Table S1: RASopathy mutations in the Ras/MAPK pathway. For each residue that mutations occur at, the reference of an animal model, if made, is given.

SHP2

Point Mutations	Model	Source
T2I		(Aoki et al., 2008)
T42A		(Aoki et al., 2008)
N58K, N58D, N58H		(Aoki et al., 2008)
G60A		(Aoki et al., 2008)
D61N, D61G	Yes	(Araki et al., 2004)
Y62N, Y62D		(Aoki et al., 2008)
Y63C		(Aoki et al., 2008)
E69Q		(Aoki et al., 2008)
F71L, F71I		(Aoki et al., 2008)
A72S, A72G	Yes	(Oishi et al., 2006)
T73I	Yes	(Jopling et al., 2007)
E76D	Yes	(Mohi et al., 2005)
Q79R, Q79P	Yes	(Nakamura et al., 2007)
D106A		(Aoki et al., 2008)
E110A		(Aoki et al., 2008)
E111A		(Aoki et al., 2008)
E139D		(Aoki et al., 2008)
Q256R		(Aoki et al., 2008)
G268S, G268C		(Aoki et al., 2008)
Y279C, Y279S	Yes	(Marin et al., 2011)
I282V		(Aoki et al., 2008)
F285L, F285S, F285C		(Aoki et al., 2008)
N308D, N308S, N308T	Yes	(Araki et al., 2009)
I309V		(Aoki et al., 2008)
G409A		(Aoki et al., 2008)
A461T	Yes	(Jopling et al., 2007)
G464A	Yes	(Jopling et al., 2007)
T468M	Yes	(Tajan et al., 2014)
P491S, P491H, P491L		(Aoki et al., 2008)
R498W		(Aoki et al., 2008)
R501K		(Aoki et al., 2008)
S502T, S502L, S502A		(Aoki et al., 2008)
G503R		(Aoki et al., 2008)
M504V		(Aoki et al., 2008)
Q506P		(Aoki et al., 2008)
Q510E, Q510P	Yes	(Schramm et al., 2012)
L560F		(Aoki et al., 2008)

NRAS

Point Mutations	Model	Source
I24N	Yes	(Runtuwene et al., 2011)
P34L		(Denayer et al., 2012)
T50I	Yes	(Runtuwene et al., 2011)
G60E	Yes	(Runtuwene et al., 2011)

HRAS

Point Mutations	Model	Source
G12S, G12C, G12A, G12V, G12E	Yes	(Schuhmacher et al., 2008)
G13C, G13D		(Sol-Church and Gripp, 2009)
Q22K		(Sol-Church and Gripp, 2009)
T58I		(Sol-Church and Gripp, 2009)
E63K		(Sol-Church and Gripp, 2009)
K117R		(Sol-Church and Gripp, 2009)
A146T, A146V		(Sol-Church and Gripp, 2009)

KRAS

Point Mutations	Model	Source
K5N		(Aoki et al., 2008)
G12D	Yes	(Tuveson et al., 2004)
V14I	Yes	(Hernández-Porras et al., 2014)
Q22E, Q22R		(Aoki et al., 2008)
P34R, P34L, P34Q		(Aoki et al., 2008)
I36M		(Aoki et al., 2008)
T58I		(Aoki et al., 2008)
G60R		(Aoki et al., 2008)
N116S	Yes	(Razzaque et al., 2012)
V152G		(Aoki et al., 2008)
D153V		(Aoki et al., 2008)
F156I, F156L		(Aoki et al., 2008)

MEK

Point Mutations	Model	Source
E44G		(Bromberg-White et al., 2012)
F53S	Yes	(Anastasaki et al., 2009)
T55P	Yes	(Anastasaki et al., 2009)
D67N		(Bromberg-White et al., 2012)
P124Q		(Bromberg-White et al., 2012)
G128V	Yes	(Anastasaki et al., 2009)
Y130C	Yes	(Anastasaki et al., 2009)

BRAF

Point Mutations	Model	Source
A246P	Yes	(Anastasaki et al., 2009)
Q257K, Q257R	Yes	(Anastasaki et al., 2009)
G464V	Yes	(Anastasaki et al., 2009)
S467A	Yes	(Anastasaki et al., 2009)
F468S		(Aoki et al., 2008)
G469E		(Aoki et al., 2008)
L485F		(Aoki et al., 2008)
V487G		(Aoki et al., 2008)
K499E	Yes	(Anastasaki et al., 2009)
E501K, E501G		(Aoki et al., 2008)
G534R	Yes	(Anastasaki et al., 2009)
N580D		(Aoki et al., 2008)
N581D	Yes	(Aoki et al., 2008)
F595L		(Aoki et al., 2008)
G596V	Yes	(Anastasaki et al., 2009)
L597V	Yes	(Andreadi et al., 2012)
D638E		(Aoki et al., 2008)

