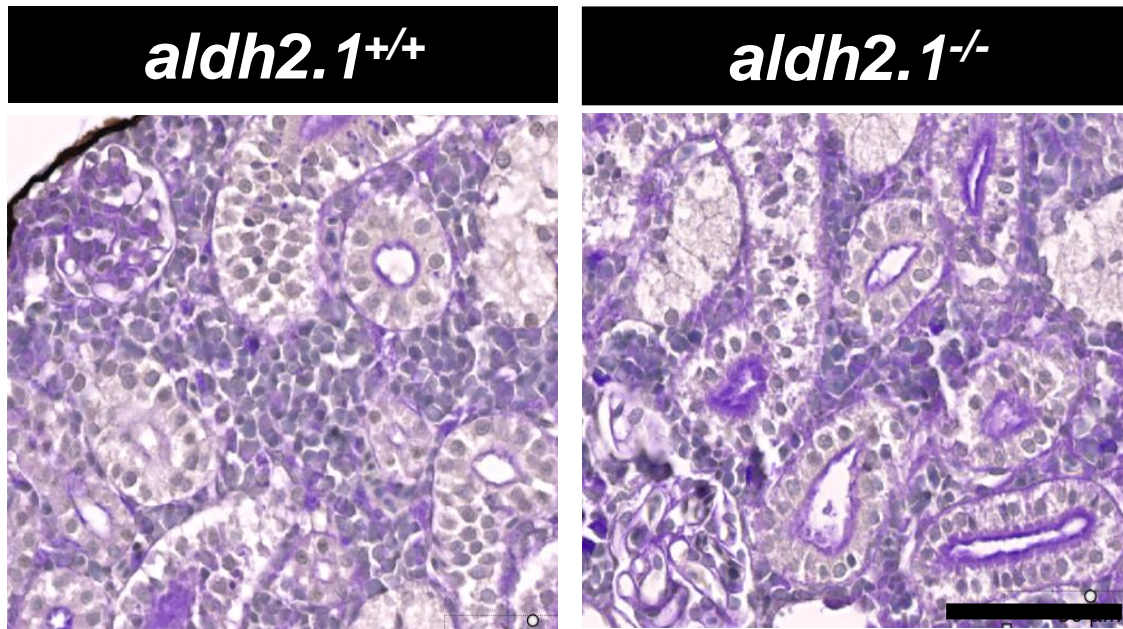
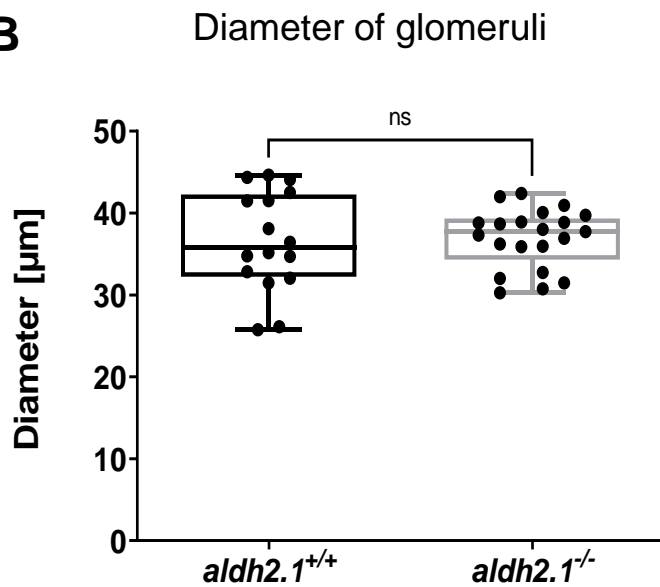
