The Regulome of Regeneration

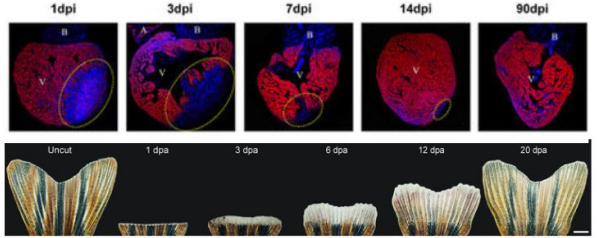
Lab meeting - Nov. 10th, 2017

Regeneration in nature

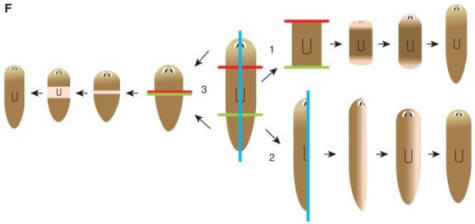
"Ability to reconstruct original shape, size and function of body parts that have been lost or damaged"

Amphibians

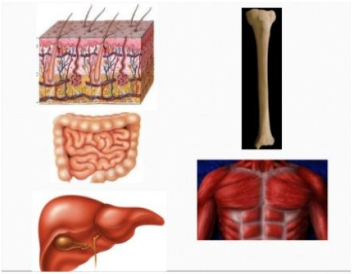
Fish



Flatworms

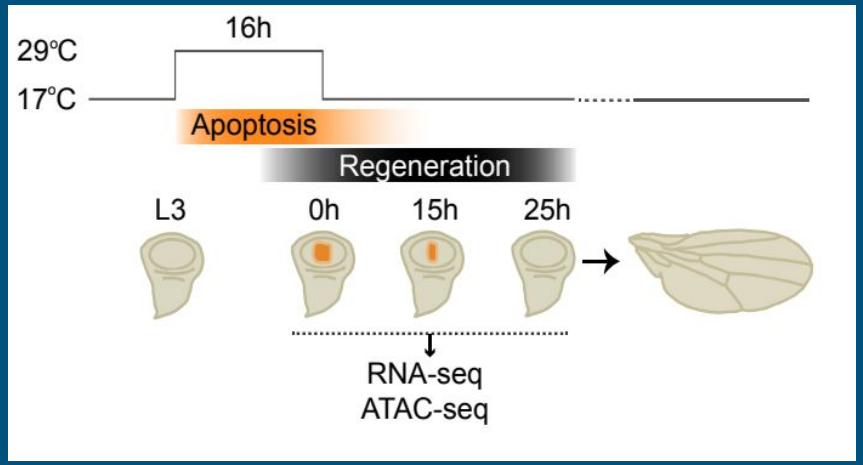


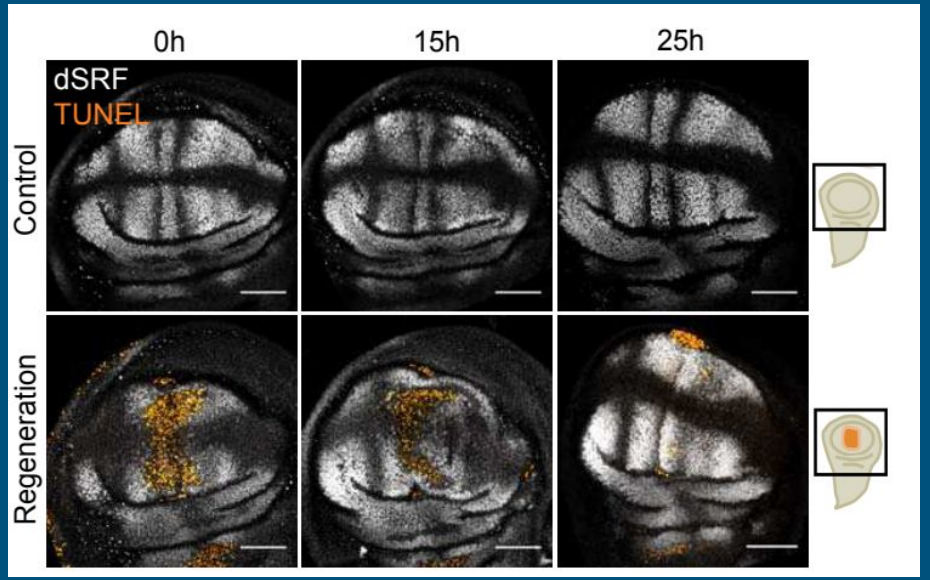
Humans



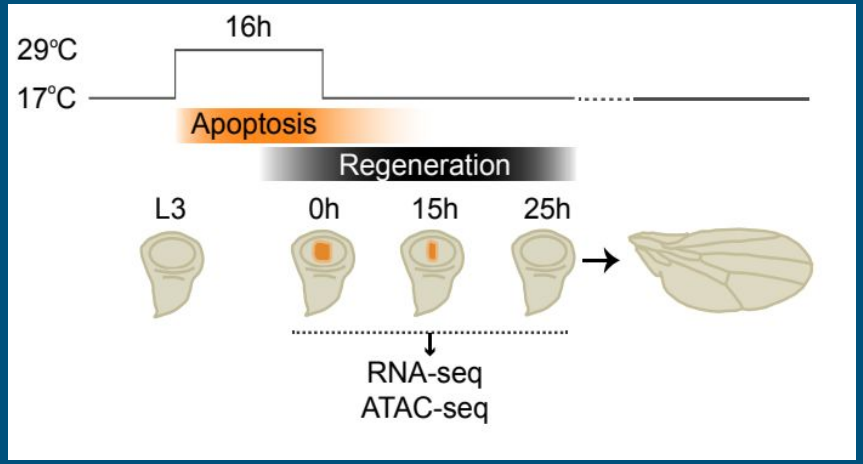
Adapted from: Gardiner et al., 2005 Pfefferli & Ja zwi nska, 2015; Rodius et al, 2016; Adell et al, 2010

