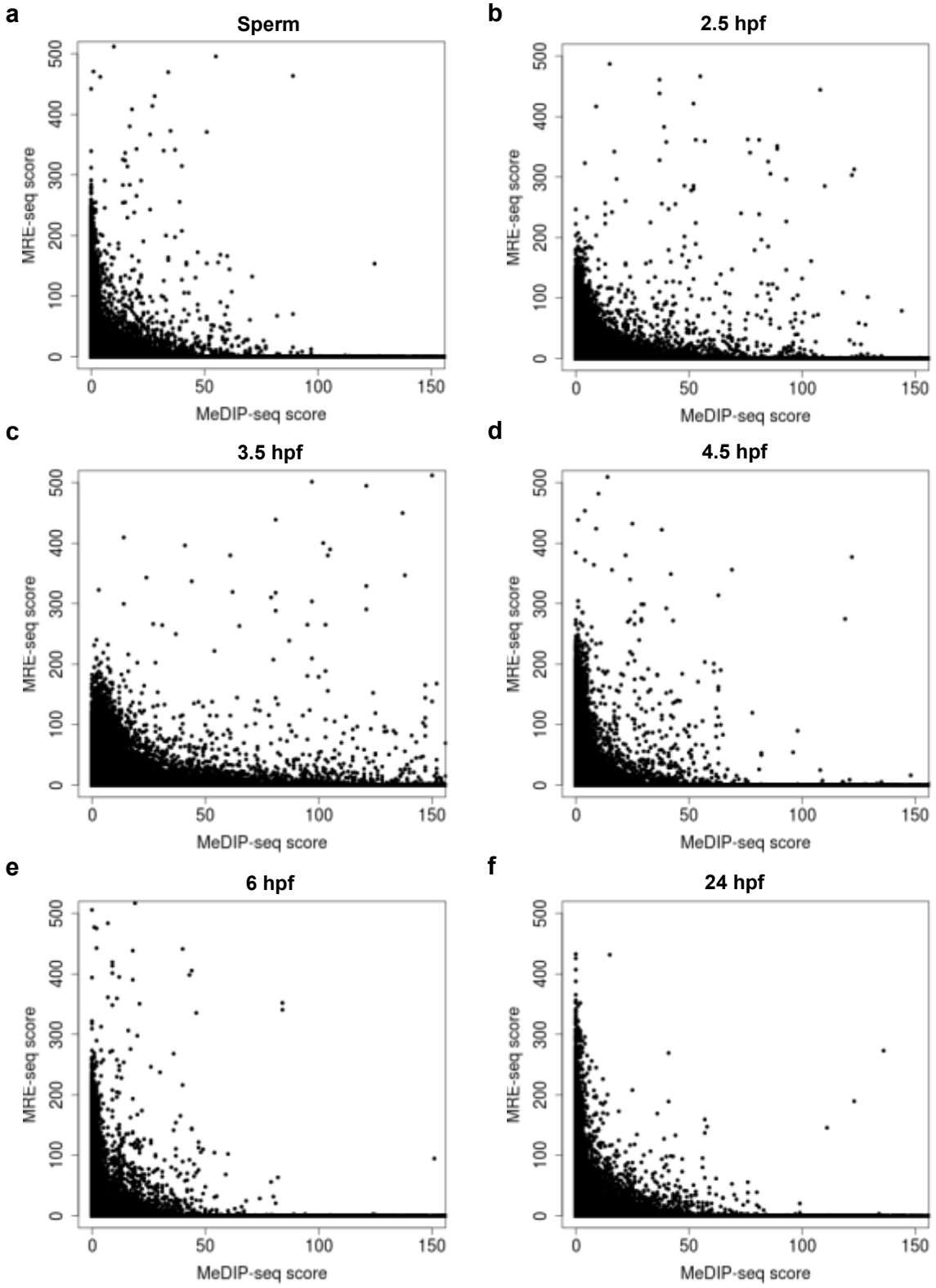
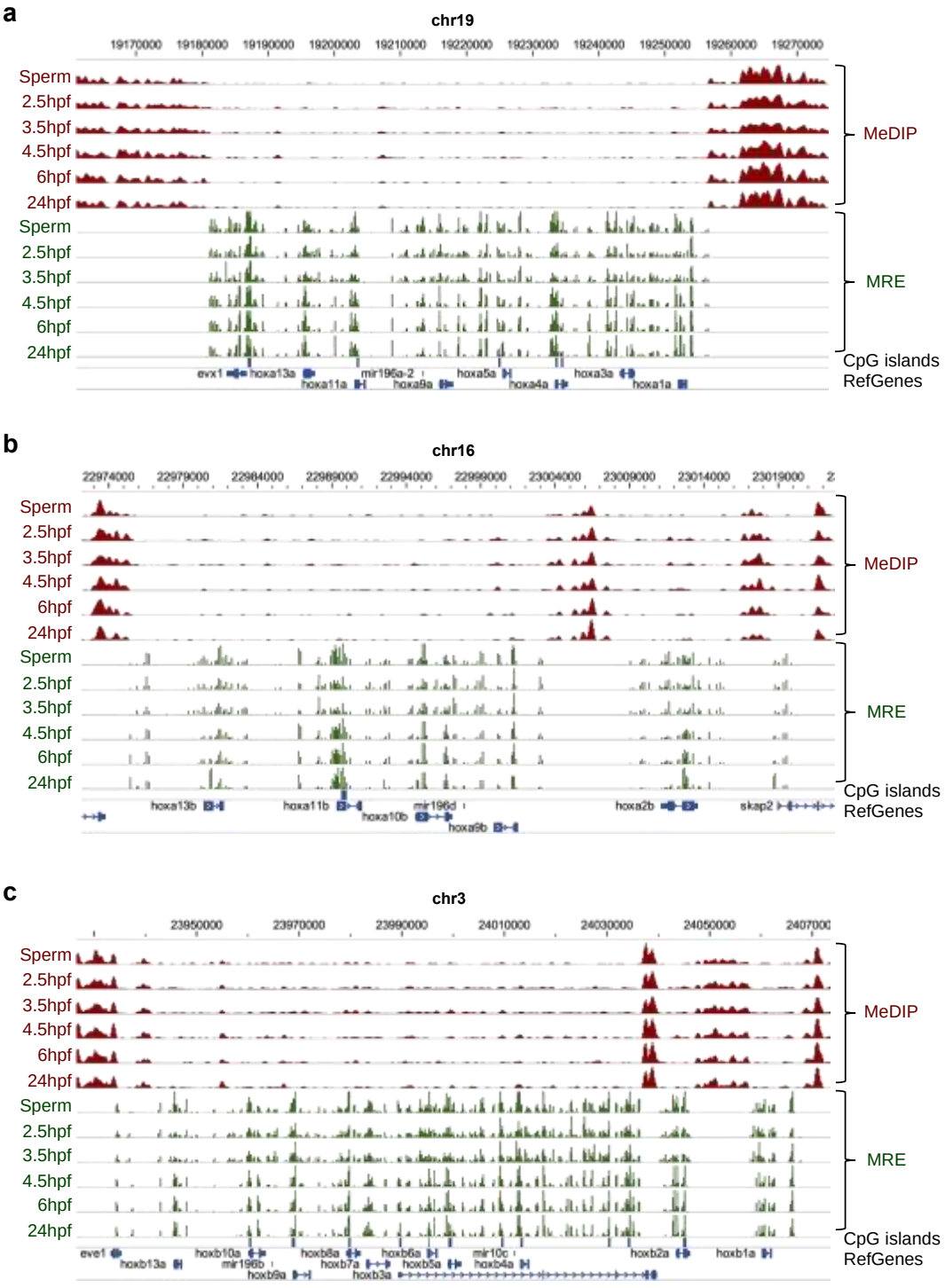
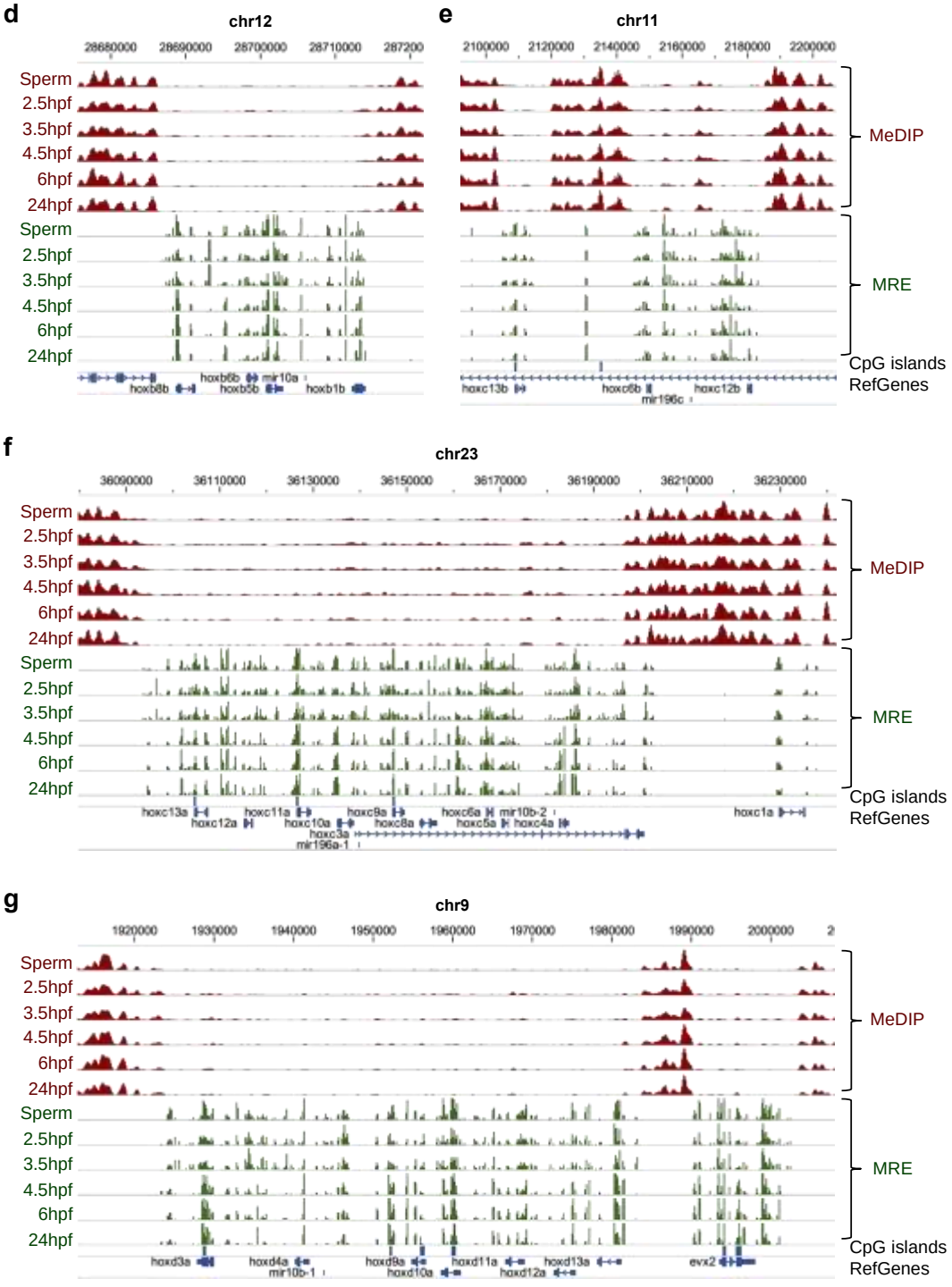
Supplementary Figure 1. Inverse correlation between MeDIP-seq and MRE-seq signals: (**a**) sperm, (**b**) 2.5 hpf, (**c**) 3.5 hpf, (**d**) 4.5 hpf, (**e**) 6 hpf and (**f**) 24 hpf embryos.



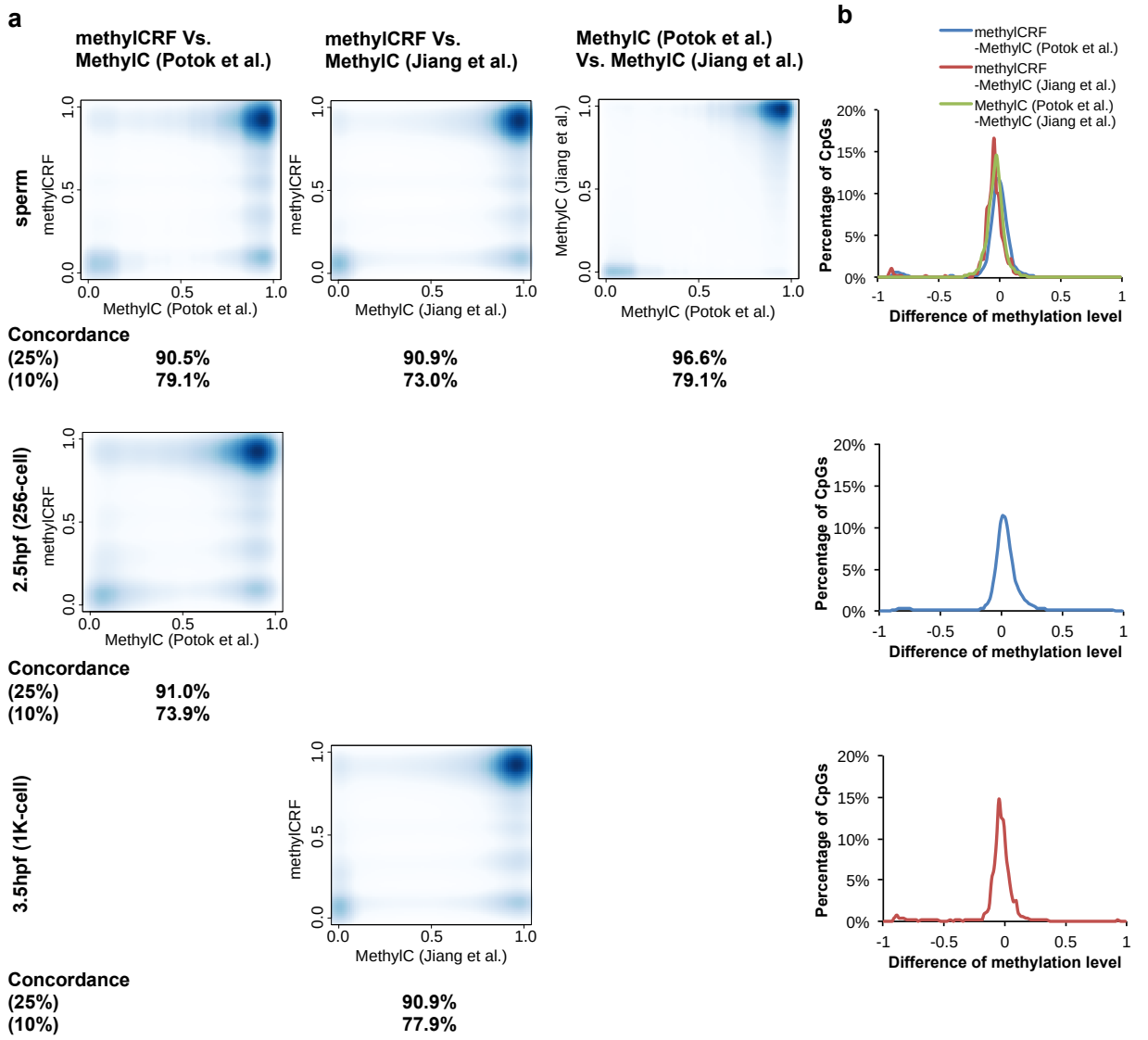
Supplementary Figure 2. Epigenome Browser views of all 7 zebrafish *hox* gene clusters: (**a**) *hoxAa*, (**b**) *hoxAb*, (**c**) *hoxBa*, (**d**) *hoxBb*, (**e**) *hoxCb*, (**f**) *hoxCa* and (**g**) *hoxDa*. The *hox* genes encode transcription factors that are important in development. All of the *hox* gene clusters are hypomethylated in all 6 developmental stages, and the neighboring regions of the clusters are mostly methylated. MeDIP-seq libraries and MRE-seq libraries covered largely non-overlapping regions.



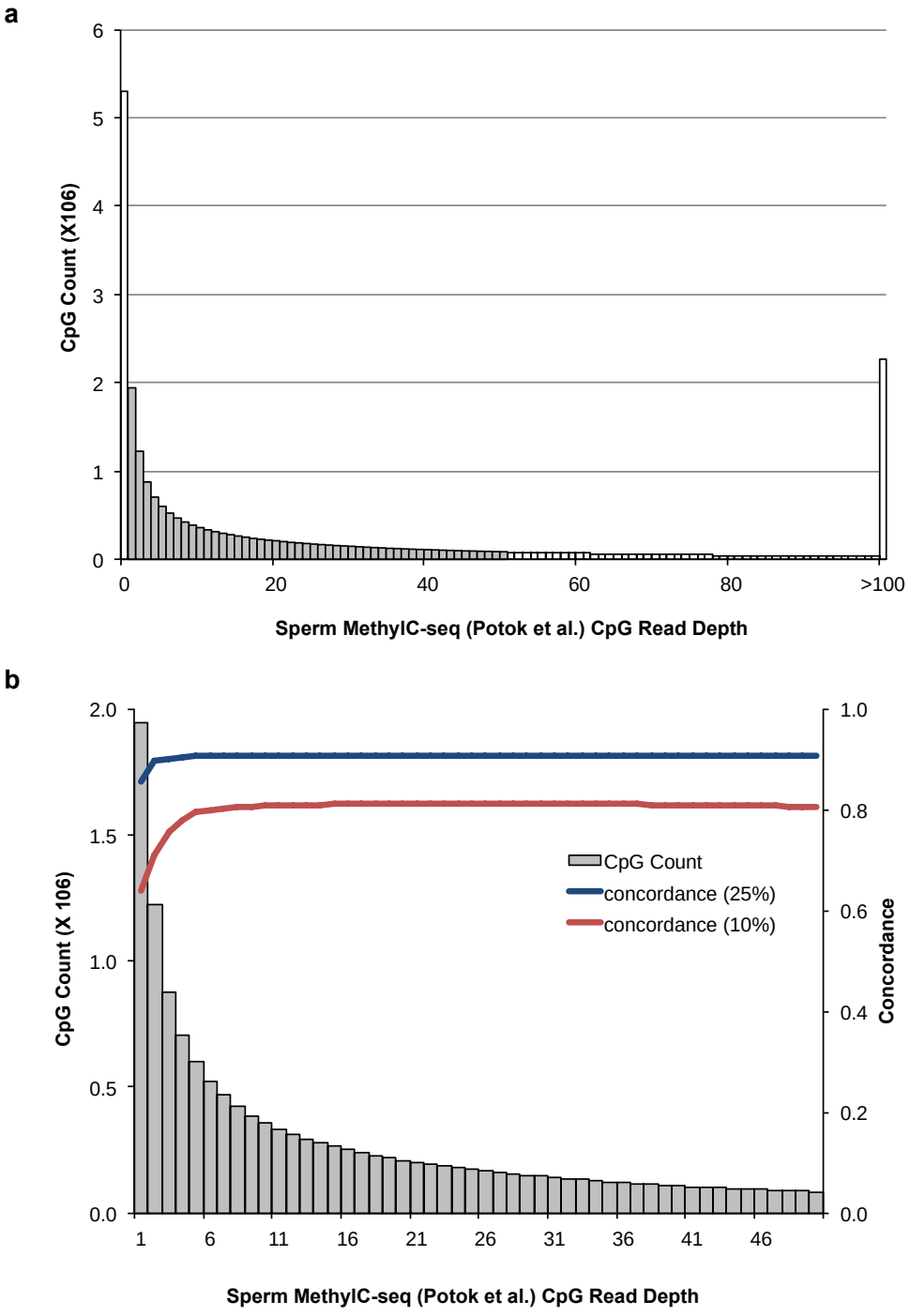
Supplementary Figure 2. Continued.



Supplementary Figure 3. Concordance between methylCRF and MethylC-seq predictions. (**a**) Density plots comparing methylCRF and MethylC-seq methylation levels at each CpG. CpGs without MethylC-seq predictions were excluded from each comparison. The concordances calculated based on 0.25 and 0.1 window differences were displayed below each density plot. (**b**) The histogram of CpGs with differences between methylCRF and MethylC-seq predictions. In each comparison, more than 90% CpGs had differences smaller than 0.25 between methylCRF and MethylC-seq.

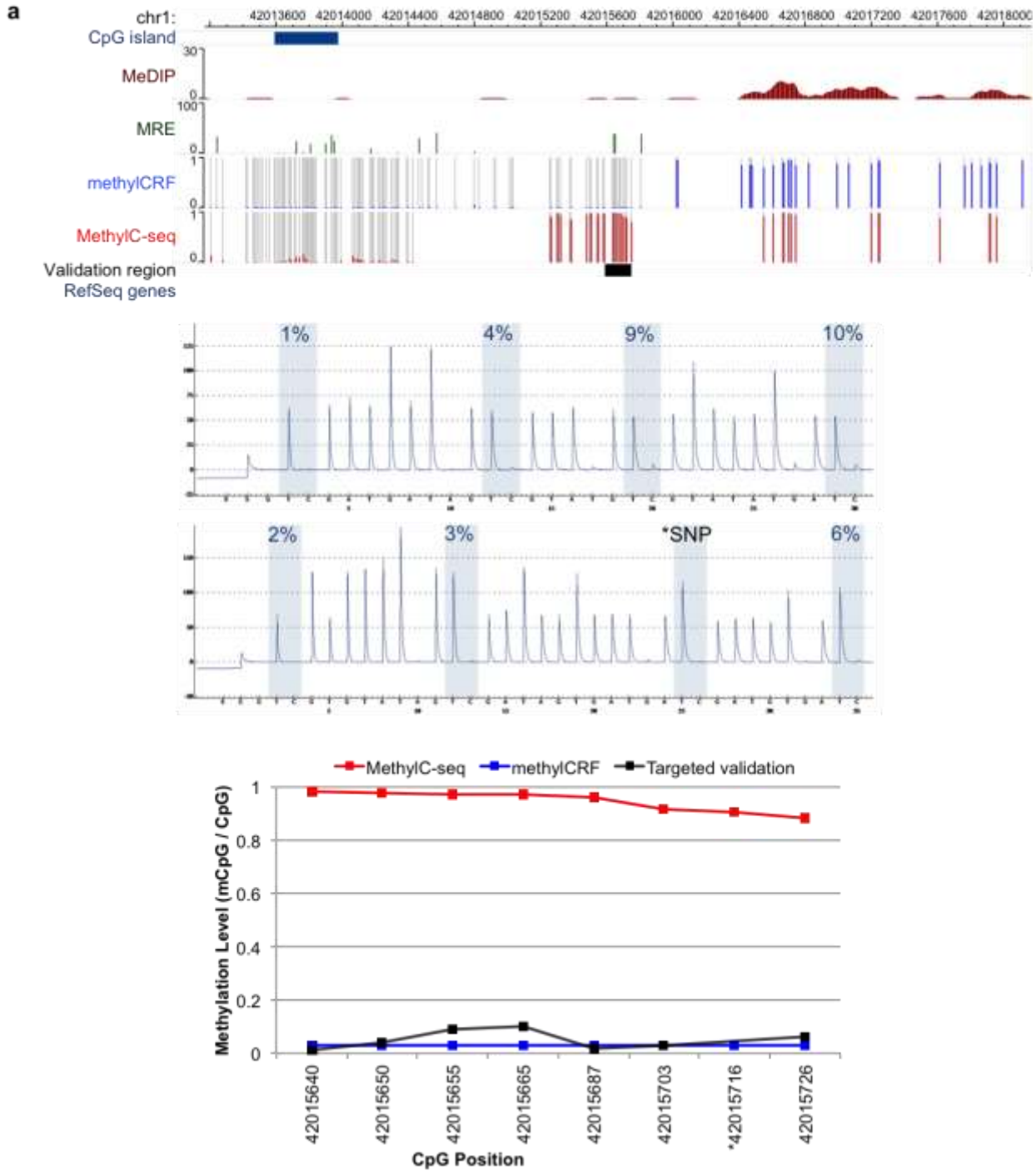


Supplementary Figure 4. The read depth of MethylC-seq affects the concordance between MethylC-seq and methylCRF. (**a**) The histograms of CpG read depths in the sperm MethylC-seq library from Potok et al. A large fraction of CpGs were not covered or only covered by a few reads (10,050,087 CpGs had < 5 reads). Grey bars indicate CpGs that are also shown in (**b**). (**b**) Concordance between MethylC-seq and methylCRF (right y-axis) as a function of MethylC-seq read depth cutoff. Concordance between MethylC-seq and methylCRF significantly increased with increasing sequencing depth cutoff of MethylC-seq.



