

SUPPLEMENTARY INFORMATION

Additional examples of biological applications

Plot of expression data

An example of how this database can also be applied to understand development is the study of the role of *ezrin* (*ezr*) genes. Diz-Muñoz *et al.* have shown that during zebrafish early development, inhibition of *ezrb* is sufficient to affect the mechanical properties of precordial plate progenitors (Diz-Muñoz *et al.*, 2010). However, the *ezra* gene was not analysed. Using this database, we can observe that the only paralogue expressed during the first hours of development is *ezrb* (Supplementary Fig. S6), which supports their results and explains why *ezra* gene inhibition was not necessary.

Correlations

An example on how this database can be used to obtain general results that are not specific to regeneration is the study of proteins involved in caveolae formation. To do that, we used all the datasets in the database to find which genes are co-expressed with *cav1*. Interestingly, some of the first genes on the list, such as *ehd2b* (Moren *et al.*, 2012), *sdprb* (Hansen *et al.*, 2009), *myo1ca* and *myo1cb* (Hernandez *et al.*, 2013) are known to form part, or are closely associated with, caveolae. However, in the top part of this list, we find other genes, such as *ccdc187* and *gypc*, which have not been previously related to caveolae. Our results suggest a possible relationship between these genes and the caveolae (Supplementary Fig. S7).

Venn diagrams

This database includes different datasets that study the regeneration of each organ. However, there are differences in their experimental setup, including the injury model used and the stages analysed. Using this application, we analysed three heart regeneration datasets from the laboratories of Poss (Goldman *et al.*, 2017), Stainier (Lai *et al.*, 2017) and Flores (Bednarek *et al.*, 2015). Besides the experimental differences, we found 269 differentially expressed genes in common in the three different datasets. This provides a high degree of confidence of the behaviour of these genes in response to injury (Supplementary Fig. S8).

Methods

Sources of RNA-Seq datasets

We collected a total of 22 datasets and 340 samples from public platforms Gene Expression Omnibus (GEO) (Barrett *et al.*, 2012), Sequence read Archive (SRA) and Bioproject (BioProject) (Goldman *et al.*, 2017; Lai *et al.*, 2017; Han *et al.*, 2014; Bednarek *et al.*, 2015; Natarajan *et al.*, 2018; King *et al.*, 2018; Sánchez-Iranzo, Galardi-Castilla, Minguillón, *et al.*, 2018; Sánchez-Iranzo, Galardi-Castilla, Sanz-Morejón, *et al.*, 2018; Mokalled *et al.*, 2016; Kang *et al.*, 2016; King and Yin, 2016; Rabinowitz *et al.*, 2017; Jiang *et al.*, 2014; Sifuentes *et al.*, 2016; Oosterhof *et al.*, 2017; Feng *et al.*, 2015; Louie *et al.*, 2017; PRJEB1986; Pauli *et al.*, 2012; Levin *et al.*, 2016; Herman *et al.*, 2018).

Datasets were selected according to the following criteria: they can be found in GEO or Bioproject by using the words “zebrafish regeneration” or “fish regeneration”. The model organism should be zebrafish or any other fish species, and the datasets should be of general interest, excluding any experiments that are restricted to study the effect of a specific gene. In addition, developmental datasets that are representative of a wide developmental range (defined as including at least 5 different developmental stages) were included.

SRA to Fastq conversion

SRA files were converted into fastq files by using fastq-dump (Sequence Read Archive Handbook) using its default parameters, or --split-files for all datasets that are paired-end.

Quality control and trim of low-quality reads and adapters

A quality control was performed with fastqc (Andrews). Trimmomatic (Bolger *et al.*, 2014) was used to trim low-quality reads and adaptor sequences when necessary. The following parameters were used: “LEADING:3 TRAILING:3 SLIDINGWINDOW:4:15 MINLEN:36”.

Specifically, Trimmomatic was applied to a whole dataset when, in “per base sequence quality” section of fastqc, there was at least one of the samples with at least one base with more than 10% of the reads with a quality value (Q in the fastq format) lower than 20 (lower whisker in the red area). This applied to the following datasets: “Heart regeneration (Poss lab.)”, “Heart regeneration (Stainier lab)”, “Heart regeneration (Xiong lab)”, “Heart regeneration (Yin lab.)”, “Muller glia (Raymond lab.)”, “Fin regeneration (Yin lab)”, “Developmental stages (Schier lab)”, “Developmental stages (PRJEB1986)”.

In addition, Trimmomatic was also applied when the percentage of adapters was too high. We defined too high adapter content when they were present in more than 5% of the reads of at least one of the samples of a dataset (warning in the “adapter content” section of fastqc). This applied to the “Cardiac fibrosis (Mercader lab)”, where the ILLUMINACLIP:TruSeq3-SE.fa:2:30:10” parameter was added; and for the “Liver regeneration (Cui lab)” dataset, where the parameter “ILLUMINACLIP:TruSeq2-PE.fa:2:30:10” was added.

In all the datasets that were paired-end, the option “PE” was included and both paired files were trimmed simultaneously, while when they were single-end, the option “SE” was included.

Alignment to the reference genome

RSEM 1.2.25 (Li and Dewey, 2011), calling Bowtie2 2.2.6 (Langmead and Salzberg, 2012), was utilised to align the reads to the *Danio rerio* reference transcriptome (ENSEMBL release 89). Default parameters were used, except for “--estimate-rspd” in RSEM that was set to “on”. The parameter “--paired-end” was included in RSEM when necessary.

RSEM aligned files for the dataset “Spinal cord regeneration P. marinus (Bloom lab.)” were directly downloaded from GEO.

“Expected counts” and “fragments per kilobase of transcript per million mapped reads” (fpkm) were used for further analyses. Fig. 1 shows a schematic representation of this workflow.

Web interface and R analysis

Data was analysed and displayed using R (Team., 2014). Specifically, the Shiny R (Chang W *et al.*, 2015) package was used to build the web interface.

