An updated SYSCILIA gold standard (SCGSv2) of known ciliary genes, revealing the vast progress that has been made in the cilia research field

Suly Saray Villa Vasquez¹, John van Dam² Gabrielle Wheway*¹

1. Faculty of Medicine, University of Southampton, UK  
2. Theoretical Biology and Bioinformatics, Department of Biology, Science Faculty, Utrecht University, Netherlands

Running Head. Provide a running head fewer than 40 characters.

Abbreviations. List only nonstandard abbreviations that are used three or more times in the text.

*corresponding author

Brief report 20,000 characters exc spaces max excluding materials and methods and references

18,810 characters

Abstract (200 words or less) 173 words
Cilia are microtubule-based organelles with important functions in motility and sensation. They contribute to a broad spectrum of developmental disorders called ciliopathies, and have recently been linked to common conditions such as cancers and congenital heart disease. There has been increasing interest in the biology of cilia and their contribution to disease over the past two decades. As a result, in 2013 we published a ‘Gold Standard’ list of genes confirmed to be associated with cilia. This was published as part of the SYSCILIA consortium systems biology study dissecting the contribution of cilia to human health and disease, and was named the Syscilia Gold Standard (SCGS). Since this publication, interest in cilia and understanding of their functions has continued to grow, and we now present an updated SCGS version 2. This includes an additional 383 genes, more than doubling the size of SCGSv1. We use this dataset to conduct a review of advances in understanding of cilia biology 2013-2021, and perspectives on the future of cilia research. We hope that this continues to be a useful resource for the cilia community.

Introduction
Cilia are microtubule-based cell surface organelles with important functions in motility and sensation. There are three subclasses of cilia defined by their microtubule ultrastructure. Firstly, motile cilia are found in large numbers on the epithelial cells of the reproductive tracts, brain ventricles and respiratory tract. As a result, cells with motile cilia are often called multiciliated cells (MCCs). These cilia have a backbone (axoneme) of a ring of 9 microtubule doublets, with a central pair of microtubules, and dynein arms allowing the cilia to beat in a coordinated motion to facilitate fluid flow over their surface (Legendre et al., 2021). Secondly, nodal cilia are a population of cilia which exist transiently in embryonic development at the embryonic node. They lack the central pair of microtubules and retain motility, and function in directional fluid flow at the node to establish left-right asymmetry in the embryo (Nonaka et al., 1998). Finally, primary cilia are single non-motile organelles found on the surface of all other epithelial cells in the body, and some other cell types such as fibroblasts. They lack the central pair of microtubules and dynein arms. They do not beat and their primary functions are in chemosensation, mechanosensation and, in the retina, photosensation (Wheway et al., 2018). The outer segment of the photoreceptor cell of the retinal is a huge and highly specialised primary cilium (Bujakowska et al., 2017).
Until several decades ago primary cilia were believed to be vestigial organelles with no significant function. They were assumed to have lost their motility and been rendered redundant. This view was challenged in the early 2000s when it was demonstrated that primary cilia are required for normal kidney function, with the discovery that IFT88, mutated in a mouse model of polycystic kidney disease, is required for cillum assembly (Pazour et al., 2000). This led to molecular investigations which identified the primary cillum as a sensory organelle, with mechanosensory roles in the kidney mediated by polycystins in the cilium membrane (Yoder et al., 2002; Nauli et al., 2003). This was an important discovery as it uncovered the role of the primary cilium in autosomal dominant polycystic kidney disease, one of the most common human genetic diseases (Ong and Wheatley, 2003). Primary cilia have subsequently been shown to be a central signalling organelle, with roles signal transduction in the Hedgehog (Huangfu et al., 2003), Wnt and PDGFRα signalling pathways (Schneider et al., 2005; Simons et al., 2005). They play important roles throughout development, from very early embryogenesis. The clinical consequences of the aberrant development or function of primary cilia extend beyond polycystic kidney disease to encompass a spectrum of severe inherited human disorders known collectively as the ciliopathies (Oud et al., 2017).

