

Supplemental Table 1: JS-MKS gene candidates and suspect gene-condition associations

Gene	Reported condition	Rationale	Ref
<i>ADAMTS9</i>	JS	**Strong candidate with only two families identified so far	(36, 126)
<i>CBY1</i>	JS	**Strong candidate with only two families identified so far	(54)
<i>CELSR2</i>	JS	only one family in each of two papers, specific variants not reported in one paper, biallelic variants in a well-established JS gene (<i>TOGARAM1</i>) in the other paper	(165, 193)
<i>CEP164</i>	JS	only one family with JS, variants reported in families with other ciliopathies	(27, 193)
<i>CLUAP1</i>	JS	only one family with JS	(92)
<i>EXOC2</i>	JS	only single family with MTS (2 families reported w/MRIs of 3 peps)	(188)
<i>EXOC4</i>	MKS	only single families with JS or MKS	(160)
<i>EXOC8</i>	JS	only single family with JS	(49)
<i>KIF14</i>	MKS	single family with MKS	(60)
<i>POC1B</i>	JS	only one family with JS	(16)
<i>TTC21B</i>	JS	no biallelic variants in JS, biallelic variants reported in families with other ciliopathies	(46)
<i>ZNF423</i>	JS	only one family with possible JS, variants reported in families with NPH	(27)

Supplemental Table 2: Common Hh signaling phenotypes in JS-MKS-NPH models

Human gene	Localization				Western blot		mRNA			in situ		Neural tube	Polydactyly
	SMO	GLI2	GLI3	GPR161	GLI2	GLI3	GLI1	PTCH	SHH	PTCH	GLI1		
<i>ADAMST9</i> (36, 129)	AB	ND	ND	ND	ND	AB	AB	AB	ND	ND	ND	ND	ND
<i>AHI1</i> (128)	NL	ND	ND	ND	ND	ND	AB	NL	ND	ND	ND	ND	ND
<i>ARL13B</i> - KO/null (25, 56, 66, 101, 110, 124, 131, 173)	AB NL	NL	AB	AB	ND	NL	AB NL	AB	AB	ND	ND	AB	AB
<i>ARL13B</i> - KD (15, 66, 124)	AB	NL	AB	ND	ND	ND	AB	AB NL	ND	ND	ND	ND	ND
<i>ARL3</i> (97, 156)	AB	ND	AB	ND	ND	AB	ND	ND	ND	ND	ND	ND	ND
<i>ARMC9</i> (19)	NL	AB	AB	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
<i>B9D1</i> (35, 50)	AB	ND	ND	ND	ND	AB	AB	AB	ND	ND	ND	AB	AB
<i>B9D2</i> (50)	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	AB
<i>C2CD3</i> (20, 28, 81)	ND	ND	ND	ND	AB	AB	ND	AB	AB	AB	AB	AB	AB
<i>CC2D2A</i> (35, 64, 191)	AB	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	AB	AB
<i>CEP104</i> (63, 205)	AB	ND	ND	AB	ND	ND	AB	ND	ND	ND	ND	ND	ND
<i>CEP164</i> (95)	ND	AB	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
<i>CEP290</i> - KD (87, 93, 166, 169)	AB NL	AB	AB	ND	ND	AB	AB NL	AB	AB	ND	ND	ND	ND
<i>CPLANE1</i> (7)	ND	ND	ND	ND	ND	ND	AB	AB	ND	ND	ND	ND	ND
<i>CSPP1</i> (63, 164)	AB	ND	ND	ND	ND	ND	AB	ND	ND	ND	ND	ND	ND
<i>DCDC2</i> (125)	ND	ND	ND	ND	ND	ND	ND	ND	AB NL	ND	ND	ND	ND
<i>FAM149B1</i> (162)	ND	ND	ND	ND	ND	ND	AB	AB	ND	ND	ND	ND	AB
<i>HYLS1</i> (30)	ND	ND	AB	AB	ND	ND	AB	AB	ND	ND	ND	ND	ND
<i>IFT172</i> (62, 67, 70, 85, 86, 132, 133)	AB	ND	ND	ND	ND	AB	AB	ND	ND	AB	AB	AB	AB