Plot fpkm application

fpkm values were plotted by using ggplot2 (Wickham, 2009). In the box plots, the hinges correspond to the first and third quartiles (25th and 75th percentiles). The whiskers extends from the hinges to the highest and lowest values as long as they don’t extend more than 1.5 interquartile ranges from the hinges.

In datasets where there are no replicates, boxplots are substituted by lines.

Moreover, individual data points were overlaid.

In the “Developmental stages (Yanai lab.)” dataset, as there is a big number of points with only one replicate and equally spaced in time, a continuous line was displayed.

Correlations application

Every sample present in the selected datasets is used to calculate the correlations.

Correlations were calculated by using the *cor* function (stats package) with its default parameters. Correlations are calculated using the Pearson method.

t-statistic was calculated by using the following equation:

$$t = r \sqrt{\frac{n - 2}{1 - r^2}}$$

where *r* is the correlation coefficient, and *n* is the number of samples used to calculate a correlation.

The two-tailed p-value was calculated as $2 * pt(t, df = (n-1))$, where t is the t-statistic, n is the number of samples used to calculate a correlation and pt the R function (stats package).

Differentially expressed genes application

Differentially expressed genes were calculated with the edgeR R package (Robinson *et al.*, 2010).

First, a dataframe is generated, which includes the expected counts of only the samples present in the two groups that are being compared.

Then, low-expressed genes are filtered. To keep a gene for the differential expression analysis, it has to be expressed at more than 1 count per million (cpm) level in at least as many samples as the size of the smallest group that is being compared. For example, if we are comparing a condition including 4 biological replicates to other condition including 3 biological replicates, only genes that are expressed at least at 1 cpm in 3 of the samples are kept.

Normalization is done by using the calcNormFactors function (edgeR package) with its default parameters, which includes the TMM-normalization method (trimmed mean of M-values).

Dispersion is calculated by using the estimateDisp function (edgeR package) with its defaults parameters. For datasets where there were no replicates, a bcv value of 0.4 was used.

exactTest function (edgeR package) with its default parameters is used to calculate differentially expressed genes. When there were no replicates, the parameter dispersion was set to 0.4^2 .

Volcano plots are made using plotly (Plotly Technologies, 2015).

Datasets information

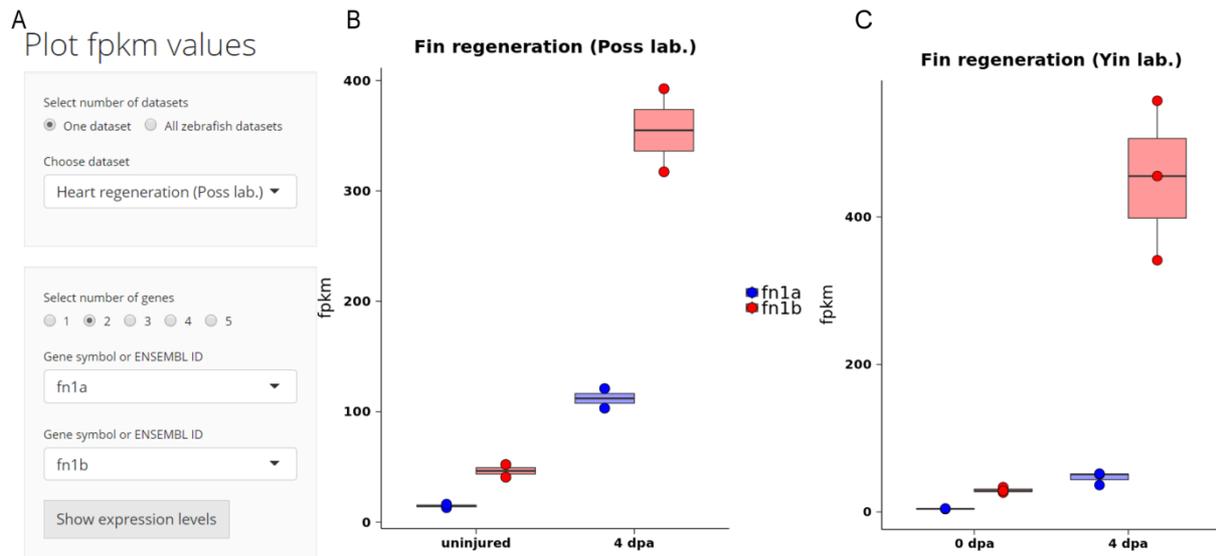
Information on each sample and links to publications were manually introduced and displayed in the database, according to the information available in GEO.

