

Table of contents

Appendix Figure S1

Expression profiling reveals genes downstream of Melanopsin.

(A) Annotated heat map of all over- (red) and underexpressed (green) genes in the *opn4* dko anterior brain with 3 biological replicates for wild-type and 3 for the *opn4* dko. For significance testing an exact test analogous to Fisher's exact with consideration of overdispersion and adjusted p-values for the false discovery rate was applied. The cutoff for differential expression was set at a significance level of $\alpha=0.05$. Pathways indicated with a blue dot for phototransduction, red for metabolism, orange for melatonin synthesis, green for MAPK, and grey for cAMP signalling. Genes assigned to light-dependent processes (GO) are indicated with a double dagger. Homeobox genes are indicated with komejirushi (*), genes with a function in the immune response with triangle, genes with a function in cell division with a circle and core clock genes with a square.

(B) Heat map of the differentially expressed genes in the *opn4* dko posterior brain.

(C) Heat map of the differentially expressed genes in the *opn4* dko eyes.

(D-V) Plots with read counts normalised to *actb1* for (D) *tph1a*, (E) *tph2*, (F) *aanat2*, (G) *otx5*, (H) *crx*, (I) *lhx4*, (J) *otx2*, (K) *mcm7*, (L) *cdk9*, (M) *caspb*, (N) *ly6pge*, (O) *pigr13.5*, (P) *mhc1uba*, (Q) *mhc1uka*, (R) *creb3l1*, (S) *cdk5*, (T) *rora*, (U) *per1a*, and (V) *per2*.

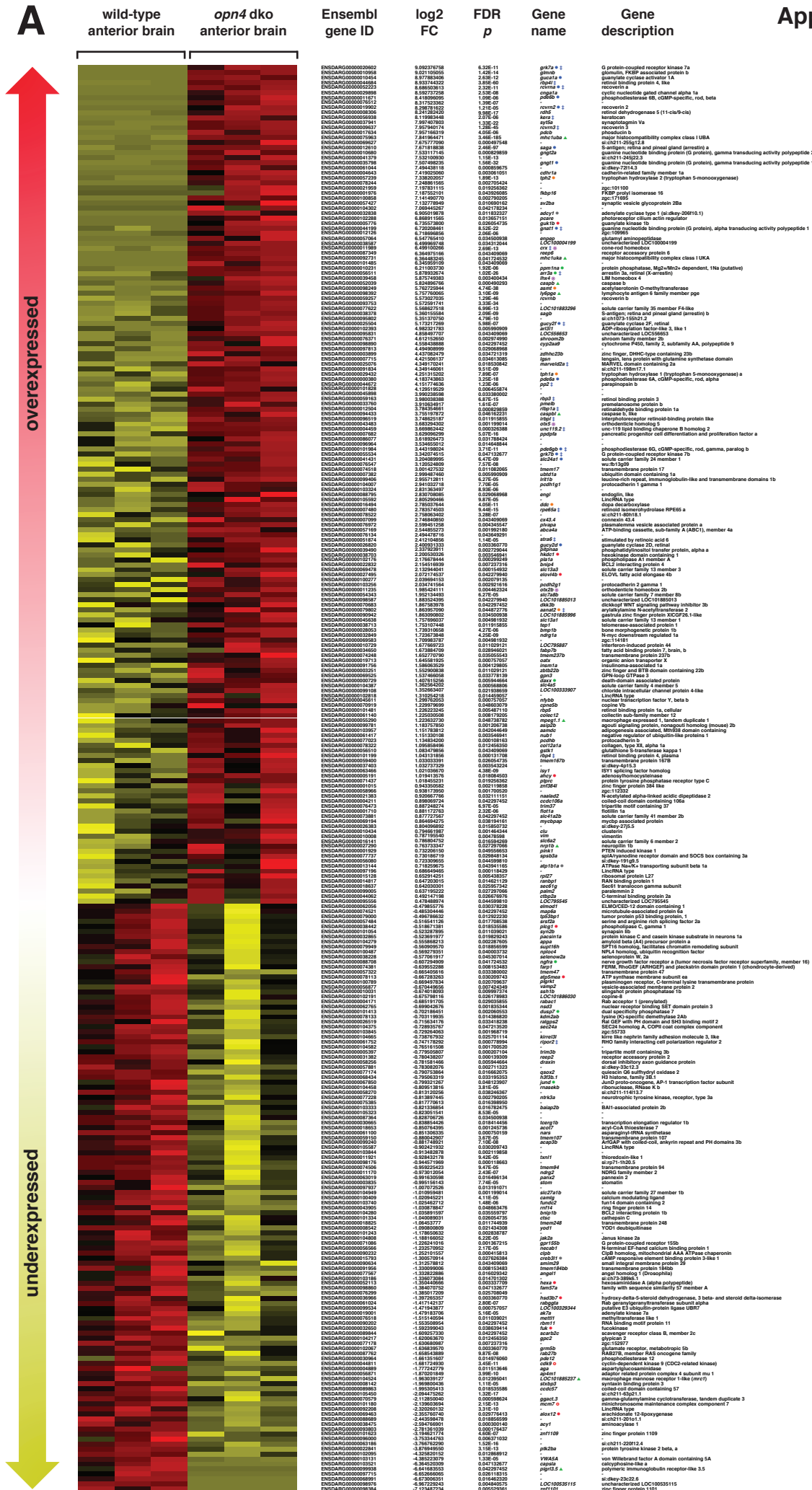
Data information: In D-V, blue markers indicate wild-type, grey markers indicate *opn4* dko and red bar indicates mean. Biological replicates are indicated with round, triangular, and square markers (n=3). Asterisks indicate significance ($0.01 < p[*] < 0.05$, $0.001 < p[**] < 0.01$, $p[***] < 0.001$, ns = not significant).