RAF1

Point Mutations	Model	Source
R256S		(Tartaglia and Gelb, 2009)
S257L		(Tartaglia and Gelb, 2009)
S259F		(Tartaglia and Gelb, 2009)
T260R, T260I		(Tartaglia and Gelb, 2009)
P261S, P261L, P261A		(Tartaglia and Gelb, 2009)
V263A		(Tartaglia and Gelb, 2009)
D486N	Yes	(Wu et al., 2012)
T491I, T491R		(Tartaglia and Gelb, 2009)
S612T		(Tartaglia and Gelb, 2009)
L613V	Yes	(Wu et al., 2011a)

Table S2: Mouse models of NF1

Gene	Defect	Phenotype	Signaling	Reference
Nf1	General	*Nf1*+/-: Predisposition to various tumors, *Nf1*-/-: Mid-gestational embryonic lethality, and cardiac defects such as double outlet right ventricle; hyperplasia of neural crest-derived sympathetic ganglia and delay in renal, hepatic and skeletal muscle development and exencephaly		(Brannan et al., 1994; Ismat et al., 2006; Jacks et al., 1994; Lakkis and Epstein, 1998; Lakkis et al., 1999)
Nf1	Leukemia	Mice can be induced into chronic myeloproliferative disease which is similar to various human leukemias including JCML		(Chang et al., 2013; Gitler et al., 2004; Largaespada et al., 1996)
Nf1	OPG	Complete deletion of *Nf1* in astrocytes and reduced NF1 expression in other cells is required to increase astrocyte proliferation and cause optic pathway gliomas (OPGs). Furthermore, astrocytes differentiating from different germinal zones have different capacities to respond to glioma-causing genetic changes	PI3K/mTOR/Akt pathway	(Bajenaru et al., 2002; Bajenaru et al., 2003; Banerjee et al., 2011a; Banerjee et al., 2011b; Dahiya et al., 2011; Dasgupta et al., 2005a; Dasgupta et al., 2005b; Hegedus et al., 2007; Lee et al., 2010a; Lee et al., 2012; Solga et al., 2014; Yeh et al., 2009; Zhu et al., 2001; Zhu et al., 2005)
Nf1	OPG	Neuronal support cells, microglia, are needed for astrocyte proliferation and OPG formation		(Daginakatte and Gutmann, 2007; Daginakatte et al., 2008; Pong et al., 2013; Simmons et al., 2011; Sun et al., 2010; Warrington et al., 2007; Warrington et al., 2010)
Nf1	Neurofib-roma	Dermal, plexiform neurofibromas and Malignant Peripheral Nerve Sheath Tumor (MPNST)		(Cichowski et al., 1999; Jessen et al., 2013; Le et al., 2009; Mayes et al., 2011; Reilly et al., 2006; Rosenbaum et al., 1997; Vogel et al., 1999; Wu et al., 2008; Yang et al., 2008; Zhu et al., 2002)
Nf1	Bone	*Nf1*+/-: less bone formation and impaired healing of distal tibial fractures , tissue specific *Nf1*-/-: bowing of the tibia (*Prx1*), congenital limb shortening (*Prx1*), defective fracture healing (*Prx1*, *Col2.3*, *Osx1*), reduced muscle fibers and strength (*Prx1*), abnormal development of joints (*Prx1*), reduced bone mass (*Col2.3*) , short stature (*Prx1* and *Col2*), impaired bone strength, short vertebral segments (*Col2.3*), altered muscle metabolism (*Prx1* and muscle)	Increased TGF-β1 signaling, increased pyrophosphates, impaired mitochondrial activity	(de la Croix Ndong et al., 2014; de la Croix Ndong et al., 2015; El Khassawna et al., 2012; Kossler et al., 2011; Rhodes et al., 2013; Schindeler et al., 2008; Wang et al., 2011; Wu et al., 2011b; Zhang et al., 2011)
Nf1	Behavior	Motivational disturbances, spatial learning defects, attention defects, working memory defects, motor learning defects, social learning defects, sex-specific learning defects	Ras/MAPK pathway and dopamine homeostasis	(Brown et al., 2010; Costa et al., 2001; Costa et al., 2002; Cui et al., 2008; Diggs-Andrews et al., 2013; Diggs-Andrews et al., 2014; Guilding et al., 2007; Li et al., 2005; Shilyansky et al., 2010; Silva et al., 1997; van der Vaart et al., 2011; Wozniak et al., 2013)
Nf1	Brain	Increase in size of cerebral cortical surface area, increased thickness of corpus callosum	Ras/MAPK pathway	(Wang et al., 2012)
Nf1	Heart defects	Mice display Ras/MAPK-dependent defects in endocardial cushions which obstructs blood flow. Embryos with endothelial cell-specific biallelic deletion have defects in endocardial cushions and myocardium, while embryos with myocardial cell-specific biallelic deletion display some adult-onset heart defects.	Ras/MAPK pathway	(Gitler et al., 2003; Ismat et al., 2006; Lakkis and Epstein, 1998; Lasater et al., 2008; Lasater et al., 2010; Xu et al., 2007; Xu et al., 2009)