References

- Andrews, S. FastQC: A quality control tool for high throughput sequence data.
- Barrett, T. *et al.* (2012) NCBI GEO: archive for functional genomics data sets—update. *Nucleic Acids Res.*, **41**, D991–D995.
- Bednarek, D. *et al.* (2015) Telomerase Is Essential for Zebrafish Heart Regeneration. *Cell Rep.*, **12**, 1691–1703. BioProject <https://www.ncbi.nlm.nih.gov/bioproject>.
- Bolger, A.M. *et al.* (2014) Trimmomatic: A flexible trimmer for Illumina sequence data. *Bioinformatics*, **30**, 2114–2120.
- Chang W *et al.* (2015) Shiny: Web Application Framework for R. <http://cran.r-project.org/package=shiny>.
- Diz-Muñoz, A. *et al.* (2010) Control of Directed Cell Migration In Vivo by Membrane-to-Cortex Attachment. *PLoS Biol.*, **8**, e1000544.
- Feng, G. *et al.* (2015) Transcriptomic characterization of the dorsal lobes after hepatectomy of the ventral lobe in zebrafish. *BMC Genomics*, **16**, 1–11.
- Goldman, J.A. *et al.* (2017) Resolving Heart Regeneration by Replacement Histone Profiling. *Dev. Cell*, **40**, 392–404.e5.
- Han, P. *et al.* (2014) Hydrogen peroxide primes heart regeneration with a derepression mechanism. *Cell Res.*, **24**, 1091–1107.
- Hansen, C.G. *et al.* (2009) SDPR induces membrane curvature and functions in the formation of caveolae. *Nat. Cell Biol.*, **11**, 807–814.
- Herman, P.E. *et al.* (2018) Highly conserved molecular pathways, including Wnt signaling, promote functional recovery from spinal cord injury in lampreys. *Sci. Rep.*, **8**, 742.
- Hernandez, V.J. *et al.* (2013) Cavin-3 dictates the balance between ERK and Akt signaling. *Elife*, **2**, e00905.
- Jiang, L. *et al.* (2014) Gene-expression analysis of hair cell regeneration in the zebrafish lateral line. *Proc. Natl. Acad. Sci.*, **111**, E1383–E1392.
- Kang, J. *et al.* (2016) Modulation of tissue repair by regeneration enhancer elements. *Nature*, **532**, 201–206.
- King, B.L. *et al.* (2018) RegenDbase: a comparative database of noncoding RNA regulation of tissue regeneration circuits across multiple taxa. *npj Regen. Med.*, **3**, 10.
- King, B.L. and Yin, V.P. (2016) A conserved microRNA regulatory circuit is differentially controlled during limb/appendage regeneration. *PLoS One*, **11**, 1–25.
- Lai, S.L. *et al.* (2017) Reciprocal analyses in zebrafish and medaka reveal that harnessing the immune response promotes cardiac regeneration. *Elife*, **6**, 1–20.
- Langmead, B. and Salzberg, S.L. (2012) Fast gapped-read alignment with Bowtie 2. *Nat. Methods*, **9**, 357–359.

- Levin, M. *et al.* (2016) The mid-developmental transition and the evolution of animal body plans. *Nature*, **531**, 637–641.
- Li, B. and Dewey, C.N. (2011) RSEM: Accurate transcript quantification from RNA-Seq data with or without a reference genome. *BMC Bioinformatics*, **12**, 323.
- Louie, K.W. *et al.* (2017) Temporally distinct transcriptional regulation of myocyte dedifferentiation and Myofiber growth during muscle regeneration. *BMC Genomics*, **18**, 854.
- Mokalled, M.H. *et al.* (2016) Injury-induced *ctgfa* directs glial bridging and spinal cord regeneration in zebrafish. *Science (80-.)*, **354**, 630–634.
- Moren, B. *et al.* (2012) EHD2 regulates caveolar dynamics via ATP-driven targeting and oligomerization. *Mol. Biol. Cell*, **23**, 1316–1329.
- Natarajan, N. *et al.* (2018) Complement Receptor C5aR1 Plays an Evolutionarily Conserved Role in Successful Cardiac Regeneration. *Circulation*, **137**, 2152–2165.
- Oosterhof, N. *et al.* (2017) Identification of a conserved and acute neurodegeneration-specific microglial transcriptome in the zebrafish. *Glia*, **65**, 138–149.
- Pauli, A. *et al.* (2012) Systematic identification of long noncoding RNAs expressed during zebrafish embryogenesis. *Genome Res.*, **22**, 577–591.
- Plotly Technologies, I. (2015) Collaborative data science Publisher: Plotly Technologies Inc. PRJEB1986 <https://www.ncbi.nlm.nih.gov/bioproject/PRJEB1986>.
- Rabinowitz, J.S. *et al.* (2017) Transcriptomic, proteomic, and metabolomic landscape of positional memory in the caudal fin of zebrafish. *Proc. Natl. Acad. Sci.*, **114**, E717–E726.
- Robinson, M.D. *et al.* (2010) edgeR: a Bioconductor package for differential expression analysis of digital gene expression data. *Bioinformatics*, **26**, 139–40.
- Sánchez-Iranzo, H., Galardi-Castilla, M., Minguillón, C., *et al.* (2018) Tbx5a lineage tracing shows cardiomyocyte plasticity during zebrafish heart regeneration. *Nat. Commun.*, **9**, 428.
- Sánchez-Iranzo, H., Galardi-Castilla, M., Sanz-Morejón, A., *et al.* (2018) Transient fibrosis resolves via fibroblast inactivation in the regenerating zebrafish heart. *Proc. Natl. Acad. Sci.*, **115**, 4188–4193.
- Sifuentes, C.J. *et al.* (2016) Rapid, dynamic activation of Müller Glial stem cell responses in Zebrafish. *Investig. Ophthalmol. Vis. Sci.*, **57**, 5148–5160.
- SRA <https://www.ncbi.nlm.nih.gov/sra/>.
- Team, R.C. (2014) R: a language and environment for statistical computing. <http://www.r-project.org>.
- Wickham, H. (2009) ggplot2: Elegant Graphics for Data Analysis. *Springer-Verlag New York*.

Supplementary Figures



Supplementary Figure 1. Expression of the *fn1a* and *fn1b* genes by using the “Plot fpkm” application. (A) Screenshot of the selection menu. Screenshot of the plots showing the expression levels of *fn1a* and *fn1b* in the “Fin regeneration (Poss lab.)” dataset (B) and the “Fin regeneration (Yin lab.)” dataset (C).

A Calculate correlations

Choose datasets

- Heart regeneration (Poss lab.)
- Heart regeneration (Stainier lab.)
- Heart regeneration (Xiong lab.)
- Heart regeneration (Flores lab.)
- Heart regeneration (Lee lab.)
- Heart regeneration (Yin lab.)
- Cardiomyocyte subtypes (Mercader lab.)
- Cardiac fibrosis (Mercader lab.)
- Cardiac fibroblast inactivation (Mercader lab.)
- Spinal cord regeneration (Poss lab.)
- Fin regeneration (Poss lab.)
- Fin regeneration (Yin lab.)
- Fin proximodistal (Moon lab.)
- Lateral line (Piotrowski lab.)
- Muller glia (Raymond lab.)
- Microglia (van Ham lab.)
- Liver regeneration (Cui lab.)
- Skeletal muscle (Kahana lab.)
- Developmental stages (PRJEB1986)
- Developmental stages (Schier lab.)
- Developmental stages (Yanai lab.)

