

Supplemental Information for:

**Fish as model systems to study epigenetic drivers
in human self-domestication and
neurodevelopmental cognitive disorders**

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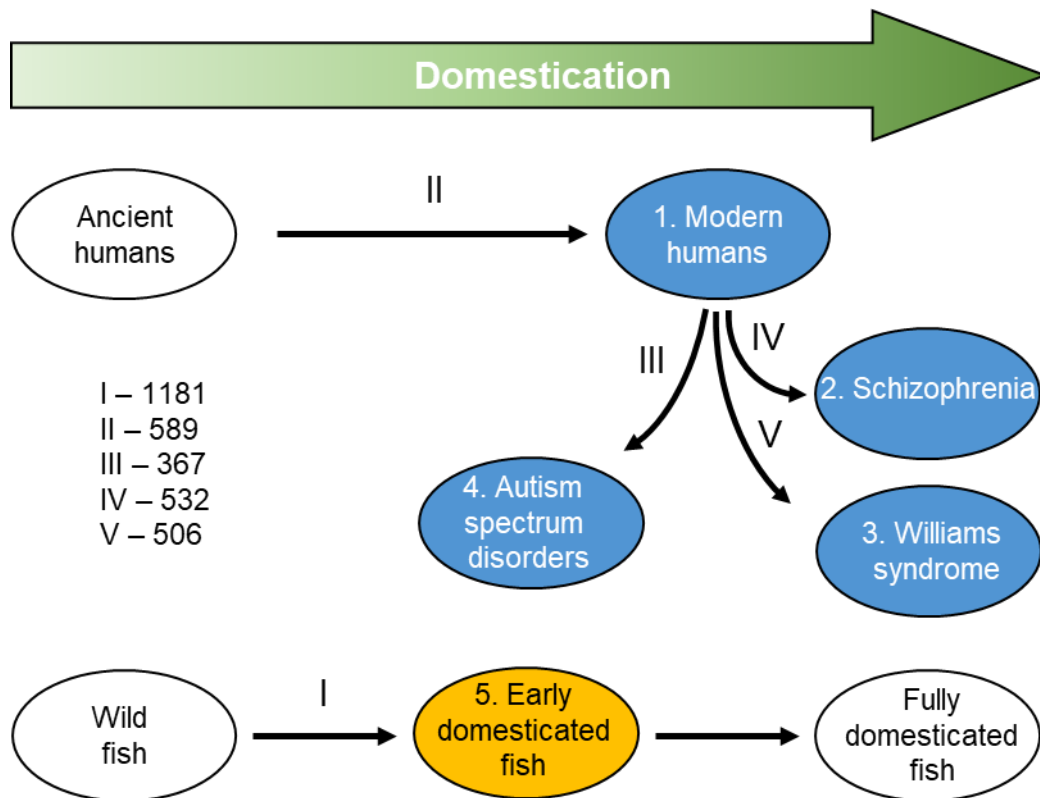


Figure S1. Conceptual design of the study. The level of domestication is shown from left to right, from less domesticated phenotypes (ancient humans and wild fish) to more domesticated (patients with schizophrenia or Williams syndrome and fish selected for specific phenotypes). The five groups used in our study are shown by their colored background (blue, humans; orange, fish). The number of genes showing epigenetic changes between groups are shown on the left after the Roman numbers. For comparisons II, III, IV and V, the number of unique orthologues in the European sea bass genome is reported.

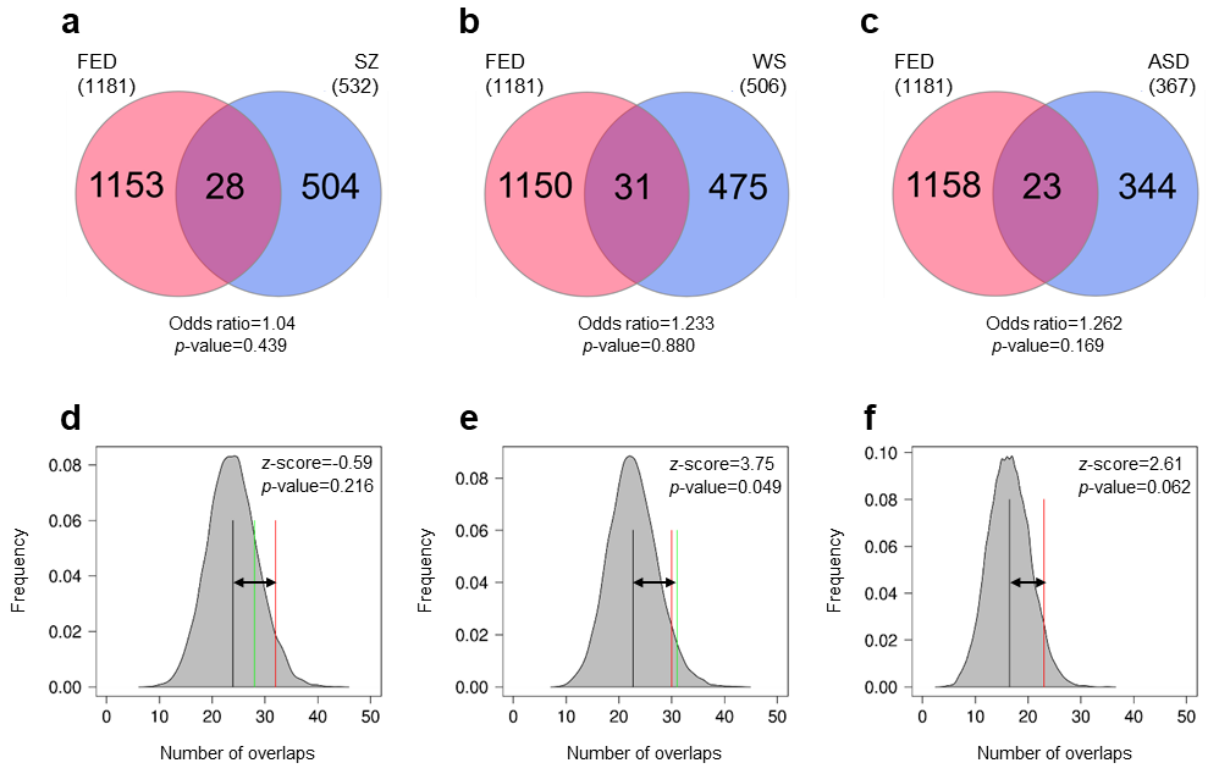


Figure S2. Overlap of orthologue genes with epigenetic changes in fish early domesticates (FED) and neurodevelopmental cognitive disorders. Pairwise comparisons are shown for FED vs schizophrenia (SZ; a, d), Williams syndrome (WS; b, e), and autism spectrum disorders (ASD; c, f). The overlaps were tested using Fisher's exact test for count data (a–c) and permutations (d–f). The results of permutations are represented as the distribution of number of overlaps (shaded grey areas) with mean number of permuted overlaps (black vertical lines) and significance threshold set to 0.05 (red lines). Observed number of overlaps is shown by the green lines and the distance of observed vs expected (random) overlaps is shown with the black arrow. The z-scores and the p -values indicate the significance of the overlaps.

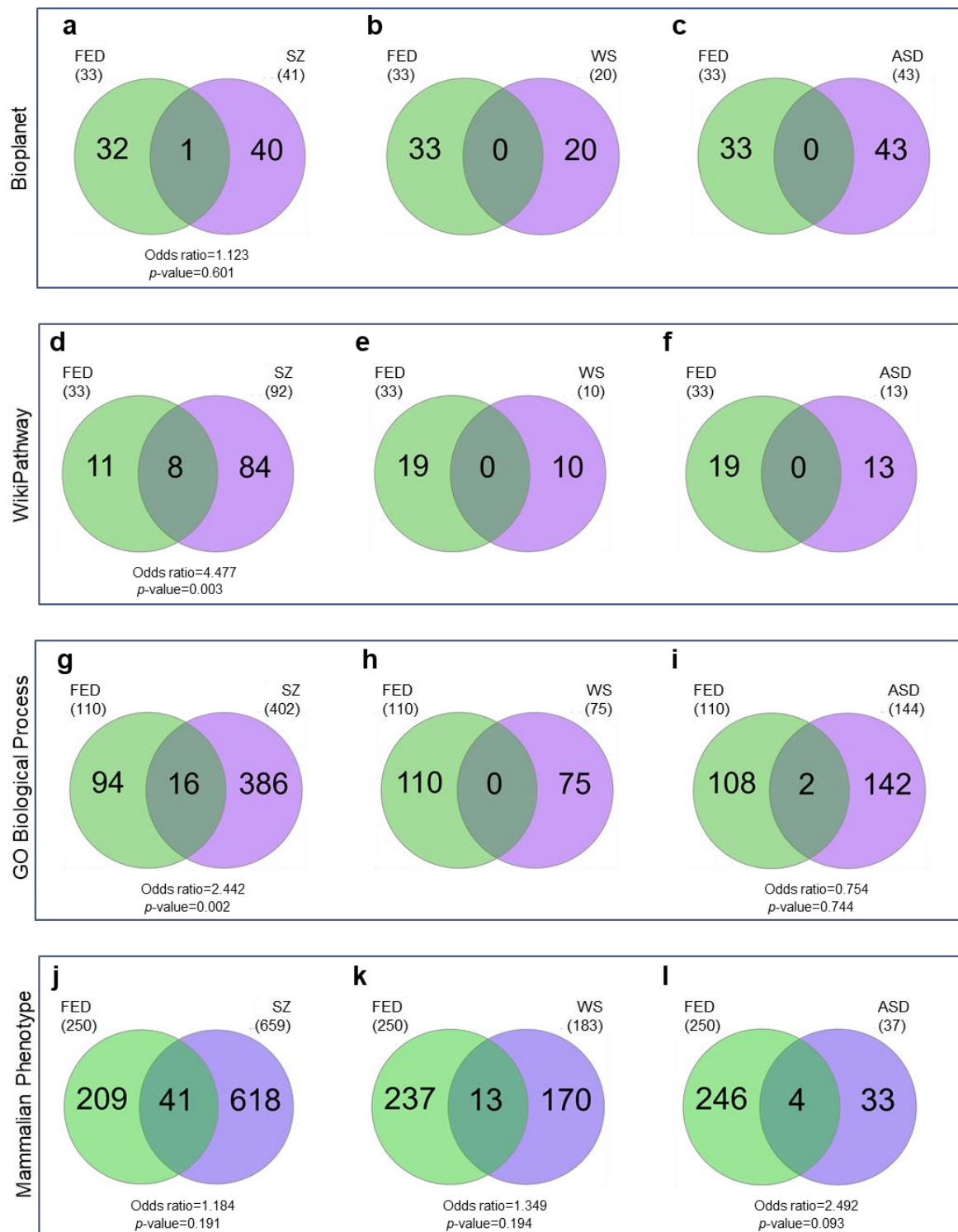


Figure S3. Overlap of pathways enriched associated with orthologue genes with epigenetic changes in fish early domesticates (FED) and cognitive disorders. Pairwise comparisons are shown for FED vs schizophrenia (SZ; a, d, g, j), Williams syndrome (WS; b, e, h, k) and autism spectrum disorders (ASD; c, f, i, l). Enriched terms from Bioplanet (a–c), WikiPathways (d–f), Gene Ontology (GO) Biological Process (g–i) and Mammalian Phenotype (j–l) were detected using Enrichr.