Supplementary Figure 5. Experimental validation of regions that exhibited discordance between MethylC-seq (Potok et al.) and methylCRF of sperm. Eight regions were validated using either clonal sequencing or pyrosequencing from PCR amplicons of bisulfite-treated genomic DNA of sperm. (**a-h**) Comparison of the eight validated regions. Within each panel, the top part is an Epigenome Browser view containing the validated region, directly comparing genomic data (i.e. methylCRF vs MethylC-seq) in and around the validated region. The validated regions are marked by a black bar. The middle part is the validation experiment (either targeted clonal validation, shown as aligned open/closed circles, or pyrosequencing result, shown as a pyrogram). The bottom part is a line graph of methylation levels in validated region, directly comparing methylCRF values, MethylC-seq values, and values from validation experiments. Open circles indicate unmethylated CpG; closed circle, methylated CpG. The asterisk * indicates absence of CpG site due to a SNP. (**a**) chr1:42015593-42015753 (**b**) chr14:25157201-25157370 (**c**) chr20:39657499-39657620 (**d**) chr22:12335157-12335326 (**e**) chr24:27012514-27012771 (**f**) chr14:20461146-20461441 (**g**) chr21:8582721-8582922 (**h**) chr5:46270017-46270621 (**i**) A table that summarizes the comparison. The root-mean-squared error (RMSE) was calculated between MethylC-seq or methylCRF and targeted experimental validation.

Supplementary Figure 5. Continued.



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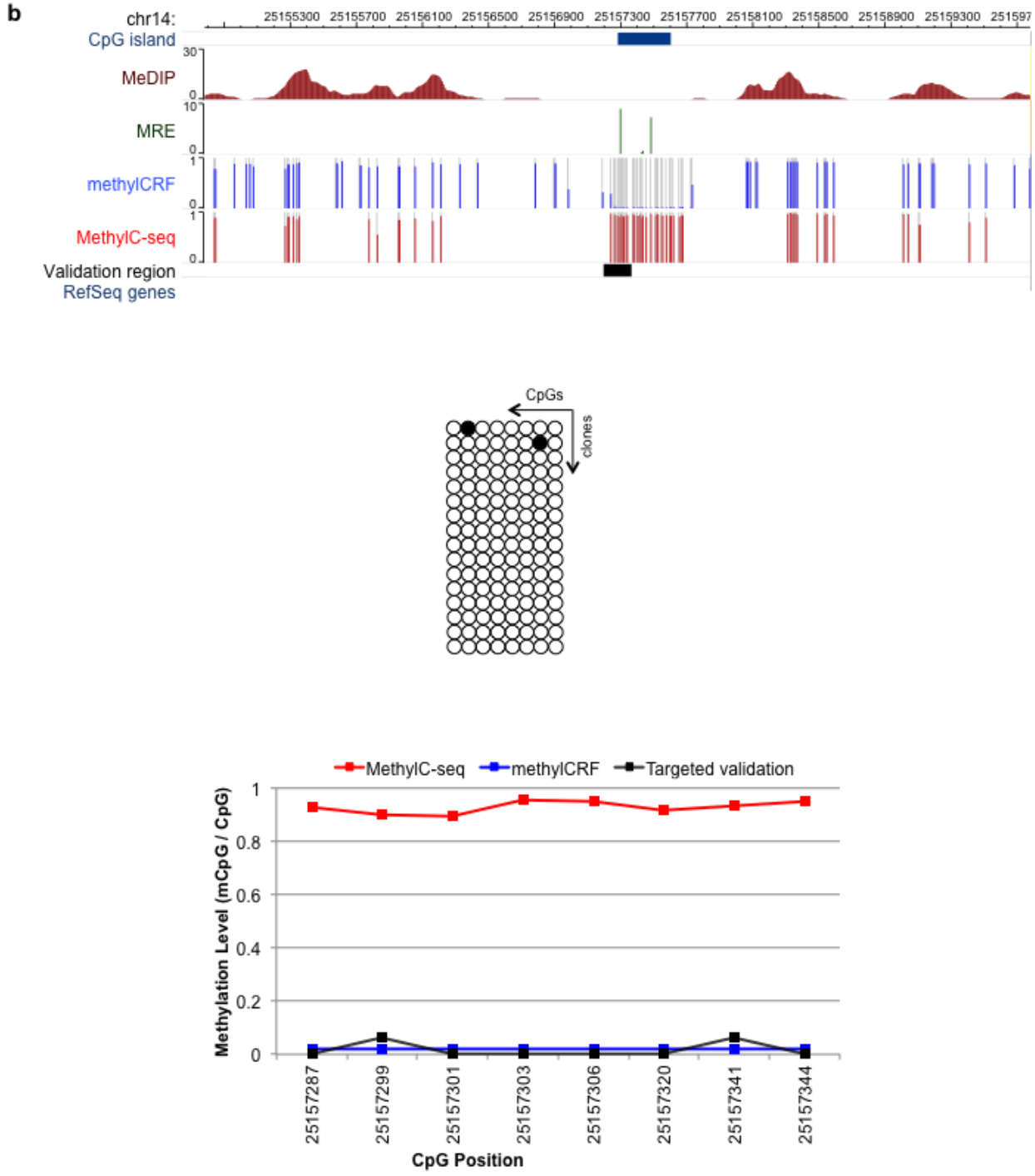
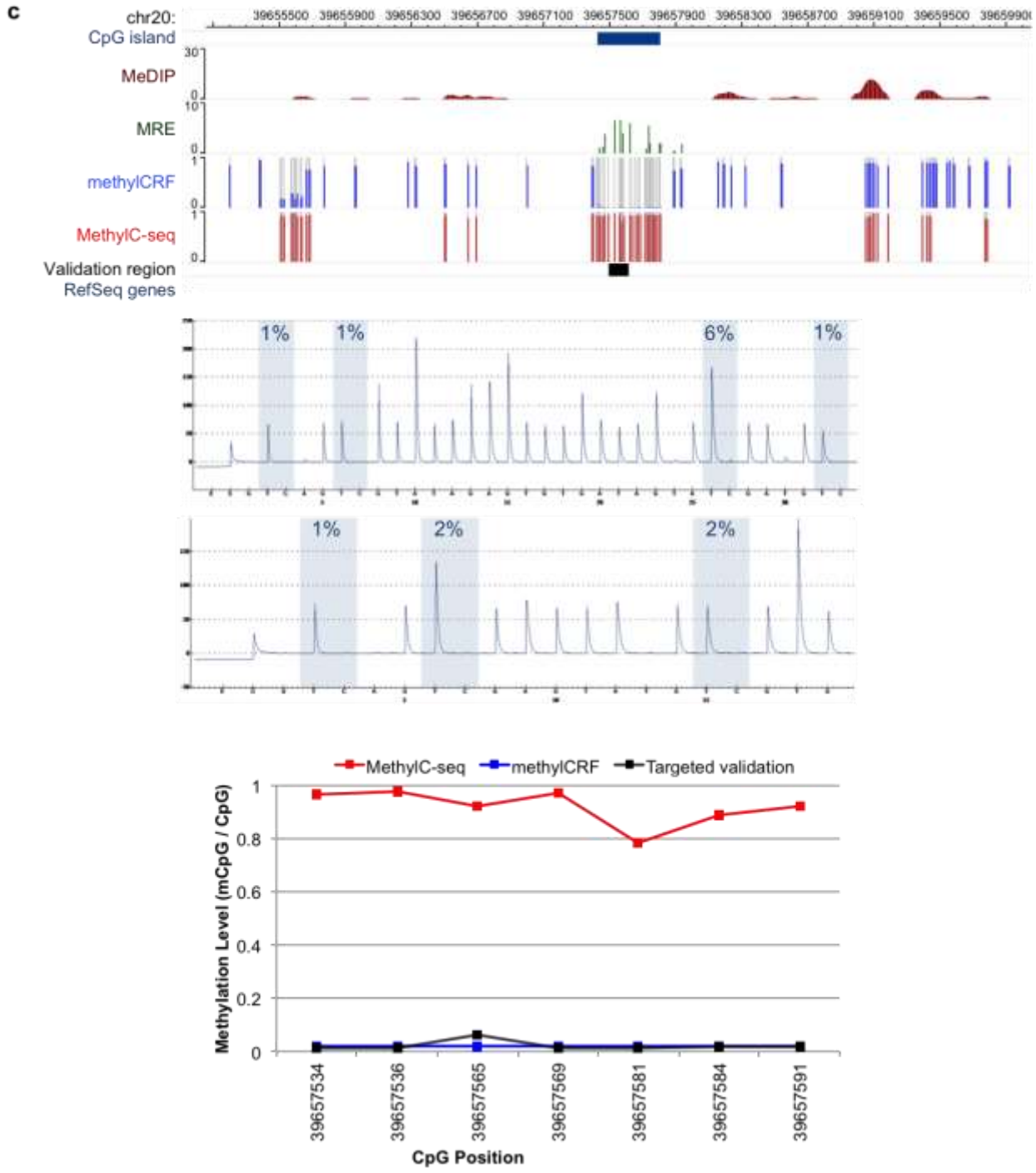


Supplementary Figure 5. Continued.



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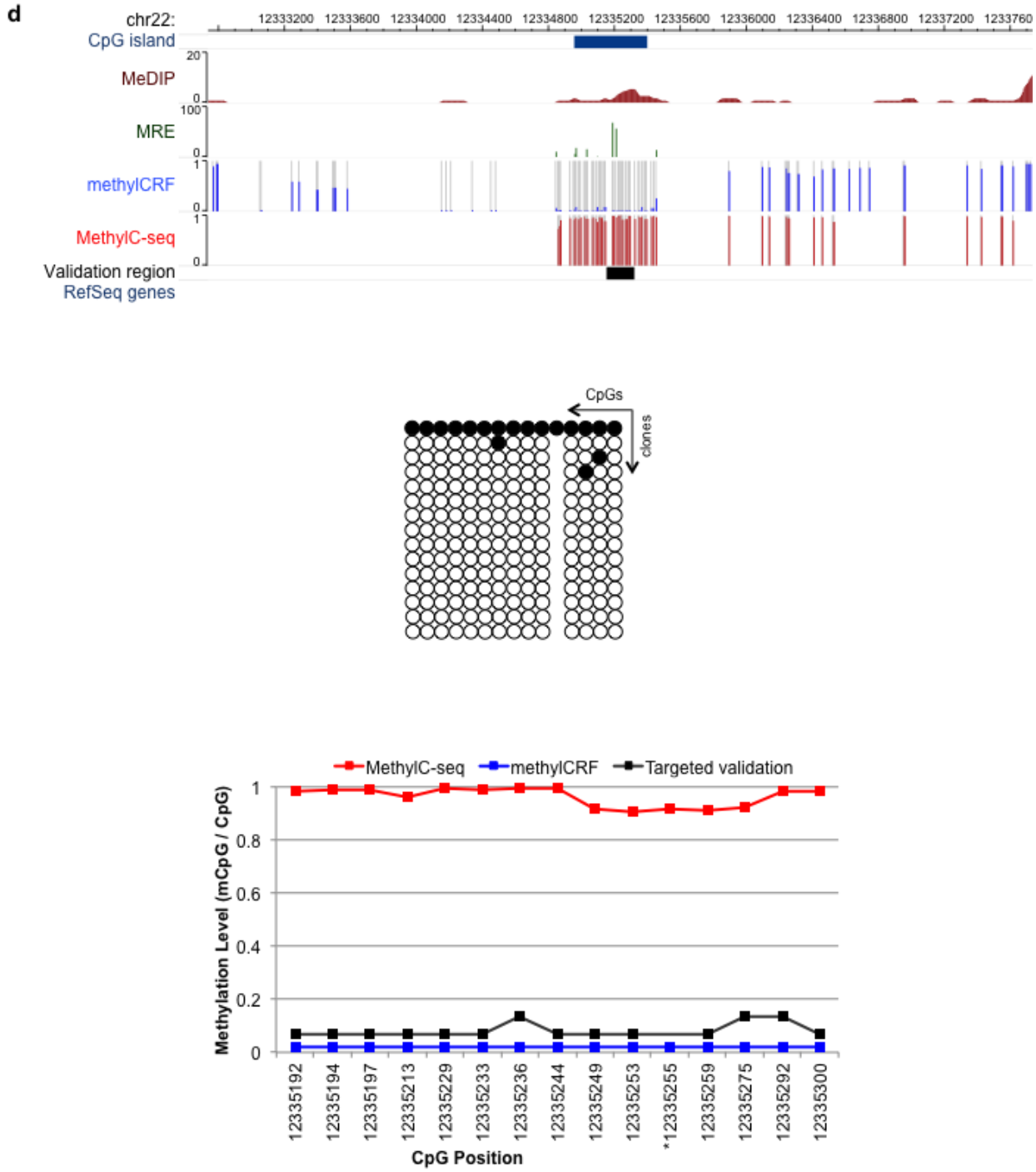

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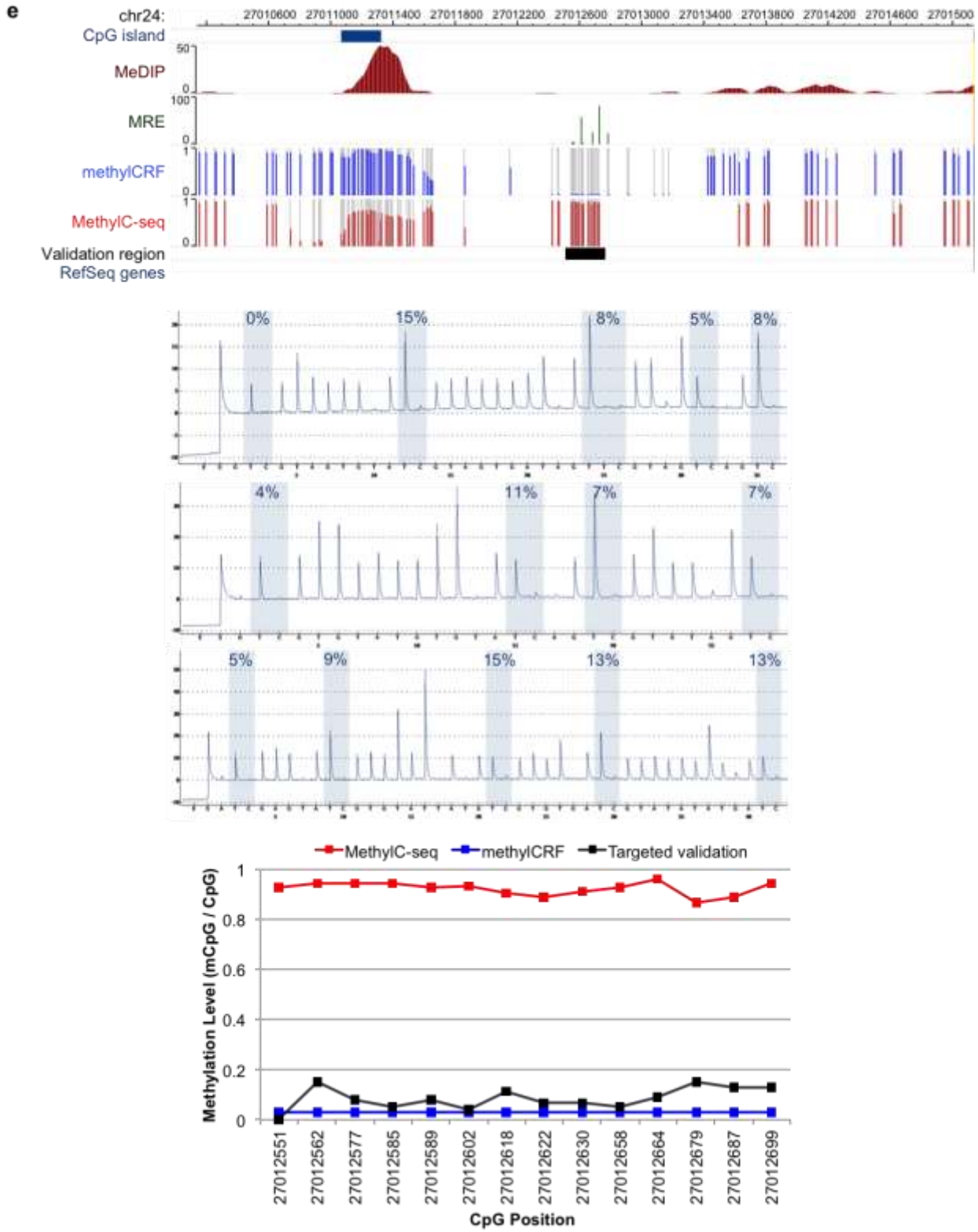

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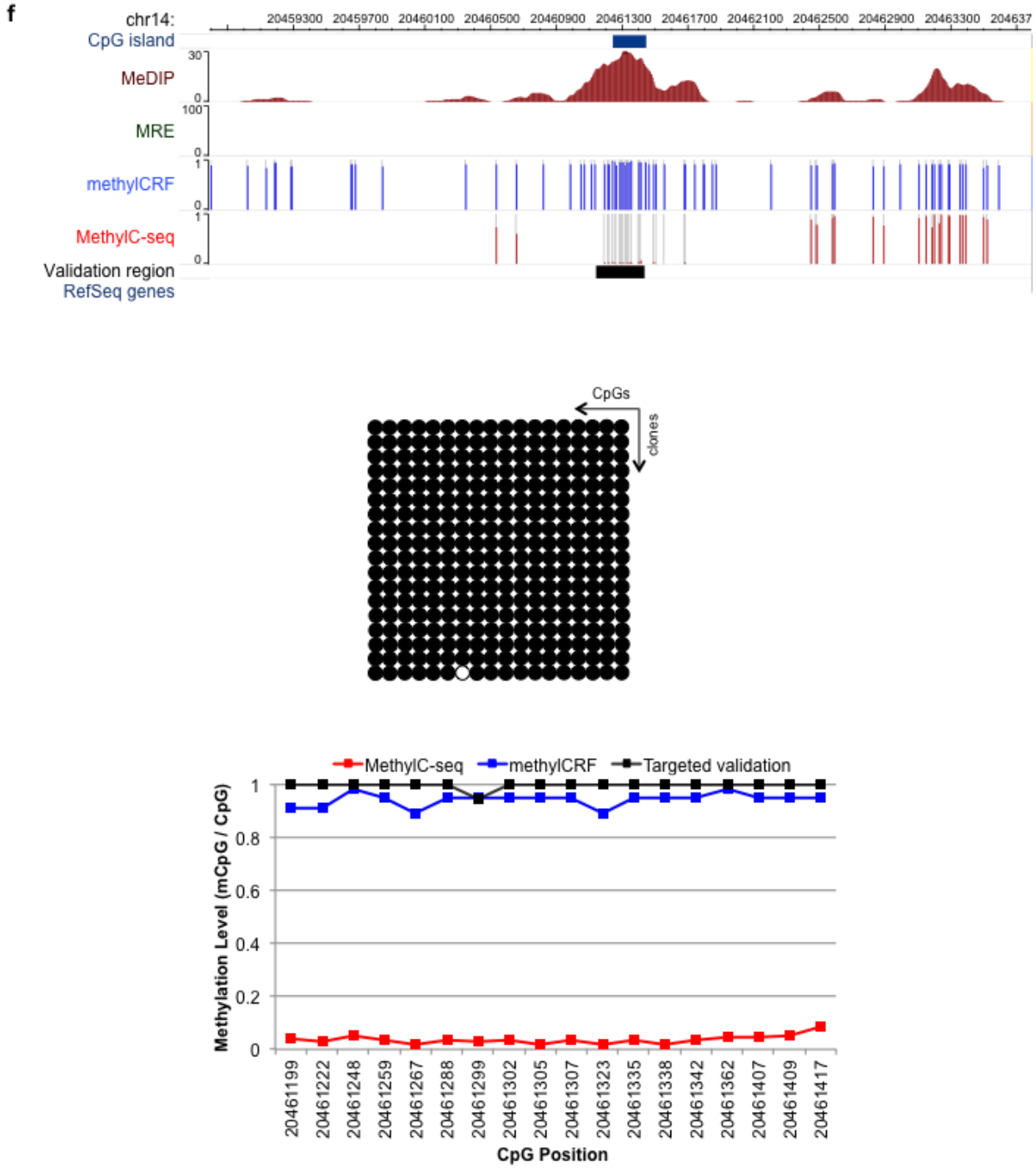
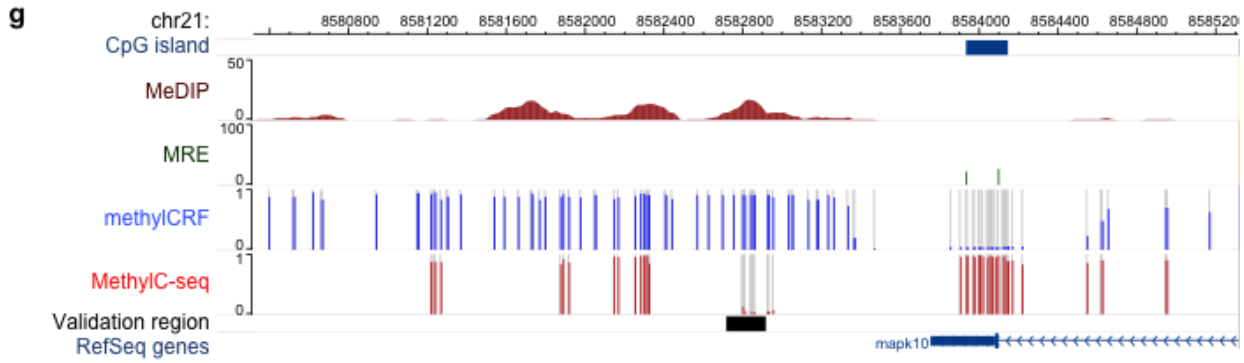
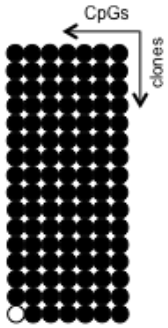
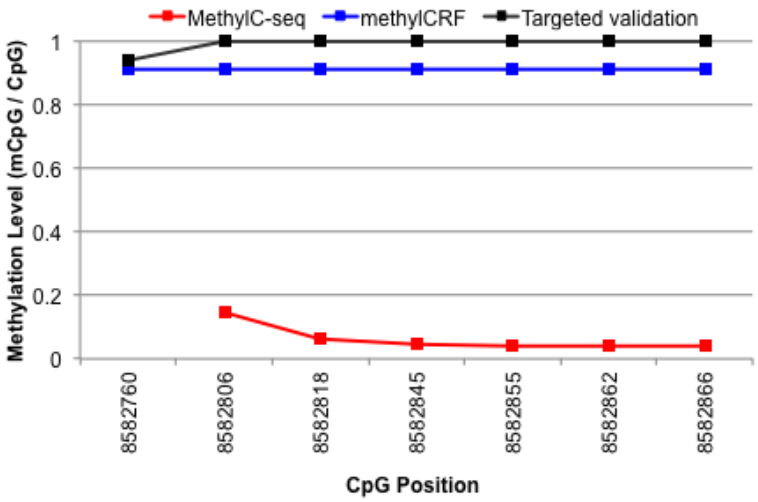