Gene symbol or EMSEMBL ID

col1a2

Calculate correlated genes

Download the table

B

Ensembl gene ID	Gene symbol	Correlations
ENSDARG00000020007	col1a2	1.0000000
ENSDARG00000035809	col1a1b	0.9843652
ENSDARG00000002235	mmp14a	0.9346462
ENSDARG00000012405	col1a1a	0.9170508
ENSDARG00000009014	col11a1b	0.9130619
ENSDARG00000059367	mfap2	0.9095764
ENSDARG00000031678	col5a2a	0.8895317
ENSDARG00000025641	gli2a	0.8766321
ENSDARG00000079049	cercam	0.8713788
ENSDARG00000044074	loxl2b	0.8639827
ENSDARG00000028071	bmp1a	0.8596621
ENSDARG00000094752	rpe65b	0.8456597
ENSDARG00000021948	tnc	0.8444393
ENSDARG00000104267	postnb	0.8397433
ENSDARG00000089162	afap11a	0.8387874
ENSDARG00000019353	sparc	0.8331497
ENSDARG00000068036	tmem119b	0.8322230
ENSDARG00000076862	fam198a	0.8303862
ENSDARG00000036558	col18a1	0.8297215
ENSDARG00000078494	ADAMTS14	0.8265787
ENSDARG00000059693	adam19a	0.8255913
ENSDARG00000026165	col11a1a	0.8253985
ENSDARG00000032831	htra1a	0.8221051
ENSDARG00000020072	thbs4b	0.8220285
ENSDARG00000102464	wnt5b	0.8214248

Supplementary Figure 2. Correlation of the *col1a2* expression with all the other genes in the zebrafish genome. All the regeneration data sets were used to calculate correlations. (A) Selection panel of the datasets and the gene to be used to calculate the correlations. (B) Genes showing a higher correlation value with the selected gene.

A

Calculate differentially expressed genes

Choose dataset
Heart regeneration (Flores lab.)

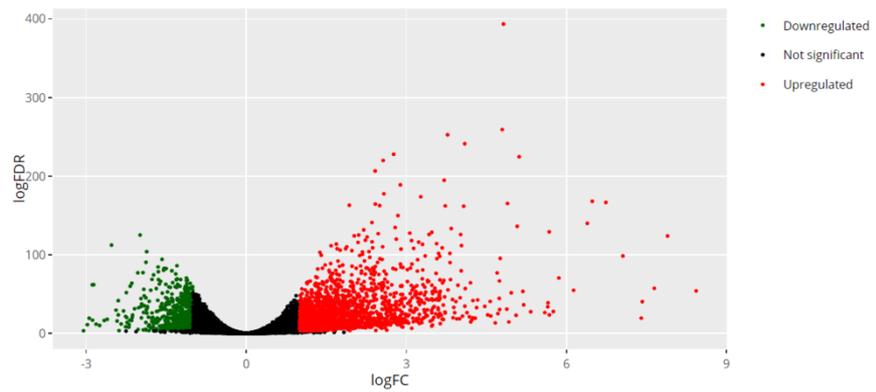
Sample group 1
uninjured

Sample group 2
3 dpi

Calculate DEG

Download the table

Show volcano plot

B**C**

Ensembl gene ID	Symbol	logFC	logCPM	PValue	FDR	logFDR	Legend
ENSDARG00000075263	ankrd1a	4.821193	5.324303	7.309077e-176	1.196204e-171	393.5629	Upregulated
ENSDARG00000019815	fn1a	4.797434	9.346662	2.904799e-117	2.376997e-113	259.3263	Upregulated
ENSDARG00000037997	tubb5	3.773298	5.001189	3.530555e-114	1.926036e-110	252.6289	Upregulated
ENSDARG00000009014	col11a1b	4.094623	4.436410	3.917284e-109	1.602757e-105	241.2997	Upregulated
ENSDARG00000053091	DAB2	2.762112	7.425201	3.472724e-103	1.136692e-99	227.8278	Upregulated
ENSDARG00000044125	txn	5.114308	5.721516	9.187156e-102	2.505950e-98	224.7347	Upregulated
ENSDARG00000011821	plod2	2.565402	6.474365	1.235004e-99	2.887440e-96	219.9878	Upregulated
ENSDARG00000013415	lmna	2.414015	6.835250	8.625862e-94	1.764636e-90	206.6647	Upregulated
ENSDARG00000036036	mdka	3.709869	8.300990	1.230288e-88	2.237211e-85	194.9145	Upregulated
ENSDARG00000055226	slc7a7	2.888318	5.142137	5.067317e-86	8.293170e-83	188.9991	Upregulated
ENSDARG00000010434	clu	2.578411	5.508846	5.159267e-81	7.676051e-78	177.5635	Upregulated
ENSDARG00000059049	zgc:174904	3.270931	6.183739	2.504511e-79	3.415736e-76	173.7681	Upregulated
ENSDARG00000089362	grn1	6.484748	6.833140	8.949943e-77	1.126729e-73	167.9694	Upregulated
ENSDARG00000088641	grn2	6.740608	5.171708	3.951698e-76	4.619534e-73	166.5584	Upregulated
ENSDARG00000096979	NPC2	4.895844	4.979053	1.513245e-75	1.651051e-72	165.2847	Upregulated
ENSDARG00000043081	ctsz	2.417885	6.743727	3.317210e-75	3.393091e-72	164.5644	Upregulated
ENSDARG00000040251	ctsk	1.931087	7.422065	1.685078e-74	1.622235e-71	162.9997	Upregulated
ENSDARG00000095627	c1qc	2.499741	5.928172	2.734149e-74	2.485949e-71	162.5729	Upregulated
ENSDARG00000093748	sl:ch211-217k17.11	3.729388	4.689974	3.933477e-74	3.388173e-71	162.2633	Upregulated
ENSDARG00000001452	adam8a	4.074256	5.062048	6.434118e-74	5.265039e-71	161.8225	Upregulated
ENSDARG00000040178	havcr1	2.842657	4.354924	9.905156e-69	7.719418e-66	149.9269	Upregulated
ENSDARG00000044613	c1qa	2.354285	5.550918	7.425902e-65	5.524196e-62	141.0511	Upregulated
ENSDARG00000019601	col12a1b	6.392603	6.613110	2.217030e-64	1.577562e-61	140.0018	Upregulated
ENSDARG00000008803	marcksb	5.077147	3.730108	9.914065e-63	6.760566e-60	136.2440	Upregulated
ENSDARG00000093440	tnfaip6	2.790729	5.375003	4.719312e-62	3.089450e-59	134.7245	Upregulated

