

Fig. S1

AAH91653.1	---GKSGGCVLVRIWTMDLLLSVFLLLCSIH-----QTFT---	32
NP_001121223.1	-----MEHLFLFFLYL--CS-----MFSSHFAAYG---	23
XP_009485548.1	NAIEAIDEFAFLEGLRRLVLLYKYLTRCRMQDP-LAV-----VVFAGLLHAPVFASA---	51
XP_016767342.2	-----MSSIGD-----E	7
KZS05952.1	-----MFRLRELFVIFLLFSFSAITIGFSVSKLRRLDNNKAMEDTMLTEISESSTSER	53
AAH91653.1	SVLG--RNTRNLFTERVCCRKQSHVIYIGKDISGSPVNVVDVGVCRTHCGQSAHFVALEAG	90
NP_001121223.1	SVMNRQNDRRNLFAERGCCKRQSNFVYIGQDISGSPVSDVGLCRSHCGVPRINAYNQA	83
XP_009485548.1	GAIGREDEQGNLFAERGCRRRQSHFLHIGHDVSGSPVSDVGVKCRSSCL-SQRISPPHPG	110
XP_016767342.2	NEGNESRTHREEVRQHVCCARHERMIDVGYGISGEIIQIDAGHCRKLCPRHV-LDDPGD-	65
KZS05952.1	IRLDSWLNHPAINIKSCCERVPKKYFVVGQGLDGEIL-VDIGQCRQSCSTKR-TKINRKE	111
	. . . : * * . . : * . . . : * * * * *	
AAH91653.1	L-RASKYSSMLDFLRHKKIRHLDPSSEVIIGSPSCGLSSSCPEAGVRVDPVMLYEGLE	149
NP_001121223.1	LPGLAKHSSMLDILKNKLRERVPDPHPSSGSEPCPQEYTCQSTKVGIERVLLFQGIQE	143
XP_009485548.1	LLGLSRHSSMLDFLRSKKLQVRHPDSPLQTGAPRSCPAGSCCEPARVHMERLLLFEGVQE	170
XP_016767342.2	-----ASRPTVQRCPFESHCRPKASKLERVSTIQGVRV	98
KZS05952.1	FEAILKANYSVDPVELF-----LAMQRDISPKSCGDDSHCLPTRTVVERHMTMSGMQE	164
	* * : : . * : :	
AAH91653.1	IEIIQDCHCEAKISQCVRAPALKTYHSNTLYETVIDVGKCVGSKGAPEGFSCVPTKFDST	209
NP_001121223.1	VEVIEDCQCSLIPEDCIRMPFLKTFPPDSPFESTVDVGKCSSPTK-TTGLLCSPTKFDTV	202
XP_009485548.1	VEVVDGCHCSTCPPECLRLPALKTFFPDPSPWEVTVDVGKCSDPITYSADGLLCVPTKFSTA	230
XP_016767342.2	IEVTEACECTSDSS-CRRESFTHLVHSGTPHQAVMDVGVCMGHCAK--DLGCKPVRNSTV	155
KZS05952.1	VAVIEDCSCLSDPELCHRVEERAIHFPGTPFETSVDVGRCSGPCSSGNSLRCRSTRNKTV	224
	: : * * . * * . . : : : * * * . . : * . . : . .	
AAH91653.1	FIQTPNKVELIQTVAQCKLIEGCIYRMLMEYHYETYSDD-----GVQIESLKEIDVGR	263
NP_001121223.1	VVESPNGAEIVQTVNCEMKENCYRISYLEYYYEVVYHSN-----GSKEERVKEIDVGR	256
XP_009485548.1	LVKNPQGGEVVQTLNCEMKEKCYRVSQVEYYYEIVHSSA-----GHREERLKEIDVGR	284
XP_016767342.2	SIKGPNQDEVYQVIEKCGCAGTCHKMDHMETVLDVDFSEVEIKDGTNTDVRPVVQRINVGQ	215
KZS05952.1	AIAGPNGDTCVEVIDKCGCASSCYRASSMEHIYDFVSPMD----DETTDSPVIKVVVDVGK	280
	: * : : : * * : : * : : : : * : : : * : :	
AAH91653.1	CLGSC TSG---SRCLLRSVSDLGECLIWAEGQGKACV PQSFESH TILA QNGQIYTVDAIT	320
NP_001121223.1	CLGGCSSG---SHCLLDRSRNRDHCIVWAEGSGNGCV PQDYETH TFRSRNGH IRSVFAIK	313
XP_009485548.1	CLGSCSSG---DPCLLRESQGGEKCLVWAEAAASGRCAPHHYDVHTFRSRRDRVRTVVAIR	341
XP_016767342.2	CVGTC PGN-ETEMCLLDRDKREPSRCLAGLYSKQHTCTPARFKVHEYRTRRGSKREIIQIT	274
KZS05952.1	CVGECNTSHHKEHCVLDRDKDDSSKCLMSLRTRENNCVPLGFQLHFRNKNGTAKSMLSIT	340
	* : * * . . * : * . : * * : . * * : . . : : * * : *	
AAH91653.1	SCVCQS	326 Danio rerio, 46%
NP_001121223.1	TCKCQM	319 Xenopus laevis
XP_009485548.1	QCKCRW	347 Pelecanos crispus, 55%
XP_016767342.2	QCACV-	279 Apis mellifera, 27%
KZS05952.1	DCGCQ-	345 Daphnia magna, 33%
	* *	

Figure S1. Alignment of Pnhd homologs. Multiple protein sequences that are similar to Pnhd from different species have been aligned using ClustalOmega from EBI. Percent identity to *Xenopus laevis* Pnhd.L protein is shown for Pnhd homologs from *Danio rerio*, *Pelecanos crispus*, *Apis mellifera*, and *Daphnia magna*. All three cystine knot domains marked by characteristic Cys residues appear conserved in different Pnhd proteins (asterisks).

Fig. S2

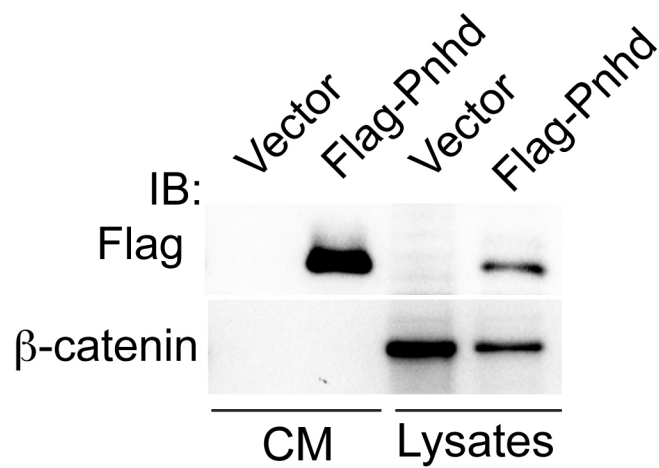


Figure S2. Pnhd secretion in cultured cells. A, HEK293T cells were transfected with *Pnhd-Flag-pCS2* DNA or control *pCS2* DNA and cultured for 48 hrs. Proteins from cell lysates or corresponding conditioned media were separated by SDS-PAGE and immunoblotted with anti-Flag antibodies. β -catenin is a control for protein loading.