Table S1. Enrichment of Gene Ontology (GO) Biological Process (BP) terms associated with genes shared between early fish domesticates and anatomically modern humans

Biological Process GO	ID	Overlap	<i>p</i> -value	Adjusted <i>p</i> -value	Odds Ratio	Combined Score	Genes
negative regulation of alpha-beta T cell differentiation	GO:0046639	2/8	1.20E-04	0.028	166.3	1501.6	<i>RUNX3;GLI3</i>
positive regulation of alpha-beta T cell differentiation	GO:0046638	2/14	3.86E-04	0.045	83.1	653.3	<i>RUNX3;GLI3</i>
actin filament polymerization	GO:0030041	2/29	0.002	0.098	36.9	235.7	<i>PREX1;CORO7</i>
limb development	GO:0060173	2/29	0.002	0.098	36.9	235.7	<i>SMOC1;GLI3</i>
actin polymerization or depolymerization	GO:0008154	2/50	0.005	0.150	20.7	110.1	<i>PREX1;CORO7</i>
protein polymerization	GO:0051258	2/59	0.007	0.150	17.5	87.1	<i>PREX1;CORO7</i>
regulation of Rho protein signal transduction	GO:0035023	2/73	0.010	0.150	14.0	64.1	<i>BCR;EPS8L2</i>
negative regulation of CD4-positive, alpha-beta T cell differentiation	GO:0043371	1/5	0.010	0.150	121.7	554.9	<i>RUNX3</i>
positive regulation of CD8-positive, alpha-beta T cell differentiation	GO:0043378	1/5	0.010	0.150	121.7	554.9	<i>RUNX3</i>
positive regulation of protein kinase C activity	GO:1900020	1/5	0.010	0.150	121.7	554.9	<i>CEMIP</i>
copper ion import	GO:0015677	1/5	0.010	0.150	121.7	554.9	<i>ATP7B</i>
peripheral nervous system neuron differentiation	GO:0048934	1/5	0.010	0.150	121.7	554.9	<i>RUNX3</i>
regulation of protein kinase C activity	GO:1900019	1/5	0.010	0.150	121.7	554.9	<i>CEMIP</i>
mesodermal cell fate commitment	GO:0001710	1/6	0.013	0.150	97.3	426.2	<i>EYA2</i>
peripheral nervous system neuron development	GO:0048935	1/6	0.013	0.150	97.3	426.2	<i>RUNX3</i>
regulation of Ras protein signal transduction	GO:0046578	2/86	0.014	0.150	11.8	50.4	<i>BCR;EPS8L2</i>
T cell apoptotic process	GO:0070231	1/7	0.015	0.150	81.1	342.8	<i>GLI3</i>
nose development	GO:0043584	1/7	0.015	0.150	81.1	342.8	<i>GLI3</i>
regulation of CD8-positive, alpha-beta T cell differentiation	GO:0043376	1/7	0.015	0.150	81.1	342.8	<i>RUNX3</i>
mitochondrion-endoplasmic reticulum membrane tethering	GO:1990456	1/7	0.015	0.150	81.1	342.8	<i>PACS2</i>

hyaluronan biosynthetic process	GO:0030213	1/7	0.015	0.150	81.1	342.8	<i>CEMIP</i>
sensory perception of mechanical stimulus	GO:0050954	2/88	0.015	0.150	11.6	48.8	<i>CEMIP;EPS8L2</i>
sensory perception of sound	GO:0007605	2/91	0.016	0.150	11.2	46.4	<i>CEMIP;EPS8L2</i>
regulation of lipid metabolic process	GO:0019216	2/92	0.016	0.150	11.0	45.6	<i>NCOR2;CARM1</i>
regulation of alpha-beta T cell differentiation	GO:0046637	1/8	0.017	0.150	69.5	284.6	<i>GLI3</i>
positive regulation of CD8-positive, alpha-beta T cell activation	GO:2001187	1/9	0.019	0.150	60.8	241.9	<i>RUNX3</i>
histone arginine methylation	GO:0034969	1/9	0.019	0.150	60.8	241.9	<i>CARM1</i>
negative regulation of alpha-beta T cell activation	GO:0046636	1/9	0.019	0.150	60.8	241.9	<i>GLI3</i>
sensory organ morphogenesis	GO:0090596	1/9	0.019	0.150	60.8	241.9	<i>GLI3</i>
activation of GTPase activity	GO:0090630	2/105	0.021	0.152	9.6	37.5	<i>BCR;TBC1D22A</i>
granulocyte activation	GO:0036230	1/10	0.021	0.152	54.1	209.4	<i>PREX1</i>
protein localization to phagophore assembly site	GO:0034497	1/11	0.023	0.152	48.7	183.8	<i>PACS2</i>
copper ion transport	GO:0006825	1/11	0.023	0.152	48.7	183.8	<i>ATP7B</i>
histone modification	GO:0016570	2/114	0.024	0.152	8.9	33.1	<i>EYA2;CARM1</i>
purine nucleoside monophosphate biosynthetic process	GO:0009127	1/12	0.025	0.152	44.2	163.3	<i>LHPP</i>
negative regulation of gene silencing by miRNA	GO:0060965	1/12	0.025	0.152	44.2	163.3	<i>NCOR2</i>
regulation of CD4-positive, alpha-beta T cell differentiation	GO:0043370	1/12	0.025	0.152	44.2	163.3	<i>RUNX3</i>
negative regulation of production of miRNAs involved in gene silencing by miRNA	GO:1903799	1/12	0.025	0.152	44.2	163.3	<i>NCOR2</i>
negative regulation of CD4-positive, alpha-beta T cell activation	GO:2000515	1/13	0.027	0.153	40.5	146.5	<i>RUNX3</i>
positive regulation of ruffle assembly	GO:1900029	1/13	0.027	0.153	40.5	146.5	<i>EPS8L2</i>
negative regulation of T cell differentiation	GO:0045581	1/14	0.029	0.153	37.4	132.5	<i>GLI3</i>
T cell differentiation in thymus	GO:0033077	1/14	0.029	0.153	37.4	132.5	<i>GLI3</i>
ribonucleoside monophosphate biosynthetic process	GO:0009156	1/14	0.029	0.153	37.4	132.5	<i>LHPP</i>
cellular copper ion homeostasis	GO:0006878	1/14	0.029	0.153	37.4	132.5	<i>ATP7B</i>

regulation of primary metabolic process	GO:0080090	2/130	0.030	0.157	7.7	27.0	<i>NCOR2;CARM1</i>
negative regulation of androgen receptor signaling pathway	GO:0060766	1/15	0.031	0.157	34.7	120.6	<i>NCOR2</i>
purine ribonucleoside monophosphate biosynthetic process	GO:0009168	1/16	0.033	0.157	32.4	110.5	<i>LHPP</i>
neutrophil activation	GO:0042119	1/16	0.033	0.157	32.4	110.5	<i>PREX1</i>
Golgi to endosome transport	GO:0006895	1/16	0.033	0.157	32.4	110.5	<i>CORO7</i>
protein dephosphorylation	GO:0006470	2/139	0.034	0.157	7.2	24.4	<i>EYA2;LHPP</i>
copper ion homeostasis	GO:0055070	1/17	0.035	0.157	30.4	101.8	<i>ATP7B</i>
regulation of small GTPase mediated signal transduction	GO:0051056	2/141	0.035	0.157	7.1	23.8	<i>BCR;PREX1</i>
hyaluronan catabolic process	GO:0030214	1/18	0.037	0.157	28.6	94.2	<i>CEMIP</i>
embryonic digit morphogenesis	GO:0042733	1/18	0.037	0.157	28.6	94.2	<i>GLI3</i>
regulation of production of miRNAs involved in gene silencing by miRNA	GO:1903798	1/18	0.037	0.157	28.6	94.2	<i>NCOR2</i>
negative regulation of RNA metabolic process	GO:0051253	1/19	0.039	0.159	27.0	87.5	<i>NCOR2</i>
positive regulation of alpha-beta T cell activation	GO:0046635	1/20	0.041	0.159	25.6	81.6	<i>GLI3</i>
purine ribonucleoside monophosphate metabolic process	GO:0009167	1/20	0.041	0.159	25.6	81.6	<i>LHPP</i>
embryonic digestive tract development	GO:0048566	1/20	0.041	0.159	25.6	81.6	<i>GLI3</i>
endoplasmic reticulum calcium ion homeostasis	GO:0032469	1/20	0.041	0.159	25.6	81.6	<i>PACS2</i>
regulation of cell differentiation	GO:0045595	2/156	0.042	0.159	6.4	20.3	<i>SMOC1;RUNX3</i>
focal adhesion assembly	GO:0048041	1/21	0.043	0.159	24.3	76.4	<i>BCR</i>
limb morphogenesis	GO:0035108	1/22	0.045	0.159	23.2	71.7	<i>GLI3</i>
cell projection assembly	GO:0030031	1/22	0.045	0.159	23.2	71.7	<i>PARVB</i>
negative regulation of signal transduction in absence of ligand	GO:1901099	1/23	0.047	0.159	22.1	67.5	<i>EYA2</i>
negative regulation of smoothened signaling pathway	GO:0045879	1/23	0.047	0.159	22.1	67.5	<i>GLI3</i>
negative regulation of extrinsic apoptotic signaling pathway in absence of ligand	GO:2001240	1/23	0.047	0.159	22.1	67.5	<i>EYA2</i>

response to copper ion	GO:0046688	1/23	0.047	0.159	22.1	67.5	<i>ATP7B</i>
hyaluronan metabolic process	GO:0030212	1/23	0.047	0.159	22.1	67.5	<i>CEMIP</i>
regulation of ruffle assembly	GO:1900027	1/24	0.049	0.161	21.1	63.7	<i>EPS8L2</i>
positive regulation of protein targeting to membrane	GO:0090314	1/24	0.049	0.161	21.1	63.7	<i>CEMIP</i>

Note. The full enrichment analysis for genes shared between fish early domesticates and anatomically modern human can be accessed here: <https://maayanlab.cloud/Enrichr/enrich?dataset=5d2c407bedd97bc283c4828e2b14c47e>

Table S2. Enrichment of Mammalian Phenotype (2014) terms associated with genes shared between early fish domesticates and anatomically modern humans

