Supplementary Table 1 | *Drosophila* PCP genes and their vertebrate homologues involved in kidney development

PCP genes		Protein properties, interactions with other PCP molecules and subcellular localization	Expression patterns and mutant PCP phenotypes			Human diseases associated with PCP gene mutations
Drosophila	**Vertebrates**		***Drosophila***	**Vertebrates**	**Role in kidney development**	
Frizzled (*fz*) *Frizzled2(fz2)*[1-3]	*Fzd1*, *Fzd2*, *Fzd3**, *Fzd4**, *Fzd5*, *Fzd6**, *Fzd7*, *Fzd8**, *Fzd9*, *Fzd10*	Seven-pass transmembrane receptor, localizes asymmetrically in both *Drosophila* and vertebrate cells. Binds Wnt ligands, recruits Dvl and Dgo to the membrane. Asymmetrically localized and interacts with Fmi and Vang[4, 5].	Widely expressed. PCP defects in all tissues studied.	*Fzd* genes are often expressed in tissue-specific patterns. Multiple *Fzds* are in the neuroectoderm, skin, somites and other tissues and organs. *Xenopus Fzd8* is expressed in the pronephros[6], *Fzd3,4,6* and *8* are expressed in renal tubules[7, 8]. Double *Fzd3/6* homozygous mice exhibit PCP defects in hair organization and *craniorachischisis*[9].	*xFzd8* regulates pronephros development in *Xenopus* [6]; Double *Fzd4/Fzd8* homozygous mutant mice display renal hypoplasia due to UB branching defects [7].	*FZD4*: familial exudative vitreoretinopathy[10]; *FZD6*: various NTDs[11].
Dishevelled (dsh)[12]	*Dvl1*, *Dvl2*, *Dvl3*	A multimodular cytoplasmic protein containing the DIX, PDZ and DEP domains. Recruited by Frizzled to the cell membrane and asymmetrically localized in the cortex. Localized to the centrosome. Interacts with Fz, Vang, Pk, Daam1, Dgo and other proteins.	Widely expressed; PCP defects in all tissues studied.	Dvl1-3 proteins are widely expressed in multiple tissues in overlapping and tissue-specific patterns and have redundant functions. Simultaneous loss of two or three *Dvl* genes causes defects in multiple organs including the brain and the heart[13].	Wider and shorter pronephros in *Xenopus* expressing *xDvl2* mutant that interferes with PCP signalling[14].	*DVL1* and *DVL3*: various NTDs[11]; *DVL1*: Robinow syndrome (duplicated ureter and VUR are reported)[15]; *DVL3*: Robinow syndrome[16].
Prickle (pk)/ *Spiny legs (sple1)*[17]	*Pk1**, *Pk2*, *Pk3**, *Pk4*	PET and LIM domain-containing cytoplasmic protein. Interacts with Vangl, Dvl, Dgo and Par3 (Pk3). Recruited to the cell membrane by Vang. Asymmetrically localized in *Drosophila* wing, zebrafish and *Xenopus* neuroectoderm.	Widely expressed. PCP defects in all tissues studied; Pk and Sple1 isoforms regulate orientation of microtubule polarity[18].	Early embryonic lethality in *pk1-/-* mice[19]. *Pk1-/-* Robinow-like syndrome including facial and skeletal abnormalities[20]; *Pk3* depletion in *Xenopus* causes neural tube and cilia defects[21].	Mouse *Pk1-/-* mutants exhibit renal dysplasia; 5% of embryos display renal cysts [20].	*PK1*: various NTDs[11, 22]; *PK1*: epilepsy-ataxia syndrome and other neurological abnormalities[23].
Flamingo (fmi) or starry night (stan)[24,25]	*Celsr1*, *Celrs2*, *Celsr3*	Cadherin-EGF-LAG seven pass G-type receptor with multiple cadherin domains. Forms homodimers and interacts with Fz and Vang. Asymmetrically localized in *Drosophila* and mammalian tissues.	Widely expressed in all tissues[26], PCP defects in all tissues studied.	Redundant and specific functions. Multiple defects in mutant mice including *craniorachischisis* (*Celsr1-/-*)[27] and lethal hydrocephalus (*Celsr2,3-/-*)[28].	*Ceslr1-/-* mice: smaller kidneys with defective UB branching[29].	*CELSR1–3*: various NTDs[11, 30, 31]. NTDs caused by *CELSR1* mutations are associated with elevated frequency of kidney malformations[29].
Van Gogh (vang)[32,33] *or Strabismus (stbm)*	*Vangl1*, *Vangl2* [34]	Tetraspanin with a PDZ-binding domain. Interacts with Pk[35], Dvl, Fmi, Scribble and extracellularly with Frizzled[36]. Vang is asymmetrically localized in *Drosophila* and vertebrate tissues, including renal tubules, inner ear, neural plate and the skin.	Widely expressed in all tissues; PCP defects in all tissues studied	Multiple organ defects including *craniorachischisis*, heart, lung, gastrointestinal, skeletal and ocular defects, defective cochlea[34, 37, 38].	Homozygous *Vangl2* mutant mice: kidney hypodysplasia, abnormal diameter of renal tubules[8, 39, 40]. Abnormal glomerular maturation and injury recovery[39].	*VANGL1/2*: various NTDs[11, 41, 42]; *VANGL1*: caudal regression syndrome in association with NTDs[41].