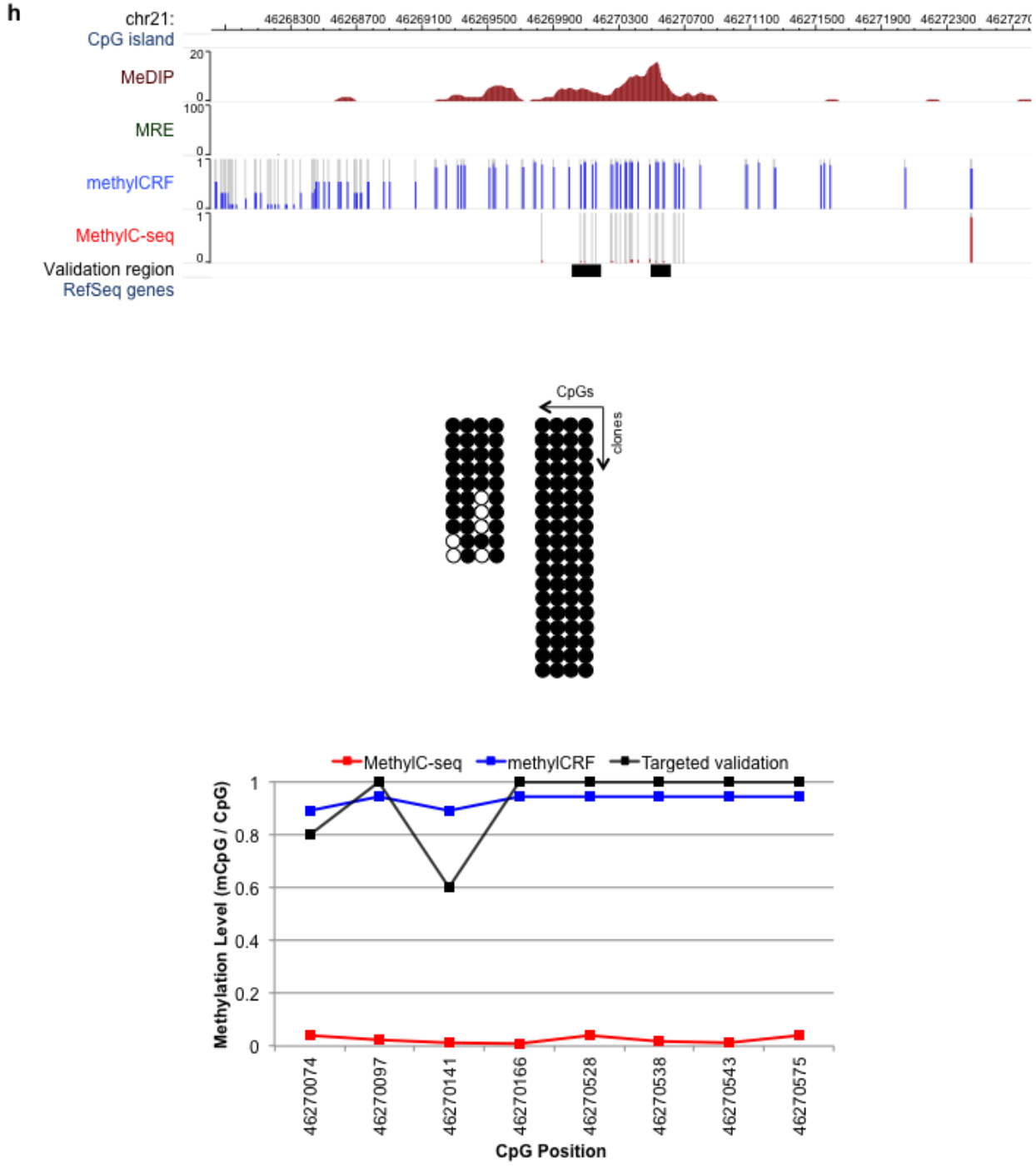
Supplementary Figure 5. Continued.







Supplementary Figure 5. Continued.

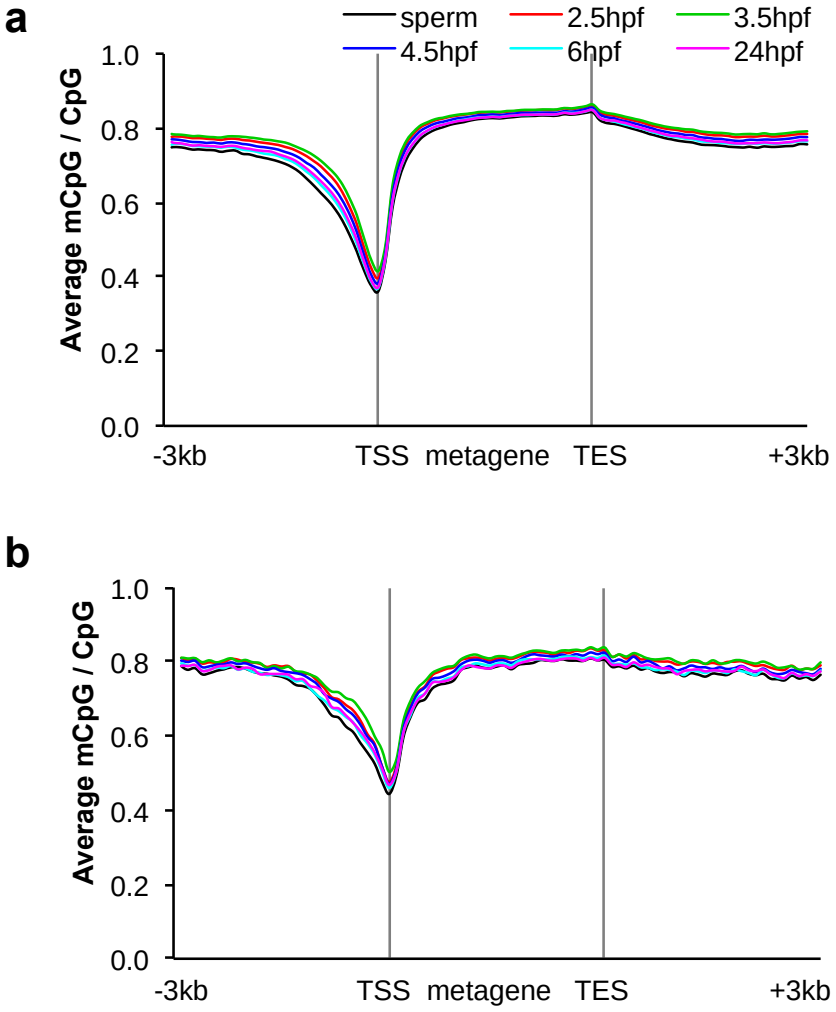


Supplementary Figure 5. Continued.

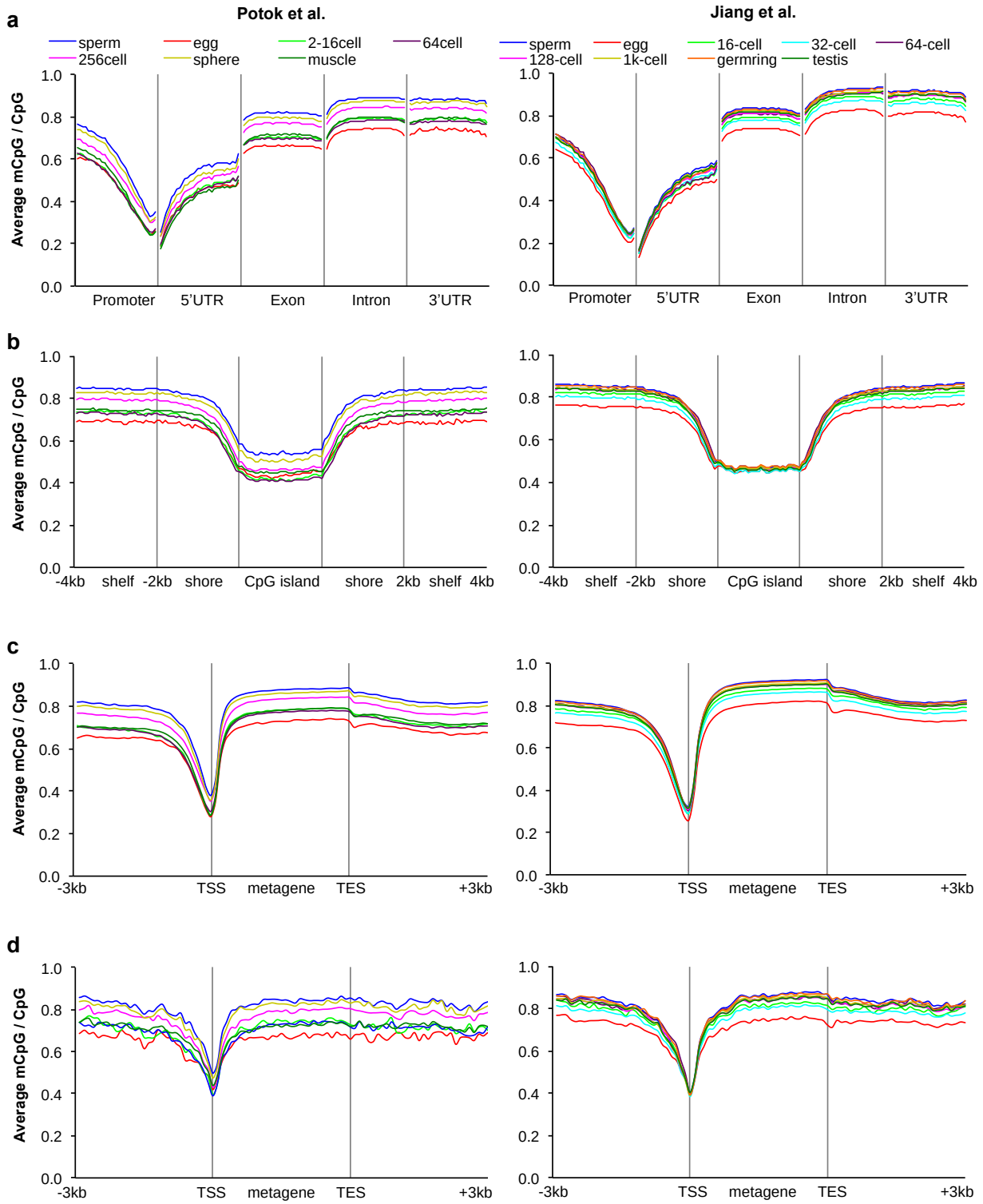
i

Validated region coordinates (Zv9)	Number of CpGs	Average DNA methylation level			RMSE	
		MethylC-seq (Potok et al.)	methylCRF	site-specific validation	MethylC-seq (Potok et al.)	methylCRF
chr1:42015593-42015753	8	0.95	0.03	0.04	0.91	0.04
chr14:25157201-25157370	8	0.93	0.02	0.02	0.92	0.03
chr20:39657499-39657620	7	0.92	0.02	0.03	0.89	0.02
chr22:12335157-12335326	15	0.96	0.02	0.08	0.88	0.07
chr24:27012514-27012771	12	0.92	0.03	0.09	0.83	0.07
chr14:20461146-20461441	18	0.04	0.94	1.00	0.96	0.06
chr21:8582721-8582922	7	0.02	0.93	0.93	0.94	0.09
chr5:46270017-46270621	8	0.06	0.91	1.00	0.91	0.12

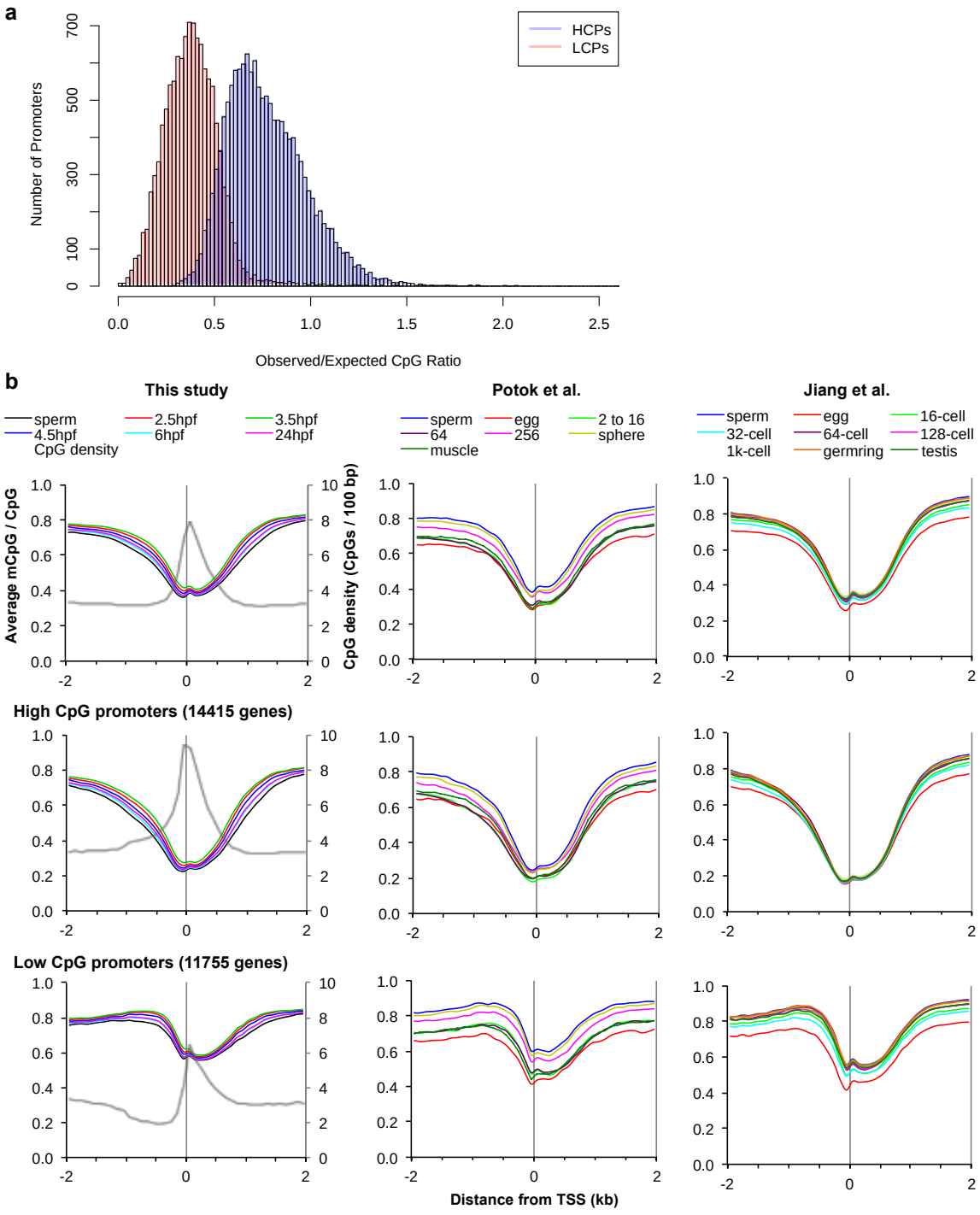
Supplementary Figure 6. The average DNA methylation level predicted by methylCRF throughout different genomic features: (**a**) protein-coding genes; (**b**) long non-coding RNA genes.



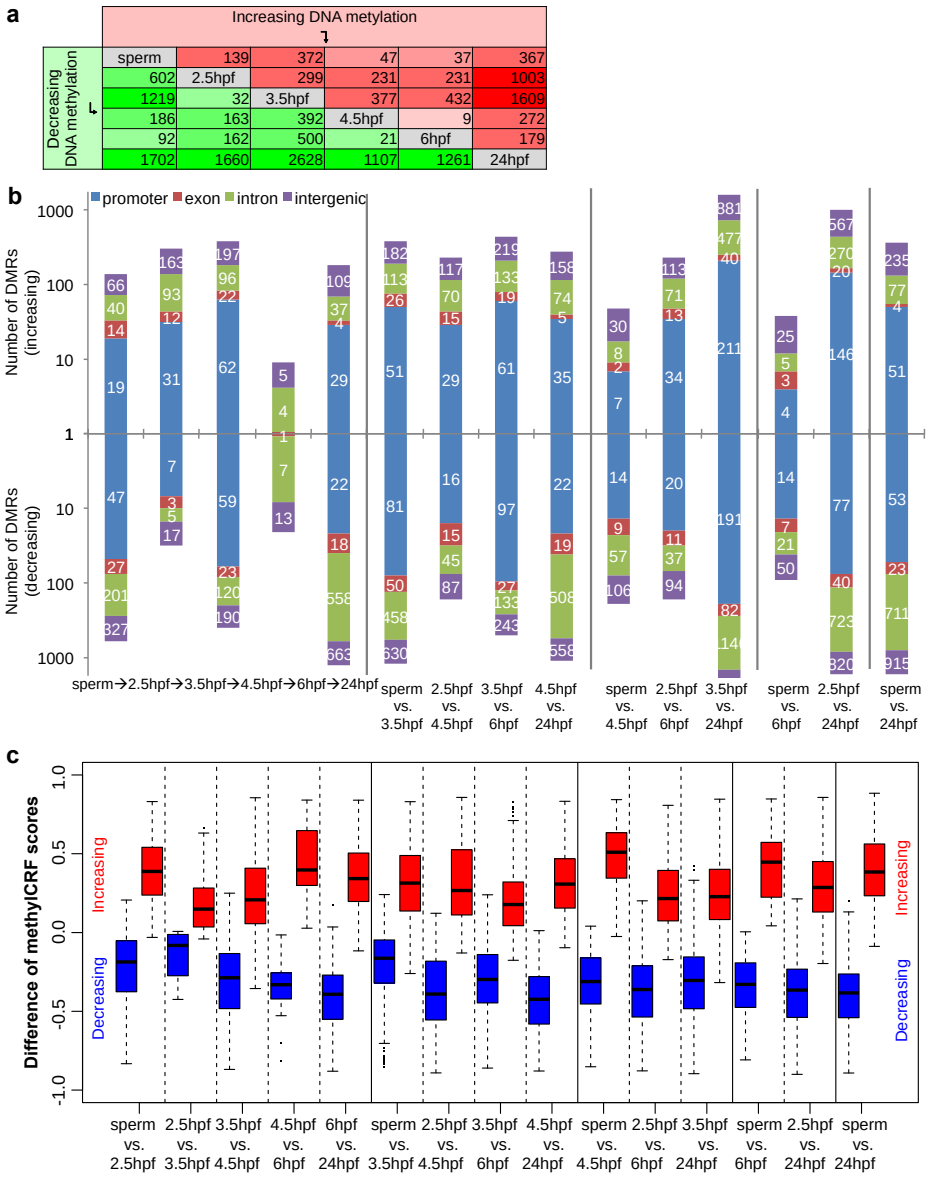
Supplementary Figure 7. The average DNA methylation level predicted by MethylC-seq throughout different genomic features: (**a**) gene-associated regions, (**b**) CpG islands and neighboring regions, (**c**) protein-coding genes, (**d**) long non-coding RNA genes.



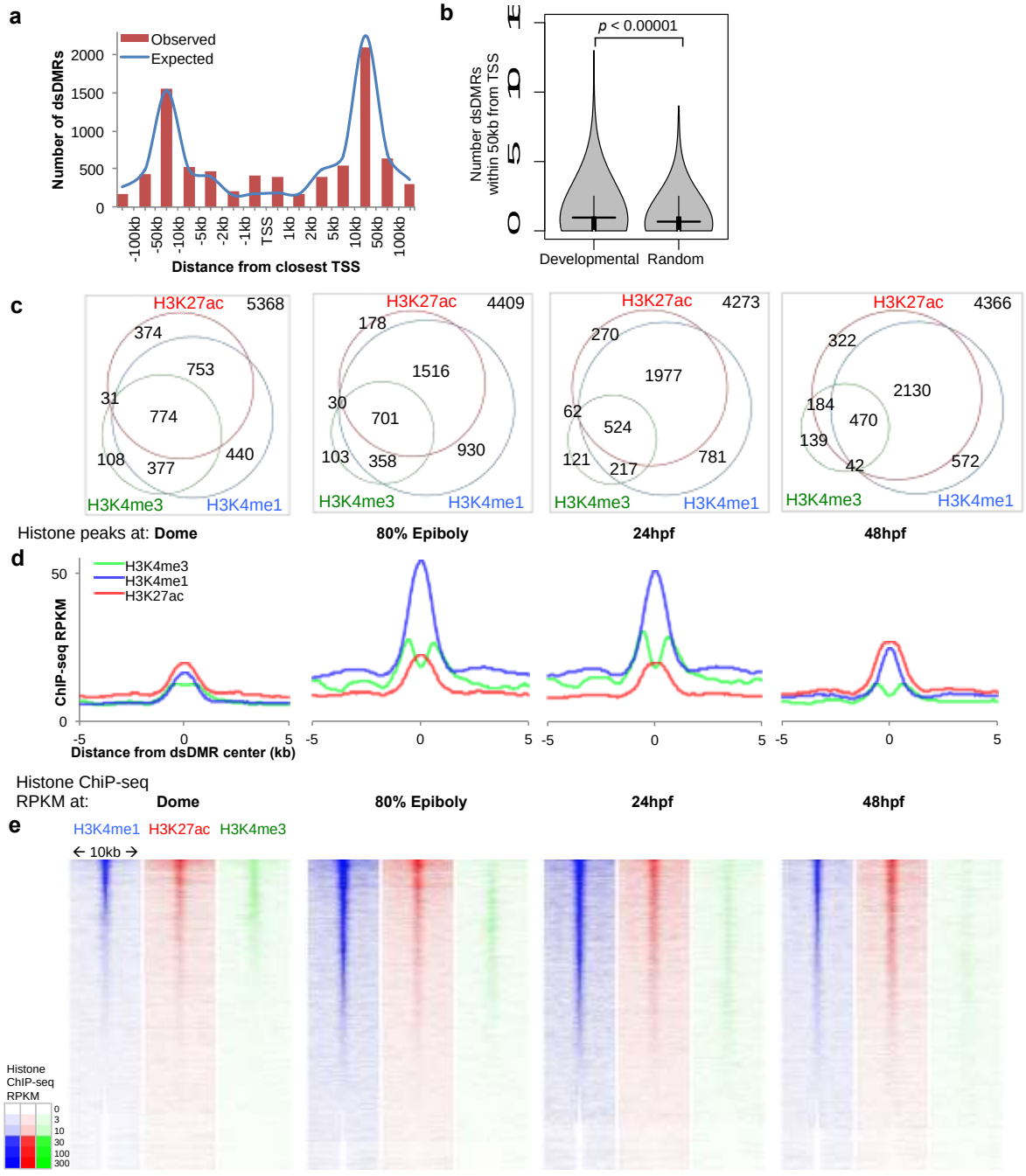
Supplementary Figure 8. Characterization of protein-coding genes according to CpG densities of their promoters. (**a**) Distribution of the number of promoters as a function of observed/expected CG ratio in the promoter sequence. (**b**) The average DNA methylation level predicted by methylCRF or MethylC-seq over all promoters (top row), HCPs (middle row) and LCPs (bottom row). The average CpG densities (grey lines) over the regions were also plotted.