Mammalian Phenotype	ID	Overlap	<i>p</i> -value	Adjusted <i>p</i> -value	Odds Ratio	Combined Score	Genes
synostosis	MP:0000566	2/7	8.98E-05	0.025	199.5	1859.2	<i>SMOC1;GLI3</i>
short humerus	MP:0004351	3/43	1.00E-04	0.025	38.3	352.7	<i>ADAMTS17;RUNX3;GLI3</i>
abnormal snout morphology	MP:0000443	3/58	2.45E-04	0.031	27.8	231.4	<i>SMOC1;AGAP1;EPS8L2</i>
abnormal cranium morphology	MP:0000438	4/147	2.52E-04	0.031	14.6	120.8	<i>SMOC1;AGAP1;RUNX3;GLI3</i>
interdigital webbing	MP:0000571	2/15	4.44E-04	0.032	76.7	592.1	<i>SMOC1;GLI3</i>
abnormal olfactory nerve morphology	MP:0005236	2/16	5.07E-04	0.032	71.2	540.4	<i>ZNF423;GLI3</i>
abnormal medulla oblongata morphology	MP:0000846	2/16	5.07E-04	0.032	71.2	540.4	<i>ZNF423;GLI3</i>
bowed tibia	MP:0004358	2/17	5.74E-04	0.032	66.5	496.1	<i>SMOC1;GLI3</i>
brachyphalangia	MP:0002543	2/18	6.45E-04	0.032	62.3	457.8	<i>ADAMTS17;GLI3</i>
reduced cerebellar foliation	MP:0009719	2/18	6.45E-04	0.032	62.3	457.8	<i>ZNF423;GLI3</i>
short fibula	MP:0002765	2/19	7.20E-04	0.032	58.7	424.4	<i>SMOC1;GLI3</i>
abnormal nasal cavity morphology	MP:0002237	2/20	7.99E-04	0.033	55.4	395.1	<i>ZNF423;GLI3</i>
hypopigmentation	MP:0005408	2/22	9.68E-04	0.034	49.8	345.9	<i>ATP7B;GLI3</i>
absent optic nerve	MP:0001333	2/22	9.68E-04	0.034	49.8	345.9	<i>SMOC1;GLI3</i>
short tibia	MP:0002764	4/214	0.00104	0.034	9.9	68.0	<i>PACS2;SMOC1;ADAMTS17; GLI3</i>
abnormal cerebral hemisphere morphology	MP:0008540	2/25	0.00125	0.037	43.3	289.6	<i>ATP7B;GLI3</i>
postnatal lethality, complete penetrance	MP:0011085	5/394	0.00135	0.037	6.8	44.9	<i>ATP7B;SMOC1;ZNF423;RUN X3;GLI3</i>
abnormal olfactory epithelium morphology	MP:0008789	2/26	0.00136	0.037	41.5	274.3	<i>ZNF423;GLI3</i>
decreased body weight	MP:0001262	9/1329	0.00149	0.039	3.9	25.1	<i>NCOR2;PREX1;LASP1;ATP7 B;SMOC;</i>
decreased bone strength	MP:0004991	2/29	0.00169	0.042	36.9	235.7	<i>ADAMTS17;PARVB;ZNF423; RUNX3</i>

abnormal bone mineralization	MP:0002896	3/115	0.00181	0.042	13.6	86.1	<i>NCOR2;RUNX3</i>
absent corpus callosum	MP:0002196	2/33	0.00218	0.049	32.1	197.0	<i>PARVB;RUNX3;GLI3</i>

Note. The full enrichment analysis for genes shared between fish early domesticates and anatomically modern human can be accessed here: <https://maayanlab.cloud/Enrichr/enrich?dataset=5d2c407bedd97bc283c4828e2b14c47e>

Table S3. Enrichment of Wikipathways associated with genes shared between early fish domesticates and anatomically modern humans

Wikipathways	Overlap	<i>p</i> -value	Adjusted <i>p</i> -value	Odds Ratio	Combined Score	Genes
TGF-beta Receptor Signaling	2/54	5.75E-03	0.066	19.14	98.74	<i>ZNF423;RUNX3</i>
TGF-beta receptor signaling in skeletal dysplasias	2/58	6.61E-03	0.066	17.77	89.20	<i>ZNF423;RUNX3</i>
Endochondral Ossification with Skeletal Dysplasias	2/64	7.99E-03	0.066	16.05	77.49	<i>RUNX3;GLI3</i>
Endochondral Ossification	2/64	0.008	0.066	16.05	77.49	<i>RUNX3;GLI3</i>
Androgen receptor signaling pathway	2/90	0.015	0.101	11.29	47.16	<i>NCOR2;CARM1</i>
Tgif disruption of Shh signaling	1/9	0.019	0.103	60.82	241.88	<i>GLI3</i>
NO metabolism in cystic fibrosis	1/13	0.027	0.121	40.54	146.48	<i>CARM1</i>
Cholesterol Biosynthesis Pathway	1/15	0.031	0.121	34.75	120.64	<i>MSMO1</i>
Hedgehog Signaling Pathway Netpath	1/16	3.31E-02	0.121	32.43	110.53	<i>GLI3</i>
Imatinib and Chronic Myeloid Leukemia	1/20	4.12E-02	0.136	25.60	81.64	<i>BCR</i>
GDNF/RET signaling axis	1/23	4.72E-02	0.141	22.10	67.47	<i>GLI3</i>

Note. The full enrichment analysis for genes shared between fish early domesticates and anatomically modern human can be accessed here: <https://maayanlab.cloud/Enrichr/enrich?dataset=5d2c407bedd97bc283c4828e2b14c47e>

Table S4. Enrichment of Wikipathways associated with genes shared between early fish domesticates and human groups with schizophrenia

Wikipathways	Overlap	<i>p</i> -value	Adjusted <i>p</i> -value	Odds Ratio	Combined Score	Genes
GABA receptor Signaling	2/31	0.045	0.275	6.3	19.5	<i>SLC32A1;GABRD</i>
Hair Follicle Development	3/32	0.005	0.101	9.5	50.0	<i>LAMA5;PDGFRA;FGFR2</i>
Alpha 6 Beta 4 signaling pathway	3/33	0.006	0.101	9.1	47.5	<i>LAMA5;LAMA2;LAMA3</i>
Hedgehog Signaling Pathway	3/44	0.012	0.158	6.7	29.4	<i>SMURF2;BOC;FBXL17</i>
TGF-beta receptor signaling in skeletal dysplasias	3/58	0.026	0.183	5.0	18.2	<i>ADAMTSL2;RUNX3;SMAD7</i>
Endochondral Ossification with Skeletal Dysplasias	4/64	0.005	0.101	6.1	32.0	<i>ADAMTS5;ADAMTS1;RUNX3;BMP6</i>
Endochondral Ossification	4/64	0.005	0.101	6.1	32.0	<i>ADAMTS5;ADAMTS1;RUNX3;BMP6</i>
Primary focal segmental glomerulosclerosis	3/72	0.045	0.275	4.0	12.3	<i>LAMA5;AGRN;CLDN1</i>
Arrhythmogenic Cardiomyopathy	5/74	0.001	0.058	6.7	44.3	<i>CACNB1;TCF7L1;LAMA2;ACTN1;DMD</i>
Glioblastoma signaling pathways	4/82	0.013	0.158	4.7	20.6	<i>PDGFRA;CDK6;PRKCQ;FGFR2</i>
Small cell lung cancer	4/96	0.021	0.183	4.0	15.3	<i>LAMA5;CDK6;LAMA2;LAMA3</i>
Pathways Regulating Hippo Signaling	4/98	0.023	0.183	3.9	14.7	<i>PDGFRA;TCF7L1;PRKCQ;FGFR2</i>
Osteoblast Signaling	3/14	0.000	0.038	25.0	193.4	<i>PDGFRA;TNFRSF11B;FGF23</i>
Oncogenic Pathways as Metastatic Traits	2/17	0.015	0.158	12.1	51.4	<i>TCF7L1;TNC</i>
MFAP5 effects	2/18	0.016	0.160	11.4	46.9	<i>ACTN1;PRKCQ</i>
BMP Signaling in Eyelid Development	3/20	0.001	0.058	16.1	107.5	<i>FOXC1;PITX2;FGFR2</i>
FGF23 signaling	2/22	0.024	0.183	9.1	34.0	<i>FGF23;FGFR2</i>
Hfe effects	2/7	0.002	0.086	36.5	219.6	<i>BMP6;SMAD7</i>
Angiogenesis	2/24	0.028	0.191	8.3	29.6	<i>PDGFRA;FGFR2</i> <i>TCF7L1;HDAC10;FZD4;BOC;HESX1;PAX3;T</i>
Ectoderm Differentiation	10/138	0.000	0.001	7.3	93.6	<i>NFRSF11B;DMD;KIFC3;FGFR2</i>
Neural Crest Differentiation	4/101	0.025	0.183	3.8	13.9	<i>TCF7L1;HDAC10;PAX3;FGFR2</i>
Wnt signaling pathway and pluripotency	4/102	0.026	0.183	3.7	13.7	<i>TCF7L1;FZD4;LRRK2;PRKCQ</i>
ESC Pluripotency Pathways	5/116	0.009	0.133	4.1	19.5	<i>PDGFRA;FZD4;FGF23;FGFR2;SMAD7</i>
22q11.2 copy number variation syndrome	5/131	0.015	0.158	3.6	15.4	<i>FOXC1;PAX3;PITX2;CLDN1;FGFR2</i>

TGF-beta Signaling Pathway	5/132	0.015	0.158	3.6	15.1	<i>CCNB2;SMURF2;TNC;SPTBN1;SMAD7</i>
Mesodermal commitment pathway	5/147	0.023	0.183	3.2	12.2	<i>FOXC1;TCF7L1;MEIS1;FZD4;PITX2</i> <i>PDGFRA;LAMA5;LAMA2;ACTN1;LAMA3;T</i>
Focal Adhesion	7/198	0.006	0.101	3.4	17.2	<i>NC;ARHGAP5</i> <i>DUSP4;CACNB1;PTPRR;LRRK2;RAPGEF2;F</i>
MAPK Signaling Pathway	8/246	0.006	0.101	3.1	16.0	<i>GF23;DUSP6;FGFR2</i> <i>PDGFRA;LAMA5;CDK6;LAMA2;LAMA3;TN</i>
PI3K-Akt signaling pathway	8/340	0.034	0.224	2.2	7.5	<i>C;FGF23;FGFR2</i>

Note. The full enrichment analysis for genes shared between fish early domesticates and human groups with schizophrenia can be accessed here: <https://maayanlab.cloud/Enrichr/enrich?dataset=c68dc00d311e361026f7339bd11b73e8>

Table S5. Enrichment of Wikipathways associated with genes shared between early fish domesticates and human groups with Williams syndrome

Wikipathways	Overlap	<i>p</i> -value	Adjusted <i>p</i> -value	Odds Ratio	Combined Score	Genes
Ectoderm Differentiation	9/138	1.95E-05	0.003	6.62	71.86	<i>TCF7L1;HDAC10;FZD4;BOC;HESX1;PAX3;DMD;KI FC3;FGFR2</i>
Neural Crest Differentiation	7/101	1.13E-04	0.009	7.02	63.74	<i>TCF7L1;HDAC10;CDH2;PAX3;HES1;AXIN2;FGFR2</i>
Laminopathies on Wnt signaling	4/35	5.33E-04	0.029	12.02	90.62	<i>TCF7L1;ICMT;CDK6;HES1</i>
Mesodermal commitment pathway	7/147	0.001	0.034	4.70	31.99	<i>FOXC1;TCF7L1;MEIS1;FZD4;AXIN2;PITX2;TOX</i>
Arrhythmogenic Cardiomyopathy	5/74	0.001	0.034	6.77	45.34	<i>TCF7L1;CDH2;LAMA2;ACTN1;DMD</i>
BMP Signaling in Eyelid Development	3/20	0.001	0.034	16.38	109.65	<i>FOXC1;PITX2;FGFR2</i>
White fat cell differentiation	3/32	0.005	0.079	9.59	51.04	<i>TCF7L1;MECOM;ZNF423</i>
Hair Follicle Development	3/32	0.005	0.079	9.59	51.04	<i>LAMA5;PDGFRA;FGFR2</i>

Note. The full enrichment analysis for genes shared between fish early domesticates and human groups with Williams syndrome can be accessed here: <https://maayanlab.cloud/Enrichr/enrich?dataset=b83024a0aa8fe2ff6492cb468c1d4ec0>

Table S6. Enrichment of Wikipathways associated with genes shared between early fish domesticates and human groups with autism spectrum disorders