Diego (dgo) [43]	*Inversin/NPHP2*[44] *Diversin/ANKRD6*[45]	Ankyrin repeat-containing cytoplasmic proteins. Dgo is recruited to the membrane by Fz and asymmetrically localized; Dgo interacts with Dvl, Fz, Vang and Pk[46]. ANKDR6 is asymmetrically localized in the mouse inner ear cells[47]. Inversin localizes to the ciliary transition zone. Both Inversin and ANKDR6 associate with the basal body.	Widely expressed in all tissues; PCP defects in all tissues studied.	Widely expressed. ANKRD6 and Inversin modulate convergent extension movements, regulate cilia and left–right patterning in vertebrates[44, 48]. *ANKRD6-/-* mice display PCP defects in cochlea[47].	*Inversin* knockdown in *Xenopus*: pronephros anomalies[49]. *Inversin-/-* mouse: cystic kidney with interstitial fibrosis[50, 51].	*NPHP2* mutations: nephronophthisis, type II[44]; *ANKRD6* mutations: various NTDs[11].
*Wg** *dWnt2* *dWnt4** *dWnt6* *dWnt10*	*Wnt1*, *Wnt2*, *Wnt2b/13*, *Wnt3*, *Wnt3a*, *Wnt4*, *Wnt5a**, *Wnt5b*, *Wnt6*, *Wnt7a*, *Wnt7b*?*, *Wnt8a*, *Wnt8b*, *Wnt9a*, *Wnt9b**, *Wnt10a*, *Wnt10b*, *Wnt11**, *Wnt16*	Cysteine-rich secreted signalling lipoproteins. Known to bind to multiple receptors including Fzd, Ror1/2, Ryk1 and Ptk7 via a cysteine-rich domain[52].	Often expressed in tissue-specific patterns. The combined loss of Wg or Wnt4 leads to loss of PCP in wing[53]; however, this has not been confirmed by other studies[54, 55].	Many Wnt ligands are expressed in specific patterns, often consistent with concentration gradients. Loss-of-function studies reveal major developmental abnormalities, including PCP phenotypes. Can instruct PCP in several models, but the requirement for PCP may be indirect [56]. *Wnt5a-/-* mice display caudal regression syndrome[57].	*Wnt5a-/-* mice: kidney defects range from renal agenesis and single kidney to renal hypoplasia and duplex kidneys [57-59]. *Wnt9a-/-* mice: cystic kidneys, abnormalities of nephrogenic progenitor pool and UB branching [60]; *Wnt11-/-* mice: hypoplastic kidneys due to loss of polarized NPCs behaviour, premature NPC depletion causing defective UB branching [61].	*WNT5a*: Robinow syndrome, including hypoplastic kidneys in some patients[62]; isolated solitary kidney[59].

Fat (ft) and Fat2 [63]	*Fat1**, *Fat2*, *Fat3*, *Fat4**	Proto-cadherin with a large extracellular domain containing Cadherin-, Laminin-G-like and EGF-like repeats. Binds to Dchs1 and Dchs2. Phosphorylated by Ft[64].	Widely expressed in all tissues; PCP defects in all tissues studied. Participates in Hippo signalling [65].	Multiple defects in all *Fat* mouse mutants, including neurological, eye and other anomalies[66]. *Fat4* interacts genetically with *Vangl2* and *Fjx1* [67] .	*Fat4-/-* mouse: hypoplastic cystic kidneys, duplex kidneys, expansion of nephrogenic progenitor zone [67, 68]. *Fat1-/-* mouse: congenital lack of glomerular podocyte slit diaphragm leading to neonatal death [69].	*FAT1:* novel syndrome: colobomatous-microphthalmia, ptosis, nephropathy and syndactyly[70]; isolated glomerulopathy (FSGS)[71]. *FAT4:* Van Madlergem syndrome 2 [72].
Dachsous (ds) [63]	*Dchs1*, *Dchs2*	Proto-cadherin (also known as Cadherin16 or Cadherin19), contains cadherin-, Laminin-G-like -repeats in the extracellular domain. Binds to Fat1 and Fat2 receptors. Phosphorylated by Fj. Asymmetrically localized.	Widely expressed in all tissues and forms a gradient along *Drosophila* wing blade and ey;, PCP defects in all tissues studied. Participates in Hippo signalling [64].	In mouse is widely expressed and required for organogenesis of many tissues including brain, heart, lung, intestine, kidney and ear [72]. The phenotype is similar to *Fat4-/-* [73].	Dchs1/2: expansion of nephrogenic progenitor zone, UB branching defects, hypoplastic kidney [68, 74].	Van Madlergem syndrome 1 with kidney involvement in some patients[72].