Appendix Figure S2

ddc transcription in wild-type and *opn4* dko larvae.

The *ddc* transcription pattern is unchanged between wild-type and *opn4* dko, but the *ddc* expression level is affected in the *opn4* dko pineal. Dorsal and lateral view of each biological replicate from Figure 4N is shown. *ddc* is expressed in the epiphysis cerebri [E], pretectum [PT], diencephalic catecholaminergic cluster [DCA], raphe nuclei [RN], locus coeruleus [LC], area postrema [AP], and gut. Larvae were raised under a 12:12 hour LD regime and fixed on the 6th dpf at ZT4. Eyes were removed after completion of the *ish* for optimal visibility of expression in the brain.

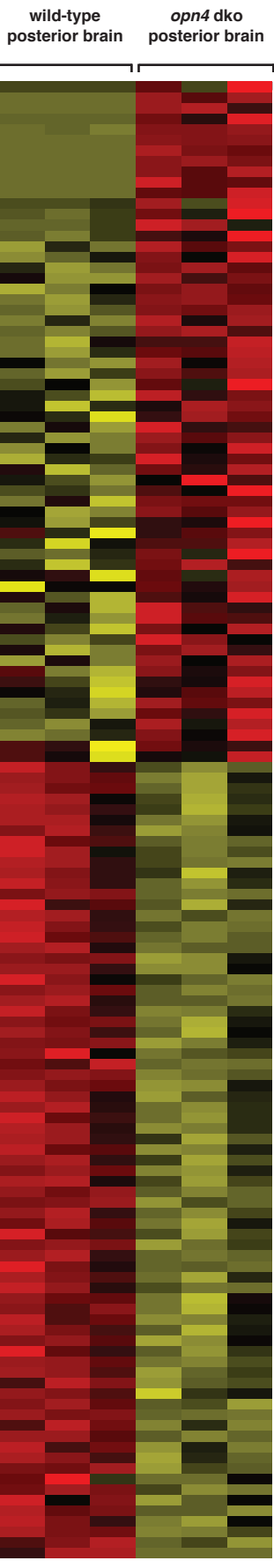
Appendix Figure S1



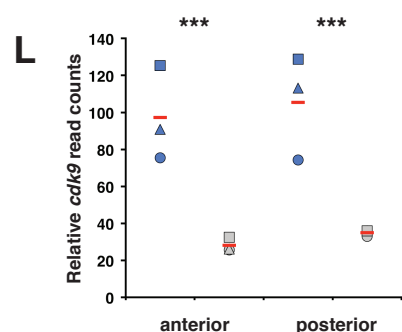
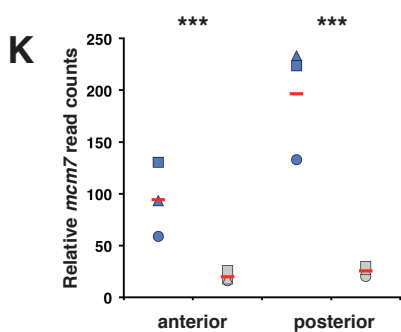
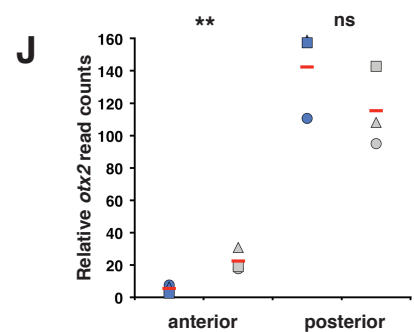
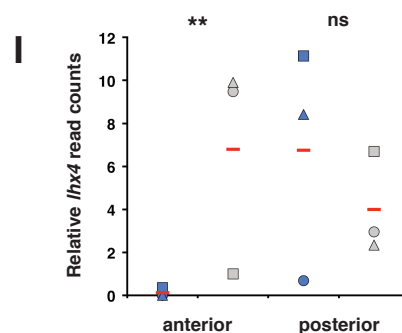
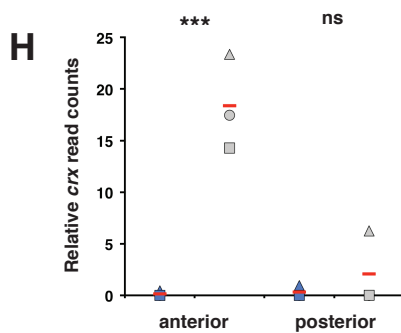
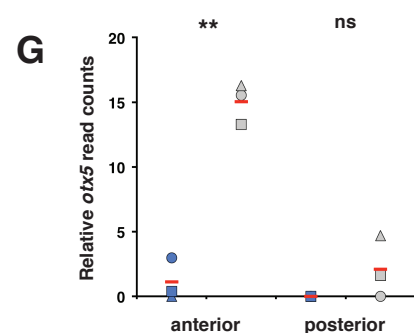
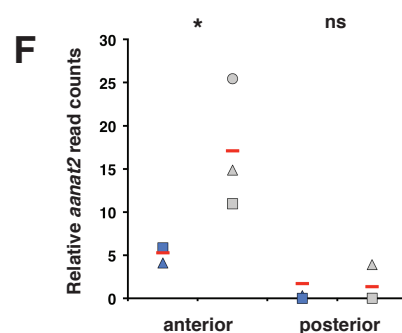
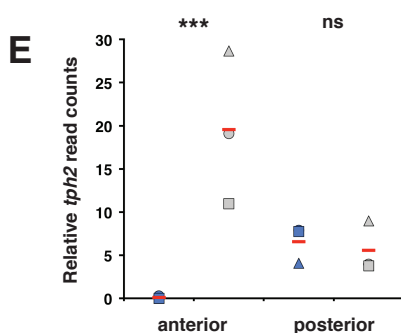
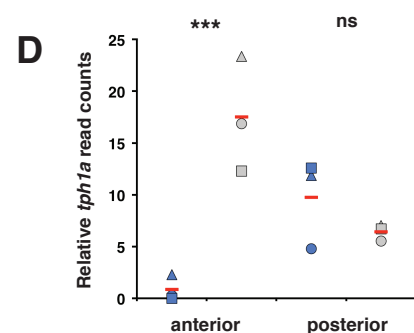
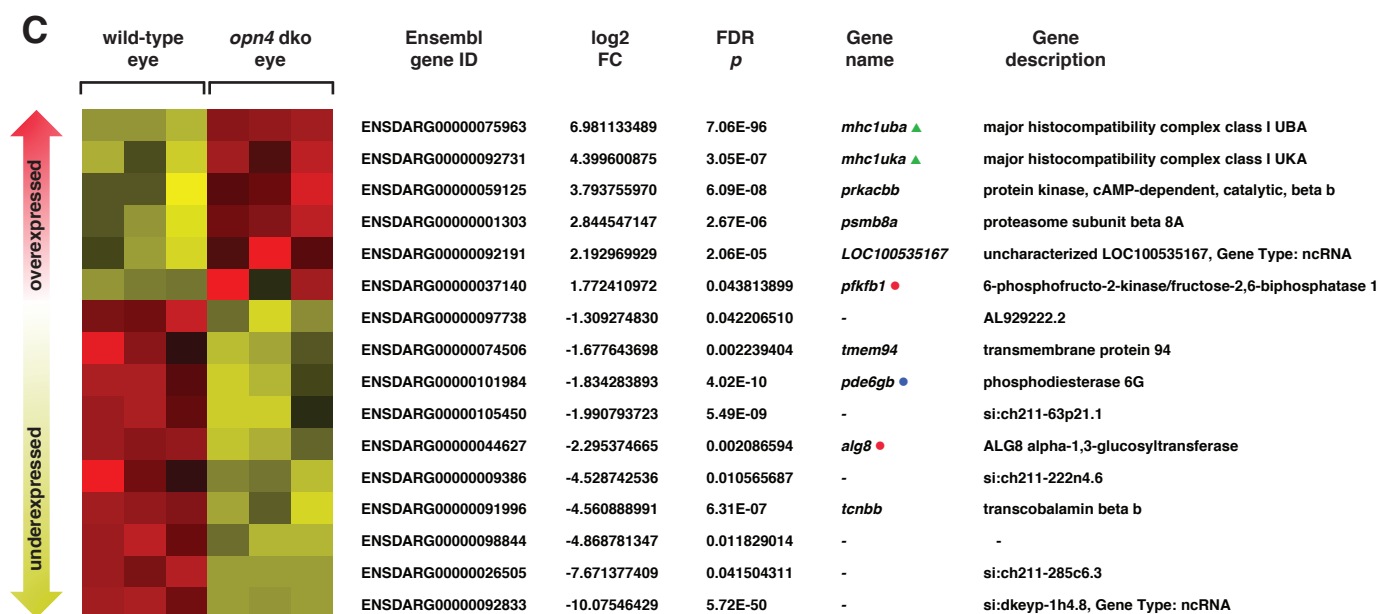
B