Wikipathways	Overlap	<i>p</i> -value	Adjusted <i>p</i> -value	Odds Ratio	Combined Score	Genes
Ectoderm Differentiation	7/138	1.15E-04	0.012	6.98	63.29	TFAP2A;BOC;HESX1;DMD;KIFC3;FGFR2;GLI3
Alpha 6 Beta 4 signaling pathway	4/33	1.28E-04	0.012	17.75	159.02	LAMA5;LAMA2;LAMA3;PIK3R1
Metastatic brain tumor	2/6	9.11E-04	0.046	63.58	445.14	CDK6;PIK3R1
Small cell lung cancer	5/96	9.90E-04	0.046	7.09	49.07	LAMA5;CDK6;LAMA2;LAMA3;PIK3R1
Neural Crest Differentiation	5/101	0.001	0.046	6.72	44.97	TFAP2A;TFAP2B;CDH2;AXIN2;FGFR2
Hair Follicle Development	3/32	0.002	0.063	13.22	81.99	LAMA5;PDGFRA;FGFR2
Arrhythmogenic Cardiomyopathy	4/74	0.003	0.074	7.34	43.10	CDH2;LAMA2;ACTN1;DMD
Glioblastoma signaling pathways	4/82	0.004	0.093	6.58	36.23	PDGFRA;CDK6;PIK3R1;FGFR2
Focal Adhesion	6/198	0.005	0.093	4.04	21.45	PDGFRA;LAMA5;LAMA2;ACTN1;LAMA3;PIK3R1
Hedgehog Signaling Pathway	3/44	0.005	0.093	9.35	49.43	SMURF2;BOC;GLI3
Pathways Regulating Hippo Signaling	4/98	0.008	0.128	5.46	26.61	PDGFRA;CDH2;PRKAR1B;FGFR2
Endometrial cancer	3/63	0.014	0.166	6.38	27.43	AXIN2;PIK3R1;FGFR2
GDNF/RET signaling axis	2/23	0.014	0.166	12.10	51.59	HSPB11;GLI3
Endochondral Ossification with Skeletal Dysplasias	3/64	0.014	0.166	6.28	26.71	RUNX3;GLI3;BMP6
Endochondral Ossification	3/64	0.014	0.166	6.28	26.71	RUNX3;GLI3;BMP6
Hippo-Merlin Signaling Dysregulation	4/120	0.015	0.166	4.42	18.50	PDGFRA;CDH2;PRKAR1B;FGFR2
Angiogenesis	2/24	0.015	0.166	11.55	48.30	PDGFRA;FGFR2
PI3K-Akt signaling pathway	7/340	0.019	0.186	2.72	10.82	PDGFRA;LAMA5;CDK6;LAMA2;LAMA3;PIK3R1;FGFR2
Primary focal segmental glomerulosclerosis	3/72	0.019	0.186	5.55	21.87	LAMA5;CDH2;AGRN
Head and Neck Squamous Cell Carcinoma	3/73	0.020	0.186	5.47	21.36	CDK6;PIK3R1;FGFR2
Tumor suppressor activity of SMARCB1	2/31	0.025	0.219	8.76	32.37	CDK6;GLI3
EGFR Tyrosine Kinase Inhibitor Resistance	3/84	0.029	0.241	4.72	16.73	PDGFRA;PIK3R1;FGFR2
Acute viral myocarditis	3/86	0.031	0.241	4.61	16.04	LAMA2;DMD;PIK3R1

Regulation of Actin Cytoskeleton	4/150	0.031	0.241	3.50	12.14	<i>PDGFRA;ACTN1;PIK3R1;FGFR2</i> <i>PDGFRA;LAMA5;LAMA2;LAMA3;PIK3R1;F</i>
Focal Adhesion-PI3K-Akt-mTOR-signaling	6/303	0.034	0.242	2.60	8.82	<i>GFR2</i>
Breast cancer pathway	4/154	0.034	0.242	3.41	11.53	<i>CDK6;PIK3R1;AXIN2;ESR1</i>
Regulation of GABA neurotransmission	2/38	0.036	0.248	7.05	23.41	<i>PIK3R1;GABRD</i>
LncRNA involvement in Wnt signaling	3/94	0.038	0.254	4.20	13.68	<i>TFAP2A;CDK6;AXIN2</i>
Splicing factor NOVA regulated synaptic proteins	2/42	0.043	0.277	6.35	19.90	<i>CDH2;AGRN</i>
Genes controlling nephrogenesis	2/43	0.045	0.280	6.19	19.15	<i>GLI3;FGFR2</i>

Note. The full enrichment analysis for genes shared between fish early domesticates and human groups with autism spectrum disorders can be accessed here:

<https://maayanlab.cloud/Enrichr/enrich?dataset=c5b8b850d070c8fa90b809675170affd>

Table S7. Enrichment of Gene Ontology (GO) Biological Process (BP) terms associated with genes shared between early fish domesticates and human groups with schizophrenia

Biological process GO	ID	Overlap	<i>p</i> -value	Adjusted <i>p</i> -value	Odds Ratio	Combined Score	Genes
extracellular structure organization	GO:0043062	12/216	4.89E-06	0.003	5.6	68.0	ADAMTS5;LAMA5;LAMA2;ADAMTS1;ADAMTS18;ADAMTS17;ADAMTSL2;LAMA3;TNC;AGRN;ADAMTS9;ADAMTS6
external encapsulating structure organization	GO:0045229	12/217	5.13E-06	0.003	5.5	67.4	ADAMTS5;LAMA5;LAMA2;ADAMTS1;ADAMTS18;ADAMTS17;ADAMTSL2;LAMA3;TNC;AGRN;ADAMTS9;ADAMTS6
extracellular matrix organization	GO:0030198	12/300	1.23E-04	0.034	3.9	35.3	ADAMTS5;LAMA5;LAMA2;ADAMTS1;ADAMTS18;ADAMTS17;ADAMTSL2;LAMA3;TNC;AGRN;ADAMTS9;ADAMTS6
neuromuscular junction development	GO:0007528	4/24	1.25E-04	0.034	18.4	165.2	CACNB1;MUSK;LRRK2;AGRNPSMB7;PDGFRA;PSMB4;DLG3;LRRK2;RAPGEF2;PRKCQ;FGF23;SPTBN1;DUSP6;FGFR2;PTPN3
MAPK cascade	GO:0000165	12/303	1.35E-04	0.034	3.9	34.6	LAMA5;LAMA3;TBX18;FGFR2
morphogenesis of an epithelium	GO:0002009	4/30	3.07E-04	0.064	14.1	114.4	LRRK2;SMAD7;PTPN3
regulation of membrane depolarization	GO:0003254	3/18	9.36E-04	0.160	18.3	127.6	TBC1D2;ATP8B1;TBC1D8;TBC1D22A;TBC1D22B
regulation of plasma membrane bounded cell projection assembly	GO:0120032	5/70	0.001	0.160	7.1	48.8	LRRK2;FGFR2
regulation of morphogenesis of a branching structure	GO:0060688	2/5	0.001	0.162	60.8	410.3	DUSP4;PTPRR;DUSP26;DUSP6
negative regulation of ERK1 and ERK2 cascade	GO:0070373	4/50	0.002	0.212	8.0	48.9	PDGFRA;ESR1;FGFR2
positive regulation of phospholipase activity	GO:0010518	3/24	0.002	0.212	13.1	79.9	CDK6;BMP6
glandular epithelial cell development	GO:0002068	2/7	0.002	0.212	36.5	219.6	

type B pancreatic cell development	GO:0003323	2/7	0.002	0.212	36.5	219.6	<i>CDK6;BMP6</i>
ventricular cardiac muscle tissue development	GO:0003229	3/25	0.002	0.212	12.5	74.8	<i>ADAMTS9;FGFR2;SMAD7</i> <i>RABGAP1L;TBC1D2;TBC1D8;RAP</i> <i>GEF2;ARAP1;AGRN;TBC1D22A;TB</i> <i>C1D22B</i>
positive regulation of GTPase activity	GO:0043547	8/214	0.003	0.212	3.6	21.5	<i>C1D22B</i>
regulation of anion transport	GO:0044070	2/8	0.003	0.225	30.4	174.5	<i>ATP8B1;FGF23</i>
forebrain neuron development	GO:0021884	2/8	0.003	0.225	30.4	174.5	<i>RAPGEF2;FGFR2</i>
receptor clustering	GO:0043113	3/28	0.003	0.225	11.0	62.2	<i>MUSK;DLG3;AGRN</i>
eye development	GO:0001654	4/58	0.004	0.225	6.8	38.0	<i>FOXC1;MEIS1;ADAMTS18;PITX2</i>
neuronal ion channel clustering	GO:0045161	2/9	0.004	0.225	26.0	143.2	<i>KCNIP2;AGRN</i>
embryonic digestive tract morphogenesis	GO:0048557	2/9	0.004	0.225	26.0	143.2	<i>PDGFRA;FGFR2</i>
type B pancreatic cell differentiation	GO:0003309	2/9	0.004	0.225	26.0	143.2	<i>CDK6;BMP6</i>
maintenance of blood-brain barrier	GO:0035633	3/30	0.004	0.225	10.2	55.5	<i>LAMA2;DMD;CLDN1</i> <i>DUSP4;PTPRR;EYA2;DUSP26;DUS</i> <i>P6;PTPN3</i>
protein dephosphorylation	GO:0006470	6/139	0.004	0.225	4.2	22.7	<i>P6;PTPN3</i>
embryonic skeletal system morphogenesis	GO:0048704	3/31	0.005	0.232	9.8	52.6	<i>PDGFRA;FGFR2;HOXA4</i>
regulation of T-helper 17 type immune response	GO:2000316	2/10	0.005	0.244	22.8	120.4	<i>PRKCQ;SMAD7</i> <i>TBC1D2;TBC1D8;TBC1D22A;TBC1</i> <i>D22B</i> <i>RABGAP1L;TBC1D2;TBC1D8;TBC1</i> <i>D22A;TBC1D22B</i>
regulation of cilium assembly	GO:1902017	4/64	0.005	0.247	6.1	32.0	<i>D22B</i> <i>RABGAP1L;TBC1D2;TBC1D8;TBC1</i> <i>D22A;TBC1D22B</i>
activation of GTPase activity	GO:0090630	5/105	0.006	0.256	4.6	23.5	<i>D22A;TBC1D22B</i>
cell-substrate junction assembly	GO:0007044	3/34	0.006	0.256	8.8	45.2	<i>ACTN1;LAMA3;SORBS1</i>
positive regulation of alcohol biosynthetic process	GO:1902932	2/11	0.006	0.256	20.2	103.1	<i>SCAP;BMP6</i>
morphogenesis of a polarized epithelium	GO:0001738	2/12	0.007	0.295	18.2	89.6	<i>LAMA5;LAMA3</i> <i>TCF7L1;LRRK2;ESR1;CXXC4;FGFR</i>
regulation of Wnt signaling pathway	GO:0030111	5/111	0.008	0.295	4.3	21.2	<i>2</i>