Much of our understanding of the basic structure and function of cilia has derived from the study of ciliated model organisms including the single-celled eukaryotes *Chlamydomonas reinhardtii, Paramecium tetraurelia, Tetrahymena thermophila* and *Trypanosoma brucei* (Vincensini et al., 2011). Study of these organisms provided us with the first proteomes of the cilium (Pazour et al., 2005; Smith et al., 2005; Broadhead et al., 2006; Arnaiz et al., 2009) and basal body (Kilburn et al., 2007), constructed using approaches such as high-throughput proteomics and comparative genomics. *Caenorhabditis elegans* and *Drosophila melanogaster* were useful models for early characterisation of genes encoding ciliary proteins, through genome-wide identification of promoters containing an X-box, and study of genes under control of ciliary transcription factors (Blacque et al., 2005; Efimenko et al., 2005; Laurençon et al., 2007). These simple model organisms show some striking conservation with humans and have been useful for identifying and characterising orthologs of human ciliopathy genes (Keller et al., 2005; Chen et al., 2006), further developed through studies of vertebrate models such as *Xenopus tropicalis* and *laevis* and zebrafish (Song et al., 2016; Rao and Kulkarni, 2021). Rat and mouse have been important mammalian models for understanding and modelling the role of cilia in human health and disease (Norris and Grimes, 2012). Collectively, many high-throughput genomic, proteomic and gene expression studies in model organisms and humans have contributed to ciliary databases such as Cildb (Arnaiz et al., 2009; Arnaiz et al., 2014), the ciliary proteome (Gherman et al., 2006) and ciliome (Inglis et al., 2006). These databases comprise lists of genes and proteins identified in high-throughput ciliary studies in different ciliated model organisms and humans but are generally assembled using computational methods and not curated by human experts (with perhaps the exception of (Nogales-Cadenas et al., 2009).

To address this, in 2013 we published version 1 of the SYSCILIA gold standard (SCGSv1) (van Dam et al.), a manually curated list of known ciliary components compiled with expert review of each entry (van Dam et al., 2013). This was borne out of a need for a robust positive control set of high confidence ciliary genes to aid interpretation of the multiple large datasets being produced by hypothesis-neutral screening approaches implemented in the collaborative European research programme ‘SYSCILIA’ [http://www.syscilia.org/index.shtml](http://www.syscilia.org/index.shtml). This positive control set proved instrumental in quantifying the enrichment of known ciliary genes in these screening results, allowing us to evaluate the success of such screening strategies and confidence in our novel findings (Sluats et al., 2015; Wheway et al., 2015; Boldt et al., 2016; Lambacher et al., 2016). This original list was focused on primary cilia genes, with less consideration for motile cilia genes.
In the eight years since this resource was published, the paper has been a useful resource for other groups analysing screening data (Gupta et al., 2015; Roosing et al., 2015; Shim et al., 2016; Pusapati et al., 2018; Gheiratmand et al., 2019), for evolutionary genetics studies (Nevers et al., 2017; Shulman and Tsou, 2017) and in prioritisation of candidate genes from exome and genome sequencing of ciliopathy patients (Shaheen et al., 2016). The field of ciliary biology has advanced rapidly since the publication of SCGSv1, and in response we now provide an updated SCGS, including updated annotation of all genes, achieved through systematic literature searching and candidate gene analysis. The result is the SCGSv2 listing 686 genes, a major increase from SCGSv1 which contained 303 genes. We advance the utility of this dataset by grouping entries into two main categories; first order and second order cilia genes, elaborating a concept first put forward by Jeremy Reiter and Michel Leroux (2017)(Reiter and Leroux, 2017). Profs Reiter and Leroux propose ciliopathies fall into two categories; first order ciliopathies which are diseases caused by aberrations in genes encoding proteins localised to the cilium and; second order ciliopathies which arise as a result of defects in genes which do not encode proteins localising to the cilium but have a role in cilium formation or function. Similarly, we annotate genes as first order if they encode proteins which localise to the cilium or basal body, and second order if they encode proteins which do not localise to the cilium or basal body but otherwise have roles in cilium structure or function. SCGSv1 was focussed on primary cilia genes, and in SCGSv2 we expand this further to more comprehensively include motile cilia genes also. We review the new entries to give a perspective on recent advances in understanding of cilium structure, function and their role in development and disease.