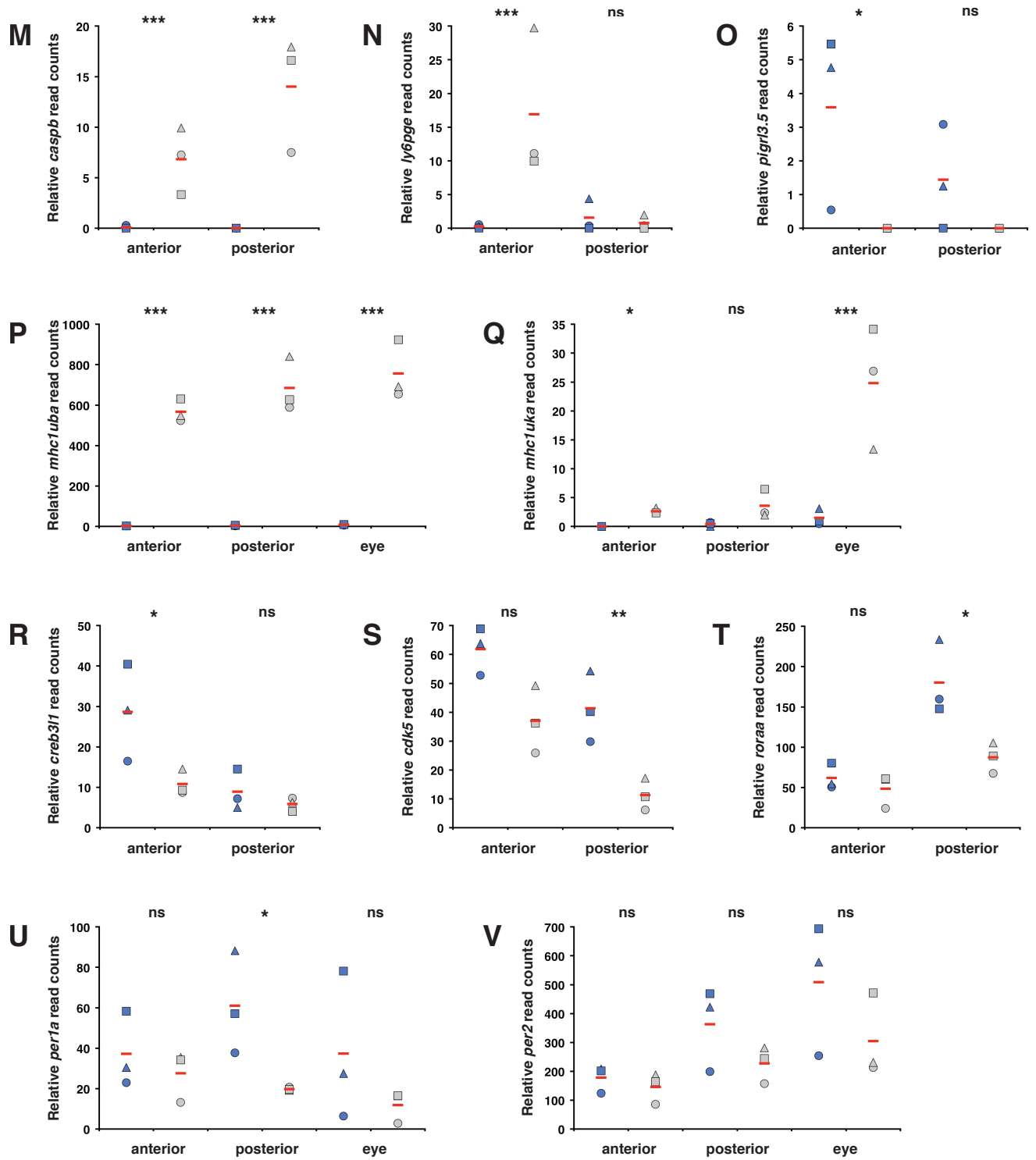
overexpressed

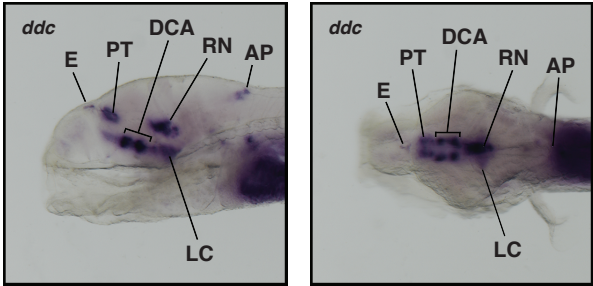
underexpressed



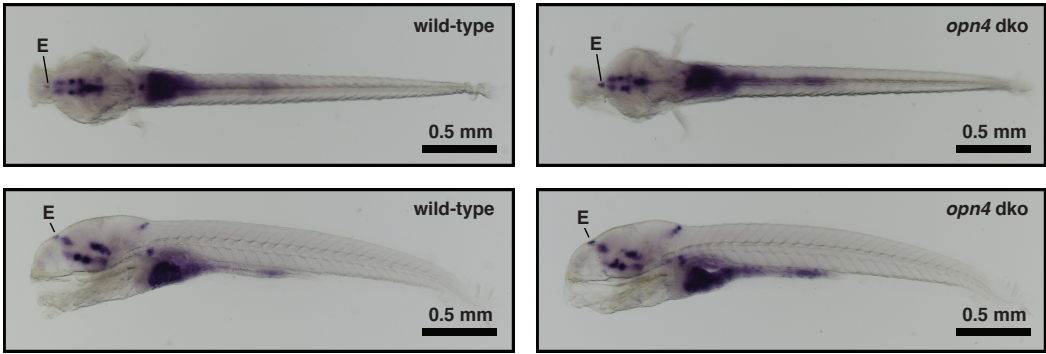
Ensembl gene ID	log2 FC	FDR p	Gene name	Gene description
ENSDARG000000044199	8.706654439	0.004842658	<i>gnat1</i> ▲	guanine nucleotide binding protein (G protein)
ENSDARG000000052039	8.608328715	4.89E-09	<i>caspb</i> ▲	caspase b
ENSDARG000000101828	8.122752389	3.43E-05	-	-
ENSDARG000000008706	7.826723409	0.000767557	<i>dicp3.3</i> ▲	diverse immunoglobulin domain-containing protein 3.3
ENSDARG000000075963	7.639764509	7.89E-210	<i>mhc1uba</i> ▲	major histocompatibility complex class I UBA
ENSDARG000000091253	7.608120380	0.00043212	<i>smyd1b</i>	SET and MYND domain containing 1b (histone methyltransferase)
ENSDARG000000098890	7.472871083	0.001541569	<i>cyp2aa9</i>	cytochrome P450, family 2, subfamily AA, polypeptide 9
ENSDARG00000001667	7.329725612	0.003280076	-	si:dkcy-222i2.7
ENSDARG00000004459	7.307471754	0.003962031	<i>unc119.2</i>	unc-119 lipid binding chaperone B homolog 2
ENSDARG00000003359	6.851564185	0.037668838	-	-
ENSDARG00000039422	6.660068170	0.048695324	<i>luom</i>	lucose mutarotase
ENSDARG00000008306	6.400965862	0.017174023	<i>rdh5</i>	retinol dehydrogenase 5 (11-cis-9-cis)
ENSDARG000000098249	5.920533880	0.000544304	<i>asmt</i> ●	acetylserotonin O-methyltransferase
ENSDARG000000096903	5.787348793	0.015402583	<i>pilpnaa</i>	phosphatidylinositol transfer protein, alpha a
ENSDARG00000039490	4.771756018	0.015402583	<i>lyrm5b</i>	LYR motif containing 5b
ENSDARG00000045827	4.134316167	0.004203160	<i>saga</i> ●	S-antigen; retina and pineal gland (arrestin) a
ENSDARG00000012610	3.924838962	0.04677231	<i>LOC100536946</i>	unc-119 lipid binding chaperone B homolog 2
ENSDARG000000095820	3.541120638	0.025823972	-	uncharacterized LOC100536946, Gene Type: ncRNA
ENSDARG000000103324	3.346453079	0.004114475	-	-
ENSDARG00000001303	3.060215177	1.25E-06	<i>psmb8a</i>	proteasome subunit beta 8A
ENSDARG000000091754	2.618741936	0.002020466	<i>chchd5</i>	coiled-coil-helix-coiled-coil-helix domain containing 5
ENSDARG000000071212	2.510199809	0.013803804	<i>c3h1</i>	prolyl 3-hydroxylase 1
ENSDARG000000107929	2.146267362	9.14E-10	<i>LOC795887</i>	interferon-induced protein 44
ENSDARG000000089343	2.053886535	0.003274852	<i>grn1</i>	granulin 1
ENSDARG000000096044	1.794509344	0.007789670	<i>plpn6</i>	protein tyrosine phosphatase non-receptor type 6
ENSDARG00000058966	1.682832794	2.90E-09	-	zgc:112332
ENSDARG000000071437	1.680832718	3.24E-07	<i>ptprc</i>	protein tyrosine phosphatase receptor type C
ENSDARG00000007682	1.568836060	0.048426581	<i>ppdpla</i>	pancreatic progenitor cell differentiation and proliferation factor a
ENSDARG00000001942	1.528323602	0.019603602	<i>lamtor5</i> ●	lysosomal/lysosomal adaptor, MAPK and MTOR activator 5
ENSDARG00000005592	1.522567345	0.037383558	<i>lap2a</i> ▲	transporter associated with antigen processing, subunit type a