Fig. S3

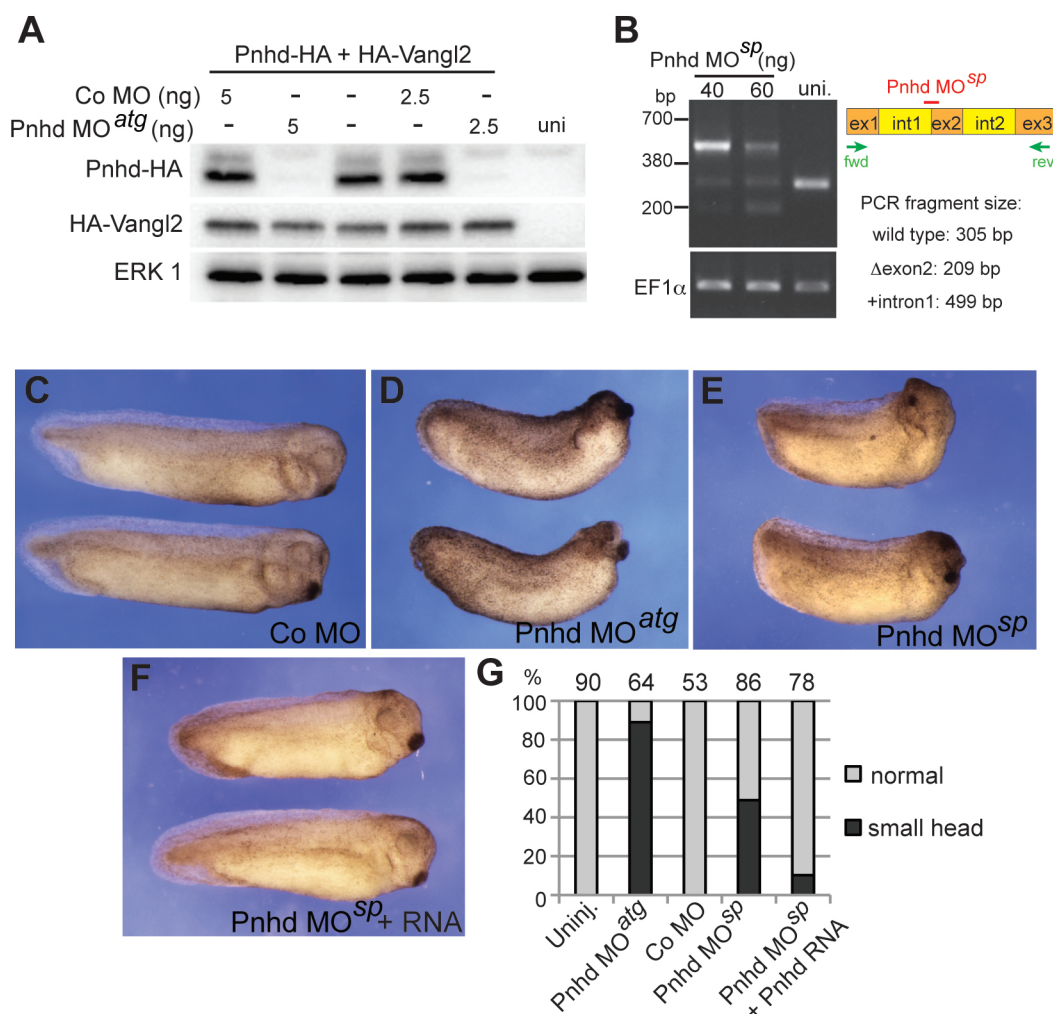


Figure S3. Validation of *pnhd* knockdown. A, Translation-blocking MO inhibits *pnhd*-HA RNA translation *in vivo*. Embryos were co-injected with *pnhd*-HA-RNA and *HA-vangl2* RNA (negative control) in the presence of a control (Co) or *pnhd* MO^{atg} (10 ng each) as indicated. Immunoblotting with anti-HA antibodies shows specific inhibitory effect of *pnhd* MO^{atg} on Pnhd protein levels. B, *pnhd* MO^{sp} (40-60 ng) interferes with endogenous Pnhd RNA splicing in morphants. C-F, Morphological phenotypes of embryos depleted of Pnhd (C-E). F, *pnhd* RNA (10 pg) rescues the morphant phenotype (F). G. Quantification of data presented in (C-F).