Results and discussion

383 additional gold standard cilia genes were identified, producing the SCGSv2 of 686 genes, a major increase from SCGSv1 which contained 303 genes. 539 of these 686 (78.6%) are first order cilia genes, and 133 are second order (19.4%). 14 have not had their protein localisation reported, and so are not designated first order or second order. A retrospective analysis of SCGSv1 shows that 273/303 genes were first order cilia genes (90.1%) and 25/303 were second order cilia genes (8.3%). This may suggest that since the publication of SCGSv1 an increasing awareness of cilia outside of the cilia community has led to more study of the cillum functions of proteins. Alternatively or additionally, it may suggest that the discovery of first order cilium genes is becoming saturated, and so a proportional increase in second order cilia gene discovery is seen more recently.

57 of the new 383 genes (14.9%) were originally qualified as predicted in SCGSv1 paper. These 57 genes appeared in experimental and bioinformatics screens without in-depth validation of their function or localisation and were provided as an appendix to the SCGSv1. 187 of the new 383 genes (48.8%) were predicted in CiliaCarta (van Dam et al., 2019), demonstrating the validity of this Bayesian-based approach to predict ciliary function from genomic, proteomic, transcriptomic and evolutionary data.

Of the novel cillum genes identified there are clear trends in the biological pathways that these genes are associated with. An enrichment analysis of Gene Ontology terms (Ashburner et al., 2000; Carbon et al., 2009; The Gene Ontology Consortium, 2019) describing Biological Processes (GO BP terms) in the list of new cillum genes compared to SCGSv1 shows that the new list of genes is particularly enriched for genes involved in cell stress responses, (de)ubiquitination, autophagy, ageing, DNA repair, chromatin remodelling, multiple signalling pathways and regulation of cardiac growth.

In the new list of cillum genes, one of the most enriched types of genes are those with GO BP terms relating to cellular response to external/environmental stimulus (GO:0071496/GO:0104004, fold enrichment 14.75/6.47, p=1.20E-13 /2.54E-10). There is particularly enrichment of genes with roles
in response to stress (GO:0006950, 2.46 fold enrichment, p=1.74E-10), cellular response to nutrient
nutrient levels/starvation (GO:0031669/GO:0042594, fold enrichment 10.87/10.09 p=5.90E-08/6.66E-07), response to decreased oxygen levels (GO:0036293, 6.21 fold enrichment, p=7.73E-06), cellular response to radiation (GO:0071478, 6.21 fold enrichment, p=7.73E-06), including DNA repair (GO:0006281, 8.54 fold enrichment, p=6.37E-05). This suggests a recent increase in understanding of
the role of ciliation in sensation of cell environment and orchestrating the response to cell stress. In
many cases of shock or stress, literature suggests that rapid responses such as ciliogenesis or cilium
resorption are executed via rapid protein degradation via the ubiquitin-proteasome system (UPS).
For example, it has been shown that MIB1, which represses ciliogenesis by ubiquitinating CEP131
and PCM1 at centriolar satellites, is abruptly inactivated in response to cell stress, leading to loss of
CEP131 and PCM1 ubiquitination and stimulation of ciliogenesis, even in proliferating cells
(Villumsen et al., 2013).