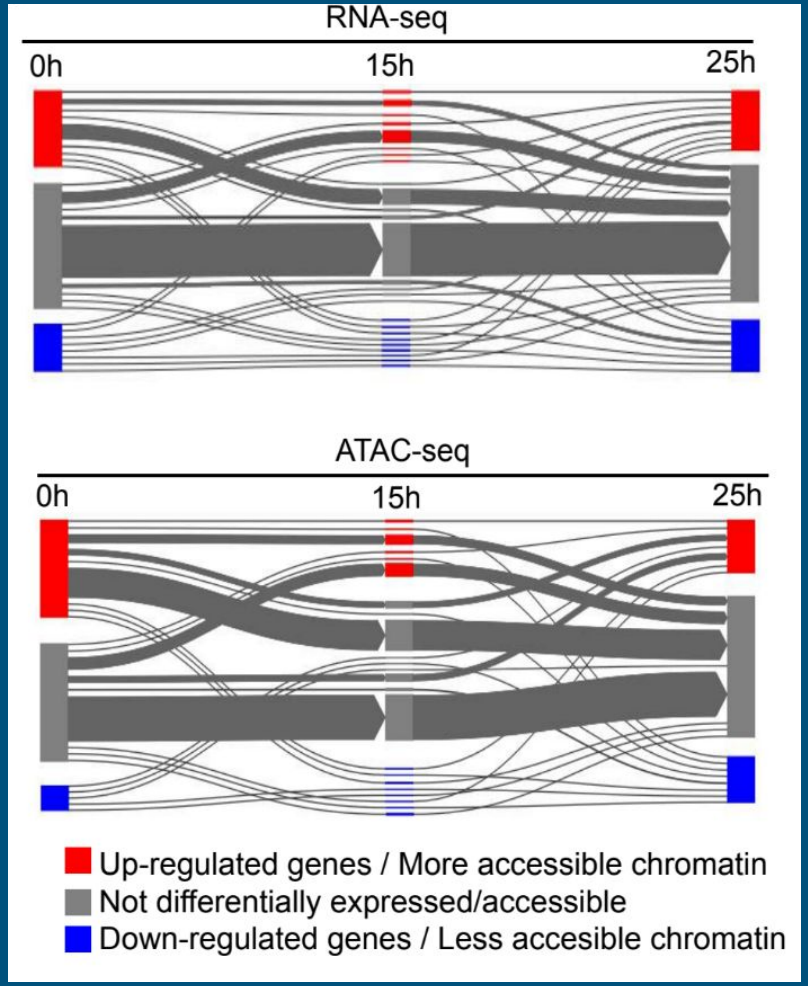
Experimental design



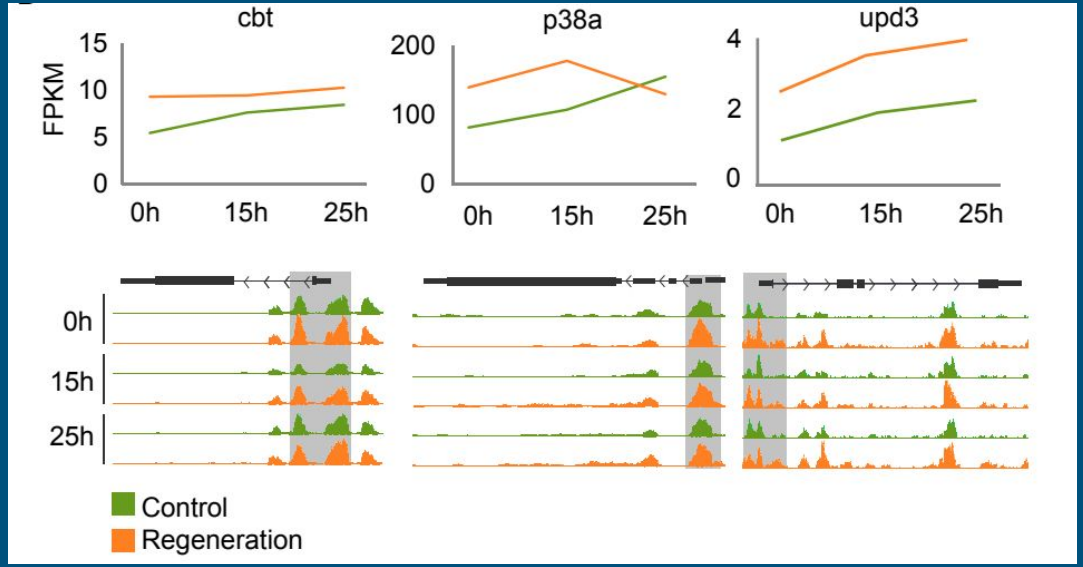


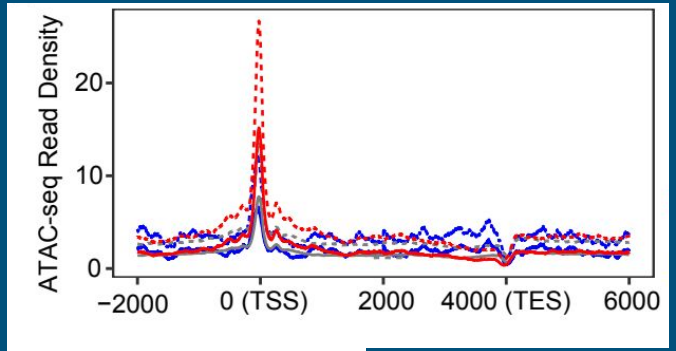
Data overview



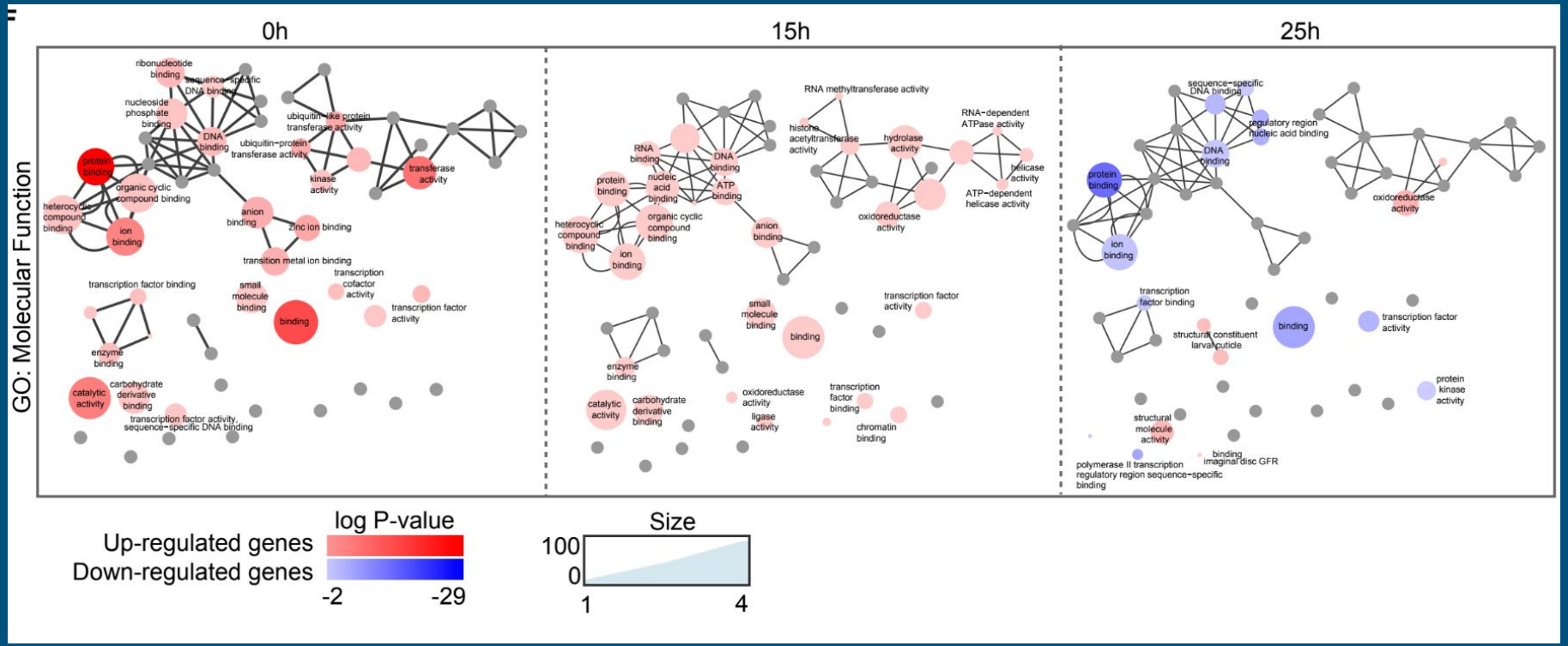


Data overview

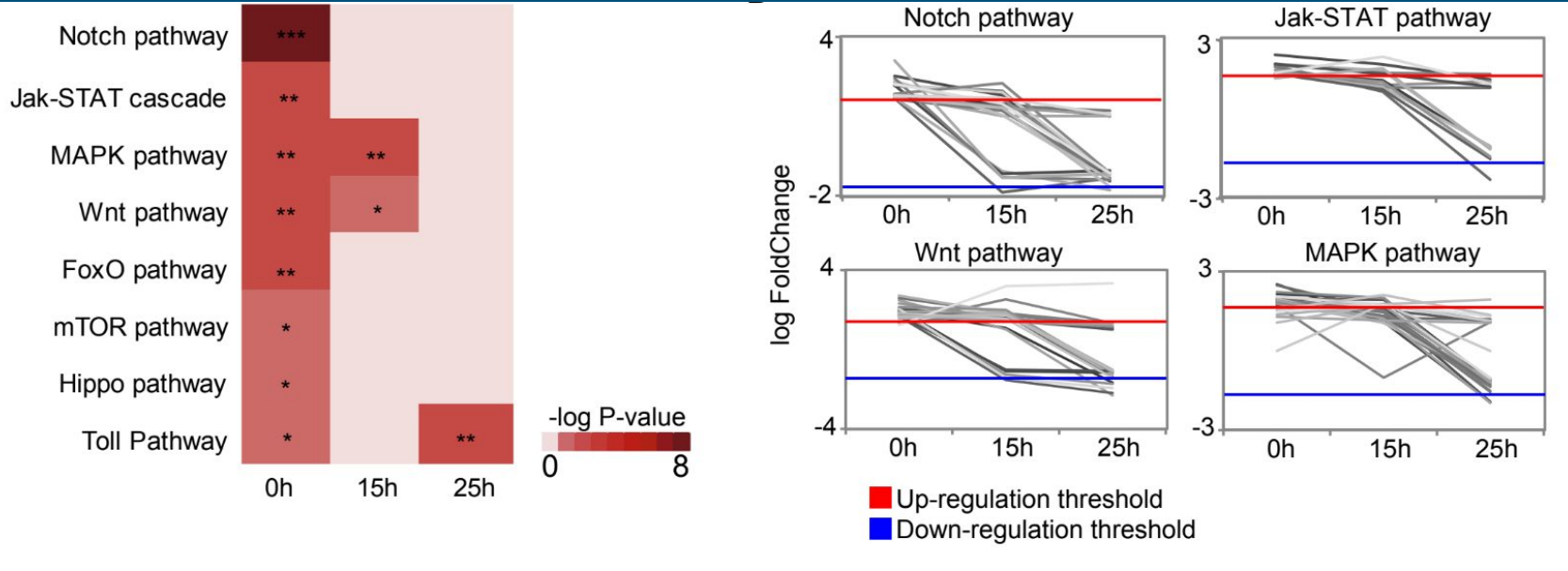