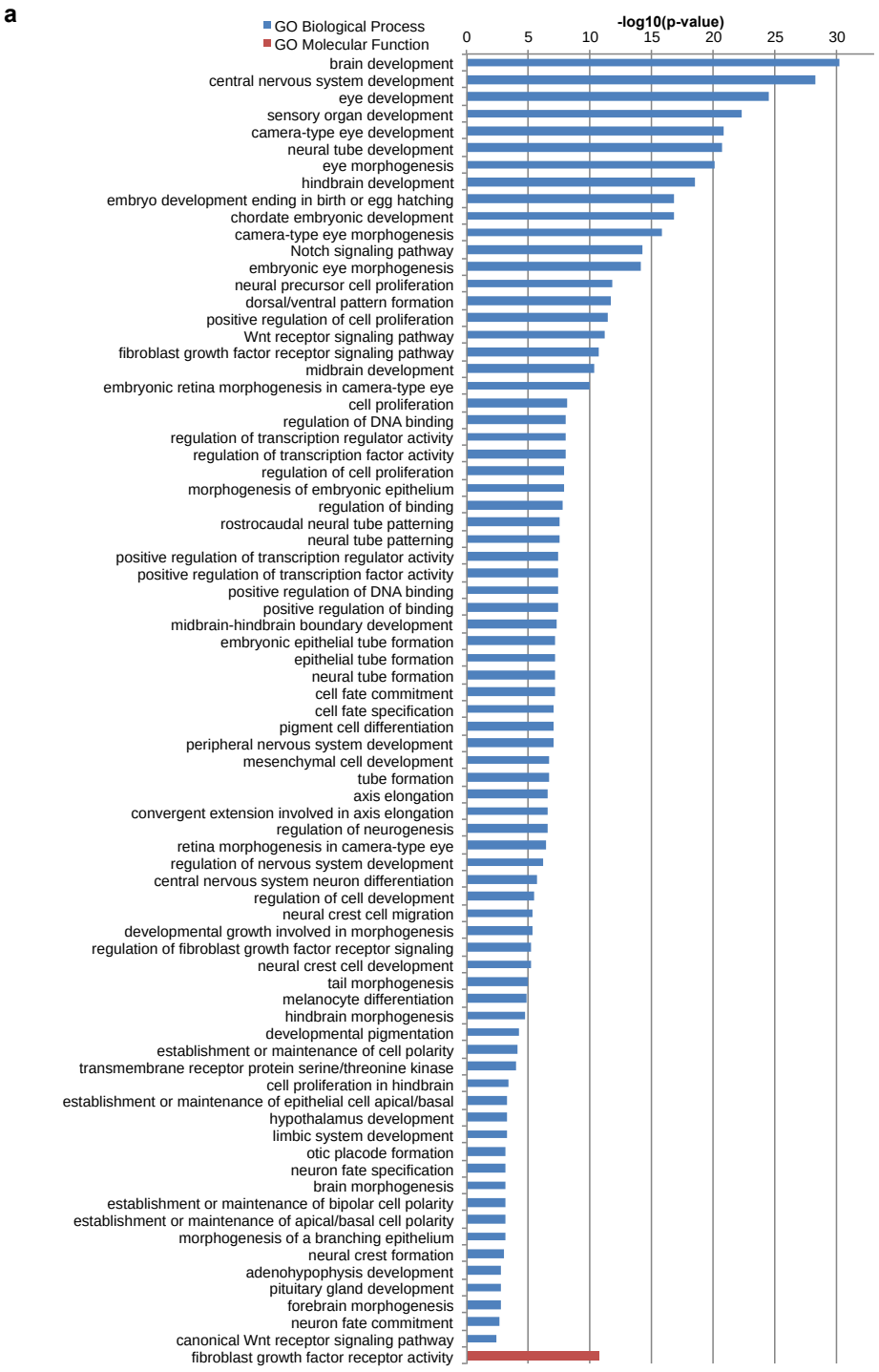
Supplementary Figure 9. Identification of the differentially methylated regions (DMRs). (**a**) The number of DMRs identified in each pair-wise comparison. DMRs were identified between two developmental stages and divided into two categories, increasing and decreasing DNA methylation, according to the relative DNA methylation levels. (**b**) The number of DMRs identified between different developmental stages. DMRs with increasing DNA methylation levels across developmental stages were plotted on the top, and DMRs with decreasing DNA methylation levels were plotted on the bottom (downward). The genomic locations of DMRs were indicated by different colors. (**c**) The boxplots of DNA methylation level differences of each DMR. Single CpG DNA methylation levels were predicted by methylCRF and averaged for each DMRs. The boxplots were plotted for each pair-wise comparison. Y-axis is the difference of the DMR region methylation levels in the later developmental time point minus that of the earlier time point.



Supplementary Figure 10. Characterization of the dsDMRs. (**a**) The distances of dsDMRs from their closest TSS. (**b**) The number of dsDMRs within 50 kb from each TSS of developmental gene or of random gene was plotted as violin plot. (**c**) A weighted Venn diagram of the number of dsDMRs overlapping with histone modification peaks from the specific developmental stages. (**d**) Histone modification signature of dsDMRs. Average ChIP-seq RPKM values from the specific developmental stages were plotted over 10 kb regions centered on the dsDMRs. **(e)** Heat maps of ChIP-seq signal over 10 kb regions centered on individual dsDMRs.

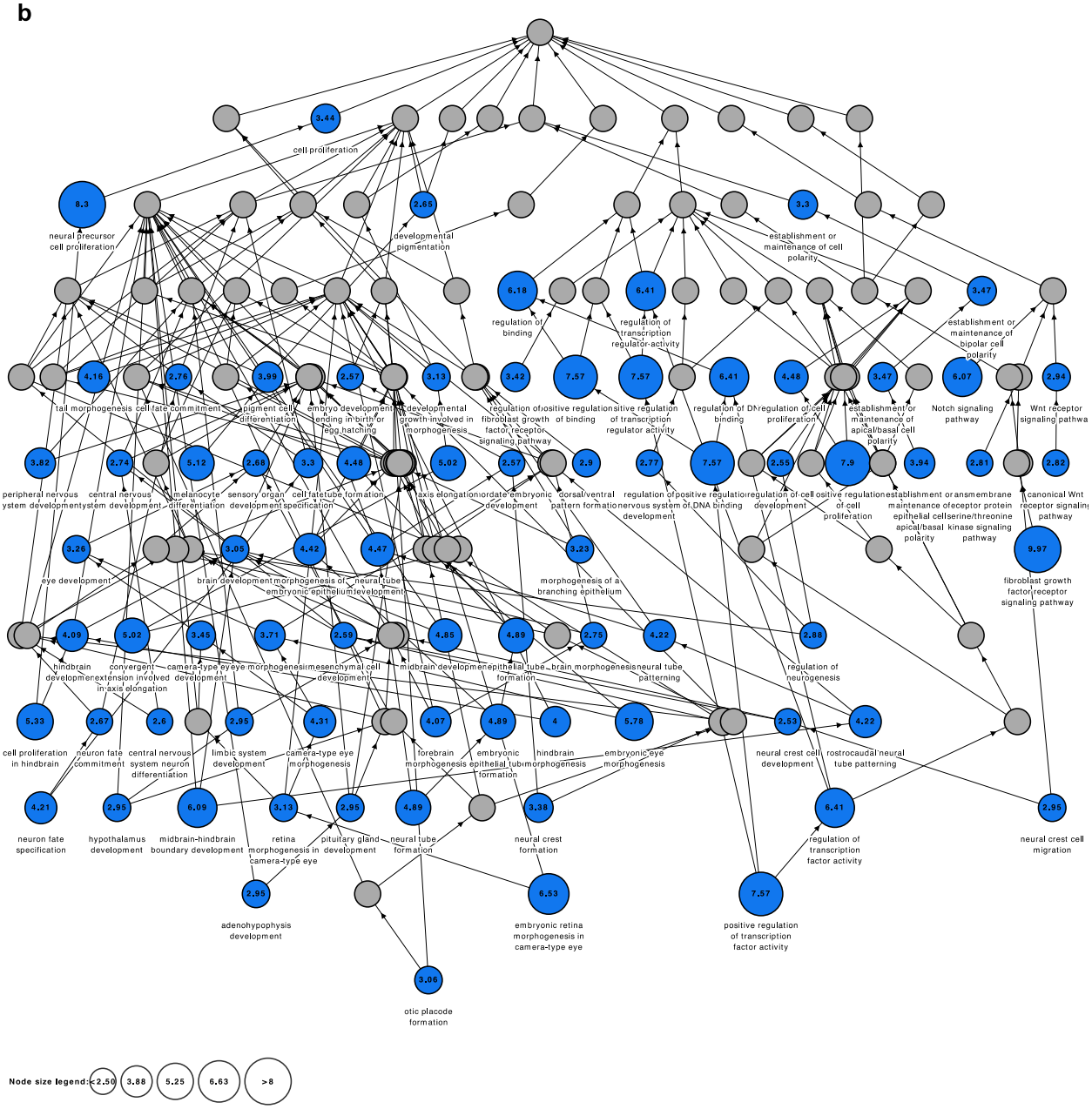


Supplementary Figure 11. Gene Ontology (GO) enrichment of dsDMRs. (**a**) A full list of enriched GO terms and their binomial p-values for dsDMRs with decreasing DNA methylation level between 6 hpf and 24 hpf. (**b**) Local directed acyclic graph based on the enriched GO Biological Process terms from a single ontology-specific table from GREAT analysis. Enriched terms were shown in blue. Nodes were sized according to binomial fold enrichment.

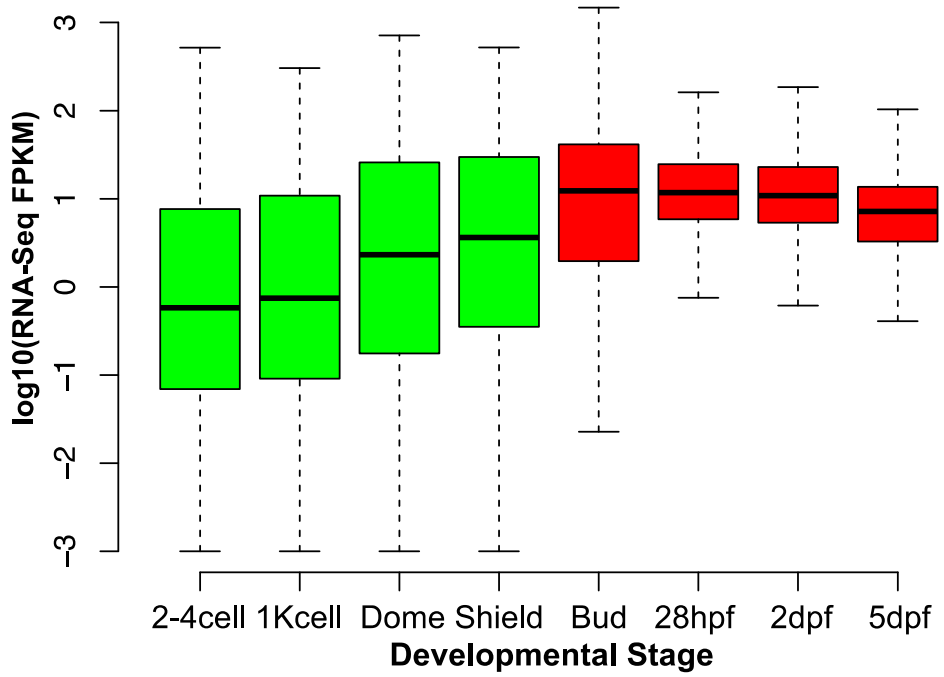


Supplementary Figure 11. Continued.

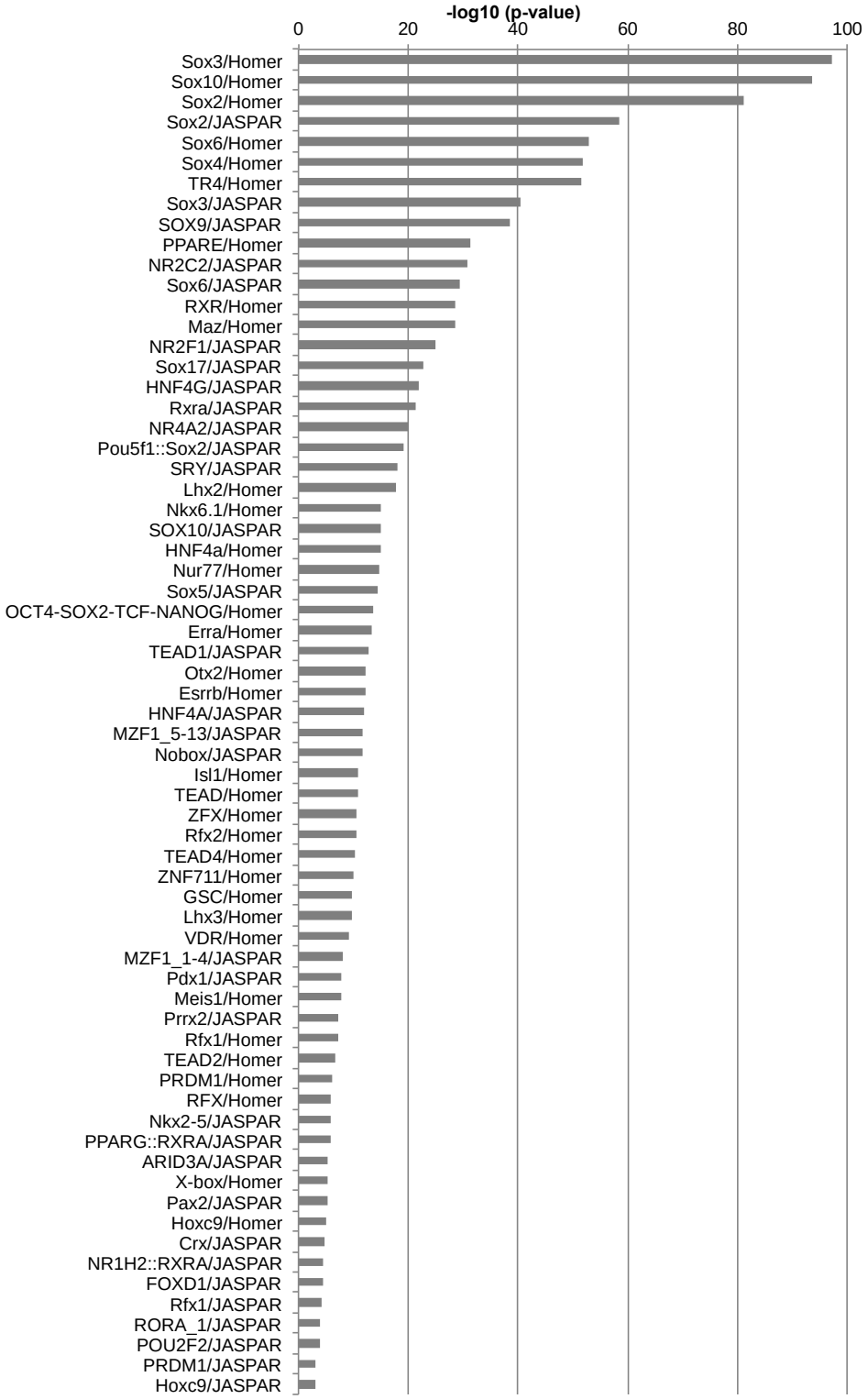
b



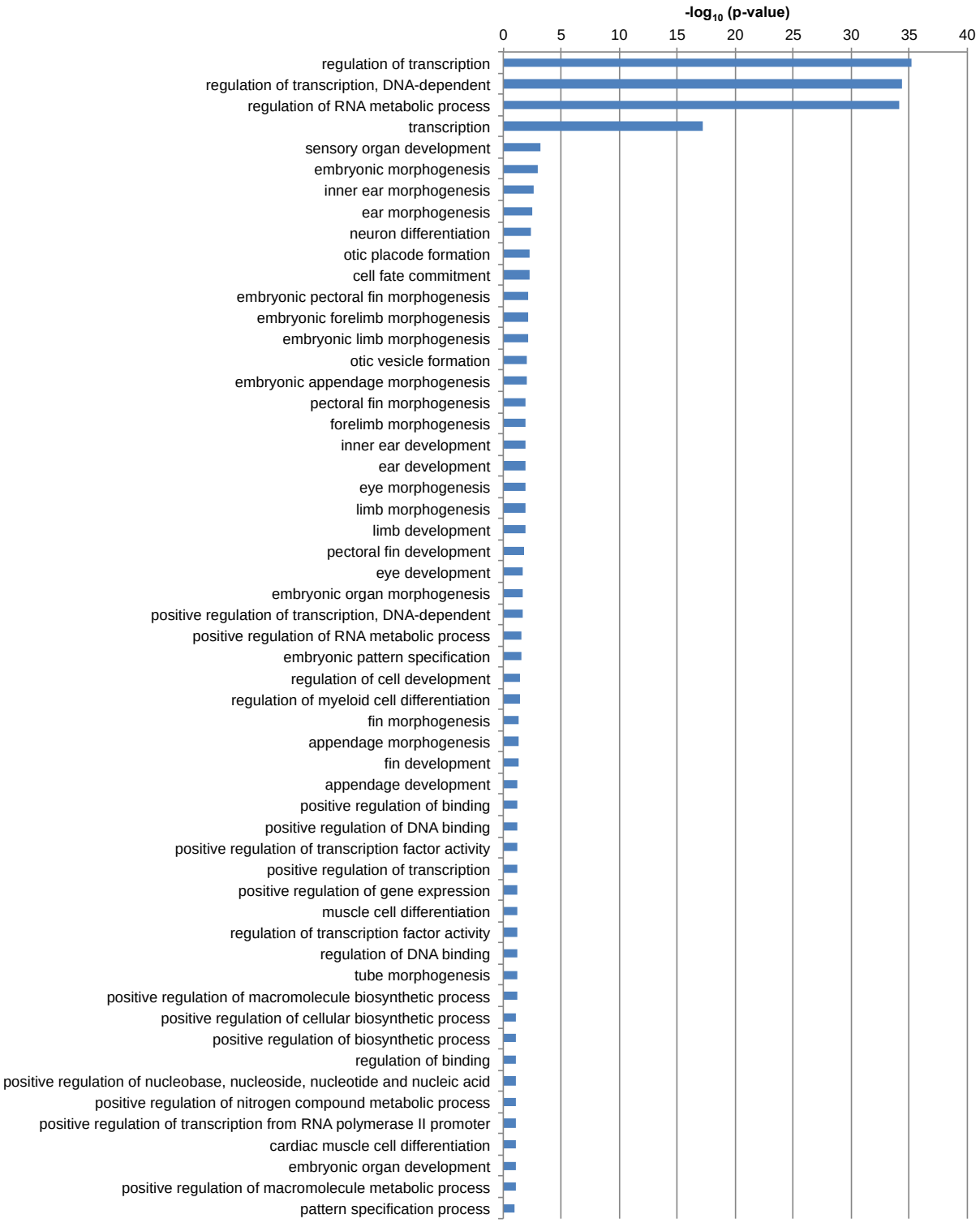
Supplementary Figure 12. Expression profiles of genes associated with dsDMRs from GO enrichment analysis across different developmental stages. The y-axis is changed to a log scale from **Fig. 3f**.



Supplementary Figure 13. A full list of enriched motifs in dsDMRs with decreasing DNA methylation level between 6 hpf and 24 hpf and their hypergeometric p-values from HOMER tool. Redundant motifs from HOMER and JASPAR are together displayed.

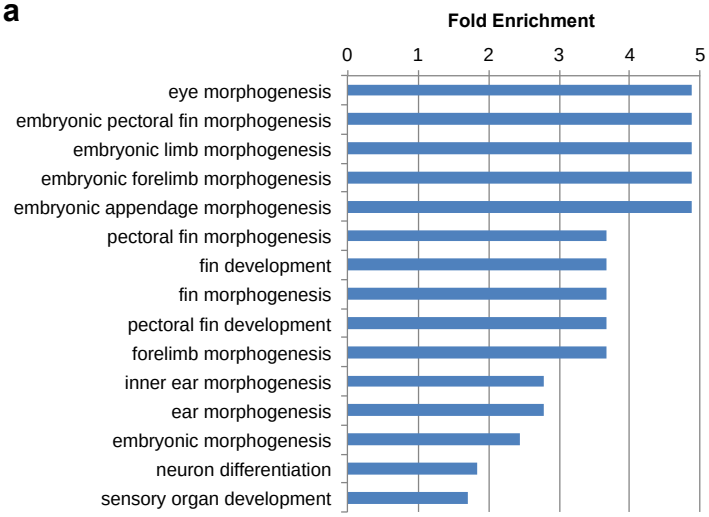


Supplementary Figure 14. A list of enriched functional annotations of transcription factors whose motifs are enriched in dsDMRs against the genomic background and their p-values from DAVID tool.



Supplementary Figure 15. Regulatory relationships among the putative targets and TFs identified in dsDMRs (**a**) A list of enriched functional annotations of transcription factors whose motifs are enriched in dsDMRs against the all TFs background and their fold enrichment scores from DAVID tool. (**b**) A table of the number of connections found by querying databases of TF-target genes. When the TFs and genes identified from dsDMRs were used, significantly larger number of connections was found than when random TFs and genes were used.