negative regulation of epithelial cell proliferation	GO:0050680	4/72	0.008	0.305	5.4	26.0	<i>CDK6;RUNX3;XDH;FGFR2</i>
							<i>PDGFRA;MUSK;AGAP2;RAPGEF2;</i>
positive regulation of kinase activity	GO:0033674	5/114	0.008	0.310	4.2	20.1	<i>FGFR2</i>
odontogenesis	GO:0042476	3/39	0.009	0.317	7.6	36.0	<i>FOXC1;PITX2;FGFR2</i>
regulation of sodium ion transmembrane transporter activity	GO:2000649	3/40	0.009	0.326	7.4	34.5	<i>NETO1;DMD;PTPN3</i>
regulation of vasculogenesis	GO:2001212	2/14	0.010	0.326	15.2	70.0	<i>RAPGEF2;XDH</i>
							<i>TBC1D2;TBC1D8;TBC1D22A;TBC1</i>
regulation of organelle assembly	GO:1902115	4/77	0.010	0.326	5.0	23.1	<i>D22B</i>
visual system development	GO:0150063	3/41	0.010	0.326	7.2	33.1	<i>FOXC1;MEIS1;ADAMTS18</i>
skeletal system morphogenesis	GO:0048705	3/42	0.011	0.337	7.0	31.8	<i>PDGFRA;FGFR2;HOXA4</i>
regulation of phospholipase C activity	GO:1900274	2/15	0.011	0.337	14.0	62.7	<i>PDGFRA;ESR1</i>
embryonic cranial skeleton morphogenesis	GO:0048701	2/15	0.011	0.337	14.0	62.7	<i>PDGFRA;FGFR2</i>
negative regulation of cell cycle	GO:0045786	4/80	0.012	0.337	4.8	21.5	<i>FOXC1;CDK6;RUNX3;PTPN3</i>
embryonic organ morphogenesis	GO:0048562	3/44	0.012	0.342	6.7	29.4	<i>PDGFRA;FGFR2;HOXA4</i>
negative regulation of platelet activation	GO:0010544	2/16	0.013	0.342	13.0	56.6	<i>PDGFRA;ADAMTS18</i>
regulation of monocyte differentiation	GO:0045655	2/16	0.013	0.342	13.0	56.6	<i>CDK6;HOXA7</i>
digestive tract morphogenesis	GO:0048546	2/16	0.013	0.342	13.0	56.6	<i>PDGFRA;FGFR2</i>
regulation of osteoblast differentiation	GO:0045667	4/83	0.013	0.342	4.6	20.1	<i>CDK6;FGF23;BMP6;FGFR2</i>
Wnt signaling pathway, planar cell polarity pathway	GO:0060071	4/85	0.014	0.350	4.5	19.2	<i>PSMB7;PSMB4;SMURF2;FZD4</i>
positive regulation of canonical Wnt signaling pathway	GO:0090263	5/130	0.014	0.350	3.7	15.6	<i>PSMB7;PSMB4;SMURF2;LRRK2;F</i>
							<i>GFR2</i>
mesonephric tubule development	GO:0072164	2/17	0.015	0.350	12.1	51.4	<i>FOXC1;FGFR2</i>
vasculature development	GO:0001944	2/17	0.015	0.350	12.1	51.4	<i>PDGFRA;SOX18</i>
regulation of establishment of planar polarity	GO:0090175	4/88	0.016	0.363	4.4	18.1	<i>PSMB7;PSMB4;SMURF2;FZD4</i>

regulation of ERK1 and ERK2 cascade	GO:0070372	7/238	0.016	0.363	2.8	11.5	<i>DUSP4;PDGFRA;PTPRR;RAPGEF2;DUSP26;DUSP6;FGFR2</i>
regulation of platelet aggregation	GO:0090330	2/18	0.016	0.363	11.4	46.9	<i>ADAMTS18;PRKCQ</i>
embryonic heart tube development	GO:0035050	2/18	0.016	0.363	11.4	46.9	<i>SOX18;PITX2</i>
regulation of cation channel activity	GO:2001257	4/89	0.017	0.363	4.3	17.7	<i>CACNB1;NETO1;DLG3;DMD;EFNB1;LAMA5;LAMA2;LAMA3;PRKCQ;SPTBN1;FGFR2</i>
axonogenesis	GO:0007409	7/240	0.017	0.363	2.8	11.3	<i>EHD4;C9;ADCY8;CLDN1</i>
protein complex oligomerization	GO:0051259	4/90	0.017	0.363	4.3	17.3	
regulation of cellular component movement	GO:0051270	3/50	0.017	0.363	5.8	23.6	<i>CDK6;ACTN1;ARAP1</i>
ureteric bud development	GO:0001657	2/19	0.018	0.367	10.7	43.0	<i>FOXC1;FGFR2</i>
mesenchymal cell differentiation	GO:0048762	3/51	0.018	0.367	5.7	22.8	<i>FOXC1;FBXL17;FGFR2</i>
Wnt signaling pathway	GO:0016055	4/92	0.018	0.367	4.2	16.6	<i>TCF7L1;FZD4;LRRK2;STRN</i>
regulation of epithelial cell proliferation	GO:0050678	4/93	0.019	0.374	4.1	16.3	<i>CDK6;RUNX3;BMP6;FGFR2</i>
negative regulation of MAPK cascade	GO:0043409	4/94	0.020	0.378	4.1	16.0	<i>DUSP4;PTPRR;DUSP26;DUSP6</i>
embryonic digestive tract development	GO:0048566	2/20	0.020	0.378	10.1	39.6	<i>PDGFRA;FGFR2</i>
negative regulation of peptidyl-serine phosphorylation	GO:0033137	2/21	0.022	0.382	9.6	36.6	<i>DMD;SMAD7</i>
focal adhesion assembly	GO:0048041	2/21	0.022	0.382	9.6	36.6	<i>ACTN1;SORBS1</i>
sensory organ development	GO:0007423	3/56	0.023	0.382	5.2	19.4	<i>FOXC1;MEIS1;ADAMTS18</i>
negative regulation of myeloid cell differentiation	GO:0045638	2/22	0.024	0.382	9.1	34.0	<i>MEIS1;CDK6</i>
peptidyl-threonine dephosphorylation	GO:0035970	2/22	0.024	0.382	9.1	34.0	<i>DUSP4;DUSP6</i>
regulation of platelet activation	GO:0010543	2/22	0.024	0.382	9.1	34.0	<i>PDGFRA;PRKCQ</i>
regulation of voltage-gated calcium channel activity	GO:1901385	2/22	0.024	0.382	9.1	34.0	<i>CACNB1;DMD</i>
proteasomal ubiquitin-independent protein catabolic process	GO:0010499	2/22	0.024	0.382	9.1	34.0	<i>PSMB7;PSMB4</i>

axon guidance	GO:0007411	6/203	0.025	0.382	2.8	10.4	<i>EFNB1;LAMA5;LAMA2;LAMA3;PRKCQ;SPTBN1</i>
regulation of pathway-restricted SMAD protein phosphorylation	GO:0060393	3/58	0.026	0.382	5.0	18.2	<i>BMP6;BMP15;SMAD7</i>
regulation of protein kinase B signaling	GO:0051896	6/207	0.027	0.382	2.7	9.9	<i>PDGFRA;STRN;XDH;FGF23;ESR1;FGFR2</i>
dephosphorylation	GO:0016311	5/153	0.027	0.382	3.1	11.2	<i>DUSP4;PTPRR;DUSP26;DUSP6;PTPN3</i>
positive regulation of Wnt signaling pathway	GO:0030177	5/153	0.027	0.382	3.1	11.2	<i>PSMB7;PSMB4;SMURF2;LRRK2;FGFR2</i>
response to organic cyclic compound	GO:0014070	3/60	0.028	0.382	4.8	17.2	<i>LRRK2;ESR1;STRN3</i>
regulation of cellular response to transforming growth factor beta stimulus	GO:1903844	2/24	0.028	0.382	8.3	29.6	<i>SMURF2;SMAD7</i>
inner ear morphogenesis	GO:0042472	2/24	0.028	0.382	8.3	29.6	<i>TBX18;FGFR2</i>
lipid translocation	GO:0034204	2/24	0.028	0.382	8.3	29.6	<i>ATP8B1;ATP11A</i>
regulation of cell differentiation	GO:0045595	5/156	0.029	0.382	3.0	10.8	<i>ZFHX3;CDK6;RUNX3;FGFR2;SMA</i>
in utero embryonic development	GO:0001701	2/25	0.030	0.382	7.9	27.7	<i>D7</i>
negative regulation of transcription, DNA-templated	GO:0045892	17/948	0.032	0.382	1.7	5.9	<i>PTPRR;FGFR2</i>
positive regulation of protein kinase B signaling	GO:0051897	5/161	0.032	0.382	2.9	10.1	<i>FOXC1;ZFHX3;L3MBTL2;HDAC10;SMURF2;ATP8B1;DUSP26;RUNX3;ESR1;BMP6;SMAD7;SOX18;PAX9;HESX1;HOXA7;FGFR2;SAMD11</i>
endothelial cell development	GO:0001885	2/26	0.033	0.382	7.6	26.0	<i>PDGFRA;STRN;FGF23;ESR1;FGFR2</i>
positive regulation of filopodium assembly	GO:0051491	2/26	0.033	0.382	7.6	26.0	<i>SOX18;RAPGEF2</i>
transmembrane receptor protein tyrosine kinase signaling pathway	GO:0007169	9/404	0.034	0.382	2.1	7.1	<i>ARAP1;AGRN</i>
BMP signaling pathway	GO:0030509	3/65	0.034	0.382	4.4	14.9	<i>PDGFRA;EFNB1;FOXC1;TIA1;MUSK;RAPGEF2;SORBS1;FGF23;FGFR</i>
positive regulation of fibroblast proliferation	GO:0048146	2/28	0.037	0.382	7.0	23.0	<i>BMP6;BMP15;SMAD7</i>
							<i>PDGFRA;CDK6</i>

positive regulation of phosphatidylinositol 3-kinase activity	GO:0043552	2/28	0.037	0.382	7.0	23.0	<i>PDGFRA;AGAP2</i>
canonical Wnt signaling pathway	GO:0060070	3/68	0.039	0.382	4.2	13.7	<i>TCF7L1;FZD4;LRRK2</i>
negative regulation of transforming growth factor beta receptor signaling pathway	GO:0030512	3/68	0.039	0.382	4.2	13.7	<i>SMURF2;ADAMTSL2;SMAD7</i>
regulation of myeloid cell differentiation	GO:0045637	3/68	0.039	0.382	4.2	13.7	<i>MEIS1;CDK6;PRKCQ</i> <i>FOXC1;ZFHX3;HDAC10;SMURF2;DUSP26;RUNX3;ESR1;BMP6;SMA</i> <i>D7;SOX18;HESX1;HOXA7;FGFR2</i>
negative regulation of transcription by RNA polymerase II	GO:0000122	13/684	0.039	0.382	1.8	5.8	<i>D7;SOX18;HESX1;HOXA7;FGFR2</i>
regulation of calcium ion transmembrane transporter activity	GO:1901019	2/29	0.040	0.382	6.7	21.7	<i>CACNB1;DMD</i>
negative regulation of myeloid leukocyte differentiation	GO:0002762	2/29	0.040	0.382	6.7	21.7	<i>CDK6;HOXA7</i>
establishment of endothelial barrier	GO:0061028	2/29	0.040	0.382	6.7	21.7	<i>SOX18;RAPGEF2</i>
artery morphogenesis	GO:0048844	2/30	0.042	0.382	6.5	20.5	<i>ADAMTS9;SMAD7</i>
cardiac muscle cell action potential	GO:0086001	2/30	0.042	0.382	6.5	20.5	<i>KCNIP2;DMD</i>
regulation of striated muscle contraction	GO:0006942	2/30	0.042	0.382	6.5	20.5	<i>DMD;SMAD7</i>
cellular response to BMP stimulus	GO:0071773	3/71	0.043	0.382	4.0	12.7	<i>BMP6;BMP15;SMAD7</i>
regulation of hematopoietic stem cell differentiation	GO:1902036	3/71	0.043	0.382	4.0	12.7	<i>PSMB7;FOXC1;PSMB4</i>
cell morphogenesis involved in differentiation	GO:0000904	3/72	0.045	0.382	4.0	12.3	<i>ATRN;LAMA5;ACTN1</i>
negative regulation of osteoblast differentiation	GO:0045668	2/31	0.045	0.382	6.3	19.5	<i>CDK6;FGF23</i>
phospholipid translocation	GO:0045332	2/31	0.045	0.382	6.3	19.5	<i>ATP8B1;ATP11A</i>
regulation of transmembrane receptor protein serine/threonine kinase signaling pathway	GO:0090092	2/31	0.045	0.382	6.3	19.5	<i>SMURF2;SMAD7</i>
non-canonical Wnt signaling pathway	GO:0035567	4/124	0.048	0.382	3.0	9.3	<i>PSMB7;PSMB4;SMURF2;FZD4</i>

cardiac muscle tissue morphogenesis	GO:0055008	2/32	0.048	0.382	6.1	18.5	<i>FGFR2;SMAD7</i>
regulation of intracellular estrogen receptor signaling pathway	GO:0033146	2/32	0.048	0.382	6.1	18.5	<i>ESR1;STRN3</i>
metal ion export	GO:0070839	2/32	0.048	0.382	6.1	18.5	<i>ATP7B;KCNIP2</i>
regulation of hematopoietic progenitor cell differentiation	GO:1901532	3/75	0.049	0.382	3.8	11.4	<i>PSMB7;FOXC1;PSMB4</i>
fibroblast growth factor receptor signaling pathway	GO:0008543	3/75	0.049	0.382	3.8	11.4	<i>TIA1;FGF23;FGFR2</i>
regulation of transcription from RNA polymerase II promoter in response to hypoxia	GO:0061418	3/75	0.049	0.382	3.8	11.4	<i>PSMB7;PSMB4;EGLN3</i>
integrin-mediated signaling pathway	GO:0007229	3/75	0.049	0.382	3.8	11.4	<i>LAMA5;ADAMTS1;LAMA3</i>
synapse organization	GO:0050808	4/126	0.050	0.382	3.0	9.0	<i>CACNB1;MUSK;LRRK2;AGRN</i>