Fig. S4

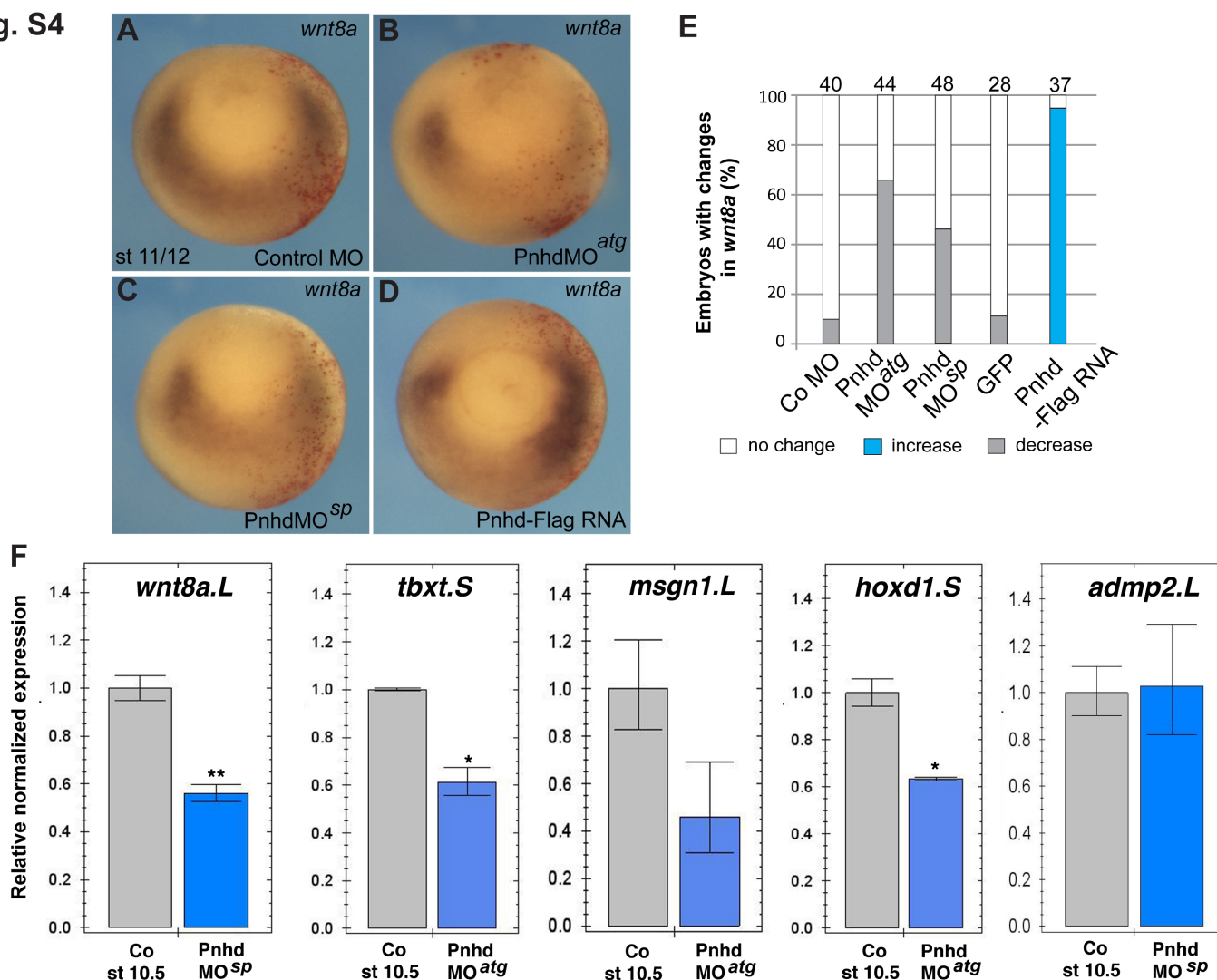


Figure S4. Regulation of *wnt8a* transcription by Pnhd. A-D, Whole mount in situ hybridization validates changes in *wnt8a* expression in embryos with manipulated *pnhd*. Injection experiments were performed as described in Fig. 5B-F. Wnt8 transcripts are visible as dark blue staining. RedGal is a lineage tracer. Representative embryos are shown. E, quantification of the results shown in A-D. F, RT-qPCR confirms downregulation of *wnt8a.L*, *tbxt.s*, *msgn1.L* and *hoxd1.s* in stage 10.5 marginal zone explants depleted of Pnhd. By contrast, the ventral marker *admp2* is not affected by Pnhd depletion.

Fig. S5

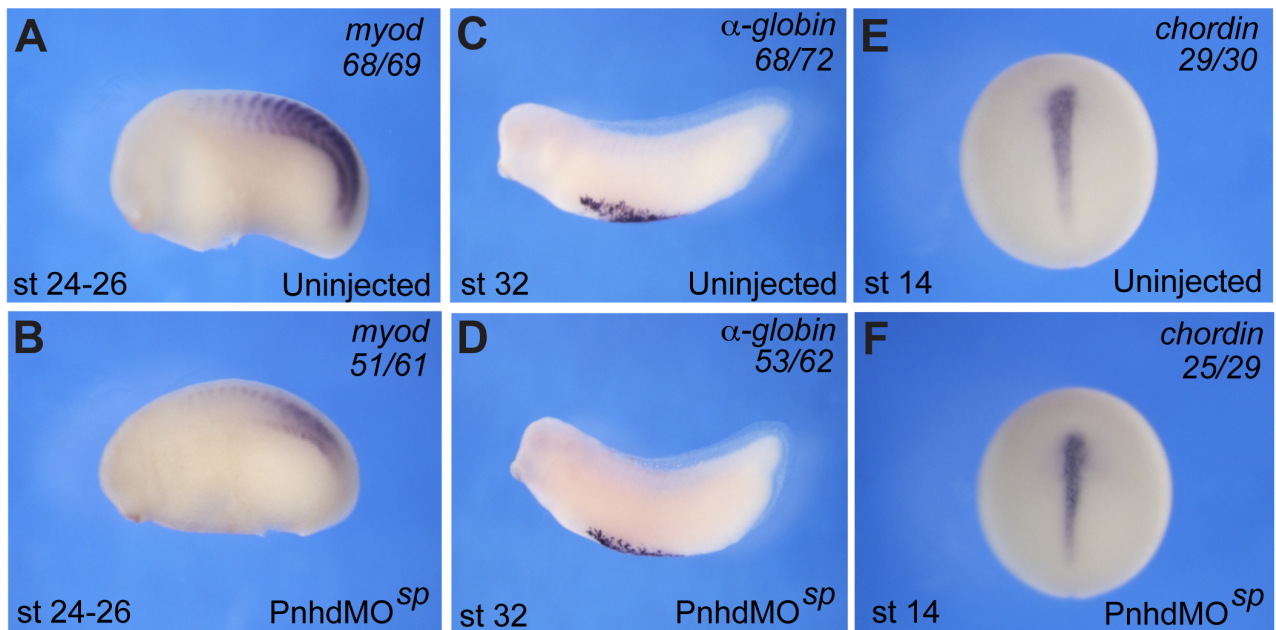


Figure S5. Regulation of mesodermal gene expression by Pnhd .

For *pnhd* depletion, each blastomere of four-cell embryos has been injected with 40 ng of *pnhd* MO^{sp}. The uninjected controls (A, C, E) or *pnhd* morphants (B, D, F) have been cultured until the indicated stages, fixed and processed for wholemount *in situ* hybridization with anti-sense probes that are specific for *myod* (A, B), α -globin (C, D) and *chordin* (E, F). Number of embryos with the presented phenotype (top) and the total number of embryos per group (bottom) are shown.