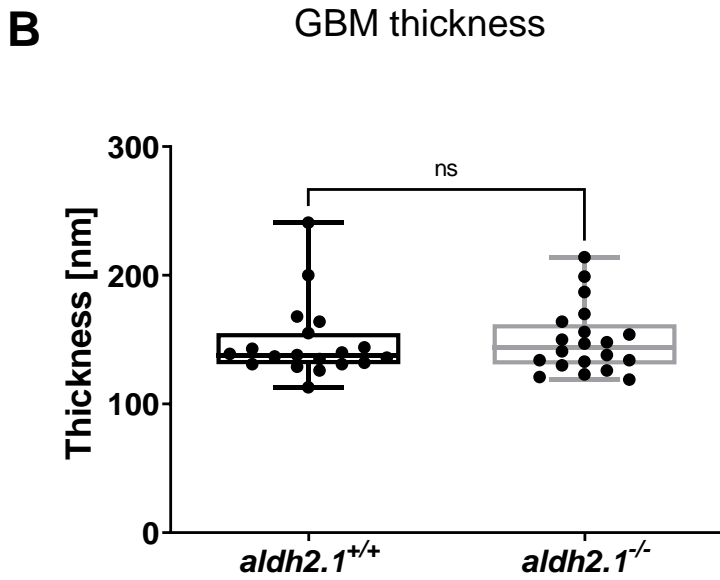
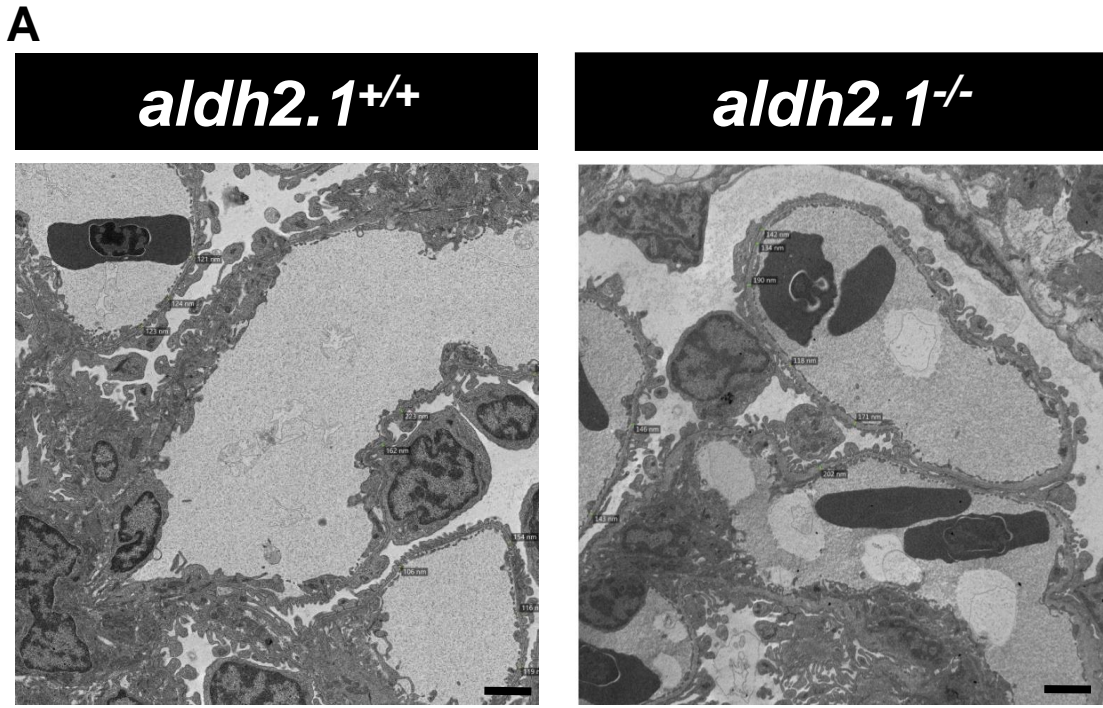