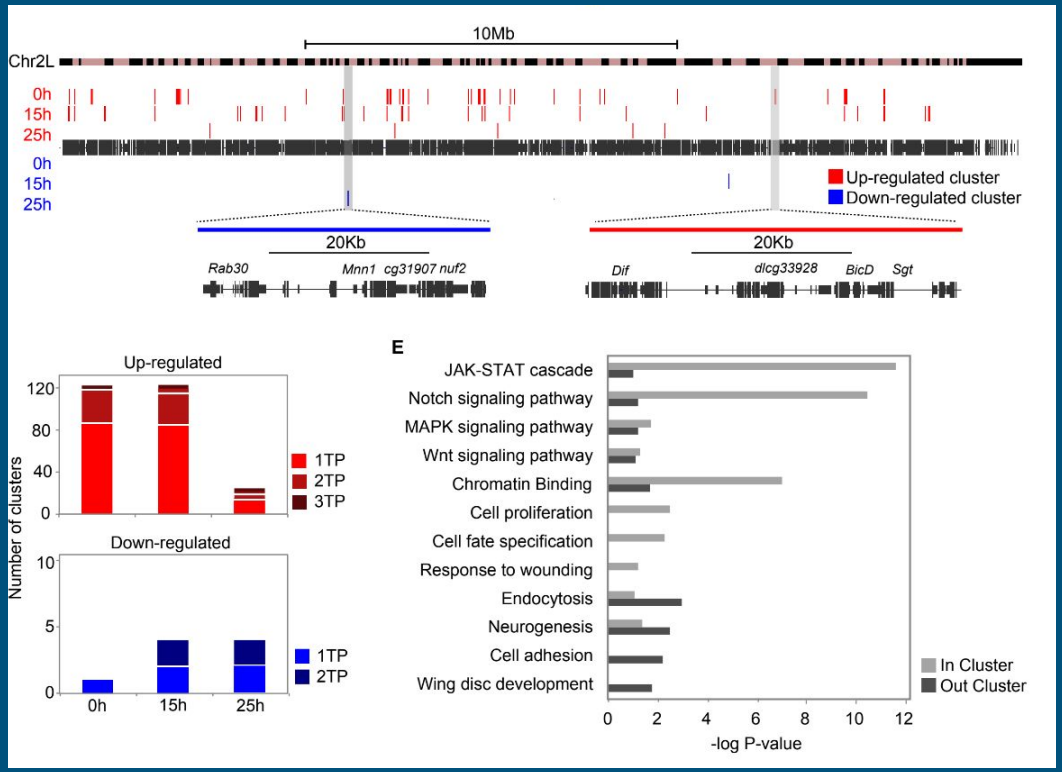
DEG through time



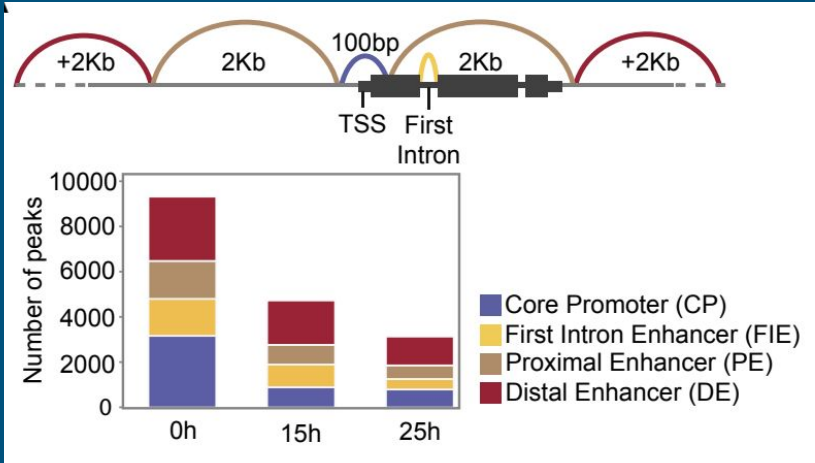
DEG through time

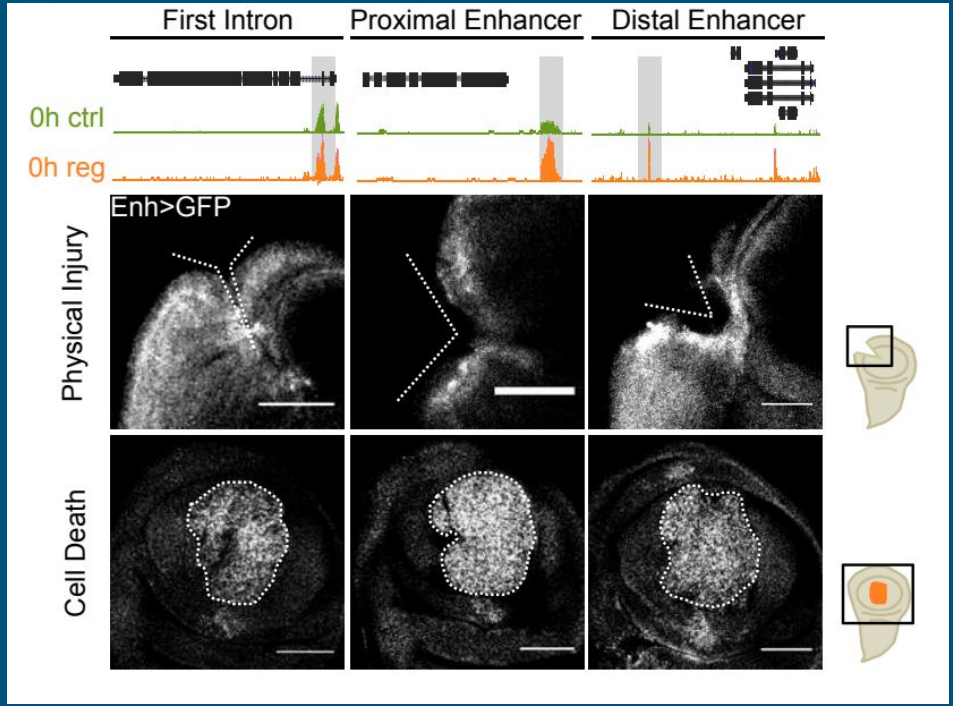


Genomic clusters

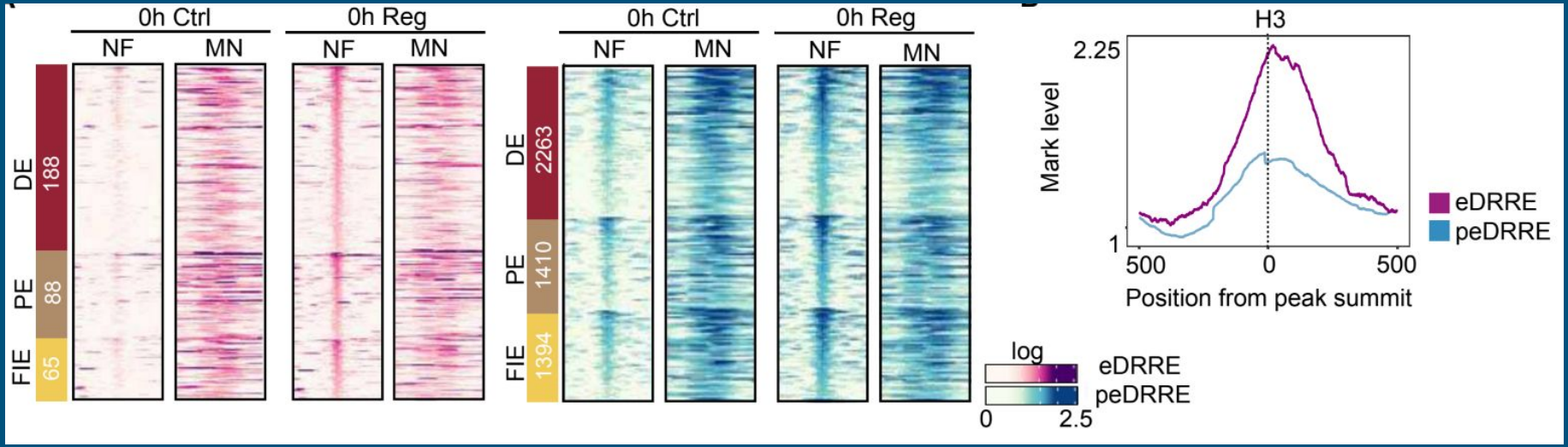


OBJ Accessible chromatin landscape after cell-death induction