Fig. S6

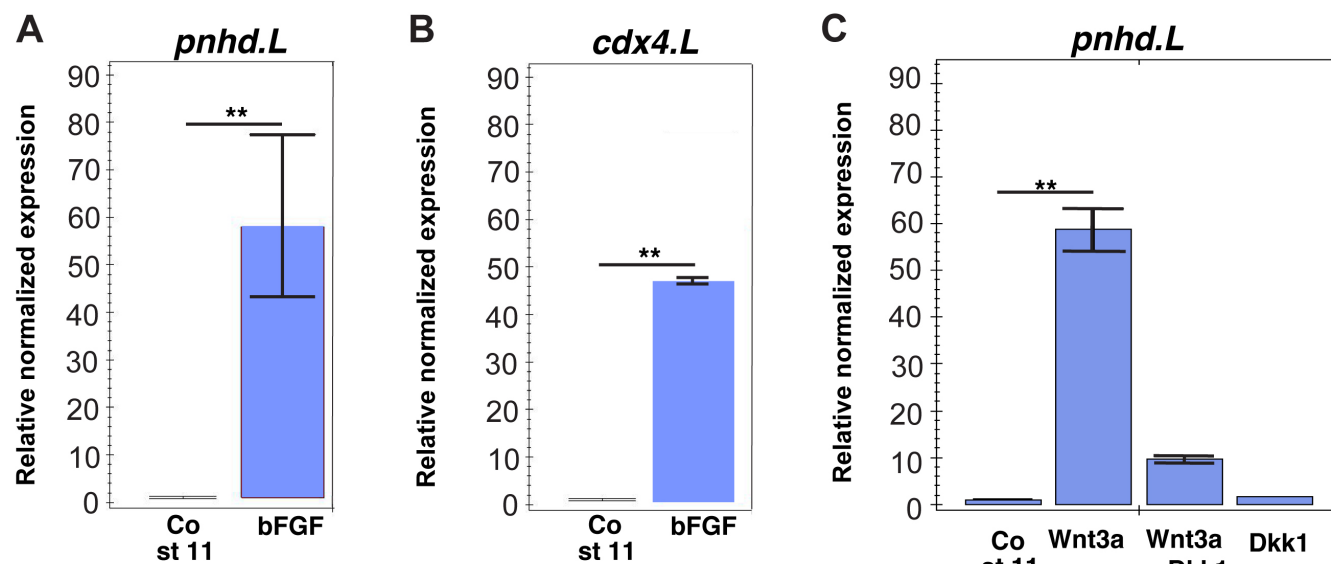


Figure S6. Pnhd transcripts are induced in ectoderm by FGF and Wnt signals. RT-qPCR data from animal caps treated with FGF or expressing Wnt3a. Ectoderm explants were dissected at stage 9-10 and cultured until stage 11. A, B, The induction of *pnhd* and *cdx4* by FGF. C, *Pnhd* transcription is activated by Wnt3a and this effect is blocked by Dkk1. Means +/- standard errors are shown. Significance was determined by the two-tailed Student's t-test, $p < 0.01$ (**).

Fig. S7

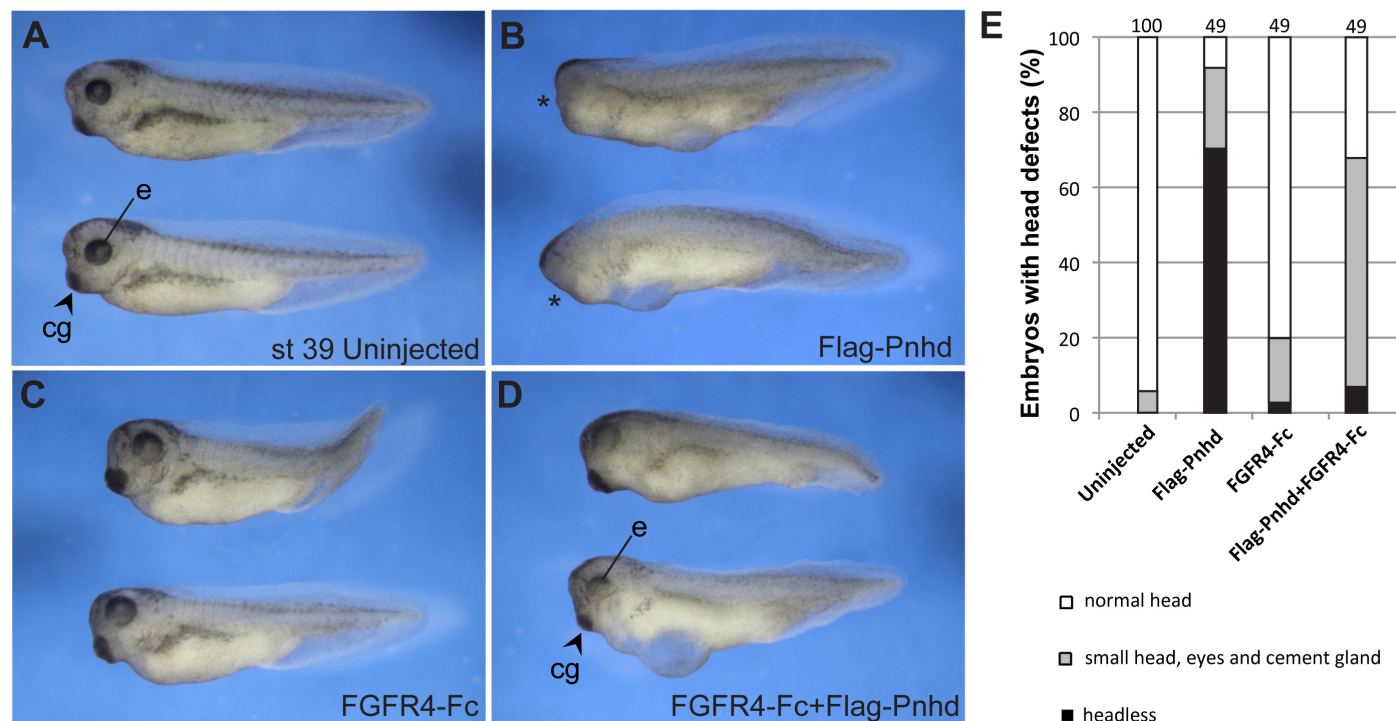
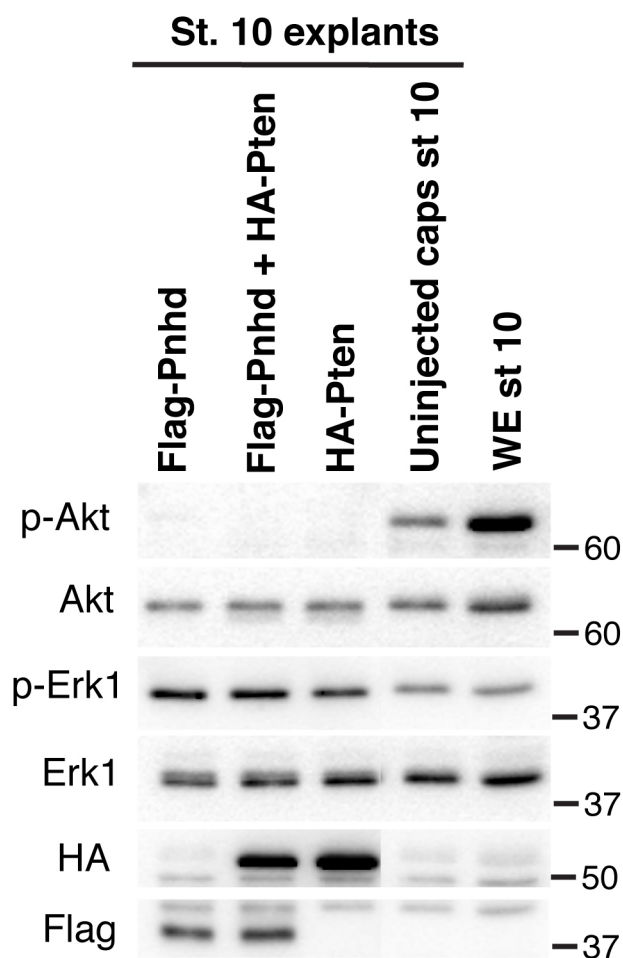