**Figure S1. Zebrafish larvae displayed no morphological alterations at 120 hpf after incubation with up to 500  $\mu\text{M}$  AA. A:** Representative microscopic images of zebrafish larvae between 24 hpf and 120 hpf displayed normal development up to 500  $\mu\text{M}$  AA treatment. Black scale bar: 500  $\mu\text{m}$ . **B:** Quantification of survival rates showed high lethality of 1000  $\mu\text{M}$  AA treated larvae.

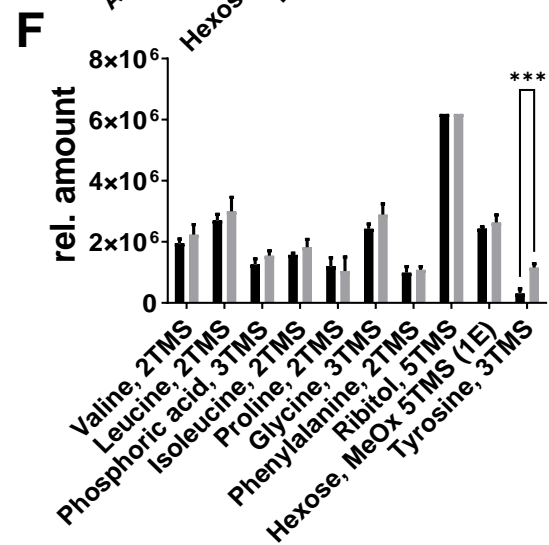
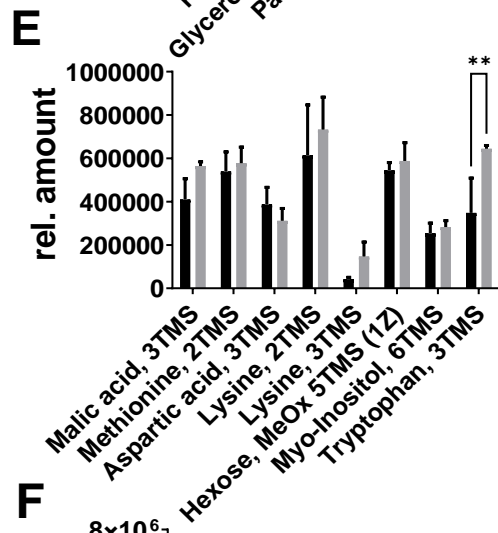
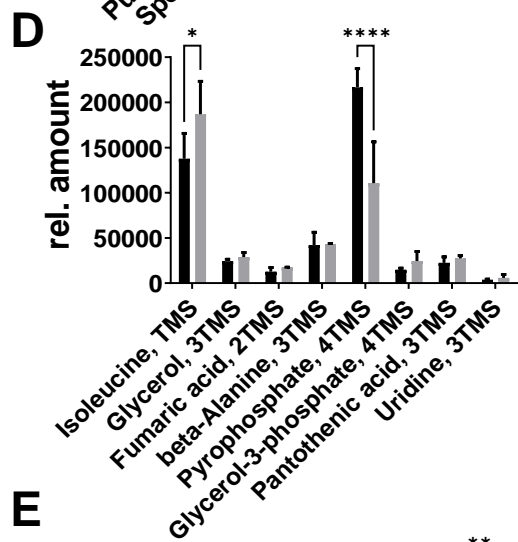
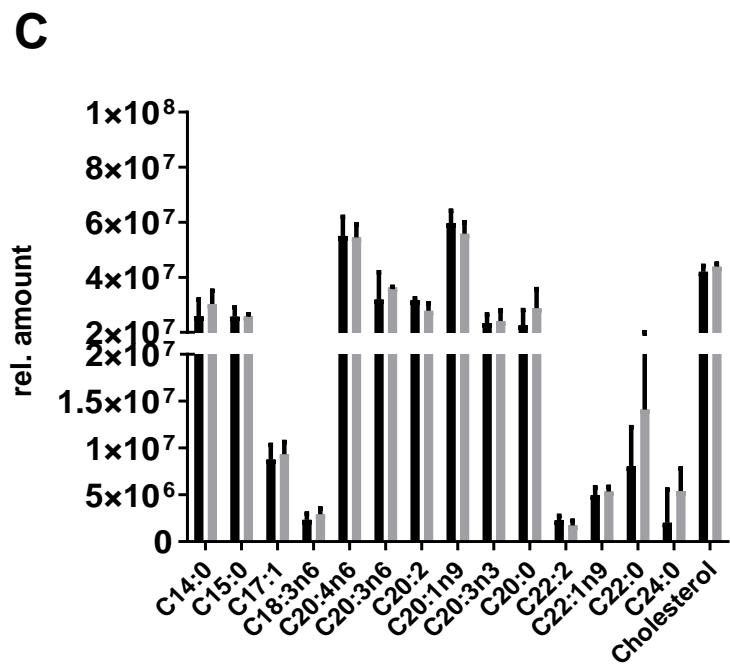
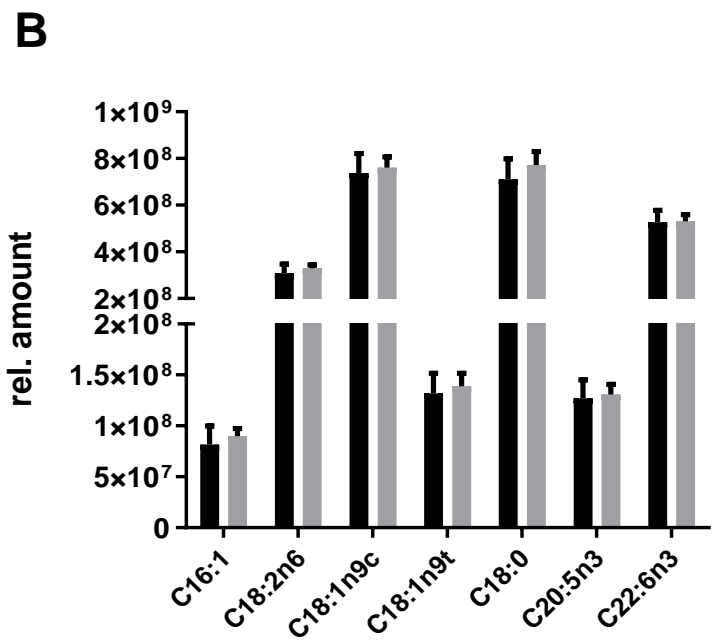
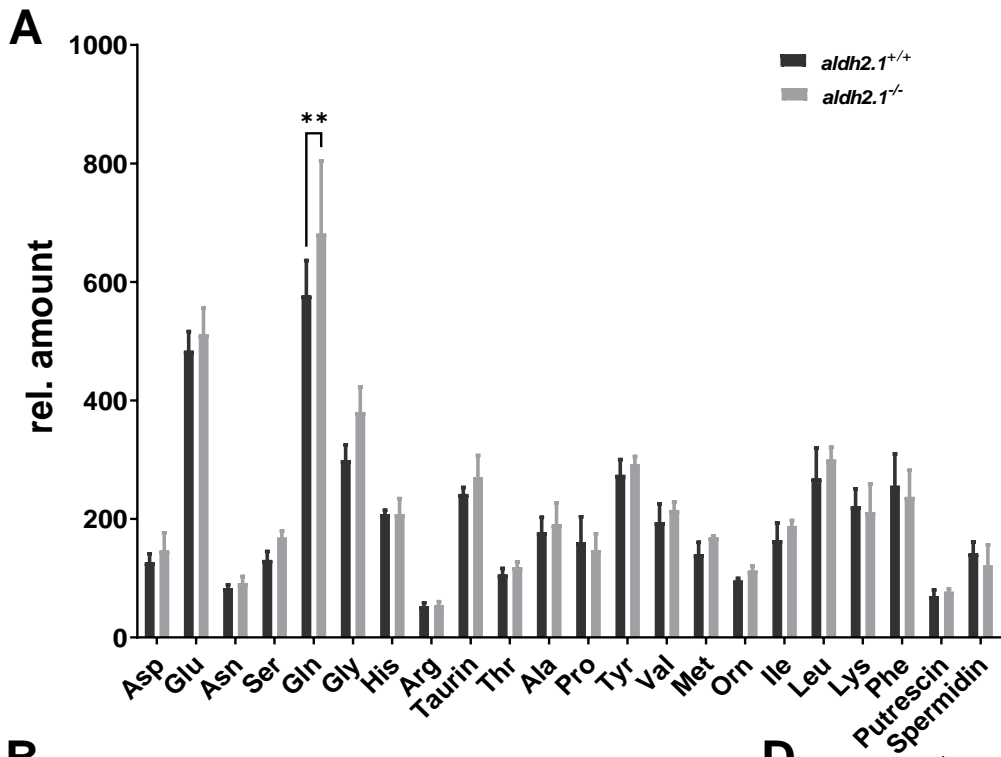