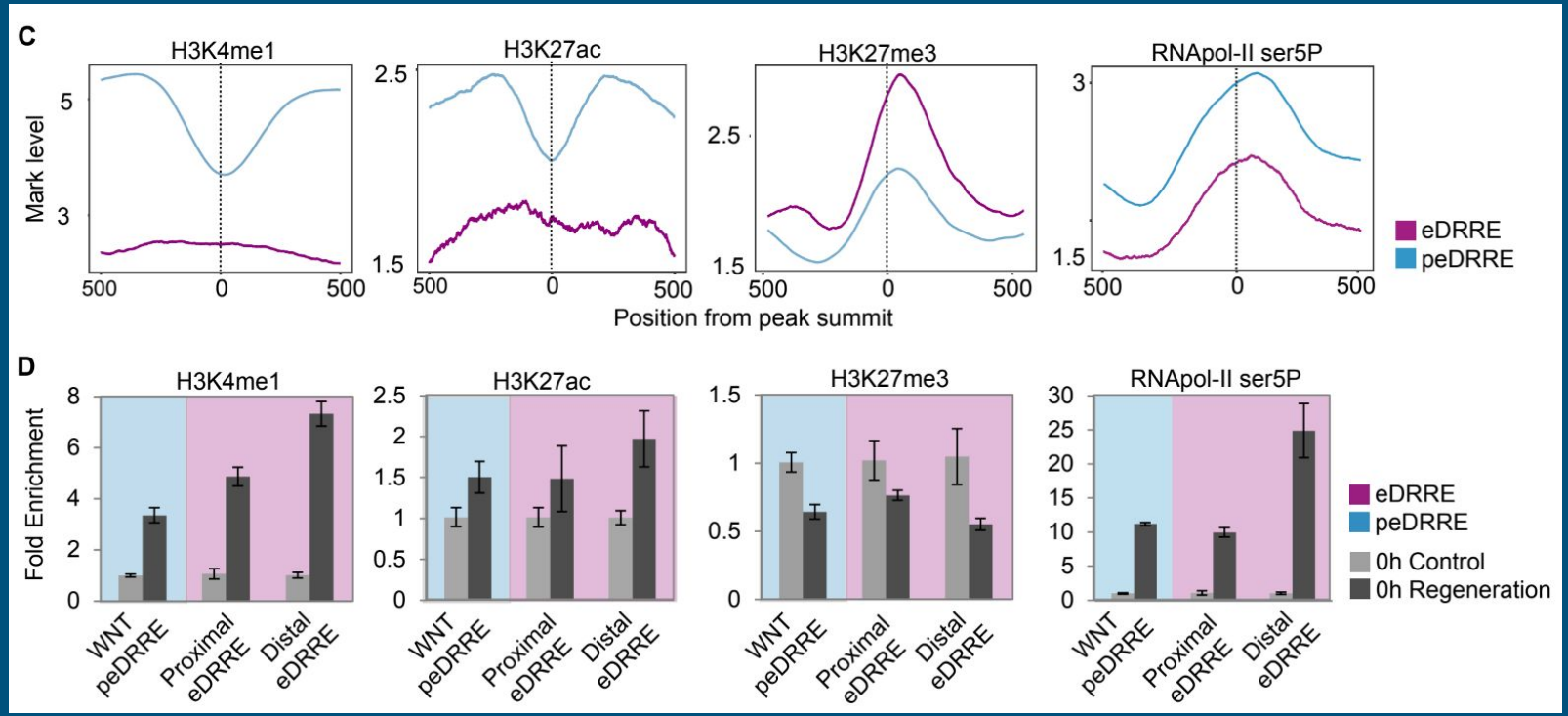




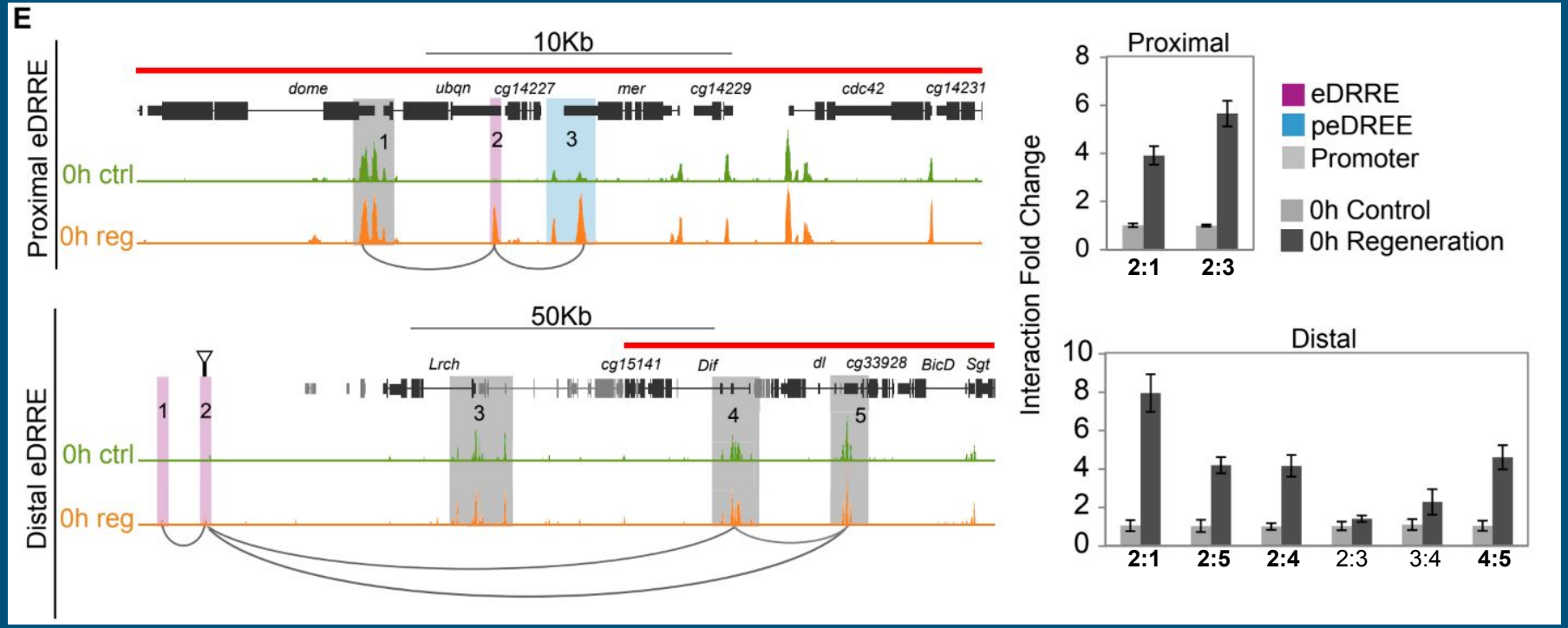
Features of Damage Responding Regulatory Elements (DRRE)



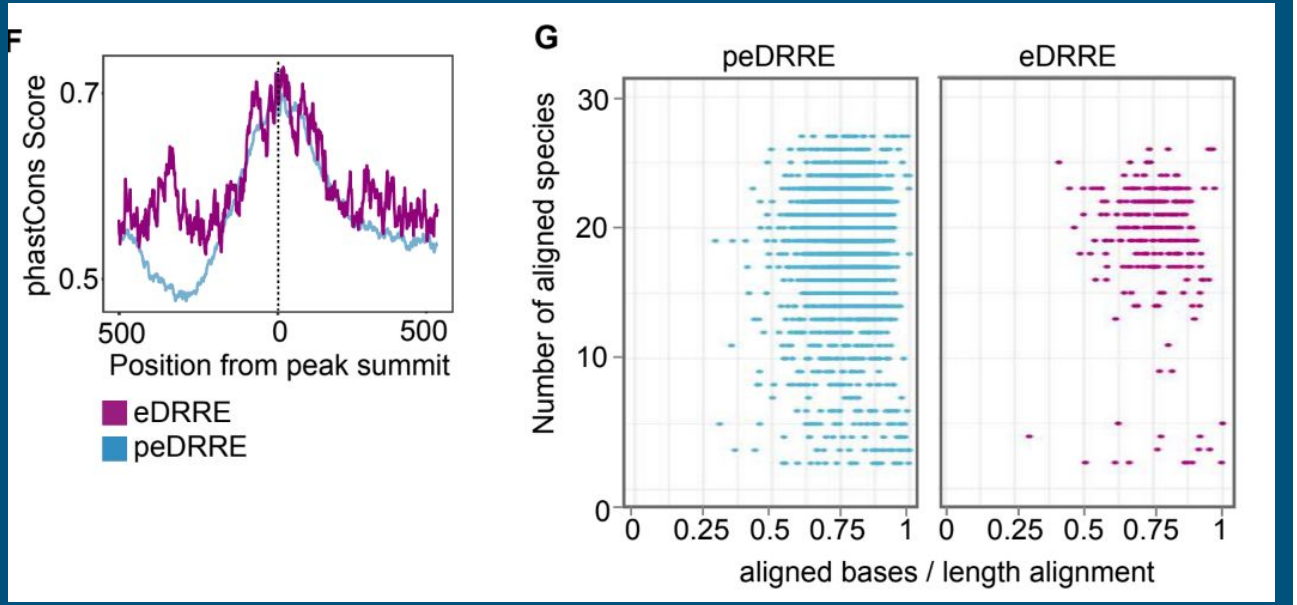
(C) Average profile of active enhancer marks
(D) ChIP-qPCR analysis on DRREs at 0h