Figure S7. Secreted dominant-interfering form of FGFR4 rescues head deficiency caused by Pnhd. Four-cell embryos have been injected with indicated RNAs, morphological phenotypes were scored at stage 39. A, Uninjected control embryos. B, Lack of head structures (*) in embryos injected with *pnhd* RNA (0.9 ng). C, Mild posterior defects in embryos injected with *FGFR4-Fc* RNA (20 pg). D, Coinjection of *FGFR4-Fc* RNA rescued the headless phenotype. Arrows and arrowheads in A and D point to eyes (e) and cement glands (CG), respectively. E, Quantification of the results. The data are representative of two different experiments.

Fig. S8**Figure S8. Akt inhibition by Pten does not influence Pnhd signaling.**

Embryos were injected with RNAs encoding Flag-Pnhd (1.5 ng) or Pten (0.5 ng), as indicated. Ectoderm explants were dissected at stage 9.5, and cultured until stage 10.25 for immunoblotting with indicated antibodies. Pnhd inhibits Akt, but induces Erk phosphorylation in ectoderm at late blastula stages. When coinjected with Pnhd, Pten further inhibits Akt but does not alter Pnhd-dependent Erk activation.

Fig. S9

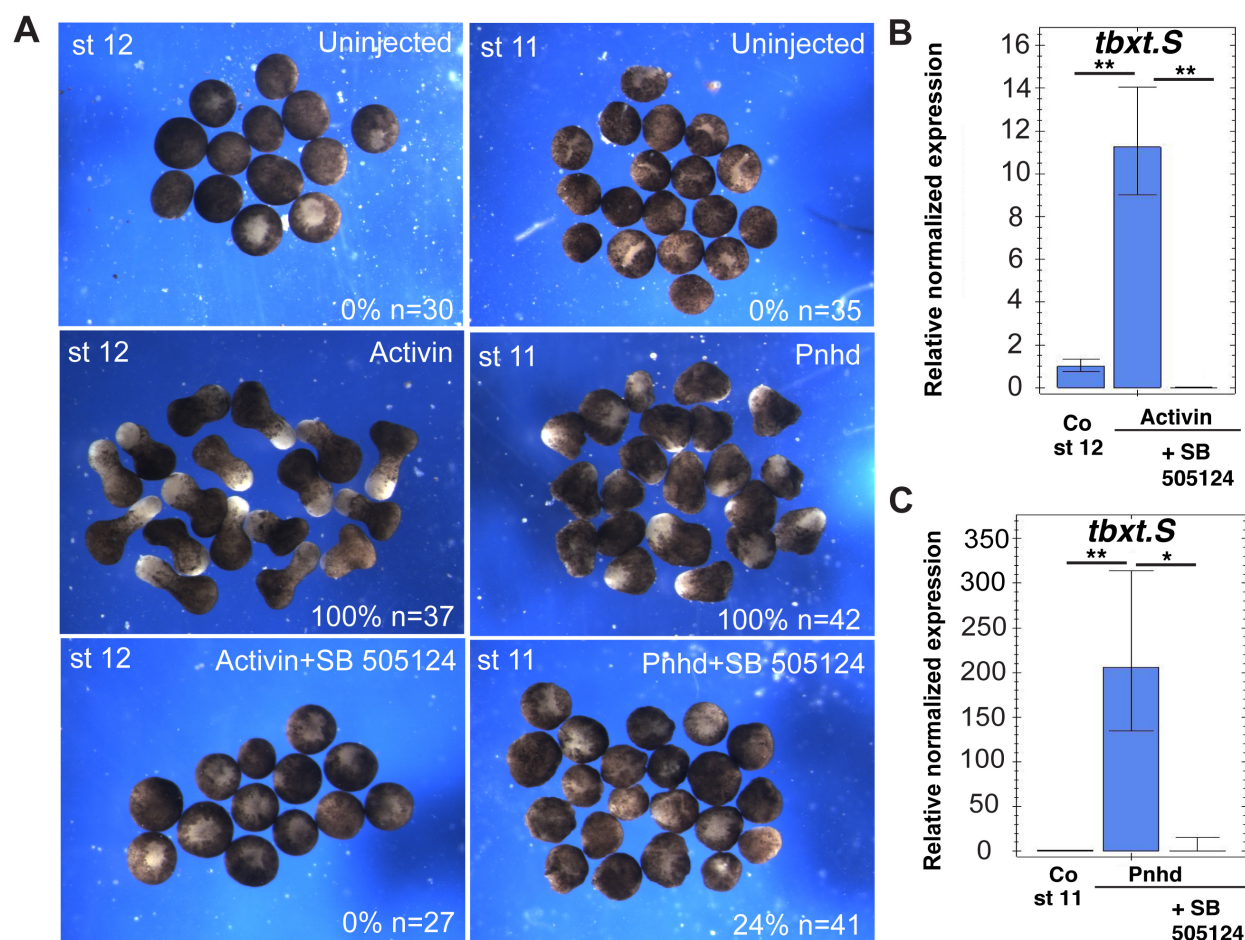


Figure S9. Pnhd activity is blocked by the Nodal/Activin inhibitor SB505124.

Animal caps were dissected at stage 9-10 and stimulated with Activin or obtained from embryos injected with pnhd RNA. RT-qPCR analysis of *tbxt.S* transcripts was carried out in animal caps incubated in the presence or absence of SB505124. A, Effect of SB505124 on Activin- or Pnhd-dependent mesoderm induction. Frequencies of the shown morphological changes and the total number of explants per group are indicated. Data are representative of three independent experiments. B, RT-qPCR analysis of *tbxt.S* transcripts in animal caps treated with Activin in the presence or absence of SB505124. C, Pnhd-dependent induction of *tbxt.S* in the presence or absence of SB505124. Means +/- standard errors are shown. Significance was determined by the two-tailed Student's t-test, $p < 0.01$ (**).