ENSDARG000000087012	1.459713622	0.031403242	-	-
ENSDARG000000011094	1.453030397	0.040492355	<i>ccna2</i> ●	cyclin A2
ENSDARG000000067797	1.447987933	0.000767557	<i>sp1a</i>	Sp1a proto-oncogene
ENSDARG00000045611	1.399277117	0.002015646	<i>nfybb</i>	nuclear transcription factor Y, beta b
ENSDARG00000043102	1.398855849	0.008888255	<i>ltn</i>	latexin
ENSDARG00000020232	1.381409300	0.016679396	<i>el1f</i>	eukaryotic translation initiation factor 6
ENSDARG00000005592	1.376007500	0.000675303	-	-
ENSDARG00000003466	1.174736198	0.000138914	<i>isy1</i>	ISY1 splicing factor homolog
ENSDARG000000061417	1.149253526	0.004494490	<i>nub1</i>	negative regulator of ubiquitin-like proteins 1
ENSDARG000000003867	1.147877678	0.037778287	<i>cdk20</i> ●	cyclin-dependent kinase 20
ENSDARG00000001015	1.11139648	0.003892332	<i>znf384l</i>	zinc finger protein 384 like
ENSDARG00000076473	1.063844034	0.010004031	<i>trim37</i>	tripartite motif containing 37
ENSDARG000000063624	1.009853636	0.023547397	<i>gfm1</i>	G elongation factor, mitochondrial 1
ENSDARG000000055504	0.996290297	0.045280108	-	si:ch211-212k18.7
ENSDARG000000231817	0.977178177	0.035581074	<i>lcp1</i> ▲	lymphocyte cytosolic protein 1 (L-plastin)
ENSDARG000000040528	0.974139146	0.028762901	<i>lgals3bpb</i>	lectin, galactoside-binding, soluble, 3 binding protein b
ENSDARG000000031776	0.877799708	0.047304254	<i>fhl27</i>	ferritin, heavy polypeptide-like 27
ENSDARG00000009753	0.869279911	0.015280802	<i>s3b6</i>	splicing factor 3b, subunit 6
ENSDARG000000068993	0.868376893	0.017174023	-	si:dkcy-271b.2
ENSDARG00000095556	0.848931055	0.000361487	<i>LOC795545</i>	uncharacterized LOC795545, Gene Type: ncRNA
ENSDARG000000077257	0.836015260	0.002494086	<i>timd4</i> ▲	T cell immunoglobulin and mucin domain containing 4
ENSDARG000000036628	0.824859364	0.015107598	<i>cd74b</i> ▲	CD74 molecule, major histocompatibility complex, class II
ENSDARG000000069421	0.805961827	0.003008655	<i>grpel2</i>	GrpE-like 2, mitochondrial
ENSDARG000000055791	0.798344650	0.005473451	-	zgc:158423
ENSDARG00000042791	0.756737184	0.041779406	<i>glt2b</i>	G protein-coupled receptor kinase interacting ArfGAP 2b
ENSDARG000000097196	0.731661684	0.001140878	-	-
ENSDARG000000100270	0.721214625	0.048426581	-	-
ENSDARG00000043697	0.642898907	0.04657951	<i>nefmb</i>	neurofilament, medium polypeptide b
ENSDARG00000006546	0.635805299	0.04589523	<i>ak4</i> ▲	adenylate kinase 4
ENSDARG000000053136	0.625023034	0.047278309	<i>b2m</i> ▲	beta-2-microglobulin
ENSDARG00000007098	0.618456375	0.003201604	<i>ltn2ba</i>	integral membrane protein 2Ba
ENSDARG000000010260	0.576383256	0.040434955	<i>mlf11</i>	MLL11 transcription factor 7 cofactor
ENSDARG00000057853	0.533515417	0.028920891	<i>atp6v0ca</i> ●	ATPase H+ transporting V0 subunit ca
ENSDARG000000010473	0.533110075	0.045280108	<i>syn2b</i>	synapsin lib
ENSDARG00000009656	0.545896568	0.045280108	<i>appa</i>	amyloid beta (A4) precursor protein a