Note. The full enrichment analysis for genes shared between fish early domesticates and human groups with schizophrenia can be accessed here: <https://maayanlab.cloud/Enrichr/enrich?dataset=c68dc00d311e361026f7339bd11b73e8>

Table S8. Enrichment of Gene Ontology (GO) Biological Process (BP) terms associated with genes shared between early fish domesticates and human groups with Williams syndrome

Biological process GO	ID	Overlap	<i>p</i> -value	Adjusted <i>p</i> -value	Odds Ratio	Combined Score	Genes
extracellular structure organization	GO:0043062	12/216	4.25E-06	0.003	5.6	69.8	ADAMTS5;LAMA5;LAMA2;ADAMTS1;ADAMTS18;ADAMTS17;ADAMTSL2;LAMA3;TNC;AGRN;ADAMTS9;ADAMTS6
external encapsulating structure organization	GO:0045229	12/217	4.45E-06	0.003	5.6	69.2	ADAMTS5;LAMA5;LAMA2;ADAMTS1;ADAMTS18;ADAMTS17;ADAMTSL2;LAMA3;TNC;AGRN;ADAMTS9;ADAMTS6
extracellular matrix organization	GO:0030198	13/300	2.46E-05	0.011	4.4	46.2	LAMA5;LAMA2;LAMA3;TNC;ADAMTS5;P4HA2;ADAMTS1;ADAMTS18;ADAMTS17;ADAMTSL2;AGRN;ADAMTS9;ADAMTS6
glandular epithelial cell development	GO:0002068	3/7	4.21E-05	0.011	69.6	701.7	CDK6;CDH2;BMP6
type B pancreatic cell development	GO:0003323	3/7	4.21E-05	0.011	69.6	701.7	CDK6;CDH2;BMP6
type B pancreatic cell differentiation	GO:0003309	3/9	9.95E-05	0.022	46.4	427.9	CDK6;CDH2;BMP6
neuromuscular junction development	GO:0007528	4/24	1.19E-04	0.022	18.6	168.5	MUSK;LRRK2;LRP4;AGRN
receptor clustering	GO:0043113	4/28	2.21E-04	0.036	15.5	130.8	MUSK;DLG3;LRP4;AGRN
morphogenesis of an epithelium	GO:0002009	4/30	2.91E-04	0.043	14.3	116.7	LAMA5;LAMA3;TBX18;FGFR2
negative regulation of multicellular organismal process	GO:0051241	9/214	5.49E-04	0.071	4.2	31.2	ADAMTS5;PTPRR;NFIB;LRP4;HOXA7;IL17D;ZNF423;N4BP1;TBX18
anterior/posterior pattern specification	GO:0009952	5/63	5.93E-04	0.071	8.1	59.9	HES6;BHLHE41;HES1;HOXA7;HOXA4
gliogenesis	GO:0042063	3/17	7.55E-04	0.082	19.9	143.0	CDK6;CDH2;NFIB
odontogenesis	GO:0042476	4/39	8.09E-04	0.082	10.6	75.8	FOXC1;AXIN2;PITX2;FGFR2
regulation of morphogenesis of a branching structure	GO:0060688	2/5	0.001	0.107	61.6	417.8	LRRK2;FGFR2
embryonic organ morphogenesis	GO:0048562	4/44	0.001	0.113	9.3	62.0	PDGFRA;HES1;FGFR2;HOXA4

positive regulation of kinase activity	GO:0033674	6/114	0.001	0.124	5.2	33.8	<i>PDGFRA;MUSK;AGAP2;SPDYA;RAPGEF2;FGFR2</i>
MAPK cascade	GO:0000165	10/303	0.002	0.136	3.2	20.5	<i>PDGFRA;ICMT;DLG3;LRRK2;RAPGEF2;FGF23;SPTBN1;DUSP6;FGFR2;PTPN3</i>
negative regulation of ERK1 and ERK2 cascade	GO:0070373	4/50	0.002	0.146	8.1	50.1	<i>DUSP4;PTPRR;DUSP26;DUSP6</i>
endosome to lysosome transport via multivesicular body sorting pathway	GO:0032510	2/7	0.002	0.146	37.0	223.8	<i>VPS4B;LYST</i>
positive regulation of synaptic plasticity	GO:0031915	2/7	0.002	0.146	37.0	223.8	<i>ADCY8;CPLX2</i>
protein localization to cytoplasmic stress granule	GO:1903608	2/7	0.002	0.146	37.0	223.8	<i>TIA1;DHX9</i>
positive regulation of protein phosphorylation	GO:0001934	11/371	0.002	0.146	2.9	17.4	<i>MARCO;MUSK;LRRK2;AGAP2;SPDYA;RAPGEF2;HCLS1;AXIN2;FGF23;BMP6;BMP15</i>
positive regulation of binding	GO:0051099	5/90	0.003	0.158	5.5	32.0	<i>FOXC1;DHX9;LRRK2;RAPGEF2;HES1</i>
regulation of anion transport	GO:0044070	2/8	0.003	0.158	30.8	177.8	<i>ATP8B1;FGF23</i>
peptidyl-proline hydroxylation to 4-hydroxy-L-proline	GO:0018401	2/8	0.003	0.158	30.8	177.8	<i>P4HA2;P4HTM</i>
forebrain neuron development	GO:0021884	2/8	0.003	0.158	30.8	177.8	<i>RAPGEF2;FGFR2</i>
positive regulation of fibroblast proliferation	GO:0048146	3/28	0.003	0.162	11.1	63.5	<i>PDGFRA;CDK6;DHX9</i>
hemopoiesis	GO:0030097	5/94	0.004	0.162	5.2	29.6	<i>MEIS1;MECOM;TOX;RUNX3;FGFR2</i>
eye development	GO:0001654	4/58	0.004	0.162	6.9	38.9	<i>FOXC1;MEIS1;ADAMTS18;PITX2</i>
embryonic digestive tract morphogenesis	GO:0048557	2/9	0.004	0.172	26.4	146.0	<i>PDGFRA;FGFR2</i>
protein dephosphorylation	GO:0006470	6/139	0.004	0.172	4.2	23.3	<i>DUSP4;PTPRR;SBF1;DUSP26;DUSP6;PTPN3</i>
regulation of ERK1 and ERK2 cascade	GO:0070372	8/238	0.004	0.179	3.3	17.7	<i>DUSP4;MARCO;PDGFRA;PTPRR;RAPGEF2;DUSP26;DUSP6;FGFR2</i>
embryonic skeletal system morphogenesis	GO:0048704	3/31	0.004	0.179	9.9	53.8	<i>PDGFRA;FGFR2;HOXA4</i>

negative regulation of nucleic acid-templated transcription	GO:1903507	12/464	0.005	0.184	2.5	13.5	<i>L3MBTL2;HDAC10;MECOM;SMURF2;ATP8B1;PAX9;BHLHE41;HES1;HOXA7;ZNF423;NPAS1;SAMD11</i>
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Note. The full enrichment analysis for genes shared between fish early domesticates and human groups with Williams syndrome can be accessed here: <https://maayanlab.cloud/Enrichr/enrich?dataset=b83024a0aa8fe2ff6492cb468c1d4ec0>

Table S9. Enrichment of Gene Ontology (GO) Biological Process (BP) terms associated with genes shared between early fish domesticates and human groups with autism spectrum disorders

Biological process GO	ID	Overlap	<i>p</i> -value	Adjusted <i>p</i> -value	Odds Ratio	Combined Score	Genes
							<i>TFAP2A;TFAP2B;LRP4;SULF1;HSP</i>
renal system development	GO:0072001	6/57	5.75E-06	0.005	15.3	184.8	<i>B11;TBX18</i>
glandular epithelial cell development	GO:0002068	3/7	1.65E-05	0.005	96.0	1056.8	<i>CDK6;CDH2;BMP6</i>
type B pancreatic cell development	GO:0003323	3/7	1.65E-05	0.005	96.0	1056.8	<i>CDK6;CDH2;BMP6</i>
type B pancreatic cell differentiation	GO:0003309	3/9	3.92E-05	0.009	64.0	649.2	<i>CDK6;CDH2;BMP6</i>
morphogenesis of an epithelium	GO:0002009	4/30	8.75E-05	0.017	19.8	185.0	<i>LAMA5;LAMA3;TBX18;FGFR2</i>
embryonic cranial skeleton morphogenesis	GO:0048701	3/15	2.05E-04	0.029	32.0	271.6	<i>TFAP2A;PDGFRA;FGFR2</i>
							<i>TFAP2A;TFAP2B;LRP4;SULF1;HSP</i>
kidney development	GO:0001822	5/70	2.31E-04	0.029	9.9	83.3	<i>B11</i>
							<i>TFAP2A;TFAP2B;SLC6A6;ZFHX3;C</i>
regulation of cell differentiation	GO:0045595	7/156	2.45E-04	0.029	6.1	50.9	<i>DK6;RUNX3;FGFR2</i>
regulation of filopodium assembly	GO:0051489	4/41	3.02E-04	0.032	13.9	112.7	<i>MYO10;PIK3R1;ARAP1;AGRN</i>
embryonic digestive tract development	GO:0048566	3/20	5.00E-04	0.048	22.6	171.6	<i>PDGFRA;GLI3;FGFR2</i>
neuromuscular junction development	GO:0007528	3/24	8.67E-04	0.058	18.3	128.8	<i>MUSK;LRP4;AGRN</i>
inner ear morphogenesis	GO:0042472	3/24	8.67E-04	0.058	18.3	128.8	<i>TFAP2A;TBX18;FGFR2</i>
positive regulation of phospholipase activity	GO:0010518	3/24	8.67E-04	0.058	18.3	128.8	<i>PDGFRA;ESR1;FGFR2</i>
cellular response to iron ion	GO:0071281	2/6	9.11E-04	0.058	63.6	445.1	<i>TFAP2A;BMP6</i>
positive regulation of hemoglobin biosynthetic process	GO:0046985	2/6	9.11E-04	0.058	63.6	445.1	<i>ABCB10;SLC6A9</i>
positive regulation of filopodium assembly	GO:0051491	3/26	0.001	0.066	16.7	113.6	<i>PIK3R1;ARAP1;AGRN</i>
regulation of hemoglobin biosynthetic process	GO:0046984	2/7	0.001	0.067	50.9	339.2	<i>ABCB10;SLC6A9</i>
sinoatrial node development	GO:0003163	2/7	0.001	0.067	50.9	339.2	<i>TBX18;CACNA1G</i>