Fig. S10

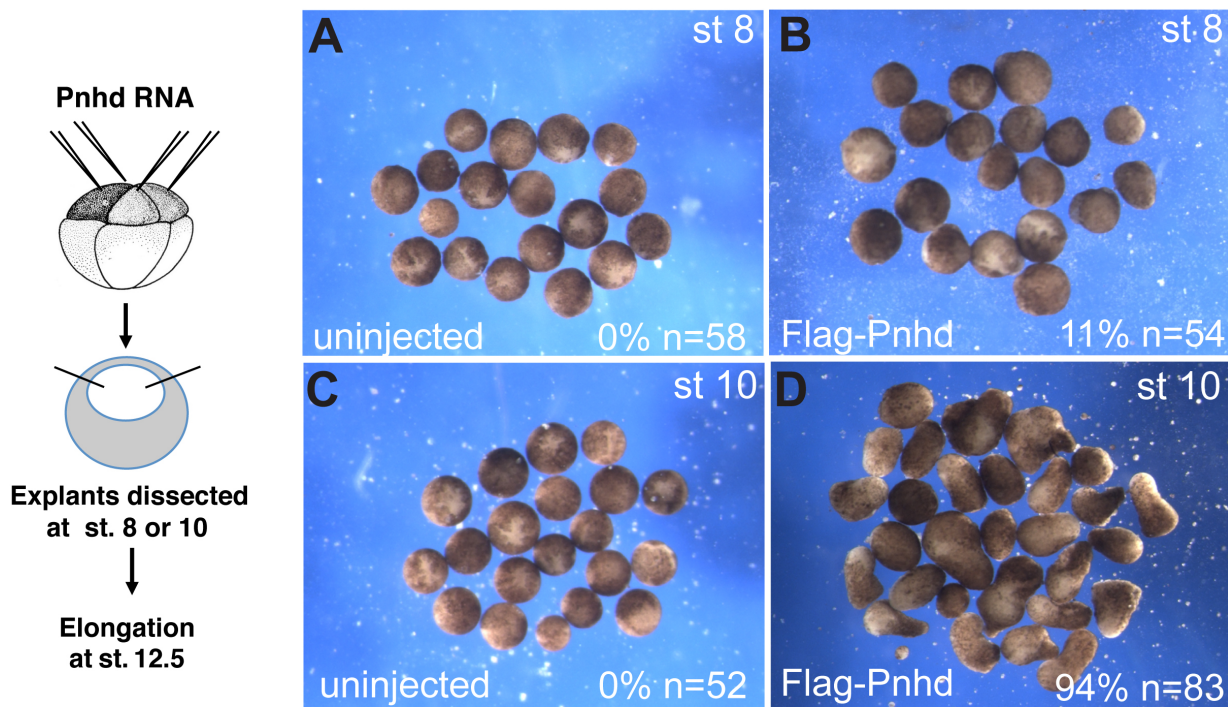


Figure S10. Pnhd-dependent elongation of animal caps isolated at the onset of gastrulation. Animal cap explants were prepared at stage 8 (A, B) or stage 10 (C, D) from the control uninjected (A, C) or *pnhd* RNA (2 ng)-injected (B, D) embryos and were cultured until stage 12.5, at which point explant morphology was imaged. Frequencies of explant elongation and total numbers of explants per group are shown. Data are representative of three independent experiments.

Fig. S11

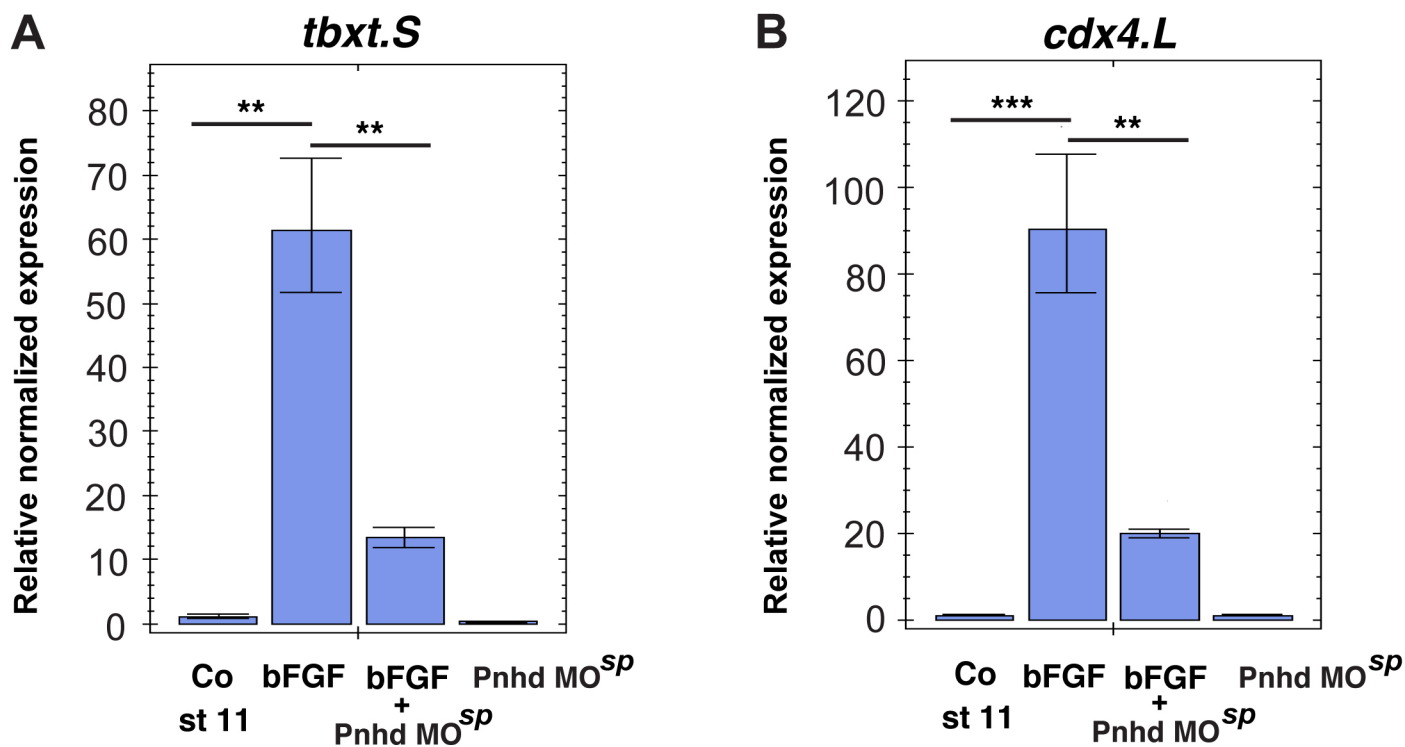


Figure S11. Pnhd is required for FGF-dependent mesoderm induction.

A, B, RT-qPCR was carried out for *cdx4* and *tbxt* in ectoderm lysates from Pnhd-depleted or control embryos after FGF stimulation as indicated. Embryos were injected into each of four animal blastomeres with Pnhd MO^{sp} (30 ng) at the 8-cell stage. Ectoderm explants were dissected at stage 8-8.5 and cultured until stage 11. Means +/- standard errors are shown.