<i>INPP5E-KO/null</i> (29, 38, 52, 65)	AB NL	AB	AB	AB	AB	AB	AB	AB	AB	ND	ND	ND	A B	A B
<i>KIAA0586</i> (4, 13, 14, 44, 45)	ND	ND	ND	ND	AB	AB	AB	AB	AB	ND	AB	AB	A B	A B
<i>KIAA0753</i> (88)	ND	ND	ND	ND	ND	ND	AB	AB	AB	AB	ND	ND	N D	N D
<i>KIF7-KO/null</i> (33, 53, 83, 103, 111, 117, 142, 210)	NL	AB	AB	ND	AB	AB	AB NL	AB	AB	ND	ND	AB	A B	A B
<i>KIF7-KD</i> (7, 76, 113, 143, 156, 178, 179, 207)	NL	AB NL	AB NL	ND	AB	AB	NL	AB NL	AB	ND	AB	ND	A B	A B
<i>MKS1</i> (23, 40, 67, 199)	AB	ND	ND	AB	ND	ND	ND	ND	ND	ND	AB	AB	A B	A B
<i>OFD1</i> (41)	ND	ND	ND	ND	ND	AB	AB	AB	AB	AB	ND	ND	N D	N D
<i>RPGRIP1L</i> (31, 192, 197)	AB	ND	ND	ND	ND	AB	AB	AB	AB	ND	AB	ND	A B	A B
<i>SUFU-KO/null</i> (1, 32, 78, 79, 109, 114, 123, 130, 140, 175, 204, 206)	ND	AB	AB	AB	AB	AB NL	AB NL	AB	AB	AB	AB	AB	A B	A B
<i>SUFU-KD</i> (47, 79, 94, 109, 123, 154, 176, 210)	AB	ND	ND	ND	AB NL	AB NL	AB NL	AB NL	NL	AB	ND	ND	A B	A B
<i>TCTN1</i> (64)	AB	ND	ND	ND	ND	AB	ND	ND	ND	ND	AB	AB	N D	A B
<i>TCTN2</i> (64, 150, 161, 200)	AB	ND	ND	ND	ND	AB	AB	AB	AB	ND	ND	ND	A B	A B
<i>TCTN3</i> (181, 196)	AB	ND	ND	ND	AB	AB	AB	AB	AB	ND	ND	ND	A B	A B
<i>TMEM67-KO/null</i> (2, 64)	NL	ND	ND	ND	ND	ND	ND	ND	ND	AB	ND	ND	A B	N D
<i>TMEM67-KD</i> (106)	ND	ND	ND	ND	ND	ND	NL	NL	ND	NL	AB	ND	N D	N D
<i>TMEM107</i> (158)	ND	ND	ND	ND	ND	ND	AB	ND	ND	ND	AB	AB	A B	A B
<i>TMEM216</i> (187)	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	N D	A B
<i>TMEM231</i> (35)	AB	ND	ND	ND	ND	ND	AB	ND	ND	ND	ND	ND	A B	A B

<i>TTC21B</i> (184, 185, 198)	NL	ND	ND	ND	ND	AB	AB	NL	ND	AB	ND	A B	N D
<i>TOGARAM1</i> (102)	AB	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	N D	N D
<i>WDR19</i> (8, 112)	NL	AB	ND	ND	ND	NL	AB	AB	ND	AB	ND	A B	A B

Supplemental Table 3: Locus heterogeneity in zebrafish models of JS-associated genes