receptor clustering	GO:0043113	3/28	0.001	0.069	15.3	101.1	<i>MUSK;LRP4;AGRN</i>
peptidyl-proline hydroxylation to 4-hydroxy-L-proline	GO:0018401	2/8	0.002	0.077	42.4	270.7	<i>P4HA2;P4HTM</i>
negative regulation of alpha-beta T cell differentiation	GO:0046639	2/8	0.002	0.077	42.4	270.7	<i>RUNX3;GLI3</i>
embryonic skeletal system morphogenesis	GO:0048704	3/31	0.002	0.077	13.7	86.2	<i>TFAP2A;PDGFRA;FGFR2</i>
renal water homeostasis	GO:0003091	3/31	0.002	0.077	13.7	86.2	<i>TFAP2B;PRKAR1B;ADCY8</i>
embryonic digestive tract morphogenesis	GO:0048557	2/9	0.002	0.086	36.3	223.1	<i>PDGFRA;FGFR2</i>
negative regulation of epithelial cell proliferation	GO:0050680	4/72	0.003	0.091	7.6	45.1	<i>CDK6;SULF1;RUNX3;FGFR2</i>
cell morphogenesis involved in differentiation	GO:0000904	4/72	0.003	0.091	7.6	45.1	<i>ATRN;LAMA5;ACTN1;PIK3R1</i>
regulation of muscle cell differentiation	GO:0051147	3/35	0.003	0.091	12.0	71.2	<i>CDH2;BOC;FGFR2</i>
forelimb morphogenesis	GO:0035136	2/10	0.003	0.091	31.8	188.3	<i>TFAP2A;TFAP2B LAMA5;LAMA2;LAMA3;PIK3R1;S100B;SPTBN1;FGFR2</i>
axonogenesis	GO:0007409	7/240	0.003	0.100	3.9	22.6	<i>00B;SPTBN1;FGFR2</i>
peptidyl-proline hydroxylation	GO:0019511	2/11	0.003	0.104	28.3	161.8	<i>P4HA2;P4HTM</i>
bone development	GO:0060348	3/40	0.004	0.113	10.4	57.6	<i>TFAP2A;SULF1;FGFR2</i>
regulation of sodium ion transmembrane transporter activity	GO:2000649	3/40	0.004	0.113	10.4	57.6	<i>NETO1;DMD;PTPN3</i>
morphogenesis of a polarized epithelium	GO:0001738	2/12	0.004	0.113	25.4	141.1	<i>LAMA5;LAMA3</i>
skeletal system morphogenesis	GO:0048705	3/42	0.004	0.125	9.8	53.3	<i>TFAP2A;PDGFRA;FGFR2</i>
response to iron ion	GO:0010039	2/13	0.005	0.125	23.1	124.5	<i>TFAP2A;BMP6</i>
bone morphogenesis	GO:0060349	2/14	0.005	0.137	21.2	111.0	<i>TFAP2A;FGFR2</i>
positive regulation of alpha-beta T cell differentiation	GO:0046638	2/14	0.005	0.137	21.2	111.0	<i>RUNX3;GLI3</i>
regulation of phospholipase C activity	GO:1900274	2/15	0.006	0.149	19.6	99.8	<i>PDGFRA;ESR1</i>
response to muscle stretch	GO:0035994	2/15	0.006	0.149	19.6	99.8	<i>CDH2;DMD</i>

regulation of epithelial cell proliferation	GO:0050678	4/93	0.006	0.150	5.8	29.2	<i>CDK6;RUNX3;BMP6;FGFR2</i>
substrate adhesion-dependent cell spreading	GO:0034446	3/48	0.006	0.150	8.5	42.9	<i>LAMA5;ATRN;PIK3R1</i>
hemopoiesis	GO:0030097	4/94	0.007	0.150	5.7	28.6	<i>MEIS1;TOX;RUNX3;FGFR2</i>
digestive tract morphogenesis	GO:0048546	2/16	0.007	0.154	18.2	90.3	<i>PDGFRA;FGFR2</i>
regulation of cellular component movement	GO:0051270	3/50	0.007	0.157	8.2	40.2	<i>CDK6;ACTN1;ARAP1</i>
activation of protein kinase A activity	GO:0034199	2/17	0.008	0.159	16.9	82.2	<i>PRKAR1B;ADCY8</i>
regulation of cellular response to growth factor stimulus	GO:0090287	2/17	0.008	0.159	16.9	82.2	<i>TFAP2B;SULF1</i>
gliogenesis	GO:0042063	2/17	0.008	0.159	16.9	82.2	<i>CDK6;CDH2</i>
synaptic transmission, glutamatergic	GO:0035249	2/18	0.009	0.174	15.9	75.3	<i>GRIK5;GRIK4</i>
cellular response to glucagon stimulus	GO:0071377	2/19	0.010	0.186	15.0	69.3	<i>PRKAR1B;ADCY8</i>
postsynaptic membrane organization	GO:0001941	2/19	0.010	0.186	15.0	69.3	<i>MUSK;LRP4</i>
cellular response to peptide hormone stimulus	GO:0071375	4/106	0.010	0.187	5.0	23.2	<i>PRKAR1B;PIK3R1;ADCY8;CRHR1</i>
chordate embryonic development	GO:0043009	3/58	0.011	0.200	7.0	31.5	<i>PTPRR;SULF1;FGFR2</i>
response to glucagon	GO:0033762	2/21	0.012	0.213	13.4	59.4	<i>PRKAR1B;ADCY8</i>
positive regulation of kinase activity	GO:0033674	4/114	0.013	0.217	4.7	20.3	<i>PDGFRA;MUSK;AGAP2;FGFR2</i>
negative regulation of myeloid cell differentiation	GO:0045638	2/22	0.013	0.217	12.7	55.3	<i>MEIS1;CDK6</i>
regulation of voltage-gated calcium channel activity	GO:1901385	2/22	0.013	0.217	12.7	55.3	<i>DMD;CRHR1</i>
limb morphogenesis	GO:0035108	2/22	0.013	0.217	12.7	55.3	<i>TFAP2B;GLI3</i>
negative regulation of reactive oxygen species metabolic process	GO:2000378	2/23	0.014	0.228	12.1	51.6	<i>TFAP2A;ABCB7</i>
ear morphogenesis	GO:0042471	2/23	0.014	0.228	12.1	51.6	<i>TFAP2A;FGFR2</i>
amino acid import across plasma membrane	GO:0089718	2/24	0.015	0.232	11.6	48.3	<i>SLC6A6;SLC6A9</i>
negative regulation of stress fiber assembly	GO:0051497	2/24	0.015	0.232	11.6	48.3	<i>ARAP1;PIK3R1</i>

positive regulation of neuron apoptotic process	GO:0043525	2/24	0.015	0.232	11.6	48.3	<i>TFAP2A;TFAP2B</i>
lipid translocation	GO:0034204	2/24	0.015	0.232	11.6	48.3	<i>ATP8B1;ATP11A</i>
cardiac conduction system development	GO:0003161	2/25	0.017	0.243	11.0	45.3	<i>TBX18;CACNA1G</i>
in utero embryonic development	GO:0001701	2/25	0.017	0.243	11.0	45.3	<i>PTPRR;FGFR2</i>
positive regulation of ion transmembrane transporter activity	GO:0032414	2/26	0.018	0.250	10.6	42.6	<i>SLC6A9;DMD</i>
synapse organization	GO:0050808	4/126	0.018	0.250	4.2	16.9	<i>CDH2;MUSK;LRP4;AGRN</i>
negative regulation of cation channel activity	GO:2001258	2/27	0.019	0.250	10.2	40.2	<i>SLC6A9;CRHR1</i>
positive regulation of muscle cell differentiation	GO:0051149	2/27	0.019	0.250	10.2	40.2	<i>CDH2;BOC</i>
negative regulation of actin filament bundle assembly	GO:0032232	2/27	0.019	0.250	10.2	40.2	<i>PIK3R1;ARAP1</i>
cell junction organization	GO:0034330	3/72	0.019	0.250	5.5	21.9	<i>LRP4;AGRN;LIMS2</i>
							<i>ZFH3;MEIS1;CDH2;HESX1;S100B</i>
central nervous system development	GO:0007417	6/268	0.020	0.250	2.9	11.6	<i>;NPAS1</i>
neutral amino acid transport	GO:0015804	2/28	0.020	0.250	9.8	38.0	<i>SLC6A6;SLC6A9</i>
positive regulation of fibroblast proliferation	GO:0048146	2/28	0.020	0.250	9.8	38.0	<i>PDGFRA;CDK6</i>
positive regulation of phosphatidylinositol 3-kinase activity	GO:0043552	2/28	0.020	0.250	9.8	38.0	<i>PDGFRA;AGAP2</i>
inorganic cation transmembrane transport	GO:0098662	6/274	0.022	0.250	2.9	11.0	<i>SLC6A6;KCNG3;SLC6A8;SLC6A9;A</i>
							<i>BCB7;CACNA1G</i>
limb development	GO:0060173	2/29	0.022	0.250	9.4	36.0	<i>LRP4;GLI3</i>
regulation of BMP signaling pathway	GO:0030510	3/76	0.022	0.250	5.2	19.9	<i>TFAP2B;SMURF2;SULF1</i>
cell morphogenesis involved in neuron differentiation	GO:0048667	3/76	0.022	0.250	5.2	19.9	<i>LRP4;S100B;FGFR2</i>
							<i>LAMA5;LAMA2;LAMA3;PIK3R1;S</i>
axon guidance	GO:0007411	5/203	0.023	0.250	3.2	12.3	<i>PTBN1</i>
cardiac muscle cell action potential	GO:0086001	2/30	0.023	0.250	9.1	34.1	<i>DMD;CACNA1G</i>