Table S1. Differentially expressed genes in ectoderm explants with ectopic *pnhd* RNA.

[Click here to Download Table S1](#)

Table S2. Putative *pnhd* target genes. The list of common genes upregulated by *pnhd* RNA in ectoderm explants and reduced in the marginal zones of embryos injected with *pnhd* MO^{SP}.

Table 2. Genes that are upregulated by Pinhead overexpression and reduced by Pinhead depletion with splicing-blocking MO

GeneNames	log2 FlagPin_vs_Cocaps	log2 PhtSpMo_vs_Co	Variation in the expected sense	product (DAVID).x
Total correct: 71				
182 t.S	8.82	-1.01	YES	T brachyury transcription factor S homeolog(t.S)
100 LOC108713288	7.48	-1.76	YES	protein Wnt-8-like(LOC108713288)
191 zg16.S	7.44	4.77		zymogen granule protein 16 S homeolog(zg16.S)
75 LOC108698139	7.10	3.04		lipocalin-like(LOC108698139)
42 foxc2.L	7.05	-2.55	YES	forkhead box C2 L homeolog(foxc2.L)
144 pdgfra.S	6.78	-1.11	YES	platelet-derived growth factor receptor, alpha polypeptide S homeolog (pdgfra.S)
163 sebox.L	6.73	-1.10	YES	sebox homeobox L homeolog(sebox.L)
58 hoxd1.S	6.59	-3.64	YES	homeobox D1 S homeolog(hoxd1.S)
60 kcnk6.L	6.41	-2.05	YES	potassium channel, two pore domain subfamily K, member 6 L homeolog (kcnk6.L)
24 col17a1.L	6.41	3.40		collagen, type XVII, alpha 1 L homeolog(col17a1.L)
78 LOC108699267	6.33	2.35		neuropeptide Y receptor type 2-like(LOC108699267)
104 LOC108714881	6.29	4.43		neural retina-specific leucine zipper protein-like(LOC108714881)
106 LOC108715253	6.10	3.35		catalase-like(LOC108715253)
47 frzb.S	5.74	-1.39	YES	frizzled-related protein S homeolog(frzb.S)
81 LOC108699331	5.66	4.52		C-reactive protein-like(LOC108699331)
88 LOC108703174	5.53	-1.45	YES	netrin-3-like(LOC108703174)
89 LOC108703928	5.44	-1.85	YES	T-box transcription factor TBX6(LOC108703928)
97 LOC108709615	5.38	3.36		multidrug and toxin extrusion protein 2-like(LOC108709615)
30 evx1.L	5.30	-1.38	YES	even-skipped homeobox 1 L homeolog(evx1.L)
98 LOC108709870	5.27	2.05		arf-GAP with GTPase, ANK repeat and PH domain-containing protein 2-like(LOC108709870)
188 wnt8a.L	4.99	-1.33	YES	wingless-type MMTV integration site family member 8A L homeolog(wnt8a.L)
80 LOC108699330	4.82	3.81		C-reactive protein-like(LOC108699330)
113 LOC108719482	4.80	3.11		neurogenic locus notch homolog protein 1-like(LOC108719482)
17 cdx1.S	4.72	-1.34	YES	caud+F28al type homeobox 1 S homeolog(cdx1.S)
109 LOC108716948	4.68	3.59		uncharacterized LOC108716948(LOC108716948)
169 slc26a9.S	4.66	3.69		solute carrier family 26 (anion exchanger), member 9 S homeolog(slc26a9.S)
134 nppb.S	4.62	3.87		natriuretic peptide B S homeolog(nppb.S)
156 rasl11b.L	4.55	1.05		RAS-like family 11 member B L homeolog(rasl11b.L)
93 LOC108705387	4.54	1.68		chemokine-like receptor 1(LOC108705387)
94 LOC108705532	4.52	2.42		uncharacterized LOC108705532(LOC108705532)
110 LOC108718036	4.47	2.42		multidrug resistance-associated protein 5-like(LOC108718036)
40 foxc1.L	4.45	-2.38	YES	forkhead box C1 L homeolog(foxc1.L)
57 hoxd1.L	4.37	-3.29	YES	homeobox D1 L homeolog(hoxd1.L)
19 cdx2.S	4.29	-2.24	YES	caudal type homeobox 2 S homeolog(cdx2.S)
69 LOC108696533	4.14	2.99		uncharacterized LOC108696533(LOC108696533)
137 nt5c3a.L	4.10	3.42		5'-nucleotidase, cytosolic IIIA(nt5c3a.L)
55 hars.L	4.02	2.02		histidyl-HRNA synthetase L homeolog(hars.L)
65 LOC100486127.S	4.02	1.88		cytochrome P450 2J6-like S homeolog(LOC100486127.S)
73 LOC108697694	4.00	-1.95	YES	transcription factor HES-5-like(LOC108697694)
36 fkbp9.S	3.98	1.85		FK506 binding protein 9 S homeolog(fkbp9.S)
67 LOC108696466	3.97	2.37		Down syndrome cell adhesion molecule-like protein 1 homolog(LOC108696466)
71 LOC108696801	3.96	3.59		urokinase plasminogen activator surface receptor-like(LOC108696801)
52 gjc2.L	3.92	2.86		gap junction protein gamma 2 L homeolog(gjc2.L)
20 cdx4.L	3.90	-2.09	YES	caudal type homeobox 4 L homeolog(cdx4.L)
83 LOC108700049	3.89	2.61		uncharacterized LOC108700049(LOC108700049)
43 foxd411.1.S	3.87	-1.37	YES	forkhead box D4-like 1, gene 1 S homeolog(foxd411.1.S)
107 LOC108715768	3.86	1.47		uncharacterized LOC108715768(LOC108715768)
119 mab21l2.S	3.78	1.66		mab-21-like 2 S homeolog(mab21l2.S)
142 pcdh8.2.L	3.68	-1.26	YES	protocadherin 8, gene 2 L homeolog(pcdh8.2.L)
170 socs4.S	3.65	3.16		suppressor of cytokine signaling 4 S homeolog(socs4.S)
130 mmp14.L	3.65	1.21		matrix metalloproteinase 14 L homeolog(mmp14.L)
103 LOC108714877	3.58	3.59		uncharacterized LOC108714877(LOC108714877)
190 zeb2.S	3.57	-1.88	YES	zinc finger E-box binding homeobox 2 S homeolog(zeb2.S)
62 lancl3.S	3.57	2.58		LanC like 3 S homeolog(lancl3.S)
141 parp3.L	3.55	2.81		poly(ADP-ribose) polymerase family member 3 L homeolog(parp3.L)
95 LOC108706889	3.51	-1.25	YES	uncharacterized LOC108706889(LOC108706889)
13 ccdc141.S	3.50	2.96		coiled-coil domain containing 141 S homeolog(ccdc141.S)
68 LOC108696532	3.49	3.37		uncharacterized LOC108696532(LOC108696532)
70 LOC108696558	3.47	2.03		ankyrin repeat domain-containing protein 65-like(LOC108696558)
39 foxb1.L	3.46	-2.02	YES	forkhead box B1 L homeolog(foxb1.L)
176 tmprss9.S	3.45	-1.59	YES	transmembrane protease, serine 9 S homeolog(tmprss9.S)
157 rb2.L	3.44	3.04		retinoblastoma-like 2 L homeolog(rb2.L)
21 cdx4.S	3.38	-2.18	YES	caudal type homeobox 4 S homeolog(cdx4.S)
10 c9.L	3.35	2.81		complement component 9 L homeolog(c9.L)
9 c3ar1.L	3.31	3.84		complement component 3a receptor 1 L homeolog(c3ar1.L)
7 aplnr.S	3.25	2.53		apelin receptor S homeolog(aplnr.S)
22 chst2.S	3.24	1.19		carbohydrate (N-acetylglucosamine-6-O) sulfotransferase 2 S homeolog(chst2.S)
136 nrp2.S	3.20	-1.52	YES	neuropilin 2 S homeolog(nrp2.S)
143 pdgfra.L	3.18	-1.14	YES	platelet-derived growth factor receptor, alpha polypeptide L homeolog(pdgfra.L)
26 ednra.S	3.17	-2.24	YES	endothelin receptor type A S homeolog(ednra.S)
6 aplnr.L	3.12	1.12		apelin receptor L homeolog(aplnr.L)
118 mab21l2.L	3.09	1.22		mab-21-like 2 L homeolog(mab21l2.L)
153 ptpn14.S	3.08	2.11		protein tyrosine phosphatase, non-receptor type 14 S homeolog(ptpn14.S)
18 cdx2.L	3.06	-2.16	YES	caudal type homeobox 2 L homeolog(cdx2.L)
128 MGC80829	3.05	1.53		MGC80829 protein(MGC80829)
3 adora2a.S	3.04	1.97		adenosine A2a receptor S homeolog(adora2a.S)
161 ror2.S	3.04	-1.09	YES	receptor tyrosine kinase-like orphan receptor 2 S homeolog(ror2.S)
177 tnfrsf6b.L	3.03	4.33		tumor necrosis factor receptor superfamily member 6b L homeolog(tnfrsf6b.L)
160 mf24.L	2.99	2.06		ring finger protein 24 L homeolog(mf24.L)
102 LOC108714552	2.95	1.27		urotensin-2 receptor-like(LOC108714552)
14 ccng1.L	2.92	2.11		cyclin G1 L homeolog(ccng1.L)
114 LOC398134	2.91	-1.24	YES	p75-like transmembrane protein fullback(LOC398134)
152 prickle1.S	2.90	1.04		prickle homolog 1 S homeolog(prickle1.S)
91 LOC108704851	2.81	1.99		uncharacterized LOC108704851(LOC108704851)
37 fosl1.L	2.78	-3.23	YES	FOS-like antigen 1 L homeolog(fosl1.L)
2 admp2.L	2.76	-1.94	YES	antidorsalizing morphogenetic protein 2 L homeolog(admp2.L)
145 pidd1.L	2.74	1.61		p53-induced death domain protein 1 L homeolog(pidd1.L)
86 LOC108700532	2.70	1.48		methionine-tRNA ligase, mitochondrial-like(LOC108700532)
165 sesn1.L	2.70	1.99		sestrin 1 L homeolog(sesn1.L)
132 ngfr.L	2.69	-1.18	YES	nerve growth factor receptor L homeolog(ngfr.L)
133 nif.L	2.69	2.14		low molecular weight neuronal intermediate filament L homeolog(nif.L)
150 plk2.S	2.68	3.27		polo-like kinase 2 S homeolog(plk2.S)
1 adap1.L	2.67	1.06		ArfGAP with dual PH domains 1 L homeolog(adap1.L)

