SI Table 8. Evidence of developmental role of 21 candidate genes from animal models

Gene	Inheritance[a]	Concordance[b]	Zebrafish Replication[c]	Human[d]	Mouse	Zebrafish	Frog	Fly	Combined Evidence[e]	Summary
BTBD9	mono/bi	strong	C		C	.	.	C	C	Mouse mutant shows neurochemical, learning and memory defects [1,2]. Drosophila mutant shows abnormal behaviour [3]
CHD3	mono	strong	C		.	.	.	C	C	Drosophila mutant is larval lethal [4,5]
CNOT1	mono	weak	.		.	C	.	C	C	Zebrafish mutant shows head and body size defect ([6], www.zfin.org). Drosophila knockdown shows neurodevelopmental defects and lethality [7,8].
DDX3X	mono	strong	C	GWS	C	.	C	C	C	Mouse knockdown shows early lethality [9]. Xenopus knockdown shows head, trunk and pigment defects, rescued by mRNA injection [10]. Drosophlia mutant has mitotic defects, some lethality [11].
DPEP2	bi	moderate	C		.	.	.	C	C	Drosophila knockdown has morphological defects [7]
DTWD2	mono	weak	.		.	.	.	.	.	
ETF1	mono	strong	.		.	.	.	C	C	Drosophila mutant is embryonic lethal [12]
FRYL	mono	strong	C		C	.	.	C	C	Mouse mutant shows homozygous embryonic lethality, and heart defect in heterozygous mutants (www.sanger.ac.uk/mouseportal, [13]. Drosophlia mutant shows developmental defects and larval lethality [14,15]
ILVBL	mono	weak	.		.	.	.	.	.	
NONO	mono	weak	.		C	.	C	C	C	Mouse mutant shows neurological defects [16,17]. Xenopus knockdown shows defective neural patterning [18]. Drosophlia mutant shows defective behaviour [19].
PKN2	mono	strong	C		.	.	.	C	C	Drosophila mutant is recessive lethal [15,20]
POGZ	mono	weak	.	GWS	.	.	.	C	C	Drosophila mutant is lethal [4]
PSD2	mono	moderate	C		.	.	.	C	C	Drosophila mutant shows neural patterning defect [21]
PSMD3	mono	strong	.		.	.	.	C	C	Drosophila mutant is larval lethal [22]
SAP130	mono	moderate	.		.	.	.	C	C	Drosophila mutant is recessive lethal [7,15]
SCGN	bi	strong	C		.	.	.	C/D	C/D	Drosophila knockdown shows partial lethality [7], insertional mutant is viable [23].
SETD5	mono	strong	D	GWS	C	.	.	D	C/D	Mouse mutant is homozygous lethal [24]. Drosophila mutant is infertile [25]. Gene is genome-wide significant in human patients [26].
SMARCD1	mono	weak	D		.	.	.	C	C	Drosophila mutant is embryonic lethal [27]
THNSL2	bi	strong	C		.	.	.	.	.	
WWC1	mono	none	.		C			C	C	Mouse mutant shows defects in learning, memory [28,29]. Drosophila mutant is recessive lethal [30]
ZRANB1	mono	strong	.		.	C	.	C	C	Zebrafish morphant strong embryonic phenotypes [31]. Drosophila knockdown shows lethality during eclosion [32].

Evidence of developmental role of 21 candidate genes from animal models

Concordant ('C') and Contradictory ('D') data from different animal models as to the developmental role of 21 genes showing a developmental phenotype in zebrafish knockdown experiments.

[a] Damaging variant observed monoallelic ('mono') or biallelic ('bi') in patients.

[b] Concordance between phenotype in fish knockdown and patient

[c] Results of different morpholinos targeting the same gene

[d] Genome-wide significance (GWS) of mutation enrichment in patients

[e] Summary of evidence across all organisms

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