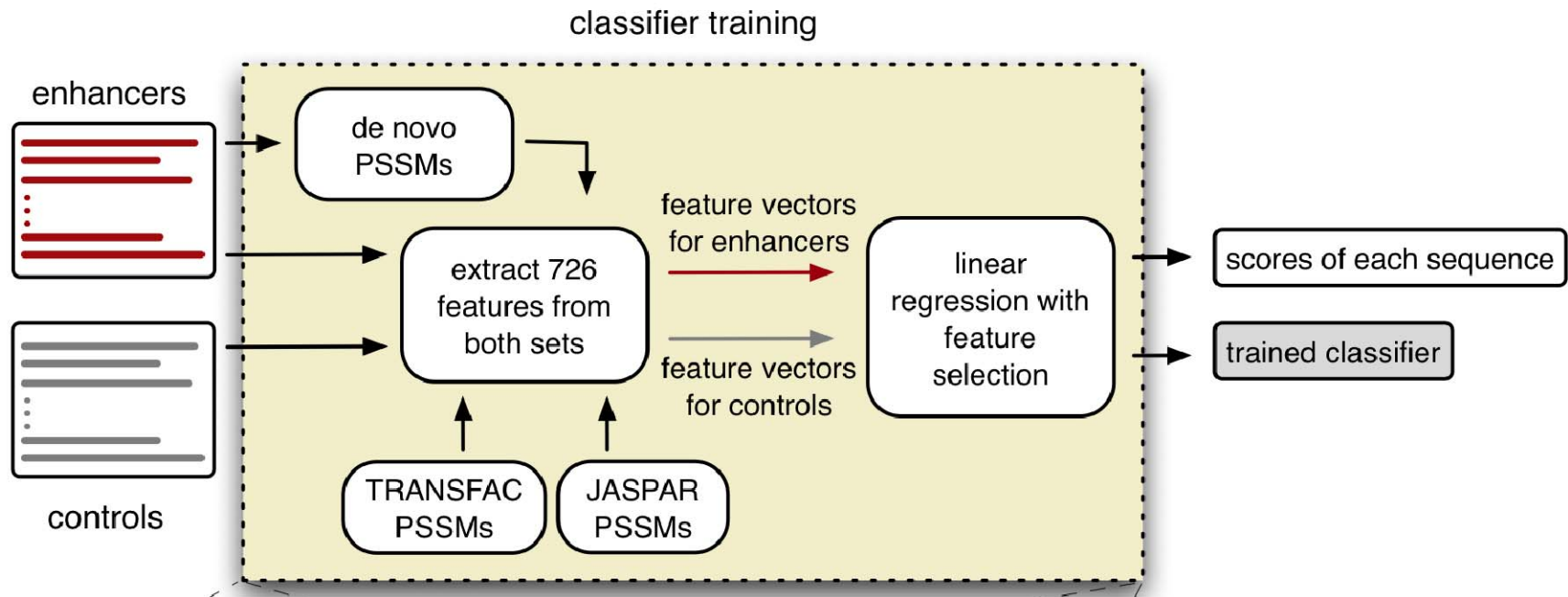
fraction of **positive** sequences with at least one match