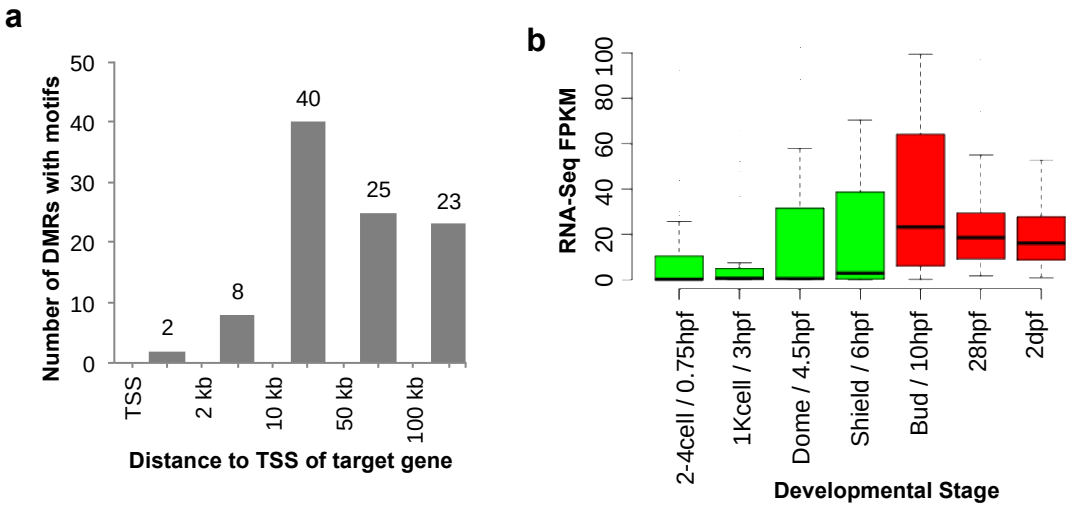
a



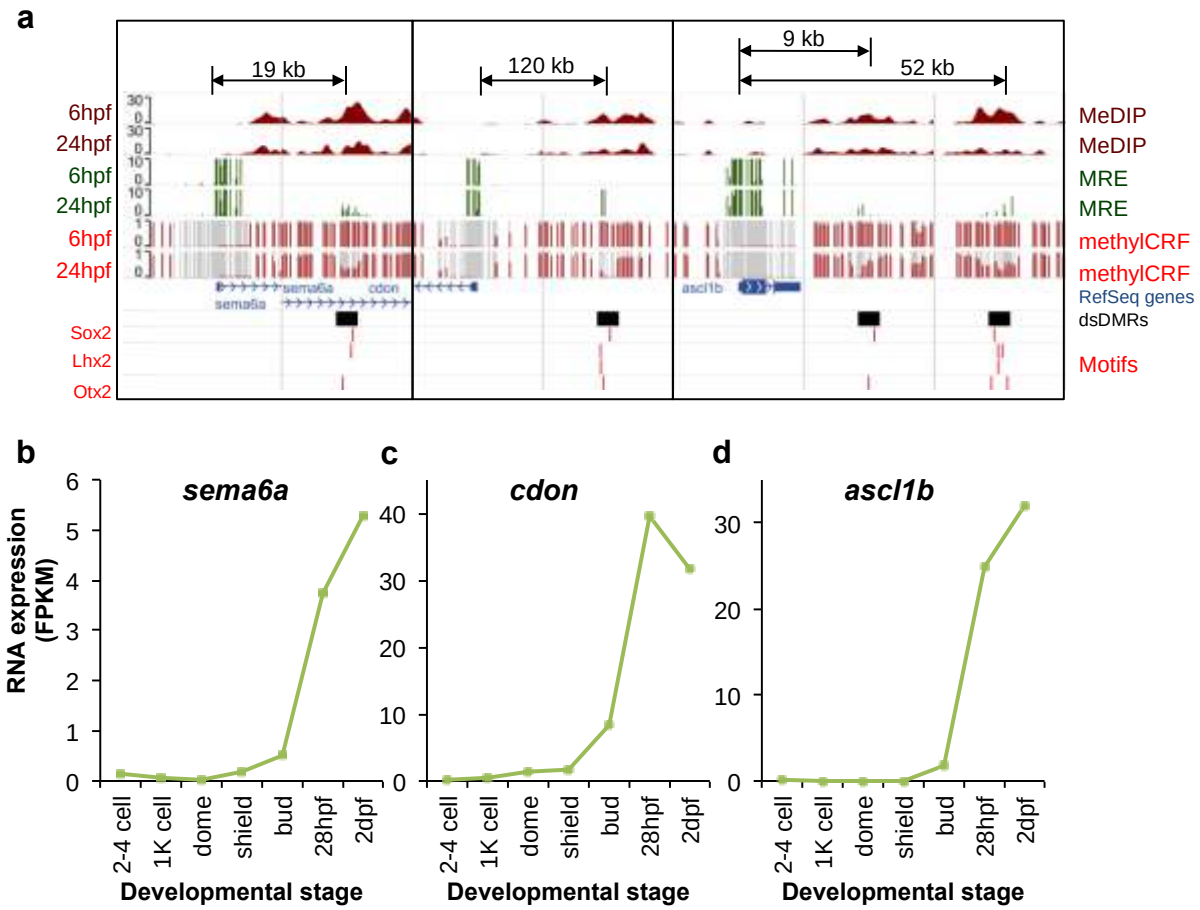
b

TFs and genes from	Number of nodes	Number of edges
dsDMRs	233	2964
random 1	234	1758
random 2	241	1970
random 3	236	1697
random 4	240	1958
random 5	244	2260
random 6	241	1985
random 7	237	1611
random 8	236	2320
random 9	233	1745
random 10	229	1556
Mean		1886
Standard deviation		260

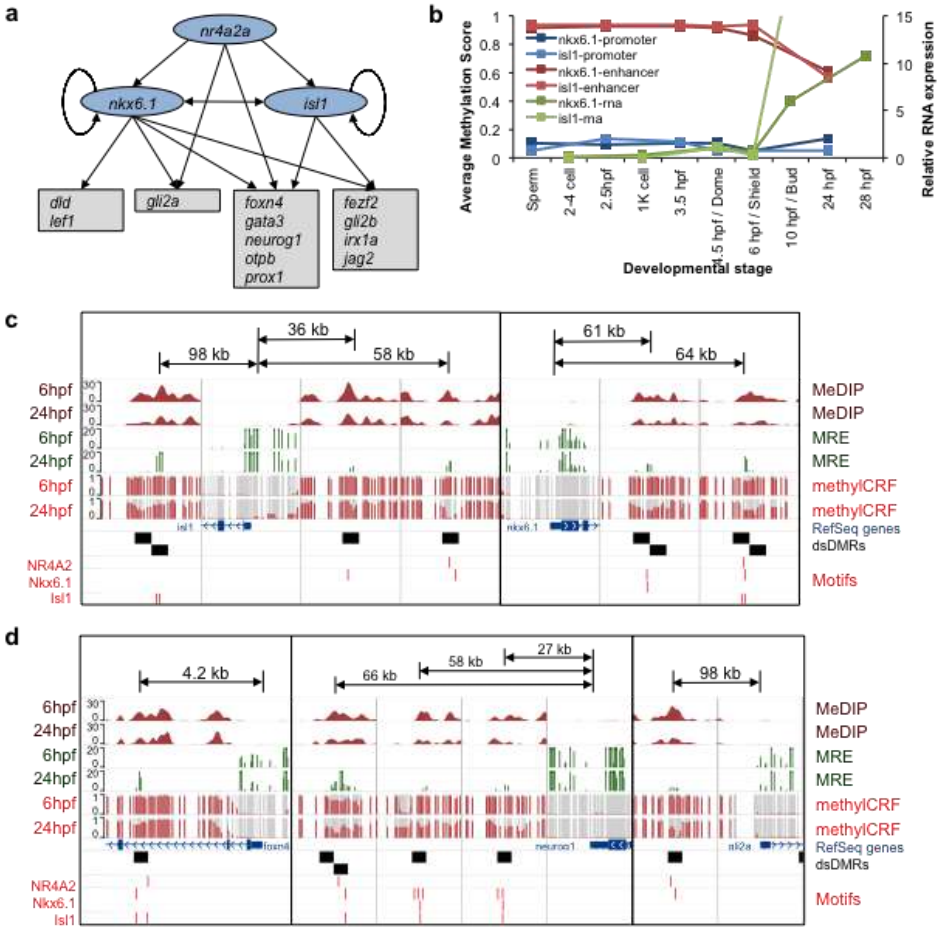
Supplementary Figure 16. Characteristics of the target genes in the regulatory network of the eye development. (**a**) Histogram of the distances of dsDMRs containing binding motifs from their linked target genes. (**b**) Expression profiles of downstream target genes of the eye development across different developmental stages. Most of the target genes showed increased expression levels from shield (6 hpf) to 28 hpf embryo stage.



Supplementary Figure 17. Identification of novel target genes for eye development (**a**) The gene set view of 7 genomic regions (chr8:204234-207234, chr8:223250-226250, chr18:42528702-42531702, chr18:42648750-42651750, chr7:51171256-51174256, chr7:51180250-51183250, chr7:51223750-51226750) from the Epigenome Browser. The left panel displayed the regions around *sema6a* promoter and its nearby dsDMR enhancer (indicated by the black box). The middle panel displayed the regions around *cdon* promoter and its nearby dsDMR enhancer. The right panel displayed the regions around *ascl1b* promoter and its two nearby dsDMR enhancers.These dsDMRs had Sox2, Lhx2, and Otx2 binding motifs (red ticks), suggesting that these genes could be downstream target genes in the regulatory network of the eye development. (**b**-**d**) The gene expression profiles of the novel target genes: *sema6a* (**b**), *cdon* (**c**), and *ascl1b* (**d**).



Supplementary Figure 18. Gene regulatory network of the central nervous system neuron differentiation. (**a**) The pupative gene regulatory network of central nervous system neuron differentiation derived from dsDMR analysis. The blue ovals were transcription factors whose motifs were enriched in dsDMRs. The genes in the grey boxes were the target genes identified in GREAT analysis. Arrows indicates that the transcription factors had their binding motifs in neighboring dsDMRs of the target genes. (**b**) The methylation profiles of the *nkx6.1* and *isl1* promoters and their neighboring dsDMR enhancers (blue and red lines, left y-axis) and the expression profile of the two genes (green lines, right y-axis). Each gene expression level was normalized to the expression level of dome stage. (**c**) The gene set view of 7 genomic regions from the Epigenome browser. The left panel displayed the regions around *nkx6.1* promoter and its nearby dsDMR enhancers (black box). The right panel displayed the regions around *isl1* promoter and its nearby dsDMR enhancers. Both dsDMRs had NR4A2, Nkx6.1 and Isl1 binding motifs (red ticks). (**d**) The gene set view of 7 genomic regions from the Epigenome browser. The left, middle, and right panels displayed the regions around *foxn4*, *neurog1*, and *gli2a* promoters and its nearby dsDMR enhancers (black box), respectively. NR4A2, Nkx6.1 and Isl1 binding motifs within each dsDMRs were displayed as red ticks, suggesting that these genes could be downstream target genes in the regulatory network of the central nervous system neuron differentiation.



Supplementary Figure 19. GFP expression patterns in G0 embryos injected with dsDMR enhancers and negative controls. G0 embryos injected with a specific putative enhancer reporter construct expressed GFP in a specific pattern. In contrast, G0 embryos injected with the negative controls did not show consistent patterns of GFP expression. Rather, GFP expression was not detected in the majority of G0 embryos. In G0 embryos with detectable GFP expression, expression was very weak and was in spotted and random patterns. Here we present examples of GFP expressions in G0 embryos injected with a validated enhancer construct in comparison to GFP expressions in G0 embryos with a negative control construct. About 40% of G0 embryos injected with *znf703-e1* reporter construct showed the same strong GFP expression patterns. However, no consistent expression pattern was observed in G0 embryos injected with negative control *six3a-ne1* reporter construct. GFP expression in these G0 embryos were very weak and in random pattern. (**a**) Table of G0 embryo numbers showing consistent GFP expression pattern, inconsistent weak GFP expression pattern, or no GFP expression. (**b**) The representative pictures of G0 embryos injected with *znf703-e1* reporter construct or *six3a-ne1* negative control construct.

a

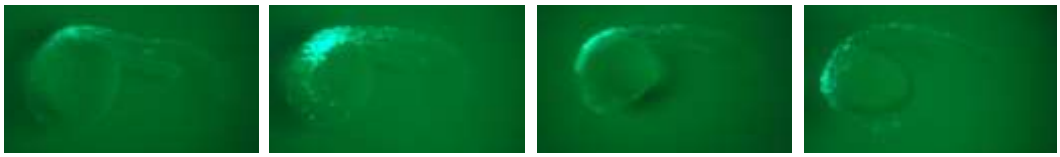
Number of G0 embryos

Tested construct	GFP with consistent patterns	Weak GFP without patterns	No GFP detected
znf703-e1	43 (shown in pictures)	58	4
six3a-ne1	0	36 (shown in pictures)	60

b

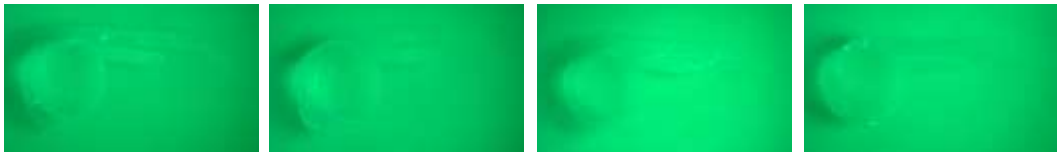
znf703-e1 (normal exposure)

GFP with consistent patterns

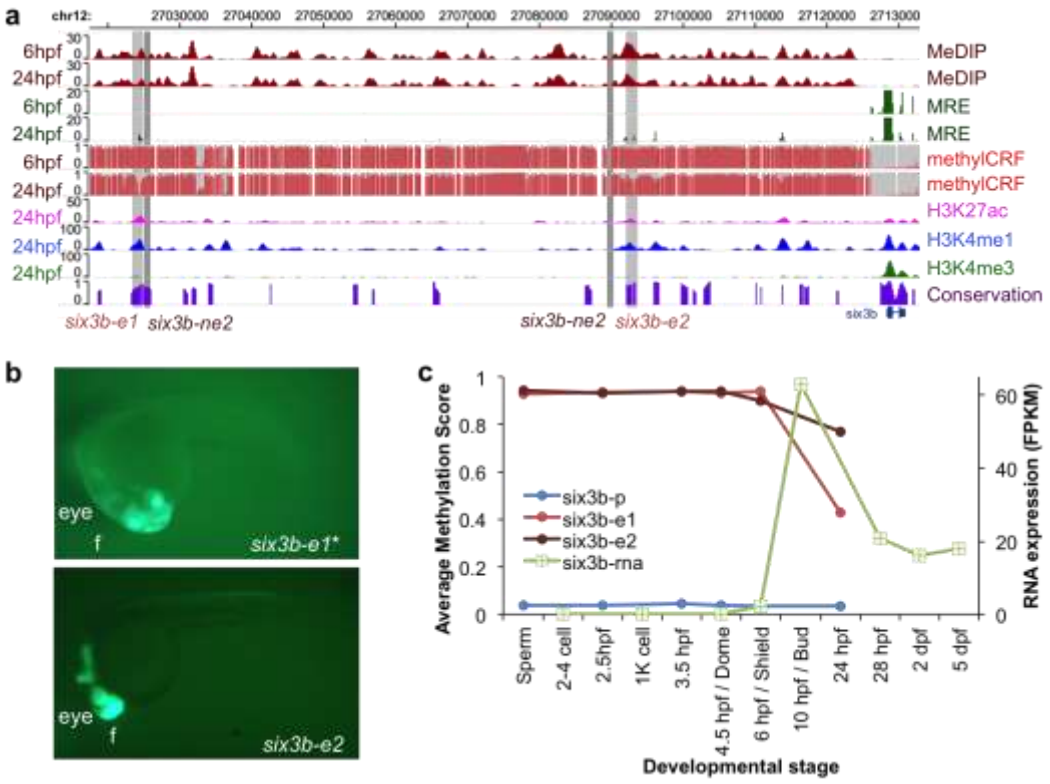


six3a-ne1 (maximum exposure)

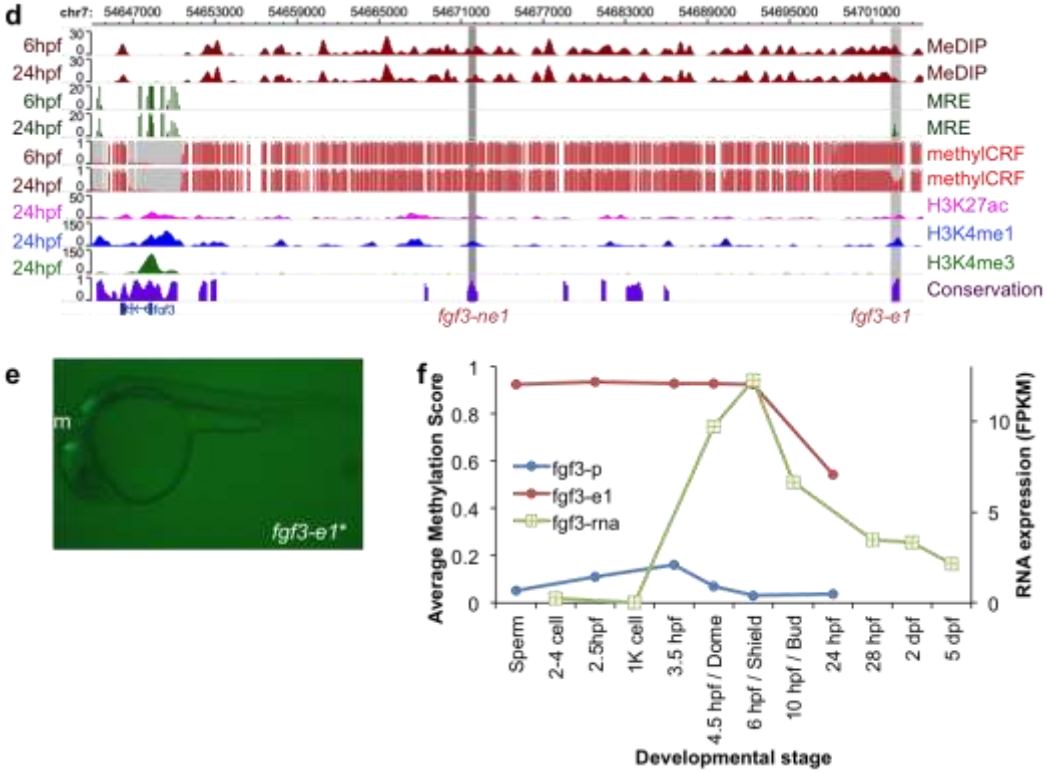
weak GFP without patterns



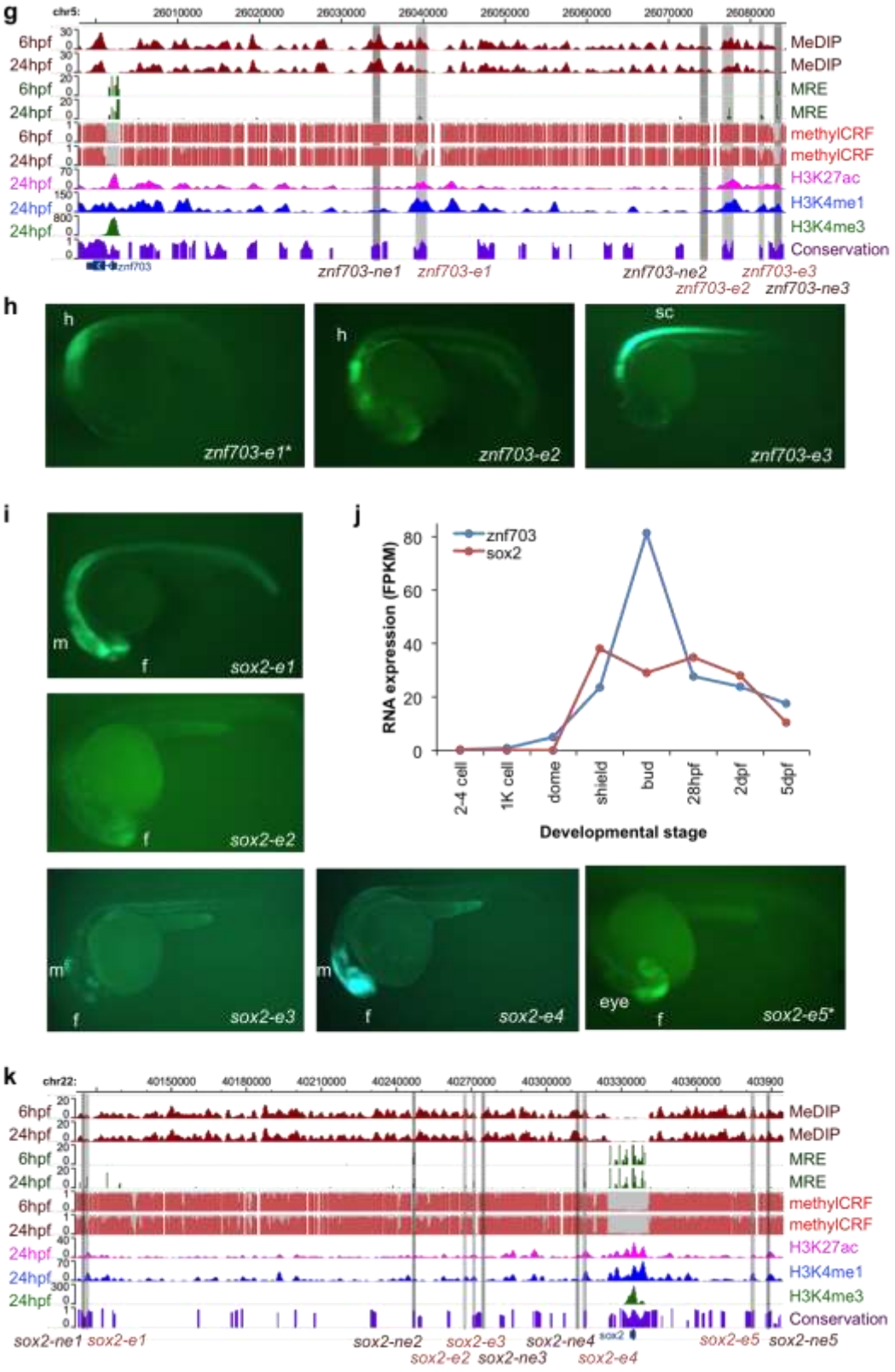
Supplementary Figure 20. *In vivo* validation of dsDMR enhancers. (**a,d,g,k,l,m**) WashU Epigenome Browser views of the *six3b* (**a**), *fgf3* (**d**), *znf703* (**g**), *sox2* (**k**), *wnt3* (**l**), and *wnt3a* (**m**) genes, their neighboring dsDMR enhancers (grey boxes), and negative controls (dark grey boxes). (**b,e,h,i,n,o**) GFP expression driven by the dsDMR enhancers of the *six3b* (**b**), *fgf3* (**e**), *znf703* (**h**), *sox2* (**i**), *wnt3* (**n**), and *wnt3a* (**o**) genes. Forbrain (f); midbrain (m); midbrain hindbrain boundary (mh); spinal cord (sc). The asterisk * indicates that only one G1 transgenic line was established. (**c,f,j,p**) The expression patterns of the nearby genes: *six3b* (**c**), *fgf3* (**f**), *znf703* and *sox2* (**j**), and *wnt3* and *wnt3a* (**p**).



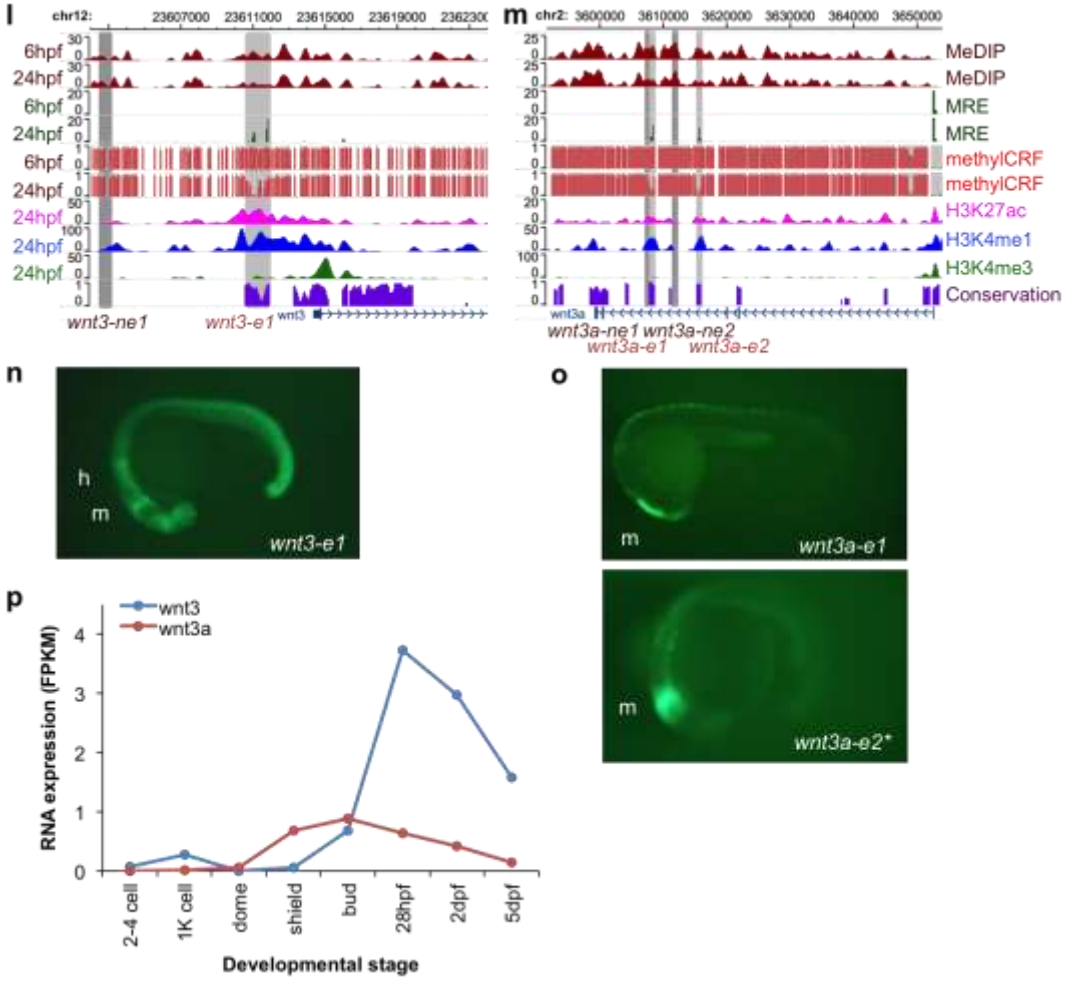
Supplementary Figure 20. Continued.