Supplementary Figure 3. Screenshot of the “Differential expression” application. (A) Selection panel. (B) Interactive volcano plot. (C) Differentially expressed genes between the selected samples.

A

Venn diagram

Number of datasets
 Two Three

Choose Dataset 1
 Heart regeneration (Poss lab.)

Sample group 1
 uninjured

Sample group 2
 14 dpa

Choose Dataset 2
 Spinal cord regeneration (Poss lab.)

Sample group 1
 2 weeks after sham

Sample group 2
 2 weeks after transection

Choose Dataset 3
 Fin regeneration (Poss lab.)

Sample group 1
 uninjured

Sample group 2
 4 dpa

B

Select one option

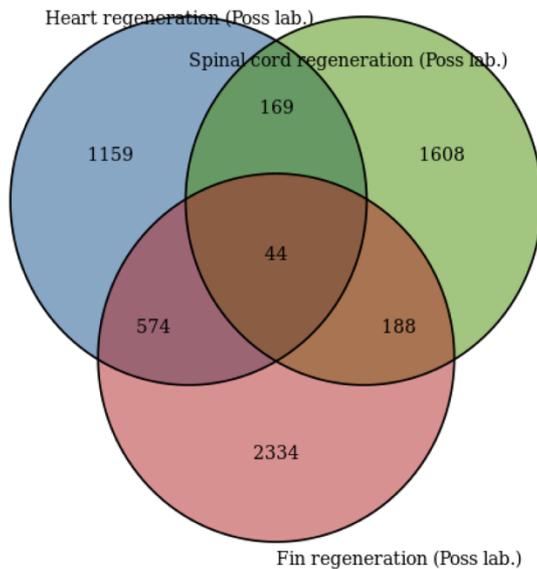
Upregulated genes

Downregulated genes

Both

Calculate [Download the table](#)

C



D

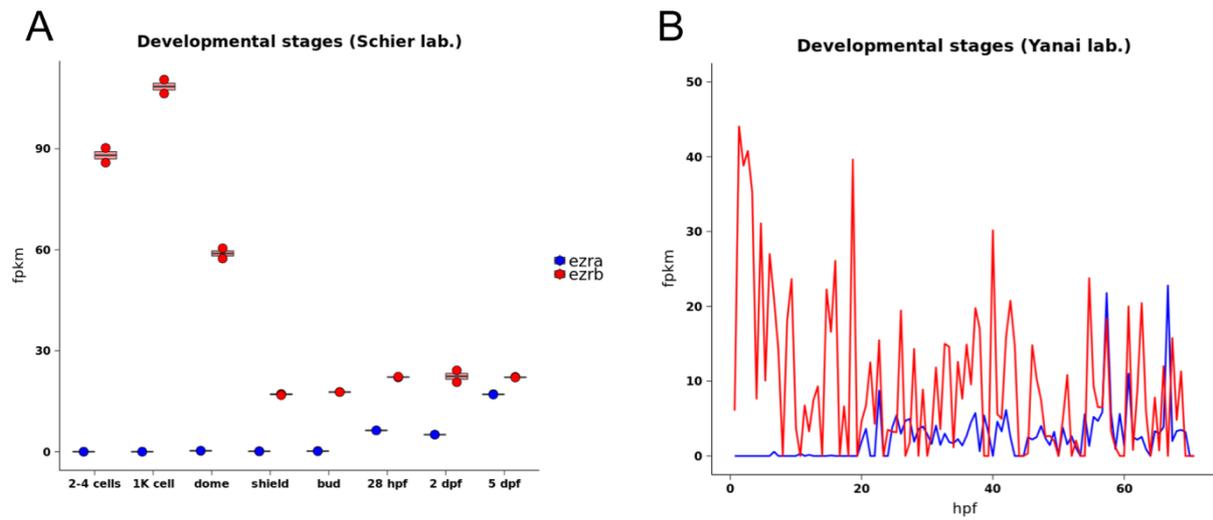
Common genes in all comparisons

Ensembl gene ID	Symbol	Mean FDR
ENSDARG00000078362	TNC	1.202395e-60
ENSDARG00000019949	serpinh1b	1.129996e-44
ENSDARG00000011797	fam46bb	5.170351e-38
ENSDARG000000037145	slc8a4b	5.507456e-37
ENSDARG000000044132	ogn	2.722156e-35
ENSDARG00000070597	prelp	6.923048e-32
ENSDARG00000077356	sypl1	1.347770e-30
ENSDARG00000003259	loxa	8.251567e-30
ENSDARG00000070141	sixh211-191i18.2	1.318002e-25
ENSDARG00000026165	col11a1a	2.516242e-23
ENSDARG00000068036	tmem119b	4.544060e-20
ENSDARG00000076357	CABZ01102039.1	5.244201e-20
ENSDARG00000071658	ywhag2	1.518708e-18
ENSDARG00000045932	cpeb1a	3.242530e-17
ENSDARG00000035809	col1a1b	7.142868e-17
ENSDARG00000021720	col7a1	1.066579e-16
ENSDARG00000045453	f13a1a.1	2.568778e-16
ENSDARG00000006526	fn1b	5.604598e-15
ENSDARG00000078494	ADAMTS14	1.115966e-14
ENSDARG00000032831	htra1a	7.459753e-14
ENSDARG00000069017	elnb	4.630516e-13
ENSDARG00000006901	AEBP1	5.480482e-13
ENSDARG00000074908	col6a1	1.294978e-12
ENSDARG00000062880	cntn3a.1	1.894471e-12
ENSDARG00000007219	actn1	5.637597e-12