Human Gene	ZF GENE ZF mutant	Renal cysts	Curved Body axis	Kinked Curved tail	Retinal involvement	Ciliogenesis	Hydrocephalus	Method
<i>AHI1</i> (108)	<i>ahi1</i> <i>ahi1^{lri46}</i>	AB	ND	AB	AB	AB	ND	TALENs
<i>ARL13B</i> (51, 68, 174)	<i>hi459</i> <i>scorpion^{hi459}</i>	AB	AB	AB	ND	AB	ND	Ins Mut
<i>ARMC9</i> (21)	<i>armc9</i>	AB	AB	ND	ND	AB	ND	CRISPR
<i>B9D2</i> (50)	<i>b9d2</i>	ND	ND	ND	ND	ND	ND	MO
<i>CC2D2A</i> (69)	<i>cc2d2a</i> <i>sentinel</i>	AB	AB	ND	ND	ND	ND	ENU
<i>CEP41</i> (104)	<i>cep41</i>	ND	ND	ND	ND	ND	ND	MO
<i>CEP104</i> (63)	<i>cep104</i>	ND	ND	AB	ND	ND	ND	MO
<i>CEP120</i> (163)	<i>cep120</i>	AB	AB	ND	ND	ND	AB	MO
<i>CEP290</i> (151, 152)	<i>cep290/</i> <i>nphp6</i>	AB	ND	ND	AB	ND	AB	MO
<i>CSPP1</i> (186)	<i>cspp1a/b</i>	AB	AB	ND	ND	ND	AB	MO
<i>IFT172</i> (119)	<i>ift172</i>	ND	ND	ND	ND	AB	ND	MO
<i>INPP5E</i> (209)	<i>inpp5e</i>	AB	ND	AB	AB	AB	ND	MO
<i>KIAA0586</i> (17, 134)	<i>talpid3</i> <i>ta3²⁶²⁻¹²⁶⁵</i>	AB	AB	ND	AB	AB	ND	ZFN
<i>KIAA0556</i> (148)	<i>kiaa0556</i>	ND	ND	AB	ND	ND	ND	MO
<i>KIAA0753</i> (74)	<i>kiaa0753</i> <i>sa22657</i>	ND	AB	ND	ND	ND	ND	Comm. EZRC
<i>MKS1</i> (107)	<i>mks1</i>	ND	ND	ND	ND	ND	ND	MO
<i>NPHP1</i> (115)	<i>nphp1</i>	AB	ND	ND	ND	ND	ND	MO
<i>NPHP4</i> (22)	<i>nphp4</i>	AB	ND	AB	AB	ND	ND	MO
<i>OFD1</i> (58)	<i>ofd1</i>	ND	AB	ND	ND	ND	AB	MO
<i>PDE6D</i> (182)	<i>pde6d</i>	AB	ND	ND	AB	ND	ND	MO
<i>RPGRIP1L</i> (122)	<i>rpgrip11l,</i> <i>mks5</i>	ND	AB	ND	ND	ND	AB	MO
<i>TCTN2</i> (116)	<i>tctn2</i>	ND	ND	ND	ND	ND	ND	MO
<i>TMEM67</i> (106)	<i>tmem67,</i> <i>mks3</i>	AB	ND	AB	AB	ND	AB	MO
<i>TMEM138</i> (105)	<i>tmem138</i>	ND	AB	ND	ND	ND	ND	MO
<i>TMEM216</i> (105)	<i>tmem216</i>	ND	AB	AB	ND	ND	AB	MO
<i>TMEM237</i> (84)	<i>tmem237a/b</i>	ND	ND	ND	ND	ND	ND	MO
<i>TOGARAM1</i> (21)	<i>togaram1</i>	AB	AB	ND	ND	AB	ND	CRISPR