Table S3: Mouse models of non-NF1 RASopathies [1]Cre-lox [2]Tissue-specific Cre-lox [3]Overexpression [4]Other

Gene	Protein (Function)	Mutation	Disease	Phenotype	Signaling	Reference
Ptpn11	Shp2 (Phosphatase)	D61G[1]	NS	Hom: embryonic lethal; Het: Short stature, craniofacial defects, and myeloproliferative diease (MPD). Severely affected embryos with cardiac defects; Increased angiogenesis; Neurocognitive defects	Increased Ras/MAPK, short stature by IGF-1	(Araki et al., 2004; De Rocca Serra-Nédélec et al., 2012; Lee et al., 2014; Wang et al., 2009; Xu et al., 2010)
Ptpn11	Shp2 (Phosphatase)	D61Y/G, E76K[1,4]	NS	Impaired hematopoiesis, increased reactive oxygen species leading to MPD		(Mohi et al., 2005; Xu et al., 2013)
Ptpn11	Shp2 (Phosphatase)	Q79R[2]	NS	Heart defects and enlarged endocardial cushions; craniofacial defects including smaller skull lengths and taller frontal bone heights; Elevated oligodendrocyte precursor cell (OPC) numbers	Increased Ras/MAPK in heart, frontal bones, and brain	(Ehrman et al., 2014; Krenz et al., 2008; Nakamura et al., 2007; Nakamura et al., 2009)
Ptpn11	Shp2 (Phosphatase)	N308D, D61Y[1,2]	NS	D61Y Het, N308D Hom: Cardiac, growth, facial, and hematologic defects similar to D61G Het; N308D Het: Less severe than N308D Hom	Increased Ras/MAPK	(Araki et al., 2009)
Ptpn11	Shp2 (Phosphatase)	Y279C[1]	NSML	Het: Short stature, craniofacial dysmorphia, hypertrophic cardiomyopathy (HCM), and increased heart to body weight ratio.	Increased AKT/mTOR	(Marin et al., 2011)
Ptpn11	Shp2 (Phosphatase)	Q510E[3]	NSML	Increased cardiomyocyte sizes, heart-to-body weight ratios, interventricular septum thickness, and cardiomyocyte disarray.	Increased mTOR	(Edwards et al., 2015; Schramm et al., 2012)
Ptpn11	Shp2 (Phosphatase)	T468M[1]	NSML	Impaired adipogenesis and better metabolic profile resulting in lean mice, splenomegaly, and larger heart.	Increased AKT and Ras/MAPK	(Tajan et al., 2014)
Sos1	Sos1 (Ras GEF)	E846K[1]	NS	Growth delay, distinctive facial dysmorphia, hematologic abnormalities, and cardiac defects.	Increased Ras/MAPK, Rac, and Stat3	(Chen et al., 2010)
Raf1	Kinase	L613V[1]	NS	Het: Short stature, craniofacial dysmorphia, splenomegaly, hematologic defects, and HCM.	Increased Ras/MAPK	(Marin et al., 2011)
Raf1	Kinase	D486N[1]	NS	Het: female mice exhibited a mild growth defect; Hom: heart defects and incompletely penetrant, but severe, growth defects.	Increased Ras/MAPK in vitro	(Wu et al., 2012)
Braf	Kinase	V600E[1]	CFC	Reduced size and body weight, craniofacial defects, cardiomegaly, and epileptic seizures	No change in Ras/MAPK	(Urosevic et al., 2011)
Braf	Kinase	L597V[1]	CFC	Short stature, craniofacial defects, HCM, cardiac enlargement, and skin papillomas	Increased Ras/MAPK	(Andreadi et al., 2012)
Braf	GTPase	Q241R[1]	CFC	Embryonic lethal, embryonic skeletal abnormalities, lymphatic defects, and cardiac defects	Increased Ras/MAPK in brain, decreased p38 & Akt	(Inoue et al., 2014)
Kras	GTPase	G12D[1,2]	NS	Small and pale embryos with brain defects and cardiomegaly		(Tuveson et al., 2004)
Kras	GTPase	V14I[1]	NS	Het: Growth delay, craniofacial defects, cardiac defects, and hematologic defects (MPD); Hom: perinatal lethality	Increased Ras/MAPK	(Hernández-Porras et al., 2014)
Kras	GTPase	G12D[2]	CFC, NS	No changes in heart size or contractility	Increased Ras/MAPK in tissue	(Dalin et al., 2014)
Hras	GTPase	G12V[1]	CS	Het: Viable but have facial dysmorphia, HCM, and hypertension; Hom: Same phenotypes but more penetrant with hyperemotivity, hypersensitivity, and cognitive impairments	No change in Ras/MAPK and Akt	(Schuhmacher et al., 2008; Viosca et al., 2009)
Hras	GTPase	G12V[1]	CS	High perinatal lethality, craniofacial defects including nasal septal deviation, teeth defects, high penetrant neoplastic phenotypes, skin papillomas under certain conditions	No change in Ras/MAPK and Akt except liver (increased Ras/MAPK)	(Chen et al., 2009; Chen et al., 2014; Goodwin et al., 2014)
Hras	GTPase	G12V[4]	CS	Increased hepatocyte growth leading to hepatomegaly		(Figueiredo et al., 2012)