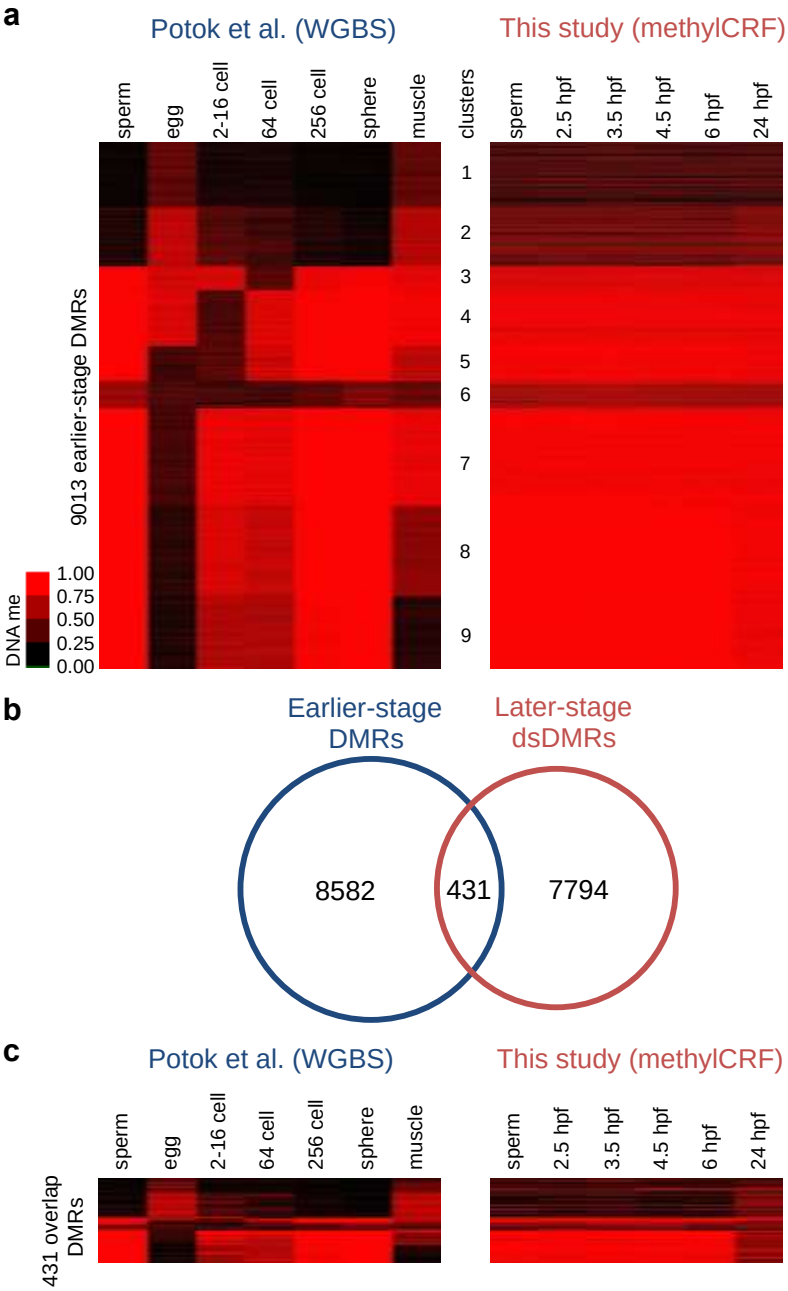
Supplementary Figure 20. Continued.



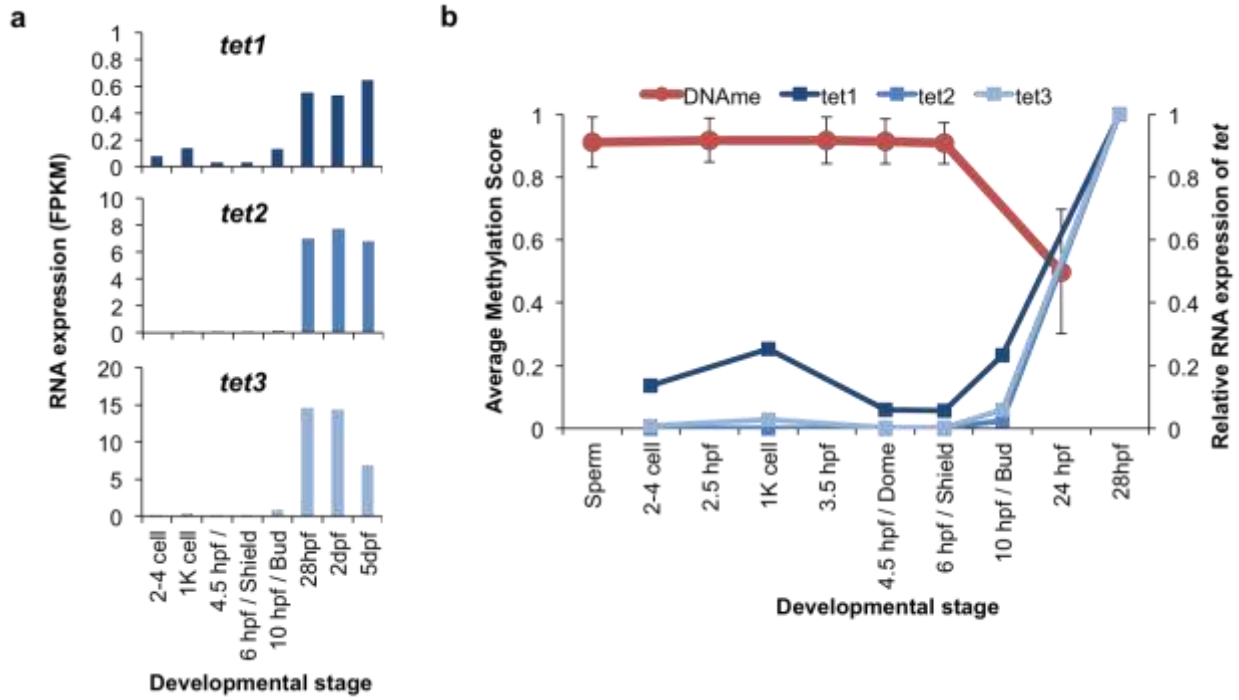
Supplementary Figure 20. Continued.



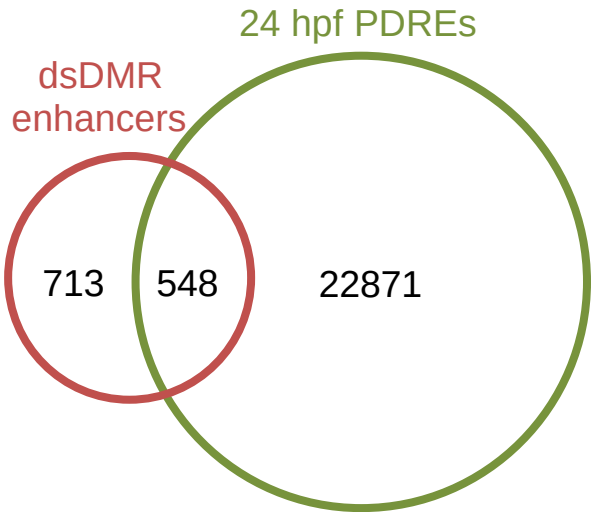
Supplementary Figure 21. DNA methylation dynamics of previously reported earlier-stage DMRs in later embryogenesis stages. (**a**) Heat map of earlier-stage DMRs' DNA methylation levels measured by either WGBS or methylCRF. Left panel: published WGBS data were used to re-draw the heat map of Figure 3A in Potok et al. (2013). Right panel: average DNA methylation in each earlier-stage DMR was calculated for six developmental stages in our study and plotted as a heat map. (**b**) A weighted Venn diagram of the overlap between earlier-stage DMRs previously reported and dsDMRs identified in our study. 431 earlier-stage DMRs were overlapped with dsDMRs by at least 50%. (**c**) Heat map of DNA methylation levels of the 431 overlapping DMRs.



Supplementary Figure 22. Expression of *tet* genes. (**a**) Expression profiles of 3 zebrafish *tet* genes across different developmental stages. (**b**) DNA methylation levels of dsDMRs are inversely correlated with *tet* expression. Each *tet* expression was normalized to the expression level in 28 hpf. DNA methylation levels are average of 1261 dsDMRs in each stage and error bars indicate the standard deviations.



Supplementary Figure 23. A weighted Venn diagram of the overlap between dsDMR enhancers and PDREs. 1261 dsDMRs used here were hypomethylated in 24 hpf embryos in the comparison between 6 hpf and 24 hpf. 23419 PDREs used here were 24 hpf-specific. 548 dsDMR enhancers were overlapped with PDREs by at least 50%.



SUPPLEMENTARY TABLES

Supplementary Table 1. Statistics for methylome sequencing across developmental stages.

	MeDIP-seq				MRE-seq			
	Total Paired Reads	Paired Reads Aligned	Alignment Rate %	CpGs Covered	Total Reads	Reads Aligned	Alignment Rate %	CpGs Covered
sperm	52520004	47698369	90.8%	18966824	37317638	35534718	95.2%	325217
2.5hpf	104923032	95684765	91.2%	21001306	57487942	51431429	89.5%	338279
3.5hpf	232029287	205771559	88.7%	22192692	79539654	68547095	86.2%	327683
4.5hpf	51256278	46089089	89.9%	20167130	38327579	35894962	93.7%	333927
6hpf	44770396	40229015	89.9%	19493410	45953510	43954427	95.6%	335045
24hpf	53222976	48160879	90.5%	19519417	40977352	39423289	96.2%	447413
Average	89786996	80605613	90.2%	20223463	49933946	45797653	92.7%	351261
Total	538721973	483633676			299603675	274785920		

Supplementary Table 2. Complete list of the enriched GO terms based on GREAT analysis

					Binomial Ontology									Hypergeometric Ontology							
Ontology	Term ID	Term Name	Rank	Raw p-value	Bonferroni p-value	FDR q-value	Fold enrichment	Expected	Observed regions	Genome fraction	Region Set coverage	Rank	Raw p-value	Bonferroni p-value	FDR q-value	Fold enrichment	Expected	Observed genes	Total genes	Gene Set coverage	Term genes coverage	Genes
GO Molecular Function	GO:0005007	fibroblast growth factor receptor activity	8	1.83E-11	3.10E-08	3.87E-09	1.11E+01	1.35E+00	15	1.07E-03	1.19E-02	9	9.78E-06	1.66E-02	1.84E-03	1.00E+01	4.98E-01	5	5	3.44E-03	1.00E+00	fgfr1a,fgfr1b,fgfr2,fgfr3,fgfr4
GO Biological Process	GO:0007420	brain development	21	5.75E-31	2.07E-27	9.85E-29	3.05E+00	4.66E+01	142	3.70E-02	1.13E-01	8	7.31E-27	2.63E-23	3.29E-24	3.98E+00	1.83E+01	73	184	5.03E-02	3.97E-01	acvr2b,adcyap1b,ascl1a,ascl1b,bdnf,bsx,cdh2,crb2,csnnp1b,disc1,disp1,dixdc1a,epha4a,fezf2,fgf3,fgf8b,fgfr1a,fmr1,foxb1.2,fsta,gli1,gli2a,gli2b,her15.1,her15.1,hoxb1a,irx1b,irx7,jhdm1db,lef1,lhx2b,lhx5,lmx1b.1,mpp5a,neurog1,nr6a1a,otp,otx1a,otx2,pard3,pax2a,pax6b,pbx4,pcdh19,pitx3,prickle1b,prkci,prox1,ralgapa1,robo2,rps15a,rx3,sema3d,sfrp5,sim1a,six3a,six3b,sox14,tbx2b,tcf7l1a,tcf7l1b,tfap2a,tgif1,usp28,vangl2,wnt10b,wnt3a,yap1,ywhag1,zic1,zic2a,zic4,zic5,znf703
GO Biological Process	GO:0007417	central nervous system development	23	6.09E-29	2.19E-25	9.52E-27	2.74E+00	5.65E+01	155	4.48E-02	1.23E-01	11	5.64E-26	2.03E-22	1.84E-23	3.51E+00	2.36E+01	83	237	5.72E-02	3.50E-01	acvr2b,adcyap1b,aldh1a2,ascl1a,asctl1b,bdnf,bsx,cdh2,crb2,csnnp1b,dbx1b,disc1,disp1,dixdc1a,dld,epha4a,fezf2,fgf3,fgf8b,fgfr1a,fmr1,foxb1.2,fsta,gata3,gli1,gli2a,gli2b,her15.1,her15.1,hoxb1a,irx1b,irx7,isl1,jag2,jhdm1db,lef1,lhx2b,lhx5,lmx1b.1,mpp5a,neurog1,nkx6.1,nr6a1a,otp,otx1a,otx2,pard3,pax2a,pax6b,pbx4,pcdh19,pitx3,prickle1b,prkci,prox1,ralgapa1,robo2,rps15a,rx3,sema3d,sfrp5,sim1a,six3a,six3b,sox14,sox3,tbx2b,tcf7l1a,tcf7l1b,tfap2a,tgif1,usp28,vangl2,wnt10b,wnt3a,yap1,ywhag1,zic1,zic2a,zic4,zic5,znf703
GO Biological Process	GO:0001654	eye development	25	3.30E-25	1.19E-21	4.75E-23	3.26E+00	3.22E+01	105	2.55E-02	8.33E-02	49	7.19E-10	2.59E-06	5.28E-08	2.64E+00	1.70E+01	45	171	3.10E-02	2.63E-01	adcyap1b,bcor,ccnd1,cdh2,cdh6,crb2,crb2l,dixdc1a,epb41l5,fgf3,fgfr1a,foxc1a,her15.1,her15.1,hs6st2,irx1a,irx7,lama1,lhx2b,lhx5,mab21l2,med24,meis1,mpp5a,nfyc,pard3,pax2a,pax6b,pbx4,pitx3,prickle1b,prkci,rab11fip4a,rbm42,rx3,sfrp1a,sfrp5,six3b,sox2,tbx2b,tcf7l1a,vangl2,zic1,zic2a,znf703
GO Biological Process	GO:0007423	sensory organ development	31	5.48E-23	1.97E-19	6.36E-21	2.68E+00	4.73E+01	127	3.75E-02	1.01E-01	45	4.13E-11	1.49E-07	3.30E-09	2.46E+00	2.40E+01	59	241	4.06E-02	2.45E-01	adcyap1b,atoh1a,atoh1b,bcor,ccnd1,cdh2,cdh6,crb2,crb2l,dachа,disp1,dixdc1a,epb41l5,fgf3,fgfr1a,foxc1a,foxi1,fsta,her15.1,her15.1,hs6st2,irx1a,irx7,lama1,lhx2b,lhx5,mab21l2,med24,meis1,mpp5a,mxrb,msxc,neurog1,nfyc,nr0b2,oc90,otx1b,pard3,pax2a,pax6b,pbx4,pitx3,prkci,ptch2,rab11fip4a,rbm42,rerea,rx3,sfrp1a,sfrp5,six3b,sox2,sox9b,tbx2b,tcf7l1a,vangl2,zic1,zic2a,znf703
GO Biological Process	GO:0043010	camera-type eye development	34	1.46E-21	5.26E-18	1.55E-19	3.45E+00	2.41E+01	83	1.91E-02	6.58E-02	65	3.96E-07	1.42E-03	2.19E-05	2.53E+00	1.31E+01	33	131	2.27E-02	2.52E-01	adcyap1b,bcor,ccnd1,cdh2,cdh6,crb2,dixdc1a,epb41l5,fgf3,foxc1a,irx1a,irx7,lama1,lhx2b,med24,meis1,mpp5a,nfyc,pard3,pax2a,pax6b,pbx4,pitx3,prkci,ptch2,rbm42,rx3,six3b,tbx2b,tcf7l1a,zic1,zic2a,znf703
GO Biological Process	GO:0021915	neural tube development	35	2.17E-21	7.79E-18	2.23E-19	4.47E+00	1.37E+01	61	1.08E-02	4.84E-02	33	8.46E-14	3.04E-10	9.22E-12	5.22E+00	4.98E+00	26	50	1.79E-02	5.20E-01	bcor,cdh2,cdx1a,fgf8b,fmr1,foxb1.2,gli1,gli2a,gli2b,lmx1b.1,mdka,mpp5a,nr6a1a,otx1a,otx2,pard6gb,pax2a,pcdh19,prkci,tcf7l1a,tcf7l1b,vangl2,wnt10b,wnt3a,zic2a,zic5
GO Biological Process	GO:0048592	eye morphogenesis	36	7.44E-21	2.68E-17	7.44E-19	3.71E+00	1.97E+01	73	1.56E-02	5.79E-02	50	5.79E-09	2.08E-05	4.16E-07	3.30E+00	8.47E+00	28	85	1.93E-02	3.29E-01	ccnd1,cdh2,cdh6,crb2l,epb41l5,fgfr1a,hs6st2,irx1a,irx7,mab21l2,med24,meis1,mpp5a,pard3,pax2a,pax6b,pbx4,prkci,rab11fip4a,rx3,six3b,sox2,tbx2b,tcf7l1a,vangl2,zic1,zic2a,znf703
GO Biological Process	GO:0030902	hindbrain development	37	2.95E-19	1.06E-15	2.86E-17	4.09E+00	1.47E+01	60	1.16E-02	4.76E-02	38	2.46E-12	8.84E-09	2.33E-10	4.51E+00	5.98E+00	27	60	1.86E-02	4.50E-01	acvr2b,ascl1a,ascl1b,cdh2,disc1,fgf3,fgfr1a,gli2b,hoxb1a,irx1b,irx7,lmx1b.1,neurog1,otx1a,otx2,pard3,pax2a,pax6b,pbx4,prickle1b,sema3d,tcf7l1b,tfap2a,vangl2,zic1,zic4,znf703
GO Biological Process	GO:0043009	chordate embryonic development	40	1.73E-17	6.23E-14	1.56E-15	2.57E+00	4.01E+01	103	3.18E-02	8.17E-02	29	1.93E-15	6.93E-12	2.39E-13	3.30E+00	1.57E+01	52	158	3.58E-02	3.29E-01	bcor,cdh2,cdx1a,ctr9,disc1,disp1,dlc,dld,dlx2a,fgf8b,fmr1,foxb1.2,foxc1a,gli1,gli2a,gli2b,her15.1,her15.1,her6,lef1,lmx1b.1,mdka,mef2a,mpp5a,msxb,naa50,neurod4,notch3,nr6a1a,rtla,otx1a,otx2,pard6gb,pax2a,pcdh19,pdlim7,prkci,pxn,rbpjb,rerea,ripply2,smtnl,tcf7l1a,tcf7l1b,tfap2a,vangl2,wnt10b,wnt3a,zeb2a,zeb2b,zic2a,zic5
GO Biological Process	GO:0009792	embryo development ending in birth or egg hatching	40	1.73E-17	6.23E-14	1.56E-15	2.57E+00	4.01E+01	103	3.18E-02	8.17E-02	29	1.93E-15	6.93E-12	2.39E-13	3.30E+00	1.57E+01	52	158	3.58E-02	3.29E-01	bcor,cdh2,cdx1a,ctr9,disc1,disp1,dlc,dld,dlx2a,fgf8b,fmr1,foxb1.2,foxc1a,gli1,gli2a,gli2b,her15.1,her15.1,her6,lef1,lmx1b.1,mdka,mef2a,mpp5a,msxb,naa50,neurod4,notch3,nr6a1a,rtla,otx1a,otx2,pard6gb,pax2a,pcdh19,pdlim7,prkci,pxn,rbpjb,rerea,ripply2,smtnl,tcf7l1a,tcf7l1b,tfap2a,vangl2,wnt10b,wnt3a,zeb2a,zeb2b,zic2a,zic5
GO Biological Process	GO:0048593	camera-type eye morphogenesis	43	1.50E-16	5.39E-13	1.25E-14	4.31E+00	1.11E+01	48	8.82E-03	3.81E-02	83	1.82E-06	6.55E-03	7.89E-05	3.41E+00	5.28E+00	18	53	1.24E-02	3.40E-01	ccnd1,cdh6,epb41l5,irx7,med24,meis1,mpp5a,pax2a,pax6b,pbx4,prkci,rx3,six3b,tbx2b,tcf7l1a,zic1,zic2a,znf703
GO Biological Process	GO:0007219	Notch signaling pathway	44	6.13E-15	2.21E-11	5.01E-13	6.07E+00	5.11E+00	31	4.05E-03	2.46E-02	59	1.47E-07	5.31E-04	8.99E-06	4.34E+00	3.69E+00	16	37	1.10E-02	4.32E-01	dla,dlb,dlc,dld,her15.1,her15.1,her6,hey1,jag1a,jag1b,jag2,lfng,notch1b,notch3,nrarpa,nrarpb
GO Biological Process	GO:0048048	embryonic eye morphogenesis	45	8.42E-15	3.03E-11	6.73E-13	5.78E+00	5.54E+00	32	4.39E-03	2.54E-02	84	2.32E-06	8.34E-03	9.93E-05	5.02E+00	2.19E+00	11	22	7.58E-03	5.00E-01	cdh2,epb41l5,hs6st2,mab21l2,pard3,pax2a,rx3,six3b,tcf7l1a,vangl2,znf703
GO Biological Process	GO:0061351	neural precursor cell proliferation	50	1.63E-12	5.86E-09	1.17E-10	8.30E+00	2.41E+00	20	1.91E-03	1.59E-02	47	9.41E-11	3.39E-07	7.21E-09	1.00E+01	9.97E-01	10	10	6.89E-03	1.00E+00	gli2b,pard3,prkci,sema3d,tcf7l1a,tcf7l1b,zic1,zic2a,zic4,zic5
GO Biological Process	GO:0009953	dorsal/ventral pattern formation	51	2.17E-12	7.80E-09	1.53E-10	2.90E+00	2.00E+01	58	1.59E-02	4.60E-02	37	2.17E-12	7.79E-09	2.11E-10	3.85E+00	8.57E+00	33	86	2.27E-02	3.84E-01	acvr1b,axin2,bmpr1aa,bmpr1ab,bmpr1bb,ctnnb1,ctnnb2,dusp6,eomesa,fgf3,fgfr1a,fsta,gli1,gli2a,gli2b,il17rd,jag1b,jrc6,mapk8,msxb,otx1,robo3,skia,skib,sox21a,spry2,tob1a,usp25,vox,wnt3a,zeb2a,zeb2b,zic2a
GO Biological Process	GO:0008284	positive regulation of cell proliferation	56	3.85E-12	1.38E-08	2.47E-10	7.90E+00	2.53E+00	20	2.01E-03	1.59E-02	152	4.90E-04	1.00E+00	1.16E-02	4.39E+00	1.59E+00	7	16	4.82E-03	4.38E-01	fgfr1a,fgfr1b,fgfr2,fgfr3,fgfr4,tcf7l1a,tcf7l1b
GO Biological Process	GO:0016055	Wnt receptor signaling pathway	58	7.35E-12	2.64E-08	4.56E-10	2.94E+00	1.84E+01	54	1.46E-02	4.28E-02	55	2.60E-08	9.34E-05	1.70E-06	3.19E+00	8.47E+00	27	85	1.86E-02	3.18E-01	axin2,ctnnb2,dact1,dixdc1a,fzd10,fzd4,fzd7a,lef1,med10,nkd2a,nrlla,nxn,sfrp1a,sfrp1b,sfrp5,tcf7l1a,tcf7l1b,tob1a,vangl2,wnt10b,wnt11r,wnt3,wnt3a,wnt7bb,wwox,zgc:158636,zic5
GO Biological Process	GO:0008543	fibroblast growth factor receptor signaling pathway	61	1.90E-11	6.85E-08	1.12E-09	9.97E+00	1.61E+00	16	1.27E-03	1.27E-02	109	2.28E-05	8.19E-02	7.52E-04	7.52E+00	7.97E-01	6	8	4.13E-03	7.50E-01	fgf8b,fgfr1a,fgfr1b,fgfr2,fgfr3,fgfr4,cdh2,csnnp1b,foxb1.2,fsta,jhdm1db
GO Biological Process	GO:0030901	midbrain development	63	5.04E-11	1.81E-07	2.88E-09	4.85E+00	5.57E+00	27	4.42E-03	2.14E-02	52	8.61E-09	3.10E-05	5.96E-07	6.21E+00	2.09E+00	13	21	8.95E-03	6.19E-01	otx1a,otx2,pax2a,pbx4,tcf7l1a,tcf7l1b,zic2a,zic5
GO Biological Process	GO:0060059	embryonic retinal morphogenesis in camera-type eye	64	1.07E-10	3.83E-07	5.99E-09	6.53E+00	3.06E+00	20	2.43E-03	1.59E-02	141	1.76E-04	6.33E-01	4.49E-03	5.02E+00	1.40E+00	7	14	4.82E-03	5.00E-01	epb41l5,irx7,meis1,mpp5a,pbx4,zic1,zic2a
GO Biological Process	GO:0008283	cell proliferation	90	6.93E-09	2.49E-05	2.77E-07	3.44E+00	9.02E+00	31	7.15E-03	2.46E-02	66	4.18E-07	1.50E-03	2.28E-05	4.30E+00	3.49E+00	15	35	1.03E-02	4.29E-01	cse1l,gli2b,ipo7,nrarpa,nrarpb,pard3,prkci,sema3d,tbx2b,tcf7l1a,tcf7l1b,zic1,zic2a,zic4,zic5
GO Biological Process	GO:0051090	regulation of transcription factor activity	91	9.82E-09	3.53E-05	3.88E-07	6.41E+00	2.50E+00	16	1.98E-03	1.27E-02	105	2.22E-05	7.97E-02	7.59E-04	6.38E+00	1.10E+00	7	11	4.82E-03	6.36E-01	fli1a,prox1,sox19a,sox19b,sox1b,sox2,sox3
GO Biological Process	GO:0051101	regulation of DNA binding	91	9.82E-09	3.53E-05	3.88E-07	6.41E+00	2.50E+00	16	1.98E-03	1.27E-02	105	2.22E-05	7.97E-02	7.59E-04	6.38E+00	1.10E+00	7	11	4.82E-03	6.36E-01	fli1a,prox1,sox19a,sox19b,sox1b,sox2,sox3
GO Biological Process	GO:0090046	regulation of transcription regulator activity	91	9.82E-09	3.53E-05	3.88E-07	6.41E+00	2.50E+00	16	1.98E-03	1.27E-02	105	2.22E-05	7.97E-02	7.59E-04	6.38E+00	1.10E+00	7	11	4.82E-03	6.36E-01	fli1a,prox1,sox19a,sox19b,sox1b,sox2,sox3
GO Biological Process	GO:0042127	regulation of cell proliferation	94	1.20E-08	4.32E-05	4.59E-07	4.48E+00	4.91E+00	22	3.90E-03	1.74E-02	186	1.95E-03	1.00E+00	3.77E-02	3.01E+00	2.99E+00	9	30	6.20E-03	3.00E-01	fgfr1a,fgfr1b,fgfr2,fgfr3,fgfr4,tcf7l1a,tcf7l1b,zic2a,zic5
GO Biological Process	GO:0016331	morphogenesis of embryonic epithelium	95	1.52E-08	5.45E-05	5.74E-07	4.42E+00	4.98E+00	22	3.95E-03	1.74E-02	92	6.79E-06	2.44E-02	2.66E-04	5.02E+00	1.99E+00	10	20	6.89E-03	5.00E-01	mdka,mpp5a,neurod4,notch3,pard6gb,pcdh19,prkci,vangl2,zic2a,zic5