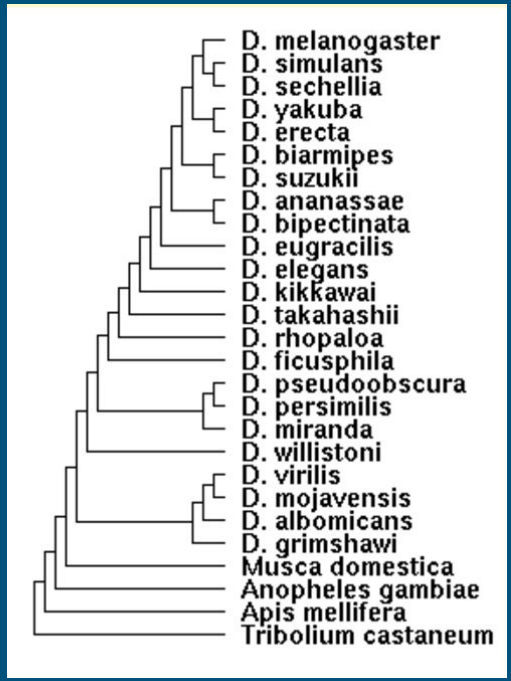


3C interactions eDRRE and genomic clusters



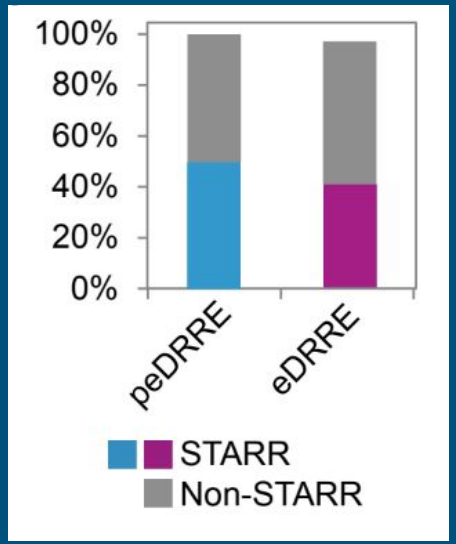
Evolutionary conservation of DRRE



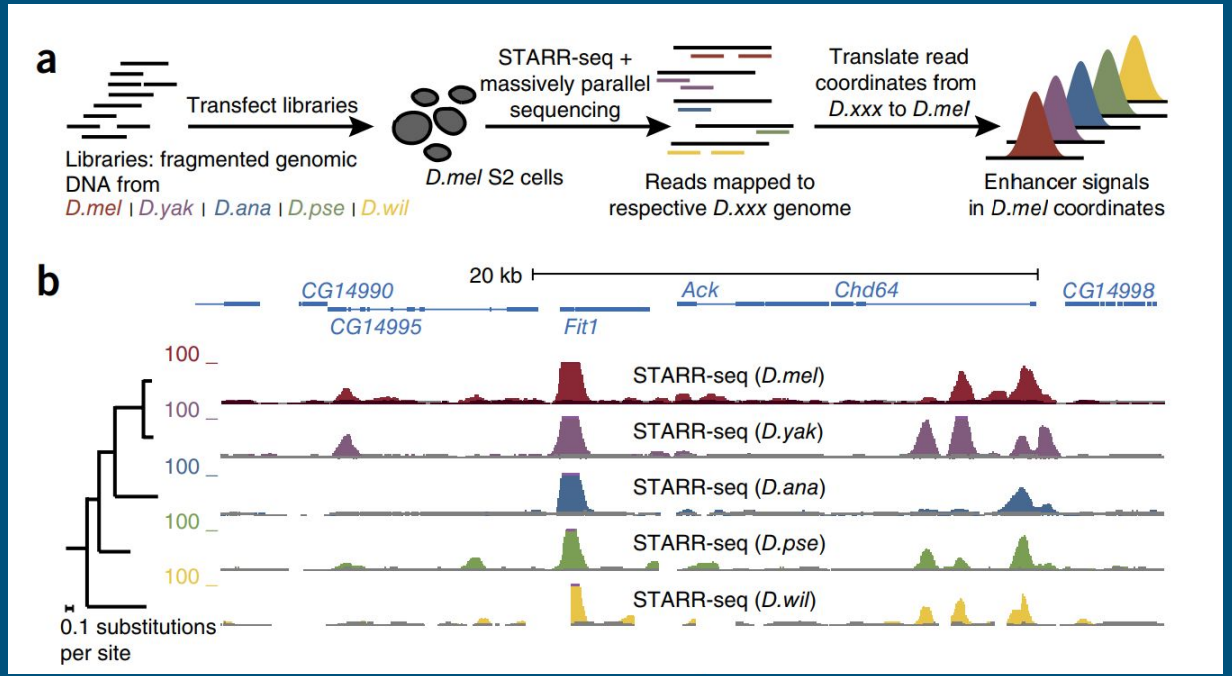


Conservation data: Multiz Alignment & Conservation (27 Species) from UCSC

Evolutionary conservation of DRRE

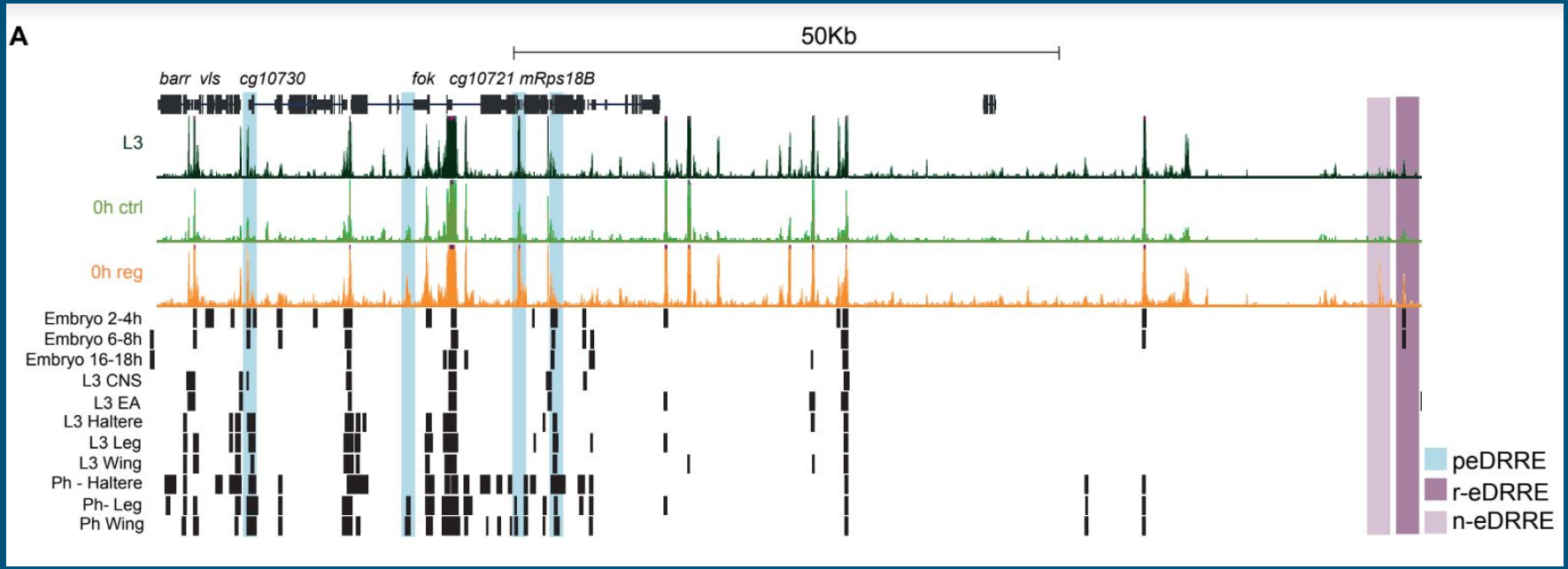


STARR-Seq: Genome-wide enhancer activity profiles



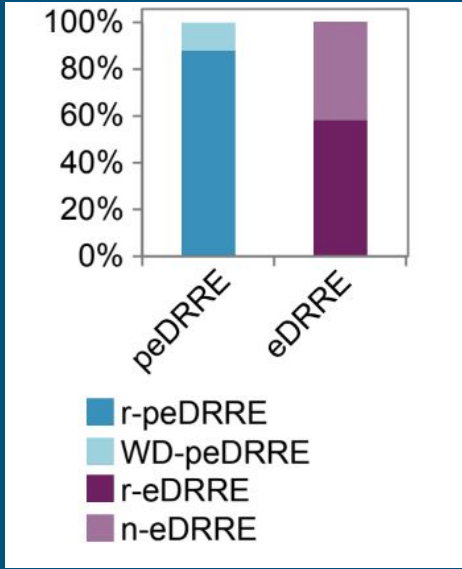
Arnold *et al*. Nat Genet (2014)

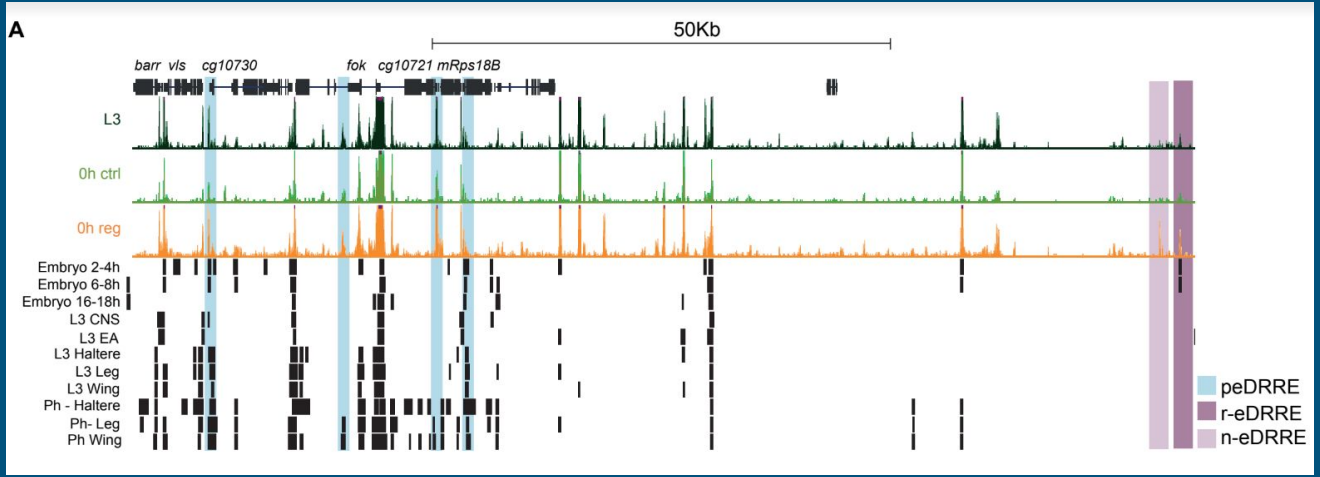
Re-activation of DRRE



FAIRE-Seq data from: McKay & Lieb, Dev Cell. (2013)

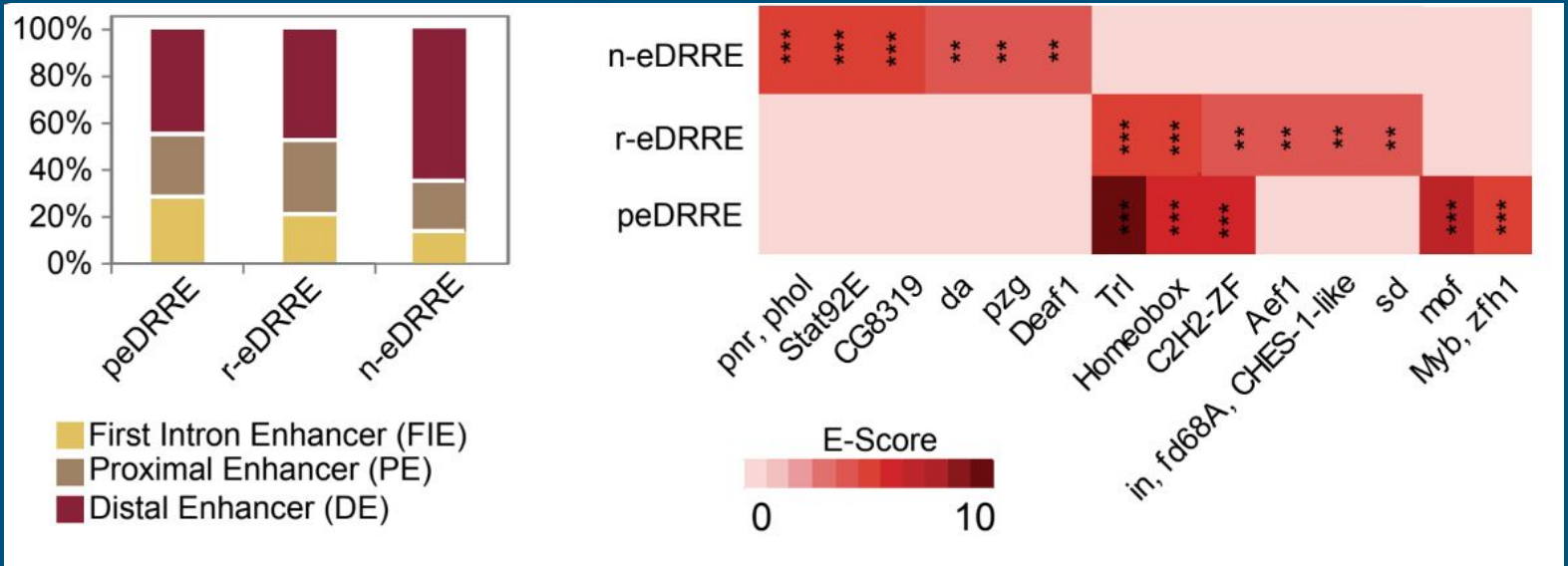
Re-activation of DRRE



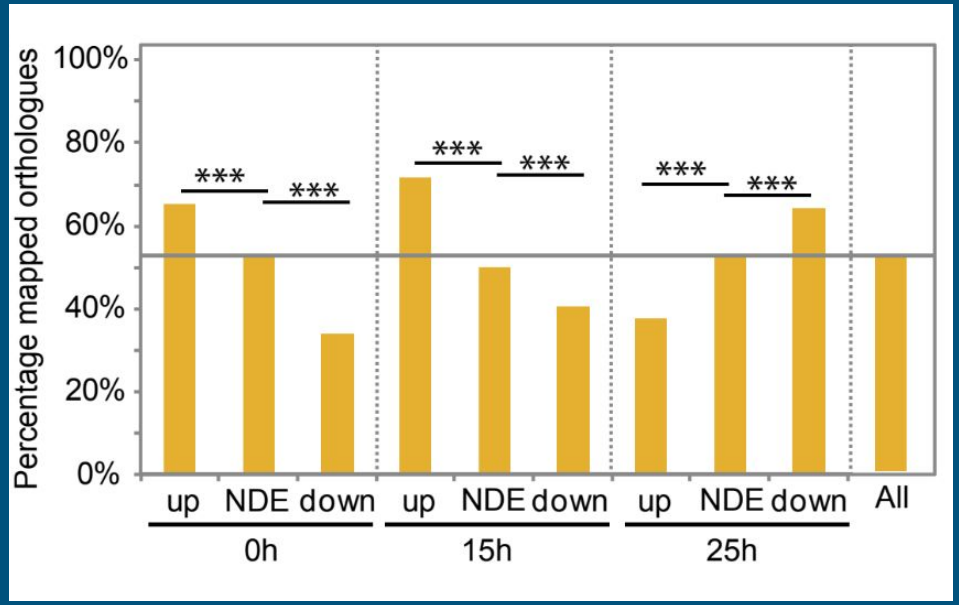


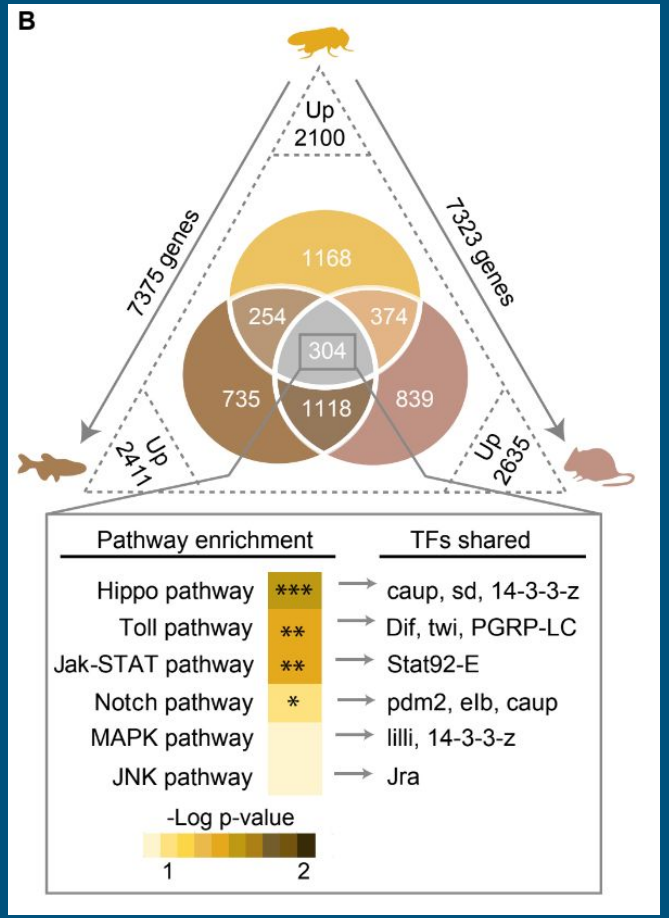
FAIRE-Seq data from: McKay & Lieb, Dev Cell. (2013)