Indeed, in addition to MIB1 E3 ligase, many other genes involved in ubiquitination and even more
involved in protein deubiquitination (GO:0016579) are found in SCGSv2 than SCGSv1 (10.87 fold
enrichment, p=5.90E-08). MIB1-mediated ubiquitination and degradation of PCM1 during serum
starvation induced ciliogenesis is antagonised by deubiquitinating enzyme USP9X (Wang et al.,
2019). USP9X further contributes to cell cycle dependent ciliogenesis; in the G0/G1/S phase, USP9X
is recruited to the centrosome by NPHP5 where it protects NPHP5 from ubiquitination, promoting
cilia assembly. In the G2/M phase, USP9X dissociates from the centrosome allowing BBS11/TRIM32
(E3 ligase) to K63 ubiquitinate NPHP5, triggering protein delocalization and loss of cilia. USP14 has
been shown to control ciliogenesis, cilia length and localisation of mediators of Hedgehog (Hh)
signalling in cilia through deubiquitination and stabilisation of KIF7 (Massa et al., 2019). USP8
deubiquitinates Hif1a to control ciliogenesis in normoxia (Troilo et al., 2014), and antagonises Smo
ubiquitination (Ma et al., 2016). SUMOylation has also been implicated in the trafficking of Smo into
cilia (Ma et al., 2016), further broadening our understanding of how protein degradation pathways
control cilia structure and function. The increase in understanding of the protein modifications
involved in protein metabolism relevant to ciliogenesis and cilia function is reflected in the
enrichment of terms in SCGSv2 related to positive regulation of phosphorylation (GO:0042327, 3.98
fold enrichment, p=7.59E-11), positive regulation of kinase activity (GO:0033674, 4.97 fold
enrichment, 1.46E-10), protein modification by small protein removal (GO:0070646, 11.64 fold
enrichment, p=4.87E-09) and positive regulation of protein modification process (GO:0031401, 2.98
fold enrichment, 4.33E-08).

In the years since the publication of SCGSv1 it has also become apparent that autophagy plays a role
in this rapid ciliogenesis/cilium resorption process. Indeed, genes with GO BP terms relating to
regulation of autophagy (GO:0010506) are enriched in the new additions to SCGSv2 (3.3 fold
enrichment, p=1.45E-02). This includes ATG3 and ATG5 which are required for rapid degradation of
OFD1 at centriolar satellites in response to serum starvation (Tang et al., 2013). This landmark
publication in Nature led to a suite of papers in recent years describing autophagic processes
removing ‘cilia roadblocks’ to promote ciliogenesis, control cilia length and control cell volume
(Jang et al., 2016; Orhon et al., 2016; Hsiao et al., 2018; Liu et al., 2018; Struchtrup et al., 2018;
Boukhalfa et al., 2020). The interest in autophagy of cilia components has even led to the suggestion
of a specific term for this process; ‘ciliophagy’ (Cloonan et al., 2014). It has long been observed that
serum starvation can induce ciliogenesis in cell culture, and this recent work studying the UPS
SUMOylation pathway and autophagy has provided insights into the mechanisms and dynamics of
this process.

Whilst cilia have been recognised as signalling hubs for a number of years now, the extent to which
the cilium plays a role in almost every signalling pathway in the cell was perhaps unprecedented.
Since the publication of SCGSv1 the cilium has been reported as playing a role in IGF signalling (Yeh
FGF signalling (Kunova Bosakova et al., 2019), Hippo/YAP/TAZ signalling (Kim et al., 2015), prostaglandin signalling (Jin et al., 2014), notch signalling (Boskovski et al., 2013), mTOR signalling (Zhong et al., 2016; Park et al., 2018) and TGFbeta signalling (Clement et al., 2013). TGFbeta signalling through the cilium was shown to be important for cardiomyogenesis (Clement et al., 2013), and GO BP terms relating to cardiac muscle growth (GO:0005021, 6.99 fold enrichment, p=4.77E-03) are also enriched in the new cilia genes of SCGSv2. Whilst one of the earliest discoveries in 9+0 cilia biology was the role of nodal cilia in establishing leftward nodal fluid flow, breaking left-right symmetry for proper heart looping (Nonaka et al., 1998) more recently there have been advances in understanding of the role of primary cilia in later heart development and function, and the contribution of cilia defects to congenital heart disease (Li et al., 2015; Scott et al., 2017; Toomer et al., 2019). Overall, however, there is a significant underrepresentation of genes involved in developmental processes such as brain development, limb morphogenesis, heart looping and left/right asymmetry the new cilia gene list compared to SCGS1, suggesting that in recent years smaller gains have been made in understanding of the role of cilia in early developmental processes.