ENSDARG00000079610	0.56953858	0.027300965	<i>akap9</i>	A kinase (PRKA) anchor protein 9
ENSDARG00000005397	0.611952534	0.027257238	<i>trim3b</i>	tripartite motif containing 3b
ENSDARG00000078904	0.630256329	0.047304254	<i>brd4</i>	bromodomain containing 4
ENSDARG000000061066	0.630676139	0.038826557	<i>c2cd2l</i>	c2cd2-like
ENSDARG000000104101	0.640739750	0.041779406	-	si:ch73-287m.1
ENSDARG000000089505	0.663293482	0.023149737	<i>bod11f</i>	bioorientation of chromosomes in cell division 1-like 1
ENSDARG000000062346	0.665637428	0.045280108	<i>cacna1e</i> ●	calcium voltage-gated channel subunit alpha1 E
ENSDARG000000100789	0.670448768	0.023158171	<i>plgrkt</i>	plasma membrane protein, C-terminal lysine transmembrane protein
ENSDARG000000174381	0.676719381	0.001609481	<i>fnr1</i>	FERM, RhoGEF (ARHGAP) and pleckstrin domain protein 1
ENSDARG000000077228	0.702465258	0.037383558	<i>ntrk3a</i>	neurotrophic tyrosine kinase, receptor, type 3a
ENSDARG000000061010	0.705142497	0.016871964	<i>nars</i>	asparaginyl-tRNA synthetase
ENSDARG000000031768	0.724617928	0.036477079	<i>roraa</i> ▲	RAR-related orphan receptor A, paralog a
ENSDARG000000058093	0.727193482	0.026710721	<i>ank1a</i>	ankyrin 1, erythrocytic a
ENSDARG000000090747	0.732267905	0.046767231	-	si:ch73-269m14.2
ENSDARG000000062744	0.735471136	0.004764247	<i>scn1lab</i>	sodium channel, voltage-gated, type I like, alpha b
ENSDARG000000061909	0.761165390	0.021234302	-	si:ch73-233f.1
ENSDARG000000078137	0.780833771	0.037119481	<i>kdm2ab</i>	lysine (K)-specific demethylase 2Ab
ENSDARG000000058877	0.811961777	0.004114475	<i>vamp2</i>	vesicle-associated membrane protein 2
ENSDARG000000086274	0.835145349	0.017174023	-	si:ch211-203b8.6
ENSDARG0000000104708	0.852808995	0.045280108	<i>ddx24</i>	DEAD (Asp-Glu-Ala-Asp) box helicase 24
ENSDARG000000037440	0.858902883	0.001609481	<i>fund2</i>	FUN14 domain containing 2
ENSDARG000000102171	0.880704925	0.005108502	<i>fnip1</i>	folliculin interacting protein 1
ENSDARG000000103962	0.882298159	0.001609481	<i>add1</i>	adducin 1 (alpha)
ENSDARG000000031382	0.905206302	0.001731688	<i>resp2</i>	receptor accessory protein 2
ENSDARG000000097337	0.934191335	0.019197071	-	-
ENSDARG000000100473	0.941325221	0.047304254	-	-
ENSDARG000000057881	0.947029724	0.009207545	-	-
ENSDARG000000068434	0.957533869	0.000860227	<i>h3f3b.1</i>	h3f3b.1
ENSDARG00000005549	0.981580254	0.047304254	<i>eml2</i>	EMAP like 2
ENSDARG000000102755	1.008199705	0.038926557	<i>eml6</i>	EMAP like 6
ENSDARG000000104582	1.015504681	1.93E-05	-	-
ENSDARG000000104088	1.041822279	0.000205290	<i>jak2a</i>	Janus kinase 2a
ENSDARG000000058549	1.052988267	0.037177827	<i>akap10</i>	A kinase (PRKA) anchor protein 10
ENSDARG000000102769	1.068303112	0.024502864	<i>LOC101886358</i>	caderin-18
ENSDARG000000075754	1.070850967	0.038926557	<i>mri1</i> ●	methylthioribose-1-phosphate isomerase 1
ENSDARG000000092867	1.084883092	0.015280802	<i>zmat4a</i>	zinc finger, matrin-type 4a