Table S4: Zebrafish Models of RASopathies [1]MO injections, [2]Zinc finger nucleases, [3]mRNA Injection, [4]Transposon-mediated integration & Heat Shock, [5]Injection of vector

Gene	Protein (Function)	Mutation	Disease	Phenotype	Signaling	Reference
nf1	Neurofibromin (Ras GAP)	Knockout[1]	NF1	Cardiac malformations and defects in vascular patterning, OPC hyperplasia, and OPC migration.	Increased Ras/MAPK	(Lee et al., 2010b; Padmanabhan et al., 2009)
nf1	Neurofibromin (Ras GAP)	Knockout[2]	NF1	OPC and Schwann cell hyperplasia, aberrant myelination, motor and learning defects, and melanophore defects.	Increased Ras/MAPK	(Shin et al., 2012; Zhu et al., 2011)
nf1	Neurofibromin (Ras GAP)	Knockout[2]	NF1	Learning and memory deficits.	Increased Ras/MAPK, PI3K, and cAMP	(Wolman et al., 2014)
ptpn11	Shp2 (Phosphatase)	D61G, T73I, A462T, G465A[3]	NS / NSML	Craniofacial defects, pericardial edema, heart jogging defects, convergence and extension (CE) defects, and shorter larvae.		(Jopling et al., 2007)
ptpn11	Shp2 (Phosphatase)	A462T[3]	NSML	Craniofacial dysmorphia, severe gastrulation phenotypes, a hammerhead phenotype, or no obvious phenotype. It alters neural crest specification and migration.	Shp2 is upstream of Ras/MAPK and Sh2 domain-dependent pathway to prevent cell death	(Stewart et al., 2010)
ptpn11	Shp2 (Phosphatase)	T468M[3]	NSML	Pericardial edema to varying degrees.		(Miura et al., 2013)
ptpn11	Shp2 (Phosphatase)	D61G, T73I, A462T, G465A[3]	NS / NSML	Defects in left-right heart jogging. These are tied to defects in cilia, Kupffer's vesicle and the propagation of Nodal in the lateral plate mesoderm.	Increased Ras/MAPK	(Bonetti et al., 2014)
ptpn11	Shp2 (Phosphatase)	Y279C, T468M	NSML	Convergence and extension defects are measured by the ratio of rhombomere width over rhombomere length.	PZR downstream of Shp2	(Overman et al., 2014)
hras	GTPase	G12V[4]	CS	Tumors, reduced size and life span, smaller heart, and craniofacial defects in adult fish.	Still largely unknown	(Santoriello et al., 2009)
nras	GTPase	I24N, T50I, G60E, G12V[3]	NS	Craniofacial defects and CE defects which cause an oblong embryo shape.	Increased Ras/MAPK	(Runtuwene et al., 2011)
kras	GTPase	N116S[3]	NS	Craniofacial dysmorphia, reduced heart size, and heart jogging defects.	Increased Ras/MAPK	(Razzaque et al., 2012)
braf/ mek	Kinase	28 mutations tested[3]	CFC	CE defects which result in an oblong embryo shape. Heart defects are reported.	Increased Ras/MAPK	(Anastasaki et al., 2009)
braf	Kinase	Q257R, G596V[3]	CFC	Similar to 2009 paper except they find that heart is sensitive to signaling perturbations.	Increased Ras/MAPK	(Anastasaki et al., 2012)
a2ml1	a-2-macroglobulin (A2M)-like-1 (Protease inhibitor)	S592L, R802H, R802L[5]	NS	Craniofacial defects scored by width over height ratio of head and heart looping.	No change in Ras/MAPK	(Vissers et al., 2015)
rit1	RIT1 (GTPase)	Q79L, E81G, G95A[3]	NS	CE defects cause an oblong embryo shape. There are craniofacial and heart defects.	Increased RIT1/MAPK	(Aoki et al., 2013)