Genomic regions and motif enrichment of DRRE

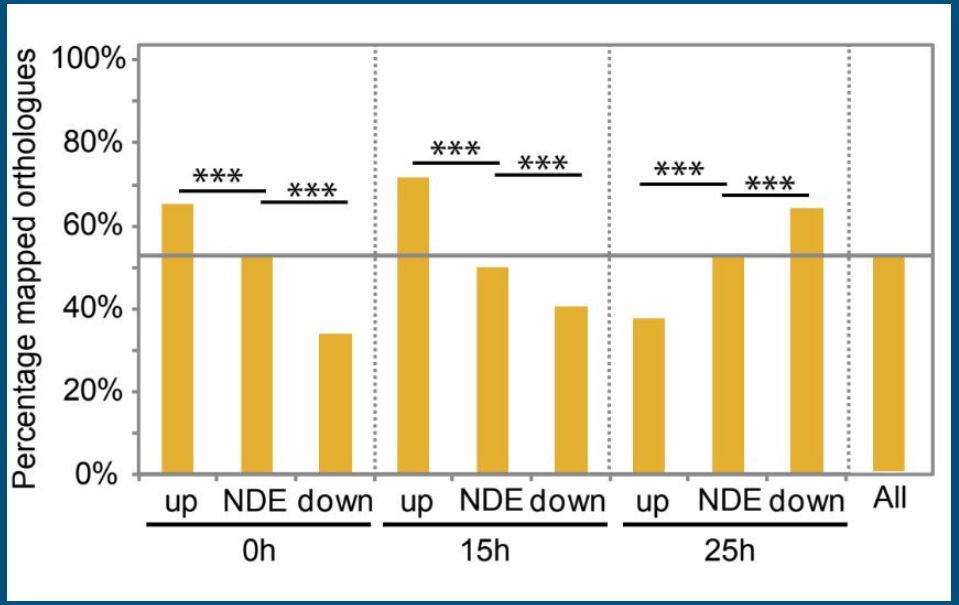


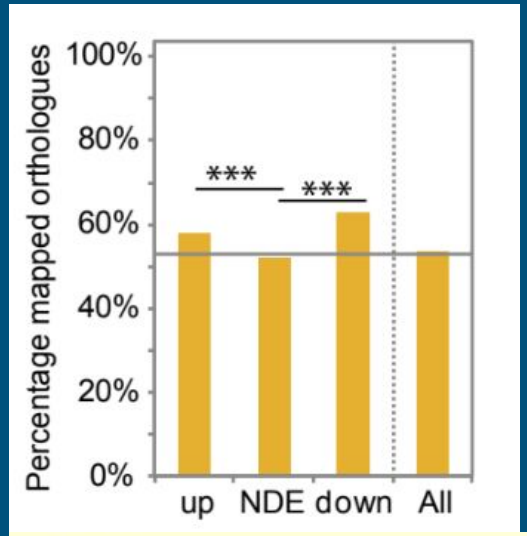
Regeneration toolkit





Eye development as positive control





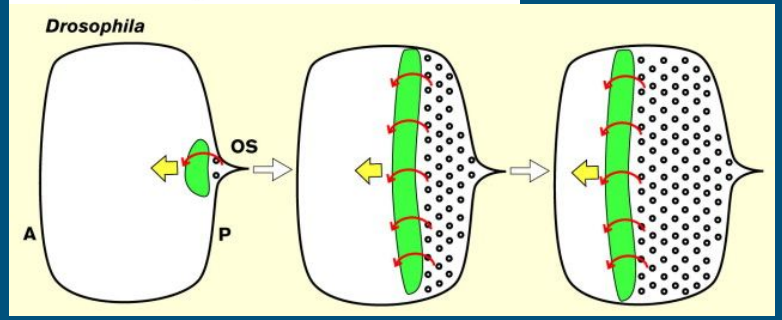
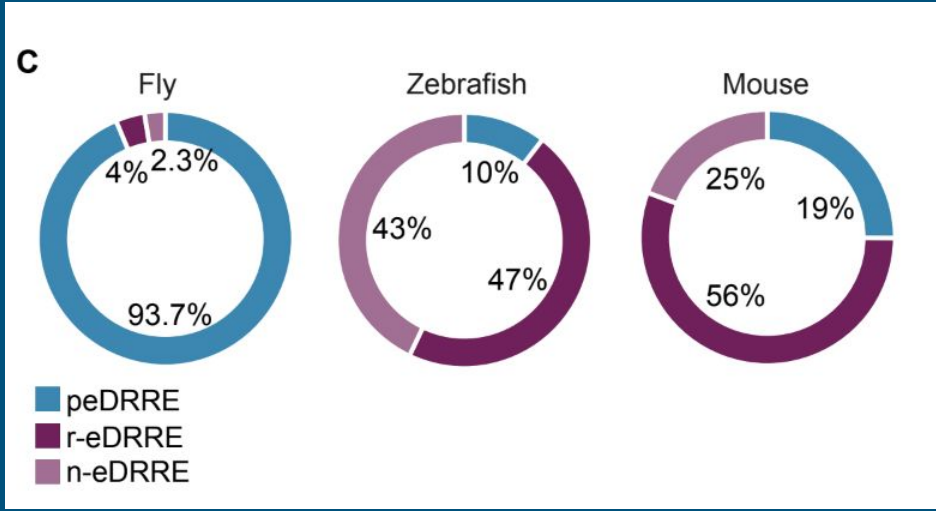
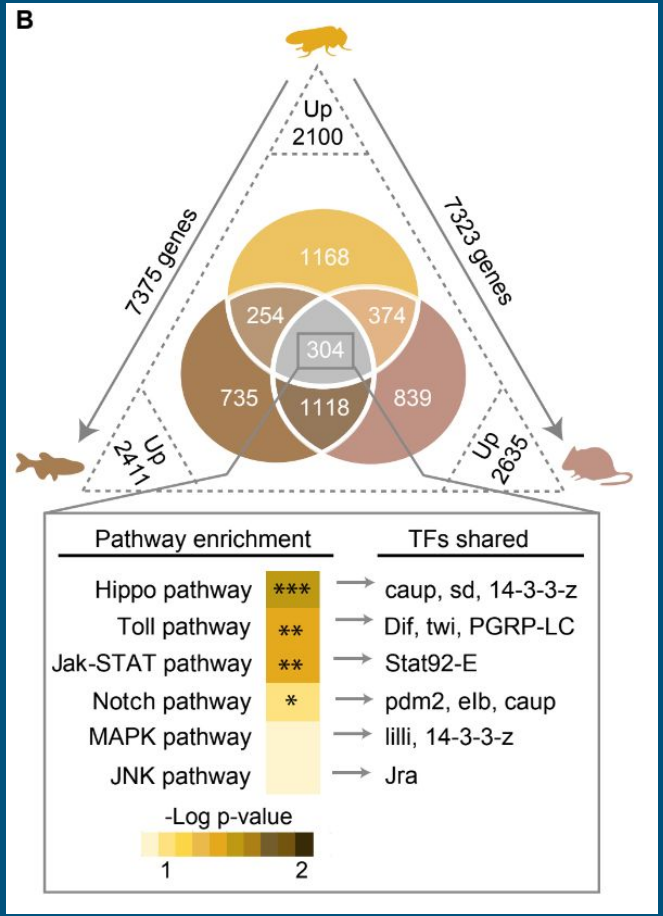


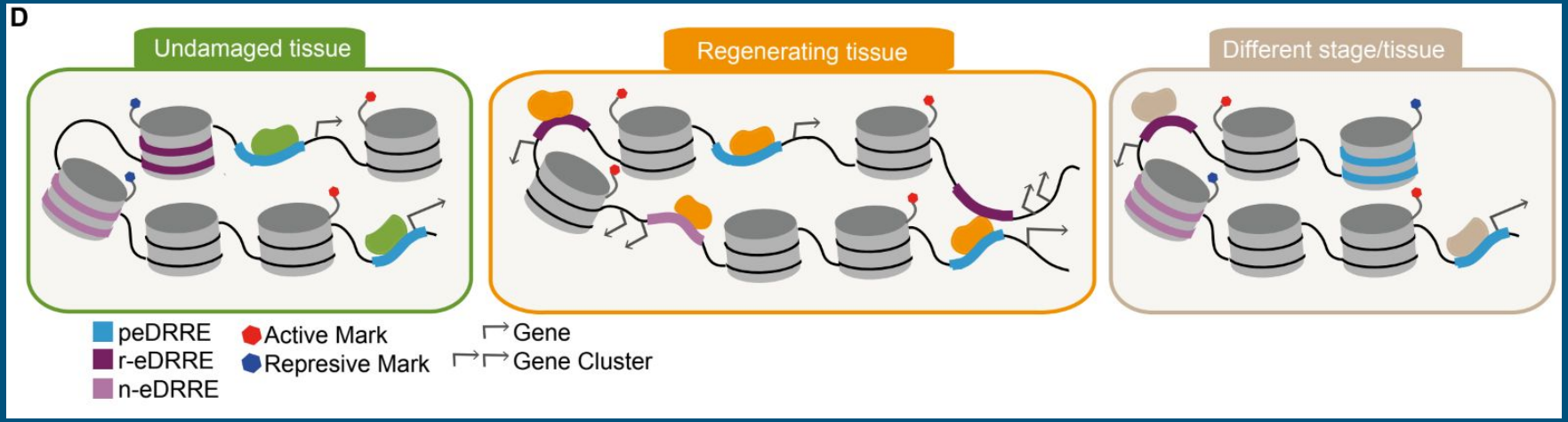
Image from: Jarman, Curr Biol (2000)

Regeneration toolkit





Regeneration regulatory logic



Thanks for your attention!

