RASopathy	Model organism	RASopathy gene	Mutation	Features	Reference
NF1	*Danio rerio*	NF1	nf1a-/- nf1b-/-	Macrocephaly and increased OPC migration within the spinal cord	81
NS	*Danio rerio*	*PTPN11*	Shp2 p.D61G	Craniofacial defects	93
		RRAS2	RRAS2 p.G24_26dup	Craniofacial defects and macrocephaly	95
			RRAS2 p.Q72H		
			RRAS2 p.Q72L	Craniofacial defects and developmental impairment	
			RRAS2 p.F75C	No aberrant in vitro or in vivo phenotypes	
		*A2ML1***	A2ML1 p.R592L	Craniofacial defects that are characteristic of NS, including a broad head	75
			A2ML1 p.R802L		
			A2ML1 p.R802H		
		SPRED2	SPRED2 p.R63*	NS evocative phenotypes, such as developmental delay and intellectual disability	4
			SPRED2 p.L100P		
			SPRED2 p.L381Hfs*95		
	Drosophila	*PTPN11*	Shp2 p.D61G	Altered cellular signaling networks	119
			Shp2 p.Y279C		
			Shp2 p.N308D		
			Shp2 p.R498W		
			Shp2 p.Q510P		
			Shp2 p.Q510E		
		BRAF	BRAF1 p.Q257R	Altered cellular signaling networks	119
			BRAF p.W531C		
		KRAS	KRAS p.G12D	Altered cellular signaling networks	119
		HRAS	HRAS p.G12S	Altered cellular signaling networks	119
		RAF1	RAF1 p.S257L	Altered cellular signaling networks	119
			RAF1 p.D486G		
			RAF1 p.L613V		
	C. elegans	*MAPK1*	MAPK1 p.I74N	Muv phenotype, consistent with aberrant RAS/MAPK pathway activity	66
			MAPK1 p.H80Y		
			MAPK1 p.A174V		
			MAPK1 p.D318G		
			MAPK1 p.P323R		
		SHOC2	SHOC2 p.S2G	Aberrant RAS/MAPK signaling	125
		RRAS	RRAS p.G39dup	Enhanced RAS/MAPK signaling	126
CS	*Danio rerio*	*HRAS*	HRAS p.G12V	CS phenotypes such as craniofacial dysmorphia and oncogene-induced senescence in the brain	99
CFC	*Danio rerio*	*BRAF*	BRAF p.Q257R	Increased major:minor axis ratio	101
			BRAF p.V600E	Early induction: truncated posterior structure and compromised forebrain. At a later stage, craniofacial deformities	102
	Drosophila	*MEK1*	Dsor1 p.Y130C	Larval cuticle deficits and ectopic wing veins	103
RASopathy-like	*Danio rerio*	*RAC1*	RAC1 p.P29S	Rasopathy-like phenotype	97
		RABL3	RABL3 p.S36*	Rasopathy-like phenotype	98

Table S2. RASopathy-associated mutations studied in non-mammalian model organisms. Collation of investigated RASopathy-associated mutations in non-mammalian models emphasized in this review, along with observed related features. In genes related to Noonan Syndrome (NS), double asterisks (**) signify an additional correlation between the mutations and Noonan-like syndrome.