Supplementary Figure 4. Up-regulated genes in three different organs during regeneration: heart, spinal cord and fin. (A, B) Screenshot of the selection menu. (C) Venn diagram. (D) List of the genes in common among the three lists. Geometric mean of the FDR values is shown and genes are ordered according to the descending order of this value.

Dataset	GEO	Pubmed	Samples description
Heart regeneration (Poss lab.)	GSE81865	Resolving Heart Regeneration by Replacement Histone Profiling. Goldman JA, Kuzu G, Lee N, Karasik J et al. Dev Cell 2017 Feb 27;40(4):392-404.	Gene expression profile of heart ventricles after cardiomyocyte genetic ablation. RNA-Seq from uninjured hearts (uninjured) and 14-day post-injured (14 dpi). Two replicates per condition.
Heart regeneration (Steinler lab.)	GSE94617	Reciprocal analyses in zebrafish and medaka reveal that harnessing the immune response promotes cardiac regeneration. Lal SL, Marrin-Juarez R, Moura PL, Kuenne C et al. Elife 2017 June 20;6.	RNA-Seq of four heart ventricles pooled at time 0 (uninjured), 6 h, and 1, 2, 3, 4, and 5 days post-sham (6 hps, 1 dps, 2 dps, 3 dps, 5 dps) and after cryoinjury (6 hpi, 1 dpi, 2 dpi, 3 dpi, 5 dpi). One replicate per condition.
Heart regeneration (Xiong lab.)	GSE50203	Hydrogen peroxide primes heart regeneration with a derepression mechanism. Han P, Zhou XH, Chang N, Xiao CL et al. Cell Res 2014 Sep;24(9):1091-107.	RNA-Seq of one heart after sham (sham) or 7 days after amputation (7 dpa).
Heart regeneration (Flores lab.)	GSE71755	Telomerase Is Essential for Zebrafish Heart Regeneration. Bednarek D, Gonzalez-Rosa JM, Guzman-Martinez G, Gutierrez-Gutierrez O et al. Cell Rep 2015 Sep 8;12(10):1691-703.	Transcriptome of hearts under the control conditions (uninjured) and 3 days after cryoinjury (3 dpi). Four replicates per condition.
Heart regeneration (Lee lab.)	GSE108493	Complement Receptor C5aR1 Plays an Evolutionarily Conserved Role in Successful Cardiac Regeneration. Natarajan N, Abbas Y, Bryant DM, Gonzalez-Rosa JM et al. Circulation 2018 Jan 18.	RNA-Seq of the lower halves of heart ventricles at 12, 24 and 48 h post-cryoinjury (12 hpi, 24 hpi, 48 hpi) or sham (12 hps, 24 hps, 48 hps). Three pools of three halves of ventricles were used per condition.
Heart regeneration (Yin lab.)	GSE106884		mRNA gene expression profiling during 0, 1, 3, 7, 14, 21 and 30 days post ventricular resection.
Cardiomyocyte subtypes (Mercader lab.)	GSE87596	Tbx5a lineage tracing shows cardiomyocyte plasticity during zebrafish heart regeneration. Sanchez-Iranzo H, Galardi-Castilla M, Mingullon C, Sanz-Morejon A et al. Nat Commun 2018 Jan 30;9(1):428.	RNA-Seq of the tbx5a-positive (tbx5a-positive) or -negative (tbx5a-negative) cardiomyocytes (CM) from an uninjured heart. Four replicates per condition obtained from the same heart.
Cardiac fibrosis (Mercader lab.)	GSE101200	Transient fibrosis resolves via fibroblast inactivation in the regenerating zebrafish heart. Sanchez-Iranzo H, Galardi-Castilla M, Sanz-Morejon A, Gonzalez-Rosa JM et al. Proc Natl Acad Sci U S A 2018 Apr 17;115(16):4188-4193.	Three to six biological replicates consisting of different cell types obtained from the ventricular apex.
Cardiac fibroblast inactivation (Mercader lab.)	GSE101199	Transient fibrosis resolves via fibroblast inactivation in the regenerating zebrafish heart. Sanchez-Iranzo H, Galardi-Castilla M, Sanz-Morejon A, Gonzalez-Rosa JM et al. Proc Natl Acad Sci U S A 2018 Apr 17;115(16):4188-4193.	postm-b-derived cells were FAC sorted from a pool of three to five biological samples. Four pools were collected at 7 dpi and three at 60 dpi. RNA was extracted from those pools and further processed for transcriptomic analysis.
Spinal cord regeneration (Poss lab.)	GSE77025	Injury-induced tctgf6 directs glial bridging and spinal cord regeneration in zebrafish. Moalalled MH, Patra C, Dickson AL, Endo T et al. Science 2016 Nov 4;354(6312):630-634.	Gene expression analysis of spinal cord after sham (2 weeks after sham) and after injury (2 weeks after transection). Two replicates per condition.
Fin regeneration (Poss lab.)	GSE76564	Modulation of tissue repair by regeneration enhancer elements. Kang J, Hu J, Karra R, Dickson AL et al. Nature 2016 Apr 14;532(7598):201-6.	Transcriptional profiles of uninjured caudal fin (uninjured) and 4 days after amputation (4 dpa). Two pools of 10 fins per condition.
Fin regeneration (Yin lab.)	GSE74415	A Conserved MicroRNA Regulatory Circuit is Differentially Controlled during Limb/Appendage Regeneration. King BL, Yin VP. PLoS One 2016;11(6):e0157106.	RNA-Seq of uninjured (uninjured) or 4 days after amputation (4 dpa). Three replicates per condition.