Developmental Biology and Genomics Lab

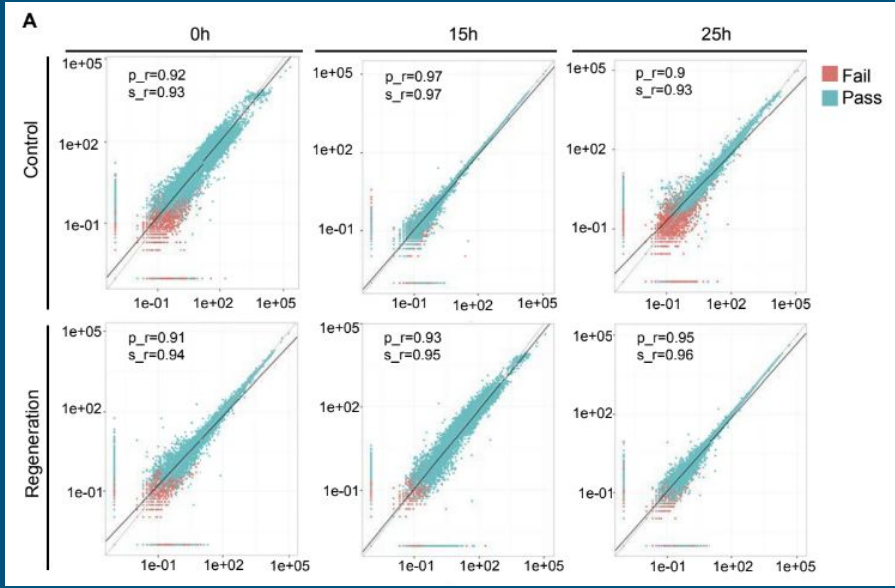
- **Montserrat Corominas**
  - **Elena Vizcaya**
  - Carlos Camillieri
- **Florenci Serras**
  - Paula Santa-Bárbara
  - José Esteban

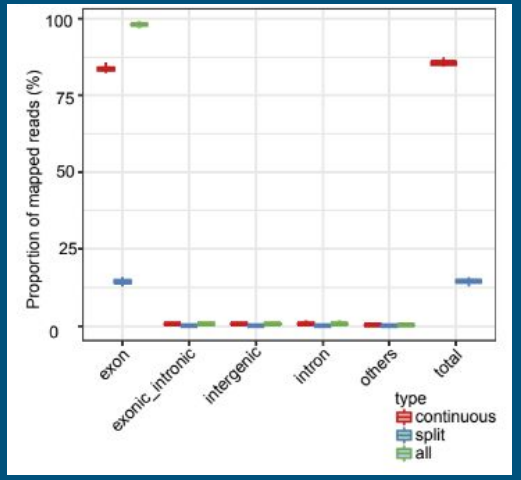
Collaborators

- Mishra's Lab (Hyderabad)
- Skarmeta

Funding

RNA-Seq summary statistics



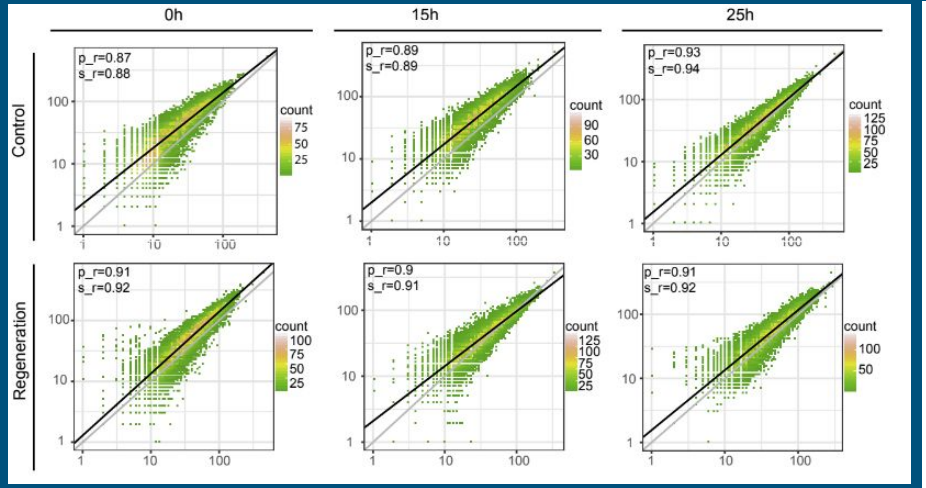


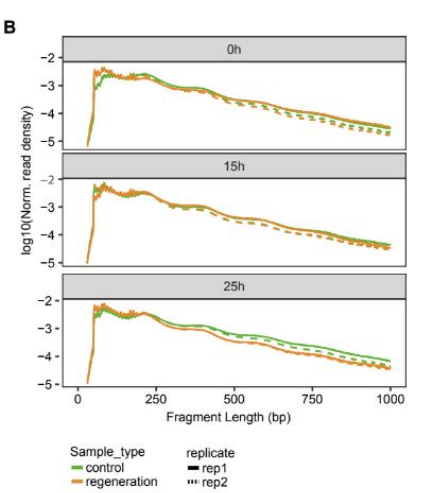
Exp-Id	nb_map_read	nb_uniq_read	prop_map_read	prop_uniq_read
0h-ctrl_rep1	19323620	19065888	83.09	98.67
0h-ctrl_rep2	36442984	35913484	92.95	98.55
0h-reg_rep1	17166784	16797954	83.74	97.85
0h-reg_rep2	19738296	19394714	88.38	98.26
15h-ctrl_rep1	52155568	51379660	95.71	98.51
15h-ctrl_rep2	68513640	67479508	96.43	98.49
15h-reg_rep1	18119846	17824258	89.62	98.37
15h-reg_rep2	18338768	17957018	85.59	97.92
25h-ctrl_rep1	18198962	17913950	93.17	98.43
25h-ctrl_rep2	38587464	37937572	91.59	98.32
25h-reg_rep1	19571362	19181440	85.10	98.01
25h-reg_rep2	26791616	26266120	87.07	98.04

DEG

	0h			15h			25h		
	Up	NDE	Down	Up	NDE	Down	Up	NDE	Down
mRNA	1997	11763	160	1631	12095	194	617	12749	554
ncRNA	99	2314	57	52	2347	71	106	2323	41
pseudogene	14	287	7	14	288	6	16	288	4
rRNA	15	126	6	12	130	5	8	135	4
tRNA	0	313	0	0	313	0	0	313	0
Total	2125	14803	230	1709	15173	276	747	15808	603

ATAC-Seq summary statistics





C

labExpId	total	uniq	prop_uniq
0h-ctrl_NF_rep1	5341626	5199086	97.3
0h-ctrl_NF_rep2	10242146	9975064	97.3
0h-reg_NF_rep1	10775260	10466302	97.1
0h-reg_NF_rep2	11857222	11559318	97.4
15h-ctrl_NF_rep1	8261020	7960502	96.3
15h-ctrl_NF_rep2	12779268	12368228	96.7
15h-reg_NF_rep1	9441288	9178988	97.2
15h-reg_NF_rep2	12362538	11997774	97.0
25h-ctrl_NF_rep1	9936622	9672454	97.3
25h-ctrl_NF_rep2	11242928	10976686	97.6
25h-reg_NF_rep1	10745466	10382710	96.6
25h-reg_NF_rep2	13657716	13253602	97.0

D

labExpId	total	uniq	prop_uniq
0h-ctrl_MN_rep1	10876938	110526732	96.7
0h-ctrl_MN_rep2	10286054	998006	97.0
0h-reg_MN_rep1	8023184	766414	96.7
0h-reg_MN_rep2	10384794	10065668	96.9
15h-ctrl_MN_rep1	7126620	6811380	95.5
15h-ctrl_MN_rep2	10716514	10293398	96.0
15h-reg_MN_rep1	12144392	11646416	95.8
15h-reg_MN_rep2	8268676	7992674	96.6
25h-ctrl_MN_rep1	11086670	10755750	97.0
25h-ctrl_MN_rep2	11732148	11411698	97.2
25h-reg_MN_rep1	8603818	8192000	95.2
25h-reg_MN_rep2	10699724	10326310	96.5