maintenance of blood-brain barrier	GO:0035633	2/30	0.023	0.250	9.1	34.1	<i>LAMA2;DMD</i>
phospholipid translocation	GO:0045332	2/31	0.025	0.250	8.8	32.4	<i>ATP8B1;ATP11A</i>
regulation of transmembrane receptor protein serine/threonine kinase signaling pathway	GO:0090092	2/31	0.025	0.250	8.8	32.4	<i>TFAP2B;SMURF2</i>
negative regulation of cell cycle	GO:0045786	3/80	0.026	0.250	5.0	18.2	<i>CDK6;RUNX3;PTPN3</i>
chondrocyte differentiation	GO:0002062	2/32	0.026	0.250	8.5	30.8	<i>SULF1;RUNX3</i>
ERBB2 signaling pathway	GO:0038128	2/32	0.026	0.250	8.5	30.8	<i>PTPRR;PIK3R1</i>
regulation of osteoblast differentiation	GO:0045667	3/83	0.028	0.250	4.8	17.1	<i>CDK6;BMP6;FGFR2</i>
positive regulation of plasma membrane bounded cell projection assembly	GO:0120034	3/83	0.028	0.250	4.8	17.1	<i>ARAP1;PIK3R1;AGRN</i>
cell-substrate junction assembly	GO:0007044	2/34	0.029	0.250	7.9	28.0	<i>ACTN1;LAMA3</i>
glucose homeostasis	GO:0042593	3/86	0.031	0.250	4.6	16.0	<i>TFAP2B;PIK3R1;ADCY8</i>
regulation of phosphatidylinositol 3- kinase activity	GO:0043551	2/35	0.031	0.250	7.7	26.7	<i>PDGFRA;PIK3R1</i>
embryonic skeletal system development	GO:0048706	2/35	0.031	0.250	7.7	26.7	<i>PDGFRA;SULF1</i>
regulation of trans-synaptic signaling	GO:0099177	2/35	0.031	0.250	7.7	26.7	<i>GRIK5;GRIK4</i>
muscle cell differentiation	GO:0042692	2/35	0.031	0.250	7.7	26.7	<i>DMD;TBX18</i>
brain development	GO:0007420	4/150	0.031	0.250	3.5	12.1	<i>ZFH3;MEIS1;CDH2;HESX1</i>
sodium ion transmembrane transport	GO:0035725	3/87	0.032	0.250	4.6	15.7	<i>SLC6A6;SLC6A8;SLC6A9</i>
activation of adenylate cyclase activity	GO:0007190	2/36	0.033	0.250	7.5	25.5	<i>ADCY8;CRHR1</i>
embryonic limb morphogenesis	GO:0030326	2/36	0.033	0.250	7.5	25.5	<i>TFAP2A;GLI3</i>
platelet aggregation	GO:0070527	2/36	0.033	0.250	7.5	25.5	<i>PDGFRA;ACTN1</i>
positive regulation of bone mineralization	GO:0030501	2/36	0.033	0.250	7.5	25.5	<i>TFAP2A;BMP6</i>
membrane assembly	GO:0071709	2/36	0.033	0.250	7.5	25.5	<i>LRP4;SPTBN1</i>
positive regulation of Wnt signaling pathway	GO:0030177	4/153	0.033	0.250	3.4	11.7	<i>SMURF2;AXIN2;SULF1;FGFR2</i>

regulation of erythrocyte differentiation	GO:0045646	2/37	0.034	0.250	7.3	24.4	<i>ABCB10;CDK6</i>
sodium ion transport	GO:0006814	3/90	0.034	0.250	4.4	14.8	<i>SLC6A6;SLC6A8;SLC6A9</i>
positive regulation of cell population proliferation	GO:0008284	8/474	0.035	0.250	2.2	7.4	<i>PDGFRA;TFAP2B;MEIS1;CDK6;TOX</i>
positive regulation of transmembrane receptor protein serine/threonine kinase signaling pathway	GO:0090100	3/92	0.036	0.250	4.3	14.2	<i>SULF1;BMP6;BMP15</i>
odontogenesis	GO:0042476	2/39	0.038	0.250	6.9	22.4	<i>AXIN2;FGFR2</i>
regulation of kinase activity	GO:0043549	3/94	0.038	0.250	4.2	13.7	<i>PDGFRA;MUSK;FGFR2</i>
protein processing involved in protein targeting to mitochondrion	GO:0006627	1/5	0.039	0.250	31.6	102.6	<i>IMMP2L</i>
negative regulation of CD4-positive, alpha-beta T cell differentiation	GO:0043371	1/5	0.039	0.250	31.6	102.6	<i>RUNX3</i>
regulation of adherens junction organization	GO:1903391	1/5	0.039	0.250	31.6	102.6	<i>BMP6</i>
regulation of chloride transport	GO:2001225	1/5	0.039	0.250	31.6	102.6	<i>ATP8B1</i>
regulation of homophilic cell adhesion	GO:1903385	1/5	0.039	0.250	31.6	102.6	<i>PTPRR</i>
cerebral cortex neuron differentiation	GO:0021895	1/5	0.039	0.250	31.6	102.6	<i>TOX</i>
neuroinflammatory response	GO:0150076	1/5	0.039	0.250	31.6	102.6	<i>ADCY8</i>
regulation of microvillus assembly	GO:0032534	1/5	0.039	0.250	31.6	102.6	<i>ATP8B1</i>
regulation of morphogenesis of a branching structure	GO:0060688	1/5	0.039	0.250	31.6	102.6	<i>FGFR2</i>
peripheral nervous system neuron differentiation	GO:0048934	1/5	0.039	0.250	31.6	102.6	<i>RUNX3</i>
positive regulation of CD8-positive, alpha-beta T cell differentiation	GO:0043378	1/5	0.039	0.250	31.6	102.6	<i>RUNX3</i>
G protein-coupled opioid receptor signaling pathway	GO:0038003	1/5	0.039	0.250	31.6	102.6	<i>ADCY8</i>

gastro-intestinal system smooth muscle contraction	GO:0014831	1/5	0.039	0.250	31.6	102.6	<i>SULF1</i>
glial cell-derived neurotrophic factor receptor signaling pathway	GO:0035860	1/5	0.039	0.250	31.6	102.6	<i>SULF1</i>
positive regulation of DNA demethylation	GO:1901537	1/5	0.039	0.250	31.6	102.6	<i>TOX</i>
response to morphine	GO:0043278	1/5	0.039	0.250	31.6	102.6	<i>ADCY8</i>
retina vasculature development in camera-type eye	GO:0061298	1/5	0.039	0.250	31.6	102.6	<i>PDGFRA</i>
positive regulation of long-term synaptic depression	GO:1900454	1/5	0.039	0.250	31.6	102.6	<i>ADCY8</i>
SA node cell to atrial cardiac muscle cell signaling	GO:0086018	1/5	0.039	0.250	31.6	102.6	<i>CACNA1G</i>
salivary gland morphogenesis	GO:0007435	1/5	0.039	0.250	31.6	102.6	<i>FGFR2</i>
positive regulation of necrotic cell death	GO:0010940	1/5	0.039	0.250	31.6	102.6	<i>SLC6A6</i>
sinoatrial node cell differentiation	GO:0060921	1/5	0.039	0.250	31.6	102.6	<i>TBX18</i>
membrane depolarization during AV node cell action potential	GO:0086045	1/5	0.039	0.250	31.6	102.6	<i>CACNA1G</i>
membrane depolarization during SA node cell action potential	GO:0086046	1/5	0.039	0.250	31.6	102.6	<i>CACNA1G</i>
trivalent inorganic anion homeostasis	GO:0072506	1/5	0.039	0.250	31.6	102.6	<i>TFAP2B</i>
ubiquitin-dependent SMAD protein catabolic process	GO:0030579	1/5	0.039	0.250	31.6	102.6	<i>SMURF2</i>
positive regulation of protein kinase B signaling	GO:0051897	4/161	0.039	0.250	3.3	10.6	<i>PDGFRA;PIK3R1;ESR1;FGFR2</i>
digestive tract development	GO:0048565	2/40	0.040	0.250	6.7	21.5	<i>GLI3;FGFR2</i>
positive regulation of ossification	GO:0045778	2/40	0.040	0.250	6.7	21.5	<i>TFAP2A;BMP6</i>
positive regulation of biomineral tissue development	GO:0070169	2/41	0.042	0.250	6.5	20.7	<i>TFAP2A;BMP6</i>
negative regulation of canonical Wnt signaling pathway	GO:0090090	4/165	0.042	0.250	3.2	10.1	<i>LRP4;AXIN2;GLI3;TBX18</i>
regulation of neuron apoptotic process	GO:0043523	3/98	0.043	0.250	4.0	12.7	<i>TFAP2A;TFAP2B;AGAP2</i>

negative regulation of protein catabolic process	GO:0042177	2/42	0.043	0.250	6.3	19.9	<i>AGAP2;PTPN3</i>
negative regulation of transcription by RNA polymerase II	GO:0000122	10/684	0.045	0.250	1.9	5.9	<i>TFAP2A;TFAP2B;ZFXH3;SMURF2;HESX1;RUNX3;ESR1;BMP6;FGFR2</i>
cellular glucose homeostasis	GO:0001678	2/43	0.045	0.250	6.2	19.2	<i>PIK3R1;ADCY8</i>
positive regulation of phospholipase C activity	GO:0010863	2/43	0.045	0.250	6.2	19.2	<i>PDGFRA;ESR1</i>
adherens junction maintenance	GO:0034334	1/6	0.046	0.250	25.3	77.5	<i>KIFC3</i>
astrocyte development	GO:0014002	1/6	0.046	0.250	25.3	77.5	<i>CDK6</i>
negative regulation of morphogenesis of an epithelium	GO:1905331	1/6	0.046	0.250	25.3	77.5	<i>SULF1</i>
regulation of DNA demethylation	GO:1901535	1/6	0.046	0.250	25.3	77.5	<i>TOX</i>
regulation of focal adhesion disassembly	GO:0120182	1/6	0.046	0.250	25.3	77.5	<i>PIK3R1</i>
nephron tubule development	GO:0072080	1/6	0.046	0.250	25.3	77.5	<i>TFAP2B</i>
chondrocyte development	GO:0002063	1/6	0.046	0.250	25.3	77.5	<i>SULF1</i>
peripheral nervous system neuron development	GO:0048935	1/6	0.046	0.250	25.3	77.5	<i>RUNX3</i>
regulation of peptidyl-cysteine S-nitrosylation	GO:2000169	1/6	0.046	0.250	25.3	77.5	<i>DMD</i>
embryonic camera-type eye morphogenesis	GO:0048596	1/6	0.046	0.250	25.3	77.5	<i>TFAP2A</i>
epithelial tube branching involved in lung morphogenesis	GO:0060441	1/6	0.046	0.250	25.3	77.5	<i>FGFR2</i>
epithelial tube formation	GO:0072175	1/6	0.046	0.250	25.3	77.5	<i>FGFR2</i>
regulation of tooth mineralization	GO:0070170	1/6	0.046	0.250	25.3	77.5	<i>TFAP2A</i>
gamma-aminobutyric acid transport	GO:0015812	1/6	0.046	0.250	25.3	77.5	<i>SLC6A6</i>
glandular epithelial cell differentiation	GO:0002067	1/6	0.046	0.250	25.3	77.5	<i>FGFR2</i>
positive regulation of focal adhesion disassembly	GO:0120183	1/6	0.046	0.250	25.3	77.5	<i>PIK3R1</i>

inner ear auditory receptor cell differentiation	GO:0042491	1/6	0.046	0.250	25.3	77.5	<i>SLC4A7</i>
sialylation	GO:0097503	1/6	0.046	0.250	25.3	77.5	<i>ST6GAL1</i>
magnesium ion homeostasis	GO:0010960	1/6	0.046	0.250	25.3	77.5	<i>TFAP2B</i>
maintenance of DNA repeat elements	GO:0043570	1/6	0.046	0.250	25.3	77.5	<i>AXIN2</i>
trigeminal nerve development	GO:0021559	1/6	0.046	0.250	25.3	77.5	<i>TFAP2A</i>
positive regulation of tooth mineralization	GO:0070172	1/6	0.046	0.250	25.3	77.5	<i>TFAP2A</i>
neurogenesis	GO:0022008	2/44	0.047	0.250	6.0	18.4	<i>CDK6;BTBD6</i>
embryonic organ morphogenesis	GO:0048562	2/44	0.047	0.250	6.0	18.4	<i>PDGFRA;FGFR2</i>
homotypic cell-cell adhesion	GO:0034109	2/44	0.047	0.250	6.0	18.4	<i>PDGFRA;ACTN1</i>
action potential	GO:0001508	2/45	0.049	0.250	5.9	17.8	<i>DMD;CACNA1G</i>
positive regulation of signal transduction	GO:0009967	5/252	0.050	0.250	2.6	7.8	<i>PIK3R1;SULF1;BMP6;FGFR2;LIMS2</i>

Note. The full enrichment analysis for genes shared between fish early domesticates and human groups with autism spectrum disorders can be accessed here:

<https://maayanlab.cloud/Enrichr/enrich?dataset=c5b8b850d070c8fa90b809675170affd>