**A****B**

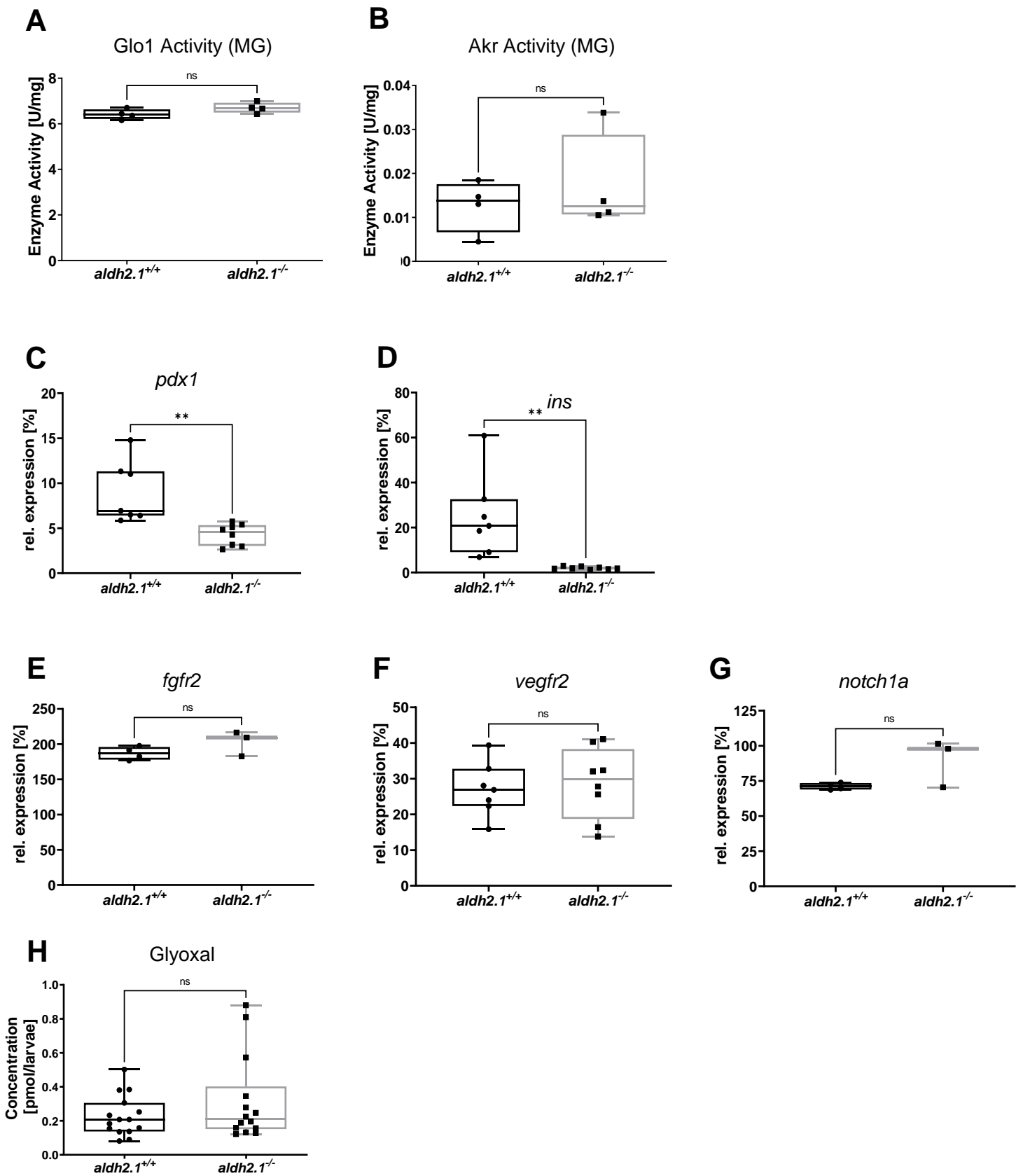
**Figure S3. Unaltered renal morphology in adult *aldh2.1*<sup>-/-</sup> zebrafish.** **A:** Representative Periodic acid-Schiff (PAS) staining showed no alterations in gross morphology of *aldh2.1*<sup>-/-</sup> kidneys. Black scale bar: 50  $\mu\text{m}$ . **B:** Quantification of glomerular diameter in zebrafish kidneys showed no changes between *aldh2.1*<sup>+/+</sup> and *aldh2.1*<sup>-/-</sup> zebrafish. Statistical analysis was done via Student's t-test, ns = not significant.