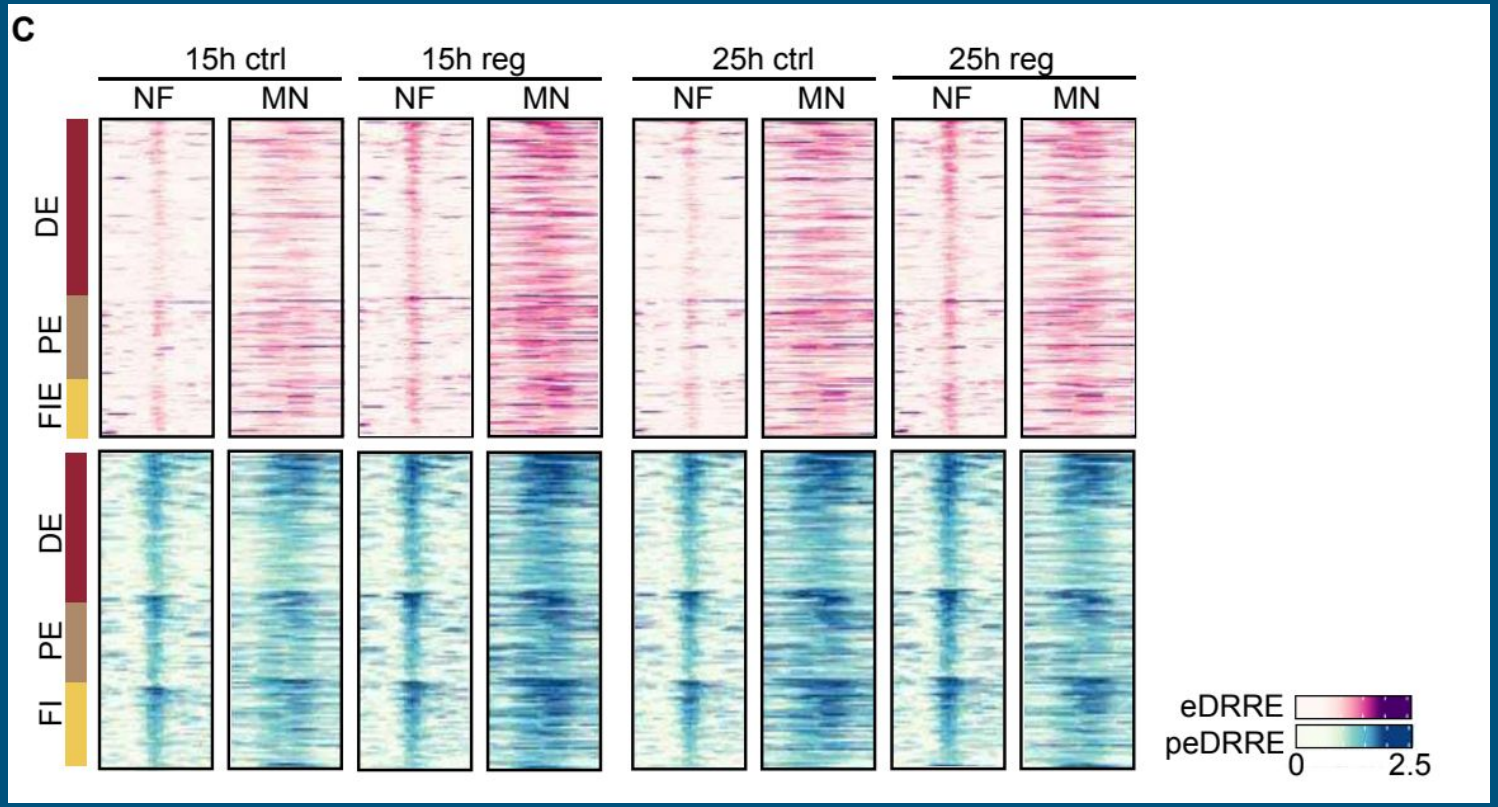
E

	0h	15h	25h
More accesible	9319	4732	3137
Less accessible	56	620	709

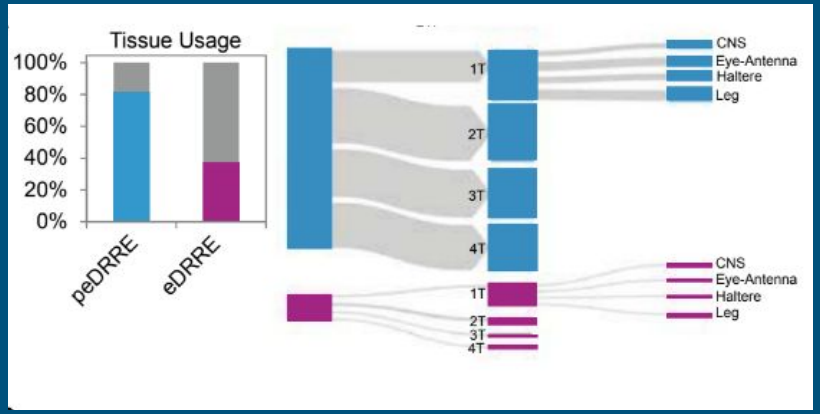
TFs in DEG


0h
15h
25h
ac pdm2 Hr78 Bug22 fd68A dys
aop zfh1 Hr96 CG17118 CG14117 Cap-D2
bi Eip78C BEAF-32 CG12299 CG17359 CG15514
bic 14-3-3zeta Rbf CG6686 CG9425 CG12054
chif ash1 Max Plzf CG8765 lilli
eg Sox15 bon RpL7-like CG11456 key
Eip75B Psc edl CG7099 MED27 CG18764
e(y)1 Ets98B Mnt CG10262 CG9727 lilli
ftz-f1 Parp drm CG10462 Zif cbt
His2Av Trf az2 Br140 nom CG31381
Hmr brat hang trsn Kdm2 Blos1
Jra woc jim sug sage Cog7
kni Taf1 Ogg1 mip120 CG4820 CG31111
knrl TfIIS MBD-like CG6701 CG6791 CG31365
crp Gug MTA1-like CG8089 CG7987 CG31875
E(spl)m3-HLH scat Ercc1 MESR4 pad
Met Iswi CHES-1-like CG10543 CG17803
E(spl)mbeta-HLH Med CG14441 CG10321 MED17
E(spl)mdelta-HLH Mlh1 CG2202 MED23 mRpL55
pk E2f1 CG1529 enok CG4424
sd Trl CG15435 CG4049 p53
svp TfIIA-S CG7818 CG11414 CG5789
RpL40 Deaf1 CG13123 CG10576 XNP
Ssrp mre11 CG3032 CG12391 CG5641
TfIIFalpha Su(z)12 CG2116 fand Rbf2
corto Zfrp8 CG7246 CG4282 CG7357
Taf6 cyc CG11696 lms SMC1
ato Chd3 CG9215 CG9890 CG31510
Taf12 Sox100B Nprl2 ebd1 SMC5
Snr1 kin17 Her hng3 CG33213
lrbp Optix Trn-SR CG2199
Mcm2 Rad17 CG3407 ERR
glu Tip60 CG17612 CG7839
SMC3 CDC45L Rat1 Pop2
Dref Dek d4 MED31
Rpd3 Hmg-2 Not3 Pbp95
Stat92E CG2790 CG1603 CG8319
Rpl1 CG12018 CG1602 CG8478
Cdk9 fu2 CG1663 MBD-R2
crm fru D19B CG6789 Asciz Opbp
E(z) RpII15 Orc1 CG9175 mkg-p CG31388
gro elB yps Sfmbt phol sc
her yem E2f2 CG10366 toe vri
kz wdn XRCC1 Clamp M1BP dalao
wek PCNA Acf1 CG12744 CG14710 CG15812
Myb dpn CG3726 row CG10214 pygo
pnr ken CG3815 CG11906 CG7928
Tbp caup Nf-YC NC2alpha Hcf
z dpa CG12075 pita CG12219
value
−1.0 −0.5 0.0 0.5 1.0
classification
0h_upregulation
15h_upregulation
25h_upregulation
2TP_0−15h_upregulation
2TP_0−25h_upregulation
2TP_15−25h_upregulation
3TP_upregulation

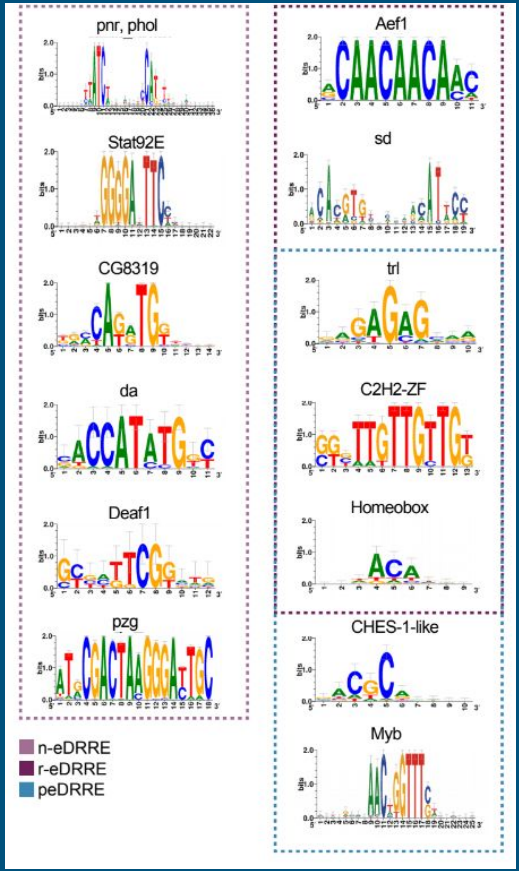
0h DRRE across time



Re-activation



Motif search



B

novel eDRRE		
	TF	Score
1	grn, **pnr**, pho, **phol**	5,01
2	CG12236	4,91
3	**Stat92E**	4,67
4	pan	4,57
5	**CG8319**	4,44
6	**da**	4,41
7	**Deaf1**	4,39
8	hth	4,26
9	CG17829	4,21
10	**pzg**	4,16

reused eDRRE		
	TF	Score
1	**trl**	5,47
2	**Homeodomain**	4,76
3	Mad	4,36
4	**C2H2-ZF**	4,34
5	Adf1	4,22
6	**Aef1**	4,22
7	dm	4,17
8	inv, en	4,06
9	**sd**	4,04
10	**mof**	3,77

peDRRE		
	TF	Score
1	**trl**	9,95
2	**in**, **fd68A**, jumu , **CHES-1-like**	7,2
3	**C2H2-ZF**	7,06
4	grh	6,59
5	CG5245, CG4360, Meics	6,45
6	**Homeodomain**	6,12
7	gem	6
8	**Myb, zfh1**	5,25
9	foxo	5,25
10	Psi	5,11

Orthologues

	0h			15h			25h		
	up	NDE	down	up	NDE	down	up	NDE	down
Mapped in both species	1269	5880	54	1154	5972	77	227	6625	351
Only mapped in zebrafish	19	133	2	23	128	3	5	141	8
Only mapped in mouse	18	83	0	14	86	1	5	92	4
non-mapped	691	5667	104	440	5909	113	380	5891	191
total	1997	11763	160	1631	12095	194	617	12749	554
% mapped	65,3980971	51,8235144	35	73,022685	51,1451013	41,7525773	38,411669	53,7924543	65,523466

	Chi-Value		P-value	
	up	down	up	down
0h	126,56	17,889	0	2,342E-05
15h	276,5	6,74	0	0,0094
25h	55,9	29,44	0	6E-08

Eye development

B

	Eye differentiation		
	up	NDE	down
Mapped in both species	978	5105	1120
Only mapped in zebrafish	29	103	22
Only mapped in mouse	7	73	21
non-mapped	758	5019	685
total	1772	10300	1848
% mapped	57,2234763	51,2718447	62,9329

Chi-Value		P-value	
up	down	up	down
21,461	85,543	3,61E-06	0