Table S3. List of primers used for RT-PCR and RT-qPCR.**Table 3****Primers used for RT-PCR**

Gene name	Forward primer	Reverse primer
wnt8a.L	5'-atg agg tcg ggt aac agt gc-3'	5'-caa agc ctc ttg cag ctt ct-3'
xbra.S	5'-gct gga agt atg tga atg gag-3'	5'-tta agt gct gta atc tct tca-3'
nodal3.1.L	5'-ctt ctg cac tag att ctg-3',	5'-cag ctt ctg gcc aag act-3'
vent2.2	5'-tga gac ttg ggc act gtc tg-3'	5'- cct ctg ttg aat ggc ttg ct-3'
cdx4.L	5'-aag ggc agc cta tgg agt tt-3'	5'-gtc cca gat gga tga gga ga-3'
krt12.4.L	5'- cac cag aac aca gag tac -3'	5'- caa cct tcc cat caa cca -3'
vegt.L	5'-caa gta aat gtg aga aac cg-3'	5'-caa ata cac aca cat ttc cc-3'
cdx4.L	5'-aag ggc agc cta tgg agt tt-3'	5'-gtc cca gat gga tga gga ga-3'
ef1a	5'-cag att ggt gct gga tat gc-3'	5'-act gcc ttg atg act cct ag-3'

Primers used for RT-qPCR

Gene name	Forward primer	Reverse primer
tbxt S	5'-tca cta gcc att cat tcc ct -3'	5'-gac tat cga ttc cct cat cc -3',
wnt8a.L	5'-atg agg tcg ggt aac agt gc -3'	5'-taa tcg gga gag tct tcg ag -3'
wnt8a-like	5'-ttc tgc acc aga aag gaa cg -3'	5'-ac cat ttt aga cat tat ctt -3'
cdx4.L	5'- tga ttt atc acc taa cca g -3'	5'- gtc cca gat gga tga gga ga -3'
nodal3.1.L	5'- ggc aaa agg tct cca tct -3'	5'- cag ctt ctg gcc aag act -3'
admp2.L	5'- ggc ttc ctt gtg atg ttc ac -3'	5'-gc agg taa gac ctt ttg ttg-3'
fgf8b.L	5'-gaa gct gat tgg gaa gac t -3'	5'- gcc ata aac cag cct tcg ta-3'
ef1a.1.S	5'-acc ctc ctc ttg gtc gtt tt -3'	5'-ttt ggt ttt cgc tgc ttt ct -3'
hoxd1.S	5'-ccc tgc aat gtg agg aca aa-3'	5'-gat gcg cct tgc tct tgt g-3'
msgn1.L	5'-gta tcc aac act ttg cca tg -3'	5'-agc act gga gaa ggt ttg tg -3'
pnhd.L	5'- tag ggc tct ggc aca aat g -3'	5'-gct cac aat gtc aca agg aatg-3'