Fin proximodistal (Moon lab.)	GSE92760	Transcriptomic, proteomic, and metabolomic landscape of positional memory in the caudal fin of zebrafish. Rabinowitz JS, Robitaille AM, Wang Y, Ray CA et al. Proc Natl Acad Sci U S A 2017 Jan 31;114(5):E717-E726.	RNA-Seq of three locations along the proximo-distal axis of the caudal fin, proximal (prox), middle (mid) and distal (dist). Five replicates per condition, each replicate is a pool of two males and two females.
Lateral line (Piotrowski lab.)	GSE56176	Gene-expression analysis of hair cell regeneration in the zebrafish lateral line. Jiang L, Romero-Carvajal A, Haug JS, Seidel CW et al. Proc Natl Acad Sci U S A 2014 Apr 8;111(14):E1383-92.	RNA-Seq of the GFP-positive cells from the sqET20 transgenic line, which labels inner and mantle support cells (GFP) and the rest of the cells (control) after neomycin treatment (neo) or non-treated (nt). Neomycin chemically ablates hair cells.
Muller glia (Raymond lab.)	GSE86872	Rapid, Dynamic Activation of Muller Glial Stem Cell Responses in Zebrafish. Sifuentes CJ, Kim JW, Swaroop A, Raymond PA. Invest Ophthalmol Vis Sci 2016 Oct 1;57(13):5148-5160.	RNA-Seq from Muller glia 0, 8 and 16 h post-injury. Three replicates per condition.
Microglia (van Ham lab.)	GSE86921	Identification of a conserved and acute neurodegeneration-specific microglial transcriptome in the zebrafish. Oostemof N, Holtman IR, Kull LE, van der Linde HC et al. Glia 2017 Jan;65(1):138-149.	Transcriptome analysis of brain cell (brain), homeostatic microglia (microglia control) (triplicates per condition) and activated microglia after cell ablation by nitroreductase at 24 (active microglia 24 h) and 48 h after treatment (active microglia 48 h). Two replicates per condition.
Liver regeneration (Cui lab.)	SRP03395	Transcriptomic characterization of the dorsal lobes after hepatectomy of the ventral lobe in zebrafish. eng G, Long Y, Peng J, U Q, Cui Z. BMC Genomics 2015. Nov 19;16:979	RNA-Seq transcriptomic analysis of 12 female livers after 6 (6 h) and 12 (12 h) h after partial hepatectomy, and from 24 h post-sham surgery (sham). One replicate per condition.
Skeletal muscle	GSE92489	Temporally distinct transcriptional regulation of myocyte differentiation and Myofiber growth during muscle regeneration. BMC Genomics 2017 Nov 9;18(1):854-Louie KW, Saera-Vila A, Kish PE, Colacino JA et al.	RNA-seq of zebrafish lateral eye muscle 0 (0 hpi), 9 (0 hpi) and 18 (18 hpi) hours post injury. Four replicates per condition.
Developmental stages (PrijEB1986)	PRIJEB1986		RNA-Seq from embryos after 1, 2, 3, 5 and 14 days post-fertilisation. 1dpf (2 replicates), 2dpf (2 replicates), 3dpf (3 replicates), 5dpf (3 replicates) and 14dpf (1 replicate).
Developmental stages (Schlier lab.)	GSE32898	Systematic identification of long noncoding RNAs expressed during zebrafish embryogenesis. Pauli A, Valen E, Lin MF, Garber M et al. Genome Res 2012 Mar;22(3):577-91. Chew GL, Pauli A, Rinn JL, Regev A et al. Ribosome profiling reveals resemblance between long non-coding RNAs and 5' leaders of coding RNAs. Development 2013 Jul;140(13):2828-34.	RNA-Seq of embryos at 2-4 cells (2-4 cells), one thousand cells (1K cell), dome (dome) and bud (bud) stages, and after 28 h post-fertilisation (28 hpf) and 2 (2 dpf) and 5 days post-fertilisation. Two replicates per condition.
Developmental stages (Yanal lab.)	GSE60619	The mid-developmental transition and the evolution of animal body plans. Levin M, Anavy L, Cole AG, Winter E et al. Nature 2016 Mar 31;531(7598):637-641.	RNA-Seq from one single embryo every 40 minutes from fertilisation. No replicates.
Spinal cord regeneration P.marinus (Bloom lab.)	GSE60619	Highly conserved molecular pathways, including Wnt signaling, promote functional recovery from spinal cord injury in lampreys. Herman PE, Papatheodorou A, Bryant SA, Waterbury CKM et al. Sci Rep 2018 Jan 15;8(1):742.	RNA-Seq from spinal cord (SC) and brain (BR) uninjured and 6 hours (6 hpi), 1 and 3 days (1 dpi, 3 dpi), 1, 2, 3, 4, 5, 6, and 12 weeks (1 wpi, 2 wpi, 3 wpi, 4 wpi, 5 wpi, 6 wpi, 12 wpi) after spinal cord injury. One replicate per condition. RNA from 4-6 animals pooled.

Supplementary Figure 5. Screenshot of the information and references provided about each dataset. Links to the publication that describes the datasets and the raw data repository are provided. To facilitate the rapid understanding of the data, a short summary of the experiment is provided.



Supplementary Figure 6. Expression of the *ezra* and *ezrb* genes using the “Plot fpkm” application. Expression of *ezra* and *ezrb* are shown in different development stages datasets from Schier lab. (A), and Yanain lab. (B).