**Figure S4. Unaltered glomerular morphology in adult *aldh2.1<sup>-/-</sup>* zebrafish.** **A:** Representative electronmicroscopy images showed no alterations in *aldh2.1<sup>-/-</sup>* glomeruli. Black scale bar: 2  $\mu$ m. **B:** Quantification of GBM thickness in *aldh2.1<sup>-/-</sup>* zebrafish glomeruli showed no changes. Statistical analysis was done via Student's t-test, ns = not significant.



**Figure S5. Metabolomic screening showed minor alterations between *aldh2.1<sup>+/+</sup>* and *aldh2.1<sup>-/-</sup>* zebrafish larvae at 96 hpf. A:** Quantification of amino acids displayed a significant increase in glutamine concentrations of *aldh2.1<sup>-/-</sup>* larvae. **B,C:** Quantification of fatty acids in 96 hpf larvae showed no change between *aldh2.1<sup>+/+</sup>* and *aldh2.1<sup>-/-</sup>* larvae. **D,E,F:** Semi-Targeted Screening identified an increase in aromatic amino acids: tryptophan and tyrosine and a decrease of pyrophosphates in *aldh2.1<sup>-/-</sup>* larvae. Statistical analysis was done via Student's t-test, ns = not significant, \*p < 0.05, \*\*p < 0.01, \*\*\*p < 0.001, \*\*\*\*p < 0.0001.



**Figure S6.** *aldh2.1*<sup>-/-</sup> larvae displayed decreased *pdx1* and *ins* expression, but unaltered expression of angiogenesis related factors. **A,B:** Quantification of enzyme activity for Glo1 and Akh showed no change in *aldh2.1*<sup>-/-</sup> zebrafish larvae. **C,D:** Strongly reduced *pdx1* and *ins* expression in *aldh2.1*<sup>-/-</sup> larvae. **E,F,G:** Quantification of gene expression of angiogenesis related factors: *fgfr2* (**E**), *vegfr2* (**F**) and *notch1a* (**G**) showed no change in *aldh2.1*<sup>-/-</sup> larvae compared to *aldh2.1*<sup>+/+</sup> larvae. Expression was quantified via RT-qPCR with 96 hpf zebrafish larvae and normalized to *arnt2*, n = 5-8 clutches, 50 larvae per clutch. Quantification of glyoxal in 96 hpf larvae (**H**) showed no difference between *aldh2.1*<sup>+/+</sup> and *aldh2.1*<sup>-/-</sup> zebrafish, n = 14, 50 larvae per clutch. Statistical analysis was done via Student's t-test, ns = not significant, \*p < 0.05, \*\*p < 0.01, \*\*\*p < 0.001, \*\*\*\*p < 0.0001.

<b>Name</b>	<b>NES</b>	<b>pvalue</b>
Pantothenate_and_CoA_biosynthesis	-2,44	0,0002
Histidine_metabolism	-2,26	0,0006
Beta-Alanine_metabolism	-2,16	0,0007
Glycerolipid_metabolism	-2,1	0,0002
Ribosome	-2,08	0,0002
Pyruvate_metabolism	-2,03	0,0007
Valine,_leucine_and_isoleucine_degradation	-2	0,0009
Tryptophan_metabolism	-2	0,0004
Arginine_and_proline_metabolism	-1,99	0,0007
Lysine_degradation	-1,97	0,0007
Fatty_acid_degradation	-1,89	0,0018
Ascorbate_and_aldarate_metabolism	-1,87	0,0039
Glycolysis_Gluconeogenesis	-1,82	0,0015
VEGF_signaling_pathway	1,46	0,0245
Endocytosis	1,53	0,0003
Apoptosis	1,53	0,0028
MAPK_Signaling_Pathway	1,58	0,0003
Cardiac_muscle_contraction	1,58	0,0027
Cellular_senescence	1,6	0,0011
Ferroptosis	1,66	0,0066
Regulation_of_actin_cytoskeleton	1,73	0,0002
Tight_junction	1,88	0,0002
Focal_adhesion	1,99	0,0002
ECM-receptor_interaction	2,04	0,0002