Supplementary Table 2. Continued.

GO:BiologicalProcess	GO:0051098	regulation of DNA binding	97	1.60E-08	5.77E-05	5.95E-07	6.18E+00	2.59E+00	16	2.05E-03	1.27E-02	121	4.86E-05	1.75E-01	1.44E-03	5.85E+00	1.20E+00	7	12	4.82E-03	5.83E-01	fli1a,prox1,sox19a,sox19b,sox1b,sox2,sox3
GO:BiologicalProcess	GO:0021532	neural tube patterning	104	3.41E-08	1.23E-04	1.18E-06	4.22E+00	5.22E+00	22	4.14E-03	1.74E-02	74	7.94E-07	2.86E-03	3.86E-05	5.02E+00	2.39E+00	12	24	8.26E-03	5.00E-01	cdx1a,fgf8b,fmr1,lmx1b.1,nr6a1a,otx1a,otx2,pax2a,tcf7l1a,tcf7l1b,wnt10b,wnt3a
GO:BiologicalProcess	GO:0021903	rostrocaudal neural tube patterning	104	3.41E-08	1.23E-04	1.18E-06	4.22E+00	5.22E+00	22	4.14E-03	1.74E-02	74	7.94E-07	2.86E-03	3.86E-05	5.02E+00	2.39E+00	12	24	8.26E-03	5.00E-01	cdx1a,fgf8b,fmr1,lmx1b.1,nr6a1a,otx1a,otx2,pax2a,tcf7l1a,tcf7l1b,wnt10b,wnt3a
GO:BiologicalProcess	GO:0043388	positive regulation of DNA binding	106	3.56E-08	1.28E-04	1.21E-06	7.57E+00	1.72E+00	13	1.36E-03	1.03E-02	109	2.28E-05	8.19E-02	7.52E-04	7.52E+00	7.97E-01	6	8	4.13E-03	7.50E-01	fli1a,sox19a,sox19b,sox1b,sox2,sox3
GO:BiologicalProcess	GO:0051099	positive regulation of DNA binding	106	3.56E-08	1.28E-04	1.21E-06	7.57E+00	1.72E+00	13	1.36E-03	1.03E-02	109	2.28E-05	8.19E-02	7.52E-04	7.52E+00	7.97E-01	6	8	4.13E-03	7.50E-01	fli1a,sox19a,sox19b,sox1b,sox2,sox3
GO:BiologicalProcess	GO:0090047	positive regulation of DNA transcription regulator activity	106	3.56E-08	1.28E-04	1.21E-06	7.57E+00	1.72E+00	13	1.36E-03	1.03E-02	109	2.28E-05	8.19E-02	7.52E-04	7.52E+00	7.97E-01	6	8	4.13E-03	7.50E-01	fli1a,sox19a,sox19b,sox1b,sox2,sox3
GO:BiologicalProcess	GO:0051091	positive regulation of DNA transcription factor activity	106	3.56E-08	1.28E-04	1.21E-06	7.57E+00	1.72E+00	13	1.36E-03	1.03E-02	109	2.28E-05	8.19E-02	7.52E-04	7.52E+00	7.97E-01	6	8	4.13E-03	7.50E-01	fli1a,sox19a,sox19b,sox1b,sox2,sox3
GO:BiologicalProcess	GO:0030917	midbrain-hindbrain boundary development	114	5.40E-08	1.94E-04	1.70E-06	6.09E+00	2.46E+00	15	1.95E-03	1.19E-02	140	1.67E-04	6.02E-01	4.30E-03	4.46E+00	1.79E+00	8	18	5.51E-03	4.44E-01	fgf8b,lmx1b.1,nr6a1a,otx1a,otx2,pax2a,wnt10b,wnt3a
GO:BiologicalProcess	GO:0072175	epithelial tube formation	116	6.95E-08	2.50E-04	2.15E-06	4.89E+00	3.68E+00	18	2.92E-03	1.43E-02	78	1.20E-06	4.31E-03	5.53E-05	7.30E+00	1.10E+00	8	11	5.51E-03	7.27E-01	mdka,mpp5a,pard6gb,pcdh19,prkci,vangl2,zic2a,zic5
GO:BiologicalProcess	GO:0001838	embryonic epithelial tube formation	116	6.95E-08	2.50E-04	2.15E-06	4.89E+00	3.68E+00	18	2.92E-03	1.43E-02	78	1.20E-06	4.31E-03	5.53E-05	7.30E+00	1.10E+00	8	11	5.51E-03	7.27E-01	mdka,mpp5a,pard6gb,pcdh19,prkci,vangl2,zic2a,zic5
GO:BiologicalProcess	GO:0001841	neural tube formation	116	6.95E-08	2.50E-04	2.15E-06	4.89E+00	3.68E+00	18	2.92E-03	1.43E-02	78	1.20E-06	4.31E-03	5.53E-05	7.30E+00	1.10E+00	8	11	5.51E-03	7.27E-01	mdka,mpp5a,pard6gb,pcdh19,prkci,vangl2,zic2a,zic5
GO:BiologicalProcess	GO:0045165	cell fate commitment	119	6.98E-08	2.51E-04	2.11E-06	2.76E+00	1.34E+01	37	1.06E-02	2.93E-02	57	5.08E-08	1.83E-04	3.20E-06	3.70E+00	5.68E+00	21	57	1.45E-02	3.68E-01	acvr1b,atoh1a,atoh1b,cdkn1c,disc1,disp1,dld,eng1b,fgf3,fmr1,foxi1,gli1,gli2a,isl1,isl2a,nkd2a,nkx6.1,pax2a,rx3,tbx2b,tfap2a
GO:BiologicalProcess	GO:0001708	cell fate specification	120	8.23E-08	2.96E-04	2.47E-06	3.30E+00	8.48E+00	28	6.73E-03	2.22E-02	73	7.51E-07	2.70E-03	3.70E-05	4.39E+00	3.19E+00	14	32	9.64E-03	4.38E-01	cdkn1c,disc1,disp1,fgf3,fmr1,foxi1,gli1,gli2a,isl1,isl2a,pax2a,rx3,tbx2b,tfap2a
GO:BiologicalProcess	GO:0050931	pigment cell differentiation	121	8.73E-08	3.14E-04	2.60E-06	3.99E+00	5.52E+00	22	4.37E-03	1.74E-02	136	1.41E-04	5.08E-01	3.74E-03	4.10E+00	2.19E+00	9	22	6.20E-03	4.09E-01	cdh2,foxd3,kitlga,mitfa,nrarpa,ric8b,sox9b,tfap2a,trpm7
GO:BiologicalProcess	GO:0007422	peripheral nervous system development	122	9.36E-08	3.37E-04	2.76E-06	3.82E+00	6.01E+00	23	4.77E-03	1.82E-02	120	4.01E-05	1.44E-01	1.20E-03	3.94E+00	2.79E+00	11	28	7.58E-03	3.93E-01	aldh1a2,cdh2,dlx2a,fgf3,foxd3,neurog1,notch1b,notch3,pax2a,sema3d,tfap2a
GO:BiologicalProcess	GO:0014031	mesenchymal cell development	128	2.23E-07	8.02E-04	6.27E-06	2.59E+00	1.47E+01	38	1.16E-02	3.01E-02	60	1.57E-07	5.64E-04	9.41E-06	3.93E+00	4.59E+00	18	46	1.24E-02	3.91E-01	acvr2b,cdh2,ctr9,disc1,dlx2a,fmr1,foxd3,lef1,mych,nrarpa,pbx4,radil,rx3,sema3d,tfap2a,tfap2c,zeb2a,zeb2b
GO:BiologicalProcess	GO:0035148	tube formation	129	2.42E-07	8.70E-04	6.74E-06	4.48E+00	4.01E+00	18	3.18E-03	1.43E-02	95	7.78E-06	2.80E-02	2.95E-04	6.17E+00	1.30E+00	8	13	5.51E-03	6.15E-01	mdka,mpp5a,pard6gb,pcdh19,prkci,vangl2,zic2a,zic5
GO:BiologicalProcess	GO:0060028	convergent extension involved in axis elongation	130	2.58E-07	9.29E-04	7.15E-06	5.02E+00	3.19E+00	16	2.53E-03	1.27E-02	152	4.90E-04	1.00E+00	1.16E-02	4.39E+00	1.59E+00	7	16	4.82E-03	4.38E-01	akap12,eaf1,gpc4,ntla,tax1bp3,zeb2a,zeb2b
GO:BiologicalProcess	GO:0003401	axis elongation	130	2.58E-07	9.29E-04	7.15E-06	5.02E+00	3.19E+00	16	2.53E-03	1.27E-02	152	4.90E-04	1.00E+00	1.16E-02	4.39E+00	1.59E+00	7	16	4.82E-03	4.38E-01	akap12,eaf1,gpc4,ntla,tax1bp3,zeb2a,zeb2b
GO:BiologicalProcess	GO:0050767	regulation of neurogenesis	133	3.25E-07	1.17E-03	8.79E-06	2.88E+00	1.08E+01	31	8.54E-03	2.46E-02	124	6.17E-05	2.22E-01	1.79E-03	3.34E+00	3.89E+00	13	39	8.95E-03	3.33E-01	cdh2,fgf3,gli1,gli2a,her9,neurod4,neurog1,notch3,olig4,robo2,sema3d,slit1a,slit2
GO:BiologicalProcess	GO:0060042	retina morphogenesis in camera-type eye	137	3.90E-07	1.40E-03	1.02E-05	3.13E+00	8.63E+00	27	6.85E-03	2.14E-02	161	6.88E-04	1.00E+00	1.54E-02	2.98E+00	3.69E+00	11	37	7.58E-03	2.97E-01	cdh6,epb41l5,irx7,med24,meis1,mpp5a,pbx4,prkci,tbx2b,zic1,zic2a
GO:BiologicalProcess	GO:0051960	regulation of nervous system development	146	7.01E-07	2.52E-03	1.73E-05	2.77E+00	1.12E+01	31	8.86E-03	2.46E-02	131	1.11E-04	3.98E-01	3.04E-03	3.18E+00	4.09E+00	13	41	8.95E-03	3.17E-01	cdh2,fgf3,gli1,gli2a,her9,neurod4,neurog1,notch3,olig4,robo2,sema3d,slit1a,slit2
GO:BiologicalProcess	GO:0021953	central nervous system neuron differentiation	156	1.84E-06	6.60E-03	4.23E-05	2.60E+00	1.23E+01	32	9.77E-03	2.54E-02	126	6.86E-05	2.47E-01	1.96E-03	3.01E+00	4.98E+00	15	50	1.03E-02	3.00E-01	disc1,dld,fezf2,gata3,gli1,gli2a,gli2b,irx1a,isl1,jag2,lef1,neurog1,nkx6.1,otpb,prox1
GO:BiologicalProcess	GO:0060284	regulation of cell development	161	3.85E-06	1.39E-02	8.61E-05	2.55E+00	1.22E+01	31	9.65E-03	2.46E-02	142	2.46E-04	8.83E-01	6.22E-03	2.96E+00	4.39E+00	13	44	8.95E-03	2.95E-01	cdh2,fgf3,gli1,gli2a,her9,neurod4,neurog1,notch3,olig4,robo2,sema3d,slit1a,slit2
GO:BiologicalProcess	GO:0001755	neural crest cell migration	162	4.45E-06	1.60E-02	9.88E-05	2.95E+00	8.14E+00	24	6.45E-03	1.90E-02	137	1.61E-04	5.81E-01	4.24E-03	3.72E+00	2.69E+00	10	27	6.89E-03	3.70E-01	acvr2b,cdh2,disc1,foxd3,lef1,nrarpa,pbx4,radil,rx3,sema3d
GO:BiologicalProcess	GO:0060560	developmental growth involved in morphogenesis	163	4.52E-06	1.62E-02	9.97E-05	3.13E+00	7.04E+00	22	5.58E-03	1.74E-02	157	5.31E-04	1.00E+00	1.22E-02	3.07E+00	3.59E+00	11	36	7.58E-03	3.06E-01	akap12,eaf1,gpc4,isl2a,ntla,plxna3,plxnb1a,robo3,tax1bp3,zeb2a,zeb2b
GO:BiologicalProcess	GO:0040036	regulation of fibroblast growth factor receptor signaling pathway	168	5.76E-06	2.07E-02	1.23E-04	3.42E+00	5.56E+00	19	4.41E-03	1.51E-02	119	3.24E-05	1.16E-01	9.79E-04	5.35E+00	1.50E+00	8	15	5.51E-03	5.33E-01	dusp6,il17rd,rerea,sall1a,sall4,spry2,spry4
GO:BiologicalProcess	GO:0014032	neural crest cell development	169	6.25E-06	2.25E-02	1.33E-04	2.53E+00	1.19E+01	30	9.40E-03	2.38E-02	81	1.49E-06	5.37E-03	6.63E-05	3.96E+00	3.79E+00	15	38	1.03E-02	3.95E-01	acvr2b,cdh2,ctr9,disc1,dlx2a,foxd3,lef1,mych,nrarpa,pbx4,radil,rx3,sema3d,tfap2a,tfap2c
GO:BiologicalProcess	GO:0035121	tail morphogenesis	178	1.16E-05	4.18E-02	2.35E-04	4.16E+00	3.36E+00	14	2.67E-03	1.11E-02	105	2.22E-05	7.97E-02	7.59E-04	6.38E+00	1.10E+00	7	11	4.82E-03	6.36E-01	bc9l,cdh2,fgf1a,fgf1b,ntla,vangl2,wnt3a
GO:BiologicalProcess	GO:0030318	melanocyte differentiation	181	1.56E-05	5.59E-02	3.09E-04	5.12E+00	2.15E+00	11	1.70E-03	8.72E-03	166	8.98E-04	1.00E+00	1.95E-02	4.63E+00	1.30E+00	6	13	4.13E-03	4.62E-01	foxd3,kitlga,mitfa,sox9b,tfap2a,trpm7
GO:BiologicalProcess	GO:0021575	hindbrain morphogenesis	189	1.80E-05	6.47E-02	3.42E-04	4.00E+00	3.50E+00	14	2.78E-03	1.11E-02	166	8.98E-04	1.00E+00	1.95E-02	4.63E+00	1.30E+00	6	13	4.13E-03	4.62E-01	ascl1a,ascl1b,disc1,irx7,neurog1,pax2a
GO:BiologicalProcess	GO:0048066	developmental pigmentation	209	5.43E-05	1.95E-01	9.34E-04	2.65E+00	8.32E+00	22	6.60E-03	1.74E-02	186	1.95E-03	1.00E+00	3.77E-02	3.01E+00	2.99E+00	9	30	6.20E-03	3.00E-01	cdh2,foxd3,kitlga,mitfa,nrarpa,ric8b,sox9b,tfap2a,trpm7
GO:BiologicalProcess	GO:0007163	establishment or maintenance of cell polarity	220	7.91E-05	2.85E-01	1.29E-03	3.30E+00	4.55E+00	15	3.61E-03	1.19E-02	164	7.62E-04	1.00E+00	1.67E-02	4.13E+00	1.69E+00	7	17	4.82E-03	4.12E-01	crb2,epb41l5,gpc4,mpp5a,pard3,prkci,vangl2
GO:BiologicalProcess	GO:0007178	transmembrane receptor protein serine/threonine kinase signaling	229	1.18E-04	4.25E-01	1.85E-03	2.81E+00	6.39E+00	18	5.07E-03	1.43E-02	186	1.95E-03	1.00E+00	3.77E-02	3.01E+00	2.99E+00	9	30	6.20E-03	3.00E-01	acvr2b,bmpr1aa,bmpr1ab,bmpr1bb,smad3a,smad7,stub1,tgfb3,tob1a
GO:BiologicalProcess	GO:0021534	cell proliferation in hindbrain	264	4.24E-04	1.00E+00	5.78E-03	5.33E+00	1.31E+00	7	1.04E-03	5.55E-03	129	9.83E-05	3.54E-01	2.74E-03	1.00E+01	3.99E-01	4	4	2.75E-03	1.00E+00	gli2b,sema3d,zic1,zic4
GO:BiologicalProcess	GO:0045197	establishment or maintenance of epithelial cell apical/basal polarity	271	6.00E-04	1.00E+00	7.97E-03	3.94E+00	2.28E+00	9	1.81E-03	7.14E-03	151	4.53E-04	1.00E+00	1.08E-02	8.03E+00	4.98E-01	4	5	2.75E-03	8.00E-01	crb2,epb41l5,pard3,prkci
GO:BiologicalProcess	GO:0021761	limbic system development	273	6.50E-04	1.00E+00	8.57E-03	2.95E+00	4.41E+00	13	3.50E-03	1.03E-02	166	8.98E-04	1.00E+00	1.95E-02	4.63E+00	1.30E+00	6	13	4.13E-03	4.62E-01	fezf2,foxb1.2,lef1,otpb,sim1a,sox14
GO:BiologicalProcess	GO:0021854	hypothalamus development	273	6.50E-04	1.00E+00	8.57E-03	2.95E+00	4.41E+00	13	3.50E-03	1.03E-02	166	8.98E-04	1.00E+00	1.95E-02	4.63E+00	1.30E+00	6	13	4.13E-03	4.62E-01	fezf2,foxb1.2,lef1,otpb,sim1a,sox14
GO:BiologicalProcess	GO:0043049	otic placode formation	278	7.59E-04	1.00E+00	9.82E-03	3.06E+00	3.92E+00	12	3.11E-03	9.52E-03	185	1.65E-03	1.00E+00	3.21E-02	3.70E+00	1.89E+00	7	19	4.82E-03	3.68E-01	fgf3,foxi1,fsta,msxb,msxc,pax2a,sox9b
GO:BiologicalProcess	GO:0048665	neuron fate specification	280	7.87E-04	1.00E+00	1.01E-02	4.21E+00	1.90E+00	8	1.51E-03	6.34E-03	148	4.23E-04	1.00E+00	1.03E-02	6.27E+00	7.97E-01	5	8	3.44E-03	6.25E-01	fgf3,gli1,isl1,isl2a,tbx2b
GO:BiologicalProcess	GO:0048854	brain morphogenesis	281	8.04E-04	1.00E+00	1.03E-02	2.75E+00	5.09E+00	14	4.04E-03	1.11E-02	156	5.28E-04	1.00E+00	1.22E-02	5.02E+00	1.20E+00	6	12	4.13E-03	5.00E-01	gli1,gli2a,gli2b,pcdh19,tgif1,zic1
GO:BiologicalProcess	GO:0061245	establishment or maintenance of bipolar cell polarity	282	8.09E-04	1.00E+00	1.03E-02	3.47E+00	2.88E+00	10	2.29E-03	7.93E-03	148	4.23E-04	1.00E+00	1.03E-02	6.27E+00	7.97E-01	5	8	3.44E-03	6.25E-01	crb2,epb41l5,mpp5a,pard3,prkci
GO:BiologicalProcess	GO:0035088	establishment or maintenance of apical/basal cell polarity	282	8.09E-04	1.00E+00	1.03E-02	3.47E+00	2.88E+00	10	2.29E-03	7.93E-03	148	4.23E-04	1.00E+00	1.03E-02	6.27E+00	7.97E-01	5	8	3.44E-03	6.25E-01	crb2,epb41l5,mpp5a,pard3,prkci
GO:BiologicalProcess	GO:0061138	morphogenesis of a branching epithelium	284	8.11E-04	1.00E+00	1.03E-02	3.23E+00	3.41E+00	11	2.70E-03	8.72E-03	165	8.73E-04	1.00E+00	1.90E-02	5.57E+00	8.97E-01	5	9	3.44E-03	5.56E-01	aldh1a2,hs6st2,plekhh1,sema3ab,unc5b
GO:BiologicalProcess	GO:0014029	neural crest formation	289	9.78E-04	1.00E+00	1.22E-02	3.38E+00	2.96E+00	10	2.35E-03	7.93E-03	180	1.25E-03	1.00E+00	2.50E-02	6.69E+00	5.98E-01	4	6	2.75E-03	6.67E-01	fmr1,tfap2a,zeb2a,zeb2b
GO:BiologicalProcess	GO:0021983	pituitary gland development	303	1.62E-03	1.00E+00	1.93E-02	2.95E+00	3.72E+00	11	2.95E-03	8.72E-03	95	7.78E-06	2.80E-02	2.95E-04	6.17E+00	1.30E+00	8	13	5.51E-03	6.15E-01	ascl1a,disp1,fgf3,gli1,gli2a,gli2b,pitx3,rx3
GO:BiologicalProcess	GO:0021984	adenohypophysis development	303	1.62E-03	1.00E+00	1.93E-02	2.95E+00	3.72E+00	11	2.95E-03	8.72E-03	95	7.78E-06	2.80E-02	2.95E-04	6.17E+00	1.30E+00	8	13	5.51E-03	6.15E-01	ascl1a,disp1,fgf3,gli1,gli2a,gli2b,pitx3,rx3
GO:BiologicalProcess	GO:0048853	forebrain morphogenesis	311	1.98E-03	1.00E+00	2.29E-02	4.07E+00	1.72E+00	7	1.36E-03	5.55E-03	129	9.83E-05	3.54E-01	2.74E-03	1.00E+01	3.99E-01	4	4	2.75E-03	1.00E+00	gli1,gli2a,gli2b,zic1
GO:BiologicalProcess	GO:0048863	neuron fate commitment	319	2.32E-03	1.00E+00	2.62E-02	2.67E+00	4.49E+00	12	3.56E-03	9.52E-03	123	5.91E-05	2.13E-01	1.73E-03	5.02E+00	1.59E+00	8	16	5.51E-03	5.00E-01	atoh1a,atoh1b,eng1b,fgf3,gli1,isl1,isl2a,tbx2b
GO:BiologicalProcess	GO:0060070	canonical Wnt receptor signaling pathway	339	3.56E-03	1.00E+00	3.77E-02	2.82E+00	3.54E+00	10	2.81E-03	7.93E-03	166	8.98E-04	1.00E+00	1.95E-02	4.63E+00	1.30E+00	6	13	4.13E-03	4.62E-01	ctnnb2,dixdc1a,lef1,tob1a,vangl2,zic5