fraction of **positive** sequences with no match

fraction of **negative** sequences with at least one match

fraction of **negative** sequences with no match

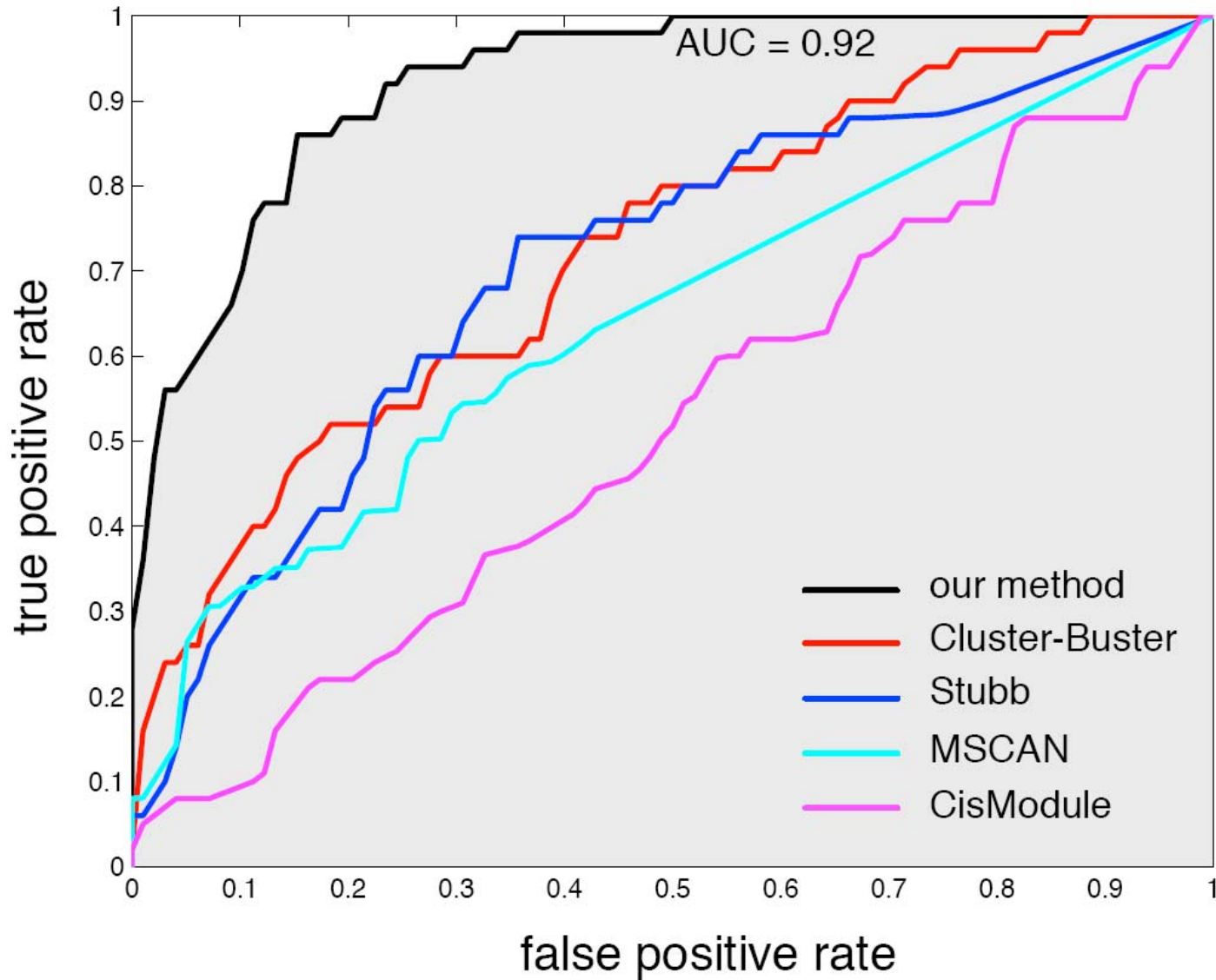
Enhancer Predictor



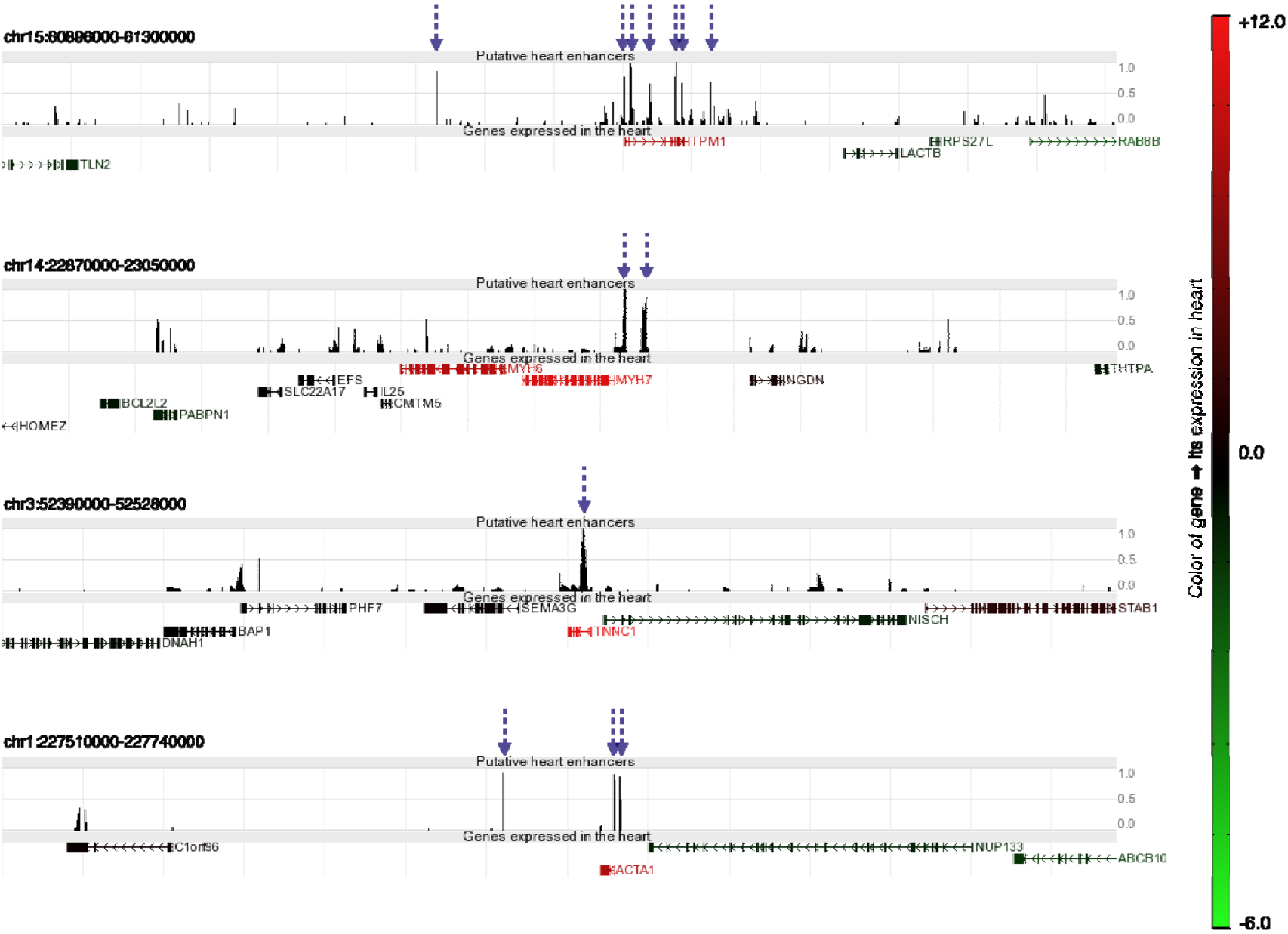
Two-step approach:

- *de novo* motif detection in the positives, TRANSFAC/JASPAR mapping of known motifs, and a set of Markov models to detect sequence features
- use these motifs to *discriminate* between positives and negatives (77 positives and 1000 random noncoding elements)

Predictor Validation

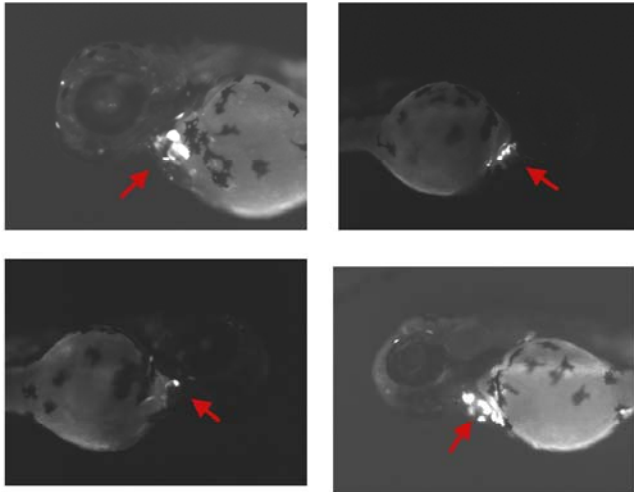


42,000 putative human heart enhancers

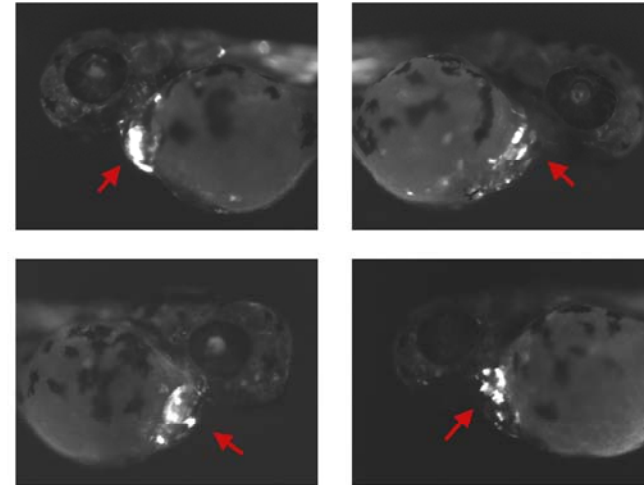


Experimental Validation

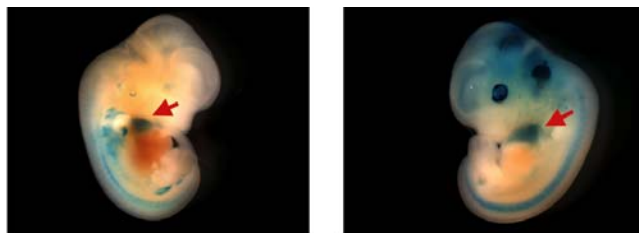
(A) chr15:65850899-65851174 injected in zebrafish



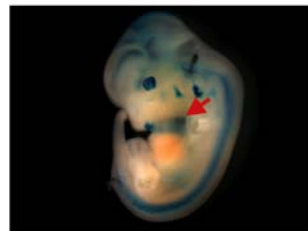
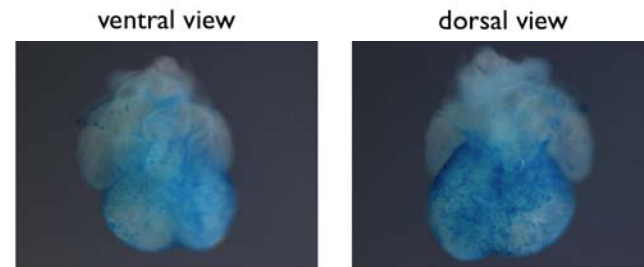
(B) chr1:26922178-26923419 injected in zebrafish



(C) chr5:172109161-172109994 injected in mouse



(D) Dissected mouse heart



12 of 20 predicted heart enhancers displayed reproducible and consistent expression in the heart. None of 10 control elements did show heart expression.

Acknowledgements

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