**Table S1. RNA-seq KEGG-Analysis values corresponding to Fig.4**



<b>CRISPR-construct name</b>	<b>Primer sequence (5' to 3')</b>
Aldh2.1-CRISPR-for	TAGGGCTCTCCCTGGCGCCGCA
Aldh2.1-CRISPR-rev	AAACTGCGGCGCCAGGGAGAGC
<b>Genotyping primer name</b>	<b>Primer sequence (5' to 3')</b>
Aldh2.1- gt 2.1 fw1	CCCTGCTGTGCAGTGTATTG
Aldh2.1- gt 2.3 fw2	CTGGCATGGCAATAAACACA
Aldh2.1- gt 2.4 rv2	TGCATCGAGAGAGATGCTGCCT
<b>qPCR primer name</b>	<b>Primer sequence (5' to 3')</b>
aldh2.1-qPCR-left	CGCACTGTATATCGCCAGTTTA
aldh2.1-qPCR-right	GGACCAAACCCTGGGATAAT

**Table S2. CRISPR constructs, primers for genotyping and qPCR for zebrafish *aldh2.1***

qPCR primer name	Primer sequence (5' to 3')	qPCR primer name	Primer sequence (5' to 3')
qPCR mapk3 fw2	GCTCCTGAGAGGGACAGTCATC	G6Pase_qPCR_Left	TCACAGCGTTGCTTTCAATC
qPCR mapk3 rv2	TCGCAGGTCGTCTGGAGTTTT	G6Pase_qPCR_Right	AACCCAGAAACATCCACAGC
qPCR mapk7 fw2	CTGGATCGGCCTTGTCGGT	G6PDH_qPCR_Left	CGTCTTTTGTGGCAGTCAGA
qPCR mapk7 rv2	GATCAATGGTTTCCGGCTGGC	G6PDH_qPCR_Right	TGATGGGTGGTGTTTTCTCA
qPCR mapk8 fw1	CCGGCCTCGCTAGCACA	cPEPCK_qPCR_Left	ATCACGCATCGCTAAAGAGG
qPCR mapk8 rv1	ACCTCGGTGGACATGGACGA	cPEPCK_qPCR_Right	CCGCTGCGAAATACTTCTTC
qPCR mapk11 fw1	GCTTCTTCGGGGCCTTAAGTACA	hk1_qPCR_Left	ATGATAGCGGCACAGCTTCT
qPCR mapk11 rv1	CATTCACGGCTACATTGCTTGGC	hk1_qPCR_Right	GTGGGTGCTCGTGCCAATC
qPCR mapk12a fw2	ACCAAATGTTAACCCGCAAGCGAT	hk2_qPCR_Left	TGAGGTCAGTCTCGTCCAGT
qPCR mapk12a rv2	CCTCTGCTGCTGTTATCCGGC	hk2_qPCR_Right	TCTTAATCGACAGGCCACCG
qPCR mapk14b fw1	TCCCGGCACAGATCACATTG	gck_qPCR_Left	AATCACCGCTGACCTGCTAT
qPCR mapk14b rv1	TTTTCATCAAGAGCTCAGGCC	gck_qPCR_Right	GCCACTTCACATACGCAATG
b2m_qPCR_Left	ACTGCTGAAGAACGGACAGG	glo1-qPCR-for	AGCAGACAATGCTGCGGGTG
b2m_qPCR_Right	GCAACGCTCTTTGTGAGGTG	glo1-qPCR-rev	CTACGGGAGAACGTCCAGGC
arnt2_qPCR_Left	AGCCAGACAGAGGTCTTCCA	2-INS_qPCR_Left	GGTCGTGTCCAGTGTAAGCA
arnt2_qPCR_Right	CCGAGGTCAGCAAAGTCTTC	2-INS_qPCR_Right	GGAAGGAAACCCAGAAGGGG
VEGFR2 (KDR):f1	TAAACAGCAGCGGTGTGCCA	Pdx1_RT-PCR_Left	ACACGCACGCATGGAAAGGACA
VEGFR2 (KDR):r1	CAGTCCACGTGGCCATCCATT	Pdx1_RT-PCR_Right	GCGGGCGCGAGATGTATTTGTT
FGFR2 F1	GGCCCATGAGCTCCCTGTTT	notch1a-qPCR-left	CATCACCCCTCCAGCAGTCT
FGFR2 R1	ACGGTCGGTCACTCACTGGA	notch1a-qPCR-right	CTGAAGAGCTCCACCCATGT

**Table S3. qPCR primers**