Table S5: *Drosophila* Models of RASopathies [1]P-element insertion at NF1 locus, [2]Chemical mutagenesis, [3]Overexpression using p-element insertion

Gene	Protein (function)	Mutation	Disease	Phenotype	Signaling	Reference
Nf1	Neurofibromin (Ras GAP)	Knockout[1]	NF1	$NF1^{-/-}$ flies have growth defects throughout development and impaired cellular response to PACAP38, a neuropeptide	Impaired cAMP	(Guo et al., 1997; The et al., 1997; Tong et al., 2002)
Nf1	Neurofibromin (Ras GAP)	Knockout[1]	NF1	Olfactory learning and short term memory defects	Impaired cAMP	(Guo et al., 2000)
Nf1	Neurofibromin (Ras GAP)	Knockout[1]	NF1	Abnormal circadian rhythms	Increased Ras/MAPK	(Williams et al., 2001)
Nf1	Neurofibromin (Ras GAP)	Knockout[2]	NF1	Growth defects throughout development	Increased Ras/MAPK	(Walker et al., 2006)
Nf1	Neurofibromin (Ras GAP)	Knockout[1]	NF1		Novel NF1-Ras-AC signaling, independent of G_{α} subunit.	(Hannan et al., 2006)
Nf1	Neurofibromin (Ras GAP)	Knockout[1]	NF1	Shortened life expectancy, vulnerability to oxidative and heat stresses, reduced mitochondrial respiration and elevated reactive oxygen species (ROS) production	cAMP regulates mitochondrial activity	(Tong et al., 2007)
Nf1	Neurofibromin (Ras GAP)	Knockout[1]	NF1	Learning and long term memory (LTM) defects	GAP-related domain needed for LTM and C-terminal essential for short- and intermediate-term memory	(Buchanan and Davis, 2010; Ho et al., 2007)
Nf1	Neurofibromin (Ras GAP)	Knockout[2]	NF1		Alk and other modifier genes involved in NF1	(Gouzi et al., 2011; Walker et al., 2013)
csw	Shp-2 (phosphatase)	D61Y, E76K[3]	NS	LTM defects	Prolonged activation or slow decay of Ras/MAPK cycle	(Pagani et al., 2009)
csw	Shp-2 (phosphatase)	N308D, A72S, E76K[3]	NS	Ectopic veins	Increased Ras/MAPK	(Oishi et al., 2006)
csw	Shp-2 (phosphatase)	Y279C,T468M[3]	NSML	Ectopic veins, rough eye	Increased Ras/MAPK	(Oishi et al., 2009)
csw	Shp-2 (phosphatase)	E76K[3]	Leukemia	Increased plasmatocyte cells	Increased Ras/MAPK	(Mohi et al., 2005)
Ras	GTPase	R68Q[2]	NS/CS/ CFC	Enhanced resistance to cell death, ectopic veins, rough eye	Increased Ras/MAPK	(Gafuik and Steller, 2011)
Ras	GTPase	G12V[3]	NS	Cardiac hypertrophy	Increased Ras/MAPK	(Yu et al., 2013)

Table S6: Phenotypes of Animal Models of RASopathies. For each phenotype that occurs in each RASopathy, a reference of an animal model is given.