Supplementary Table 3. Primer sequences for cloning candidate dsDMR enhancers and negative controls.

Enhancer	Genomic coordinate of PCR (Zv9)	Length	Forward PCR primer sequence	Reverse PCR primer sequence
six3a-e1	chr13:9844735-9845567	833	AACCGGATATCGTGCGCTGCTCAAAACATTA	ACCGCTCGAGATGCATGTGCAGGCTTAGGT
six3a-e2	chr13:9876410-9877496	1087	AACCGGATATCAGCAACCTCGGCTAACAAT	TGCGAGCTCTTAAGCATGTGCAACGGAAG
six3b-e1	chr12:27023558-27024926	1369	GGGGTACCGCACCTGTGCTTTCACTCAA	TGCGAGCTCACCATCCACACGTTACAGC
six3b-e2	chr12:27092089-27093577	1489	GGGGTACCCGCCATCTCTGAAAACATCA	ACCGCTCGAGGACAACAGGTCCATGTGTGG
fgfr2-e1	chr13:47043956-47044727	772	ACCGCTCGAGCATTGCTATCTGTGGCTCA	GGGGTACCAGCGATGCTAAATCGACGTT
fgfr2-e2	chr13:47048850-47049553	704	ACCGCTCGAGTGTGAAAAATTCCTTGCTCTGT	GGGGTACCGCGCAGAGCTGTAGCTGTTT
fgfr2-e3	chr13:47079183-47079685	503	ACCGCTCGAGTATCGCATCCTCACATGCAC	GGGGTACCGCACTTGAACCTCCCAGACT
fgfr2-e4	chr13:47147852-47148467	616	ACCGCTCGAGTGGGCAACATTTGAAAAACA	GGGGTACCACAAAAGTGGGTCCAACTCG
fgf3-e1	chr7:54702356-54703124	769	ACCGCTCGAGTCGCACATTCCACTGTAAGC	GGGGTACCGTCTGGAACTGACGGCTCTC
znf703-e1	chr5:26039075-26040431	1357	AACCGGATATCAATGCATGCCAATGATCAGA	GGGGTACCTTTAAGAAGTGCCGCTGACA
znf703-e2	chr5:26076625-26077977	1353	AACCGGATATCTGGGTTTGCAACAACAGAAA	TGCGAGCTCACTTTTTACCAACGCCATGC
znf703-e3	chr5:26081124-26081692	569	AACCGGATATCAGGGCCGTATTTCTTCCACT	TGCGAGCTCTTGCAAACAAAAGCAACAGC
sox2-e1	chr22:40116018-40116916	899	ACCGCTCGAGTCCGAGTACGGTGTCATCAA	GGGGTACCCTGACCTTAACCCTGACA
sox2-e2	chr22:40267310-40268047	738	ACCGCTCGAGCCCCACAATACCAAAAGTG	GGGGTACCATGGGCTTGTCATCTCTGA
sox2-e3	chr22:40270974-40271494	521	ACCGCTCGAGGTTAATTCCAGCCGAACAA	GGGGTACCTGGGTTAGAATGCGGGTTAG
sox2-e4	chr22:40314986-40315852	867	ACCGCTCGAGTGTAGCTCCGCCCTCTTTTA	GGGGTACCGGCAGCTGAGTTGTGATGAA
sox2-e5	chr22:40382380-40383117	738	ACCGCTCGAGCACGCTGGAAAACAGACT	GGGGTACCCCACTACTGCCCTCTTT
wnt3-e1	chr12:23610508-23612061	1554	ACCGCTCGAGACATGCTCCGCAAGGATAAC	AACCGGATATCGGTTTCAAAGCGAGTTCTGC
wnt3a-e1	chr2:3607794-3608622	829	TGCGAGCTCTGACAATGCAATGGCAGACT	GGGGTACCGAATTCCTCAGGGATCACCA
wnt3a-e2	chr2:3615290-3616091	802	AACCGGATATCAATGGTTCAAACGGCATCTC	ACCGCTCGAGCATTCTCTCCAGTGCCTTC
Negative controls				
six3a-ne1	chr13:9843819-9844508	690	CGCTAGGATCAACGAGAAGG	AGAACGCCGATGAATAATGG
six3a-ne2	chr13:9876218-9876725	534	GGCGGGGAAAATGTAGCTTA	CTCATTTTCAACCGCATTCA
six3b-ne1	chr12:27025200-27025902	703	TTCATTCGCTCATTCATTTCC	CGATGATGACGACGACAACT
six3b-ne2	chr12:27089582-27090330	749	GAGGCAGGGGGTAAGTTTTC	CAAAACGCTAACCAAGCAAA
fgfr2-ne1	chr13:47046087-47046773	687	CAATGTCACTGCCCCTTATG	CTCGCTCATGCTTGACTTTC
fgfr2-ne2	chr13:47050151-47050861	711	GCCGTTATCATATGCGTCAA	GAGCTGGCAAATGTTGTGAA
fgfr2-ne3	chr13:47082761-47083356	596	CAAGGTGTGCACTGGCATAG	AGCACCGCTCAGCTGATAAT
fgfr2-ne4	chr13:47150488-47151093	606	TCATCATTCATTTGCCCTGA	AACTGGTTTGGCCATGAGAC
fgf3-ne1	chr7:54671495-54672196	702	GGACCAAAATGTCCGAATGA	CTTTGGGGAGGGAAATGAAT
znf703-ne1	chr5:26034035-26034733	699	GCTCACGCTCTTTCTGCTTT	TTCATTTTGACAGCGAGGTG
znf703-ne2	chr5:26074122-26074815	694	AATCTTGCTCCTCAGCATGG	ATCTATGACCGGGGGTTTTC
znf703-ne3	chr5:26083204-26083808	605	CCTTTTGTTTCTCCGCTGTC	TGTTTGCTGGACTGGATTGA
sox2-ne1	chr22:40114980-40115687	708	CCATTGACTAGTGGGAAAAACC	TTGCAAGTGACGAATTTTGC
sox2-ne2	chr22:40246839-40247538	700	AACATGCAAGCTCCACACAG	CCCCTCCAACTTCACATCAG
sox2-ne3	chr22:40274332-40275071	740	GCTTCACCGTTGTTCTTGGT	TGTGCATGGGACGTGTAAAT
sox2-ne4	chr22:40312238-40312908	671	CAGCCTAAACTGCAGACAGGA	CCAACAATACCAATGGAAGTCA
sox2-ne5	chr22:40388661-40389359	699	ATGCGGTCTCCAAATCAAAA	GAAGAACCGTGCGGAATAAA
wnt3-ne1	chr12:23602504-23603203	700	TATGCGGCTGTGGTGATAAG	ATGGCTCACGTTTCAATTCC
wnt3a-ne1	chr2:3607100-3607809	710	GAATGCAGGTGAAGCCAGAT	TGCCATTGCATTGTCAGTCT
wnt3a-ne2	chr2:3611694-3612386	693	TTTATTGCAACCCATGCTCA	CCCTATCCACGAGAGCAAAA

Supplementary Table 4. Overlaps of dsDMR enhancers or negative controls with conserved sequences and enhancer histone peaks.

dsDMR enhancer or negative control	Location from TSS (kb)	Differentially methylated	Conserved seqeunces	H3K4me1 peak at 24hpf	H3K27ac peak at 24hpf
six3a-e1	-18.6	✓	✓	✓	✓
six3a-e2	-50.4	✓	✓	✓	✓
six3b-e1	-104.2	✓	✓		
six3b-e2	-35.6	✓	✓		
fgfr2-e1	-3.7	✓		✓	✓
fgfr2-e2	-8.6	✓			
fgfr2-e3	-38.8	✓	✓		
fgfr2-e4	-107.5	✓		✓	
fgf3-e1	-54.2	✓	✓		
znn703-e1	-37.1	✓	✓	✓	✓
znf703-e2	-74.7	✓	✓	✓	✓
znf703-e3	-78.8	✓	✓	✓	✓
sox2-e1	219.2	✓	✓	✓	✓
sox2-e2	68.0	✓		✓	✓
sox2-e3	64.5	✓	✓	✓	✓
sox2-e4	20.3	✓	✓	✓	✓
sox2-e5	-47.1	✓	✓	✓	✓
wnt3-e1	-3.1	✓	✓	✓	✓
wnt3a-e1	44.5	✓	✓	✓	
wnt3a-e2	37.0	✓	✓	✓	✓
six3a-ne1	-17.6		✓	✓	✓
six3a-ne2	-49.9		✓	✓	✓
six3b-ne1	-102.9		✓		
six3b-ne2	-38.4				
fgfr2-ne1	-5.8			✓	
fgfr2-ne2	-9.9				
fgfr2-ne3	-42.4				
fgfr2-ne4	-110.2				
fgf3-ne1	-23.4		✓		
znf703-ne1	-31.8		✓	✓	✓
znf703-ne2	-71.8				
znf703-ne3	-80.9		✓	✓	✓
sox2-ne1	220.4		✓		✓
sox2-ne2	88.5		✓		✓
sox2-ne3	61.0				
sox2-ne4	23.1				
sox2-ne5	-53.3		✓	✓	✓
wnt3-ne1	-11.5			✓	
wnt3a-ne1	45.2				
wnt3a-ne2	40.7				

Supplementary Table 5. The genes nearby candidate dsDMR enhancers and their ontology annotation.

Gene nearby identified enhancers	Related enriched GO terms	Ontology Term ID
six3a	brain development	GO:0007420
	central nervous system development	GO:0007417
six3b	brain development	GO:0007420
	central nervous system development	GO:0007417
	eye development	GO:0001654
	sensory organ development	GO:0007423
	camera-type eye development	GO:0043010
	eye morphogenesis	GO:0048592
	camera-type eye morphogenesis	GO:0048593
	embryonic eye morphogenesis	GO:0048048
fgfr2	positive regulation of cell proliferation	GO:0008284
	fibroblast growth factor receptor signaling pathway	GO:0008543
	regulation of cell proliferation	GO:0042127
	fibroblast growth factor receptor activity	GO:0005007
fgf3	brain development	GO:0007420
	central nervous system development	GO:0007417
	eye development	GO:0001654
	sensory organ development	GO:0007423
	camera-type eye development	GO:0043010
	hindbrain development	GO:0030902
	dorsal/ventral pattern formation	GO:0009953
	cell fate commitment	GO:0045165
	cell fate specification	GO:0001708
	peripheral nervous system development	GO:0007422
	regulation of neurogenesis	GO:0050767
	regulation of nervous system development	GO:0051960
	regulation of cell development	GO:0060284
	otic placode formation	GO:0043049
	neuron fate specification	GO:0048665
	pituitary gland development	GO:0021983
	adenohypophysis development	GO:0021984
	neuron fate commitment	GO:0048663
znf703	brain development	GO:0007420
	central nervous system development	GO:0007417
	eye development	GO:0001654
	sensory organ development	GO:0007423
	camera-type eye development	GO:0043010
	eye morphogenesis	GO:0048592
	hindbrain development	GO:0030902
	camera-type eye morphogenesis	GO:0048593
	embryonic eye morphogenesis	GO:0048048
sox2	eye development	GO:0001654
	sensory organ development	GO:0007423
	eye morphogenesis	GO:0048592
	dorsal/ventral pattern formation	GO:0009953
	regulation of transcription factor activity	GO:0051090
	regulation of DNA binding	GO:0051101
	regulation of transcription regulator activity	GO:0090046
	regulation of binding	GO:0051098
	positive regulation of DNA binding	GO:0043388
	positive regulation of binding	GO:0051099
	positive regulation of transcription regulator activity	GO:0090047
	positive regulation of transcription factor activity	GO:0051091
wnt3	Wnt receptor signaling pathway	GO:0016055
wnt3a	brain development	GO:0007420
	central nervous system development	GO:0007417
	neural tube development	GO:0021915
	chordate embryonic development	GO:0043009
	embryo development ending in birth or egg hatching	GO:0009792
	dorsal/ventral pattern formation	GO:0009953
	Wnt receptor signaling pathway	GO:0016055
	neural tube patterning	GO:0021532
	rostrocaudal neural tube patterning	GO:0021903
	midbrain-hindbrain boundary development	GO:0030917
	tail morphogenesis	GO:0035121

Supplementary Table 6. Expression pattern at 24 hpf of genes nearby candidate dsDMR enhancers.

Gene nearby identified enhancers	Gene expression pattern at 24 hpf	References	Reference PMID
six3a	forebrain midbrain hindbrain boundary medial longitudinal fasciculus rhombomere 2 anterior neural tube	Feijoo et al., 2009 Bräutigam et al., 2010 Pikulkaew et al., 2011	19544579 20533356 21360790
six3b	central nervous system diencephalon forebrain immature eye telencephalon immature eye forebrain immature eye optic stalk telencephalon immature eye optic stalk forebrain optic cup diencephalon telencephalon eye telencephalon	Thisse et al., 2001- Perkins et al., 2005 Sun et al., 2006 Loucks et al., 2007 Jeong et al., 2007 Sanek et al., 2009 Xie et al., 2011	N.A. 15844196 16696945 17647295 17164418 19855021 21915332
fgfr2	diencephalon hindbrain midbrain midbrain hindbrain boundary solid lens vesicle ventral telencephalon epibranchial placode pectoral fin bud endoderm mesoderm pancreatic bud basal plate midbrain region central nervous system diencephalon forebrain hindbrain hypochord pharyngeal arch solid lens vesicle tegmentum ventral mesenchyme ventricular zone solid lens vesicle	Tonou-Fujimori et al., 2002 Nechiporuk et al., 2005 Harvey et al., 2006 Manfroid et al., 2007 Thisse et al., 2008- Nakayama et al., 2008	14516681 16077091 16501170 17942484 N.A. 18089288
fgf3	forebrain midbrain pharyngeal arch 3-7 skeleton somite tail bud midbrain hindbrain boundary otic vesicle pharyngeal pouch 1 pharyngeal pouch 2 pharyngeal pouch 3 pharyngeal pouch tooth 4V pharyngeal pouch diencephalon midbrain hindbrain boundary optic stalk presumptive neural retina midbrain hindbrain boundary anterior macula	Kudoh et al., 2001- Walshe et al., 2003 Jackman et al., 2004 Nechiporuk et al., 2005 Plaster et al., 2007 Nakayama et al., 2008 McMahon et al., 2009 Feng et al., 2010	N.A. 14651935 15355794 16077091 17576618 18089288 19500562 20043901

Supplementary Table 6. Continued.

znf703	epidermis hindbrain mesoderm midbrain neural tube periderm pharyngeal arch 3-7 skeleton somite spinal cord vein	Thisse et al., 2001-	N.A.
	optic cup optic fissure	Brown et al., 2009	19171890
	periocular mesenchyme	Lupo et al., 2011	21555593
sox2	immature eye midbrain midbrain hindbrain boundary neural tube otic vesicle spinal cord telencephalon	Thisse et al., 2001-	N.A.
	brain diencephalon forebrain hindbrain hypochord immature eye midbrain nervous system otic vesicle spinal cord telencephalon ventral mesoderm	Rauch et al., 2003-	N.A.
	cerebellum otic vesicle presumptive neural retina	Okuda et al., 2006	16408288
	hindbrain otic vesicle	Cunliffe et al., 2006	16324829
	lateral line primordium neuromast	Hernandez et al., 2007	17443814
	brain central nervous system	Dee et al., 2008	18572157
	brain eye otic vesicle posterior neural tube	Amaral et al., 2009	19767420
wnt3	basal plate midbrain region cerebellum diencephalon hindbrain midbrain zona limitans intrathalamica	Clements et al., 2009	19452545
wnt3a	midbrain hindbrain boundary rhombomere	Riley et al., 2004	15366005
	cerebellum diencephalon midbrain	Buckles et al., 2004	15147762
	pectoral fin bud	Norton et al., 2005	16221725
	optic tectum	Nyholm et al., 2007	17215296
	neural crest cell	Huang et al., 2009	19097504

Supplementary Table 7. Primer sequences for targeted validation.

Genomic coordinate of PCR (Zv9)	Length	CpGs	Forward PCR primer sequence (genomic seqeunce in the parenthesis)	Reverse PCR primer sequence (genomic seqeunce in the parenthesis)
Targeted bisulfite clonal sequencing				
chr14:25157201-25157370	170	10	AAATTTTATAATTGTTTTGGTAATATATTT (AAACTTTATAACTGCTTTGGCAATACATTT)	ATAACTAACATTCAACAAACATCAC (ATGACTGGCATTCAACAGGCATCAC)
chr22:12335157-12335326	170	15	AATAATGATGTTAAGTTTTTGAGGAGGT (AATAATGATGCTAAGTCTCTGAGGAGGC)	ACTCTAAACTACAAATACCCTCAAC (GCTCTAAGCTGCAAGTGCCCTCAAC)
chr14:20461146+20461441	296	18	AGTTTTTTGTTATAGGGAATGTGTTGT (AGCTTTCTGCTACAGGGAATGTGCTGT)	TTCTACCAATATCATTAAAAAAC (TTCTGCCAGTGTCATTGAGGGAC)
chr21:8582721+8582922	202	7	AAATAAATTTTTGTTGTGGAAATTTAG (AAATAAACTCCTGCTGTGGAAATTTAG)	CACCCTCTTTTCTACAACCTTACATAC (CACCCTCTTTTCTGCAGCCTTGCATGC)
chr5:46270017+46270196	180	4	TTTGTATTGTTAAAAAGTTTTTTTT (TCTGCACTGCTAAAAAGTTTCCCCT)	AATAATTTTAATCTAACATTTATTTTATC (GGTGATTTTAATCTAACATTTGTTTTGTC)
chr5:46270498+46270621	124	4	TATTGTGAGGTTTTATTGTTAGGAAAAA (CACTGTGAGGTTTTACTGTCAGGAAAAA)	AAAAAAACAAAACACCAATAAACTACTAAC (AAGAGAACAAAACACCAATGAGCTACTAAC)
Targeted bisulfite pyrosequencing				
Universal biotinylated primer:				/5bioaG/GGGACACCGCTGATCGTTTA
chr1:42015593-42015753	161	8	AGTTTGTGTTGTTTGTTTGATATTTTATTA (AGCCTGTGCTGTTTGCCTGACACTCCACTA)	GACGGGACACCGCTGATCGTTTAACACACCCTATTCCAAAAAAAAC (ACACACCCTGTTCCAAAGAGGAC)
Sequencing primers:			TATTGTTAGTTATTAGTATG (TACTGTCAGTTATCAGCATG) TTATAATGTATTTGATTAAA (CCATAATGCATTTGATCAAA)	
chr20:39657499-39657620	122	7	TGGTTTTGTTGGGAAAATAATAGTT (TGGCTCTGTTGGGAAAATAACAGCC)	GACGGGACACCGCTGATCGTTTACCACACATCAAAATCTAAAAAAACA (CCACACATCAAAGTCTGAGAGAACA)
Sequencing primers:			ATAATAGTTTTAAGGTAGAT (ATAACAGCCCCAAGGTAGAC) GATTTGAGTGTAGTTGTTGT (GATCCGAGCGCAGCTGCTGC)	
chr24:27012514-27012771	258	16	TTGTTGATGTGTTTTTGTGTTTTTAG (CTGCTGATGTGCTTCTGTGCCCTCAG)	GACGGGACACCGCTGATCGTTTAATCTCCCCATTATAAATATTACTTTCATAT (GTCTCCCCATTGTAAATATTGCTTTCATGT)
Sequencing primers:			GTTTTTAGTAATAGATTAGA (GCCCTCAGTAACAGATTAGA) GGGTGTTTGGGAGGGAGTAG (GGGCGTCCGGGAGGGAGCAG) TATTTTATAGTAAAGTTATT (CATCCAACAGTAAAGCCATT)	