Supplemental Table 4: Locus heterogeneity in mouse models of JS-associated genes

Human Gene	Mouse Gene /mutant	Embryonic/ perinatal lethality	Eye defects	L-R asymmetry	Disrupted Hh/ Neural tube	Polydactyly	Kidney cysts	Ciliogenesis	Cranio-facial defects
<i>AHI1</i> (99, 100)	<i>Ahi1</i>	ND	ND	ND	ND	ND	AB	ND	ND
<i>ARL13B</i> (25, 173)	<i>Arl13b, hennin</i>	AB	AB	AB	AB	AB	ND	AN	ND
<i>ARL3</i> (75, 153)	<i>Arl3</i>	AB	AB	ND	ND	ND	AB	ND	ND
<i>B9D1</i> (50)	<i>B9d1</i>	AB	AB	AB	AB	AB	AB	AB	AB
<i>B9D2</i> (183)	<i>B9d2, stumpy</i>	ND	ND	ND	ND	ND	AB	AB	ND
<i>CPLANE1</i> <i>C5ORF42</i> (43)	<i>Cplane1</i> <i>hug</i>	AB	AB	ND	NL	AB	AB	AB	AB
<i>CC2D2A</i> (64)	<i>Cc2d2a</i>	ND	AB	AB	ND	ND	ND	ND	ND
<i>C2CD3</i> (81)	<i>C2cd3</i> <i>hty, hearty</i>	AB	ND	AB	AB	AB	ND	AB	ND
<i>CEP41</i> (104)	<i>Cep41</i>	AB	ND	ND	ND	ND	ND	ND	ND
<i>CEP120</i> (203)	<i>Cep120</i>	AB	ND	AB	AB	ND	ND	AB	ND
<i>CEP290</i> (144)	<i>Cep290</i>	AB	AB	ND	ND	ND	AB	ND	ND
<i>CSPP1</i> MGI: 2681832	<i>Cspp1</i>	ND	ND	ND	ND	ND	ND	ND	ND
<i>HYLS1</i> MGI: 1924082	<i>Hyls1</i>	AB	ND	AB	ND	ND	ND	ND	ND
<i>IFT172</i> (70, 86)	<i>lft172, wim, slb</i>	AB	AB	AB	AB	AB	ND	ND	AB
<i>INPP5E</i> (89)	<i>Inpp5e</i>	AB	AB	ND	ND	AB	AB	ND	AB
<i>KIAA0586</i> (13, 14)	<i>Talpid3</i>	AB	ND	AB	AB	AB	ND	AB	AB
<i>KIAA0556</i> (149)	<i>Kiaa0556</i>	ND	ND	ND	ND	ND	NL	NL	ND
<i>KIAA0753</i> MGI: 1921727	<i>Kiaa0753</i>	AB	ND	AB	ND	ND	ND	ND	AB
<i>KIF7</i> (113)	<i>Kif7, maki</i>	AB	ND	ND	AB	AB	ND	ND	ND
<i>MKS1</i> (40, 199)	<i>Mks1</i>	AB	AB	AB	AB	AB	AB	AB	AB
<i>NPHP1</i> (90, 91)	<i>Nphp1</i>	ND	AB	ND	ND	ND	NL	ND	ND
<i>NPHP4</i> (202)	<i>Nphp4</i> <i>nmf192</i>	ND	AB	ND	ND	ND	NL	ND	ND
<i>OFD1</i> (59)	<i>Ofd1</i>	AB	ND	AB	AB	AB	AB	AB	AB
<i>PDE6D</i> (208)	<i>Pde6d</i>	ND	AB	ND	ND	ND	ND	ND	ND
<i>PIBF1</i> MGI: 1261910	<i>Pibf1</i>	AB	ND	AB	AB	ND	ND	ND	ND
<i>RPGRIP1L</i> (192)	<i>Rpgrip1l</i> <i>ftm fantom</i>	AB	AB	AB	AB	AB	AB	AB	AB
<i>SUFU</i> (39, 79, 175)	<i>Sufu</i>	AB	AB	AB	AB	AB	AB	ND	AB
<i>TCTN1</i> (64, 145)	<i>Tctn1</i> <i>kerouac</i>	AB	ND	AB	AB	AB	AB	AB	ND
<i>TCTN2</i> (150)	<i>Tctn2</i>	AB	AB	AB	AB	AB	AB	AB	AB
<i>TCTN3</i> (195)	<i>Tctn3</i>	AB	AB	AB	AB	AB	ND	ND	ND
<i>TMEM67</i> (64)	<i>Tmem67</i>	AB	ND	ND	ND	ND	AB	AB	ND
<i>TMEM107</i> (26)	<i>Tmem107</i>	AB	AB	ND	AB	ND	ND	ND	AB
<i>TMEM138</i> MGI: 1920232	<i>Tmem138</i>	ND	ND	ND	ND	ND	ND	ND	ND
<i>TMEM218</i> (194)	<i>Tmem218</i>	ND	ND	ND	ND	ND	AB	ND	ND
<i>TMEM231</i> (146)	<i>Tmem231</i>	AB	AB	ND	AB	AB	ND	ND	ND
<i>TMEM237</i> MGI: 2138365	<i>Tmem237</i>	AB	ND	ND	ND	ND	ND	ND	ND

1. !!! INVALID CITATION !!! .
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