Diagram Part	Phenotypes	RASopathy	Reference
Mice Only	Bone defects	NF1	(Kolanczyk et al., 2007)
	Neurofibromas	NF1	(Rosenbaum et al., 1997)
	Sex-linked effects	NF1	(Diggs-Andrews et al., 2014)
	Muscle Abnormalities	NF1	(Sullivan et al., 2014)
	Attention deficits	NF1	(Brown et al., 2010)
	Working memory deficits	NF1	(Shilyansky et al., 2010)
	Leaner metabolic profile	NS	(Tajan et al., 2014)
	Hematologic disease	NS	(Araki et al., 2009)
	Triangular face	NS, CS	(Araki et al., 2004; Schuhmacher et al., 2008)
	Enlarged spleen	NS	(Araki et al., 2004)
	Liver defects	NF1,NS,CFC,CS	(Araki et al., 2004; Figueiredo et al., 2012; Hegedus et al., 2007; Inoue et al., 2014)
	Lymphatic system defects	CFC	(Inoue et al., 2014)
	Epileptic seizures	CFC	(Urosevic et al., 2011)
	Nasal septal deviation	CS	(Chen et al., 2009)
	Papilloma formation	CS	(Chen et al., 2009)
	Hyperemotivity	CS	(Viosca et al., 2009)
	Teeth defects	CS	(Goodwin et al., 2014)
***Drosophila* Only**	Mitochondrial defects	NF1	(Tong et al., 2007)
	Circadian rhythm defects	NF1	(Williams et al., 2001)
	Synaptic overgrowth	NF1	(Walker et al., 2013)
	Slower escape response	NF1	(The et al., 1997)
	Ectopic veins	NS	(Oishi et al., 2006)
	Photoreceptor defects	NS	(Oishi et al., 2006)
Zebrafish Only	Pigmentation Defects	NF1	(Shin et al., 2012)
	Motor Defects	NF1	(Shin et al., 2012)
	Schwann cell hyperplasia	NF1	(Shin et al., 2012)
	Kupffer's vesicle malformation	NS	(Bonetti et al., 2014)
	C&E defects	NS, CFC	(Runtuwene et al., 2011)
	Precocious ossification	CS	(Santoriello et al., 2009)
	Reduced blood oxygenation	CS	(Santoriello et al., 2009)
	Scoliotic spine	CS	(Santoriello et al., 2009)
	Sterility	CS	(Santoriello et al., 2009)

Mice and *Drosophila*	**Mice**		***Drosophila***	
Myeloproliferative disease	NF1, NS	(Gitler et al., 2004; Mohi et al., 2005)	NS	(Mohi et al., 2005)

Mice and Zebrafish	**Mice**		**Zebrafish**	
Neural crest cell defects	NF1	(Ismat et al., 2006)	NF1, NS	(Shin et al., 2012; Stewart et al., 2010)
Myelin sheath defects	NF1	(Cichowski et al., 1999)	NF1	(Shin et al., 2012)
OPC hyperplasia	NF1, NS	(Bennett et al., 2003; Ehrman et al., 2014)	NF1	(Shin et al., 2012)
Hypertelorism	NS	(Araki et al., 2004)	NS, CFC, CS	(Anastasaki et al., 2012; Runtuwene et al., 2011; Santoriello et al., 2009)
Gliomas	NF1	(Hegedus et al., 2009)	NF1	(Shin et al., 2012)

Mice, Zebrafish, and *Drosophila*	**Mouse**		**Zebrafish**		***Drosophila***	
Learning/cognitive defects	NF1, NS, CS	(Costa et al., 2002; Lee et al., 2014; Viosca et al., 2009)	NF1	(Wolman et al., 2014)	NF1, NS	(Buchanan and Davis, 2010; Pagani et al., 2009)
Reduced life span	NS, CFC	(Hernández-Porras et al., 2014; Urosevic et al., 2011)	CS	(Santoriello et al., 2009)	NF1	(Tong et al., 2007)
Growth defects	NS, CFC	(Araki et al., 2004; Urosevic et al., 2011)	NS, CFC, CS	(Anastasaki et al., 2009; Jopling et al., 2007; Santoriello et al., 2009)	NF1	(Walker et al., 2006)
Cardiac defects	NF1, NS, CFC, CS	(Araki et al., 2009; Inoue et al., 2014; Ismat et al., 2006; Schuhmacher et al., 2008)	NF1, NS, CS	(Bonetti et al., 2014; Padmanabhan et al., 2009; Santoriello et al., 2009)	NS	(Yu et al., 2013)

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