A Calculate correlations

Choose datasets

- Heart regeneration (Poss lab.)
- Heart regeneration (Stainier lab.)
- Heart regeneration (Xiong lab.)
- Heart regeneration (Flores lab.)
- Heart regeneration (Lee lab.)
- Heart regeneration (Yin lab.)
- Cardiomyocyte subtypes (Mercader lab.)
- Cardiac fibrosis (Mercader lab.)
- Cardiac fibroblast inactivation (Mercader lab.)
- Spinal cord regeneration (Poss lab.)
- Fin regeneration (Poss lab.)
- Fin regeneration (Yin lab.)
- Fin proximodistal (Moon lab.)
- Lateral line (Piotrowski lab.)
- Muller glia (Raymond lab.)
- Microglia (van Ham lab.)
- Liver regeneration (Cui lab.)
- Skeletal muscle (Kahana lab.)
- Developmental stages (PRJEB1986)
- Developmental stages (Schier lab.)
- Developmental stages (Yanai lab.)

Gene symbol or EMSEMBL ID

Calculate correlated genes

Download the table

B

Ensembl gene ID	Gene symbol	Correlations
ENSDARG00000103747	cav1	1.0000000
ENSDARG00000020924	myo1ca	0.7861321
ENSDARG00000071196	sdprb	0.7658510
ENSDARG00000100968	siich211-1a19.3	0.7616283
ENSDARG00000040362	ehd2b	0.7473702
ENSDARG00000054451	lox1	0.7335184
ENSDARG00000061579	myo1cb	0.7245319
ENSDARG00000053857	ccdc187	0.7219719
ENSDARG00000041546	gypc	0.7050950
ENSDARG00000040133	ackr4b	0.7015259
ENSDARG00000105653	BX323797.4	0.7011573
ENSDARG00000061941	trpv4	0.7000284
ENSDARG00000073711	mrrn2b	0.6947155
ENSDARG00000019367	tgfb3	0.6922020
ENSDARG00000105065	dock9a	0.6896928
ENSDARG00000070391	tspan4b	0.6861500
ENSDARG00000004451	tnfrsfa	0.6856331
ENSDARG00000103020	sidkey-237i9.8	0.6841137
ENSDARG00000040920	sidkey-49n23.1	0.6825790
ENSDARG00000099891	siich211-57n23.1	0.6822988
ENSDARG00000029072	klf6a	0.6816982
ENSDARG00000039881	cemip	0.6810626
ENSDARG00000034718	tfpia	0.6800483
ENSDARG00000103774	limch1b	0.6762323
ENSDARG00000035858	cnn2	0.6753525

Supplementary Figure 7. Correlation of the *cav1* expression with all the other genes in the zebrafish genome. All the datasets were used to calculate correlations. (A) Selection panel of the datasets and the gene to be used to calculate the correlations. (B) Genes showing a higher correlation value with the selected gene.

A

Venn diagram

Number of datasets
 Two Three

Choose Dataset 1
 Heart regeneration (Poss lab.)

Sample group 1
 uninjured

Sample group 2
 14 dpa

Choose Dataset 2
 Heart regeneration (Stainer lab.)

Sample group 1
 uninjured

Sample group 2
 5 dpi

Choose Dataset 3
 Heart regeneration (Flores lab.)

Sample group 1
 uninjured

Sample group 2
 3 dpi

B

Select one option

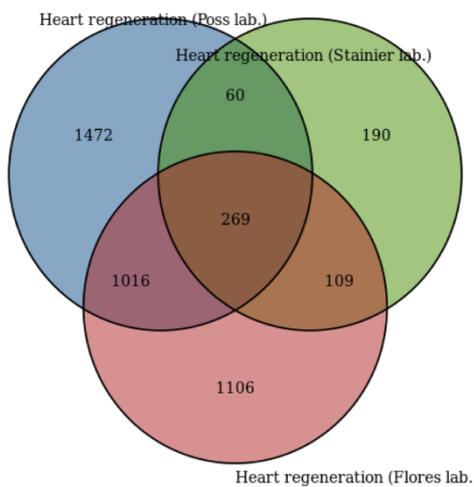
Upregulated genes

Downregulated genes

Both

Calculate [Download the table](#)

C



D

Common genes in all comparisons

Ensembl gene ID	Symbol	Mean FDR
ENSDARG00000075263	ankrd1a	1.517492e-63
ENSDARG00000019815	fn1a	6.116973e-42
ENSDARG00000009014	col11a1b	2.143921e-41
ENSDARG00000037997	tubb5	2.220153e-39
ENSDARG00000044125	txn	5.268458e-37
ENSDARG00000036036	mdka	6.205232e-33
ENSDARG00000059049	zgc:174904	2.816338e-31
ENSDARG00000088641	gm2	4.312869e-31
ENSDARG00000010434	clu	8.625036e-30
ENSDARG00000089362	gm1	1.214575e-29
ENSDARG00000019601	col12a1b	1.971203e-29
ENSDARG00000001452	adam8a	2.993890e-29
ENSDARG00000093748	slc211-217k17.11	6.578861e-29
ENSDARG00000040178	havcr1	9.265716e-29
ENSDARG00000096979	NPC2	8.633365e-28
ENSDARG00000088803	marcksb	5.151995e-26
ENSDARG00000030449	crabp2b	1.036045e-25
ENSDARG00000044613	c1qa	9.850418e-25
ENSDARG00000075891	sall1b	1.698623e-24
ENSDARG00000055439	adamts17	1.525654e-23
ENSDARG00000061120	slc43a2b	1.630468e-23
ENSDARG00000060917	anln	2.901153e-22
ENSDARG00000005789	enpp1	5.205089e-22
ENSDARG00000075261	timp2b	9.417912e-22
ENSDARG00000037859	il11a	3.982114e-21

Supplementary Figure 8. Genes differentially expressed in three heart regeneration datasets each of them performed by a different laboratory. (A, B) Screenshot of the selection menu. (C) Venn diagram. (D) List of the genes in common among the three lists. Geometric mean of the FDR values is shown and genes are ordered according to the descending order of this value.