ENSDARG000000104949	1.091630292	0.000493516	<i>sic27a1b</i>	solute carrier family 27 member 1b
ENSDARG00000018773	1.092571836	0.037810491	<i>hivp2b</i>	human immunodeficiency virus type I enhancer binding protein 2b
ENSDARG000000086326	1.102249238	0.048102752	-	-
ENSDARG000000058256	1.115998371	0.003345801	<i>draxin</i>	dorsal inhibitory axon guidance protein
ENSDARG000000059150	1.138807356	0.000676513	<i>tmem107</i>	transmembrane protein 107
ENSDARG000000062277	1.139804425	0.015402583	<i>ppp2r2cb</i>	protein phosphatase 2, regulatory subunit B, gamma b
ENSDARG000000052648	1.174760386	0.038280407	<i>hs3st4</i>	heparan sulfate (glucosamine) 3-O-sulfotransferase 4
ENSDARG00000016256	1.195331820	0.000767557	<i>nud3a</i>	nudix (nucleoside diphosphate linked moiety X)-type motif 3a
ENSDARG000000044811	1.222116158	2.47E-05	<i>cdk9</i> ●	cyclin-dependent kinase 9 (CDC2-related kinase)
ENSDARG000000056885	1.225438269	0.015280802	<i>per1a</i> ▲	period circadian clock 1a
ENSDARG000000011170	1.258652500	4.89E-09	<i>ndrg2</i>	NDRG family member 2
ENSDARG000000032865	1.295903497	1.30E-08	<i>pascin1a</i>	protein kinase C and casein kinase substrate in neurons 1a
ENSDARG000000090232	1.410702507	0.013667181	-	-
ENSDARG000000103030	1.446615950	0.039448547	-	-
ENSDARG000000058871	1.510713428	0.025145625	<i>ap4m1</i>	adaptor related protein complex 4 subunit mu 1
ENSDARG000000056683	1.576286458	0.009342008	<i>cdk5</i> ▲	cyclin-dependent kinase 5
ENSDARG000000081434	1.754995034	0.000767557	<i>stxbp3</i>	stx16 binding protein 3
ENSDARG000000063186	1.894334588	0.00192783	-	-
ENSDARG000000105450	2.040191320	4.23E-16	-	-
ENSDARG000000092208	2.073193962	3.55E-06	-	-
ENSDARG000000102959	2.226186138	0.014367227	-	-
ENSDARG000000032650	2.234388304	0.003286201	<i>luk</i> ●	leukocytosis associated 1
ENSDARG000000080762	2.363540523	4.70E-07	<i>rab27b</i>	RAB27B, member RAS oncogene family
ENSDARG000000076299	2.397128824	0.001954266	-	-
ENSDARG000000057321	2.41642965	0.000676513	<i>lut1</i>	terminal uridylyl transferase 1, U6 snRNA-specific
ENSDARG000000101180	2.581257303	2.30E-31	<i>mcm7</i> ●	minichromosome maintenance complex component 7
ENSDARG000000022399	2.712304463	0.004114475	<i>snu13b</i>	SNU13 homolog, small nuclear ribonucleoprotein B (U4/U6.U5)
ENSDARG000000022841	2.918793651	0.000767557	<i>ptk2ba</i>	protein tyrosine kinase 2 beta, a
ENSDARG000000324283	2.992498438	0.008690092	<i>coq6b</i>	coenzyme Q8A, genome duplicate b
ENSDARG00000018744	3.014377179	0.040434955	<i>prl2</i>	prolactin 2
ENSDARG000000038475	3.205365098	1.47E-07	<i>acy1</i>	aminoacylase 1
ENSDARG000000093803	3.500688613	0.047304254	-	-
ENSDARG000000075301	3.515424703	0.002960406	<i>gsdf</i>	gonadal somatic cell derived factor
ENSDARG000000102858	3.574549768	0.045280108	-	-
ENSDARG000000037813	3.913667855	0.003358031	-	-
ENSDARG000000088689	4.110502985	0.002492631	-	-
ENSDARG00000075433	6.852483543	0.046936979	<i>myom2a</i>	myomesin 2a