Four jointed (fj) [75, 76]	Fjx1 [67]	Transmembrane protein II, Golgi-associated serine-threonine protein kinase. Interacts with Ft and Ds.	Expressed in a gradient in *Drosophila* wing and eye. PCP defects in the eye and wing. Additionally controls cell growth and differentiation via Hippo signalling [64].	Required for development of multiple organs including heart, lung, eye and others [67].	Exacerbates renal hypoplasia, cystic and duplex kidney phenotypes on *Fat4-/-* background[67]; partially rescues cystic kidney phenotype in *Pkd1-/-* mice[77].	N/D
Off-track (*otk, otk2*) [78]	Ptk7 [79]	Atypical protein tyrosine kinase (enzymatically dead). Interacts with Wnt, Ror2, Dvl.	No PCP phenotypes.	Widely expressed in many tissues. *Ptk7* mutations in mice cause *craniorachischisis* and *spina bifida* as well as a decrease in hematopoietic pool [79, 80]. *Ptk7* interacts genetically with *Vangl2* to regulate neural tube closure [79].	Renal hypoplasia in mice [79]	Various NTDs [11].
Ror [81]	*Ror1*, *Ror2* [82]	Receptor tyrosine kinase, acts as Wnt5a co-receptor to regulate PCP signalling and convergent extension movements in *Xenopus* [83, 84]	No PCP phenotype for the null allele.	Often expressed in tissue-specific manner. Regulates morphogenesis of multiple organs in mice [57].	*Ror1-/-* and *Ror2-/-* mice: renal hypoplasia, duplex kidneys [57, 85].	*ROR2*: Robinow syndrome including smaller kidneys in some patients [86].
Inturned (in) [17, 87]	*Intu*[88, 89]	Interacts with Fuz, Inturned, Dvl, Daam1 and Vangl2 [90, 91]. A part of the functional module with Fuz to form Rab23GEF to control ciliogenesis [92]. Asymmetrically localized in *Drosophila* wing cells.	Expressed in *Drosophila* wing cells	Morphogenesis defects in *Xenopus*, cilia defects[88]. A wide range of defects in *Intu-/-* mice: cranial NTD or hydrocephaly, heart outflow defects, polydactyly, facial abnormalities, hypoplastic liver, lungs, anophthalmia and others, shorter cilia [89].	N/D	SRPS II OFD type II (renal hypoplasia is reported), NPHP [91]
Fuzzy (fy) [17, 93]	*Fuz* [88]	LONGIN-domain-containing protein, a part of Rab23GEF [92], interacts with Fuz, Intu, Dvl and Vangl2. Asymmetrically localized in *Drosophila* wing cells.	Expressed in *Drosophila* wing cells.	Broadly expressed. Loss-of-function phenotypes are similar to those of *Intu* morphants in *Xenopus* [88] and *Intu-/-* mice [94]. Involved in endo/exocytosis, ciliogenesis in vertebrates [91, 94].	Renal hypodysplasia (E. Torban, unpublished work).	Various NTDs[95], SRPS type II (hypoplastic kidneys are reported) [96]
Fritz [97]	*WDPCP* [98]	WD-domain-containing protein, regulator of actin and vesicle trafficking	Broadly expressed in *Drosophila* wing cells.	Multiple defects in *Wdpcp-/-* mice including heart defects, polydactyly, hypoplastic liver, lungs. Shorter cilia and abnormal ciliogenesis [98].	Renal dysplasia, duplex kidneys [98]	SRPS type II OFD type VI Joubert syndrome with renal disease [91]
Multiple wing hair (mwh)[17]	Does not exist in vertebrates	Formin-domain protein, negative regulator of actin polymerization	Broadly expressed in *Drosophila* wing cells	N/A	N/A	N/A
Daam [99]	*Daam1*, *Daam2*	Formin-domain protein, positive regulator of actin polymerization. Interacts with Dvl, RhoA, Intu [100, 101]	Regulates axon growth and tracheal cuticle pattern[102] and left–right asymmetry[99].	Mouse and *Xenopus Daam1/2* are widely expressed and may have redundant functions. *Daam1* genetically interacts with *Vangl2* and *Wnt5a* to control caudal development and neural tube closure, respectively[103].	*Daam1* knockdown in *Xenopus* and zebrafish causes defective pronephric tubulogenesis[104].	N/D

The table does not include relevant apicobasal polarity components and PCP effectors that have broad housekeeping functions, such as protein kinases, Rabs and other vesicular trafficking machinery, actin- and tubulin-associated proteins, myosins, small GTPases. GEF, guanine nucleotide exchange factor; N/A, not applicable; N/D, not determined; NPCs, nephron progenitor cells; NPHP, nephronophthisis; NTD, neural tube defects; OFD, oral-facial-digital syndrome; PCP, planar cell polarity; PKD, polycystic kidney disease; SRPS, short rib polydactyly syndrome; UB, ureteric bud; VUR, vesicoureteral reflux.
*Members of the large gene group known to participate in PCP signalling.

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