BR1



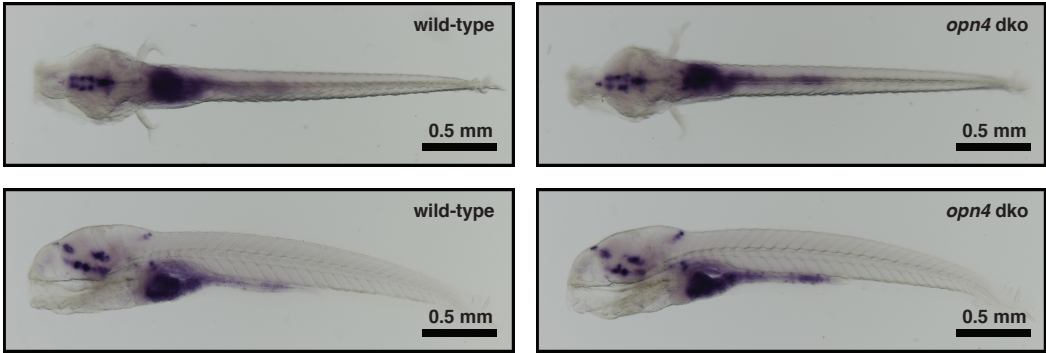
BR2

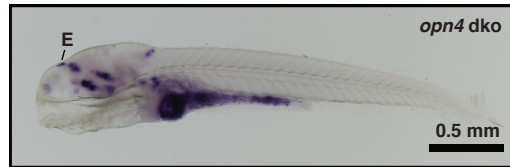
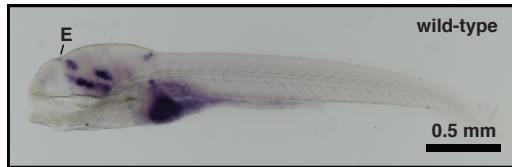
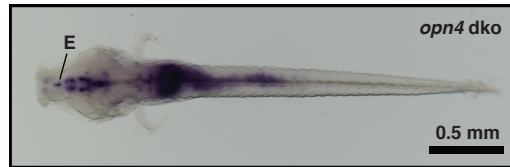
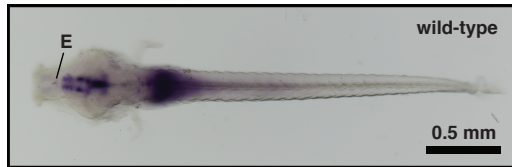
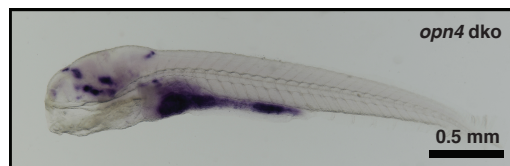
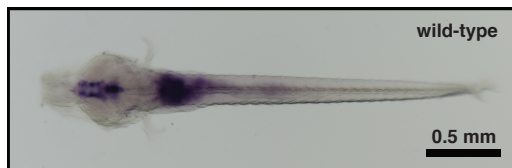
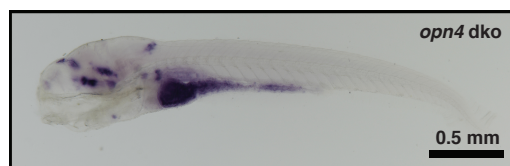
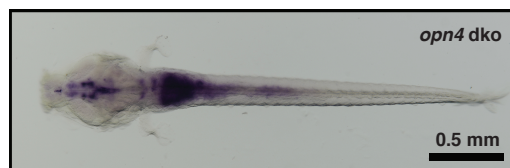
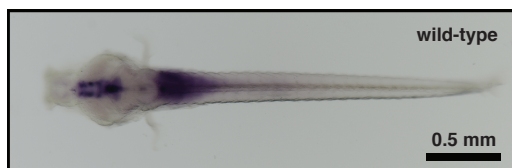


BR3



BR4



BR5**BR6****BR7****BR8**