Enrichment of genes with GO BP terms chromatin organization (GO:0006325, 11.64 fold enrichment, p=4.87E-09), histone modification (GO:0016570) and covalent chromatin modification (GO:0016569) (both 9.32-fold enriched, p=6.97E-06) in SCGSv2 represents an increase in understanding of transcriptional regulation of ciliogenesis, and also of the dual roles of histone modifying enzymes in histone modification and other roles in the cilium. This includes KDMSC which is involved in regulating ciliogenesis by regulating actin gene expression, and also through directly binding to the actin cytoskeleton, creating a responsive "actin gate" that involves ARP2/3 activity and IFT (Yeyati et al., 2017) and TRRAP, an essential component of multiple histone acetyltransferase complexes, which regulates multillicated cell formation (Wang et al., 2018). There has also been an increase in understanding of how various transcription factors regulate ciliogenesis, such as MCM2 which binds to transcription start sites of cilia inhibiting genes to control ciliogenesis in postmitotic cells (Casar Tena et al., 2019) and MYB transcription factor which plays a role in multiciliogenesis, as progenitors exit the cell cycle and amplify their centrioles (Tan et al., 2013). Furthermore, transcription factor ATOH1 controls ciliogenesis in neuron progenitors (Chang et al., 2019) and transcription factor SREBF1 activates expression of PLA2G3 to repress cilium formation in cancer cells (Gijs et al., 2015). Recent studies have also expanded understanding of the role of RFX transcription factors RFX2 and 7 in regulating coordinated ciliogenesis (Chung et al., 2014; Manojlovic et al., 2014). Furthermore, it has been shown that some transcription factors have secondary functions in cilia, such as SALL1 transcription factor which Interacts with factors related to cilia function, including the negative regulators of ciliogenesis CCP110 and CEP97 (Bozal-Basterra et al., 2018). Additionally, post-transcriptional regulation of cilia genes is beginning to be understood with the discovery that pre-mRNA splicing factors regulate splicing of cilia genes (Wheway et al., 2015; Buskin et al., 2018), and NUDT16L1 (SDOS) post-transcriptionally regulates cilia genes by binding and regulating translation of cilia mRNAs (Avolio et al., 2018).

Finally, it is an interesting observation that the new genes in SCGSv2 are enriched for GO BP term aging (GO:0007568, 9.32 fold enrichment, p=6.97E-06). Whilst there are few publications directly linking cilia to ageing (Carroll and Korolchuk, 2018) it is well known that the cilium plays a central role in nutrient sensing, and reduced responsiveness of nutrient sensing pathways is associated with ageing. The nutrient-sensing role of cilia in ageing may become more apparent in future research. Furthermore, recent research has linked cilia defects to induction of cell senescence (Jeffries et al., 2019) and conversely that depolarization of senescent cell plasma membrane leads to primary cilia defects and a resultant failure to inhibit growth factor signaling (Carroll et al., 2017). Senescence has been described as a feature of some ciliopathies such as nephronophthisis type 7 (Lu et al., 2016). This is significant, because cilia are classically associated with developmental
disorders, yet may also play a role in ageing and associated disease, which are some of the most costly burdens to our society today, both economically and socially.

The aim of this study was to produce a high confidence list of cilia genes annotated by cilia experts. The approach prioritised the exclusion of false positives over the exclusion of false negatives, and as a result the list is highly stringent and not a completely comprehensive list of all cilia and basal body genes. Absence of a gene from this list does not necessarily mean that gene does not play a role in ciliogenesis, cilium structure or function but inclusion of a gene in this list means that it is highly confidently associated with these processes in humans. The literature search did not include grey literature or literature in pre-print servers prior to peer review and as a result, the most recently identified and characterised genes will not be included. The literature search focussed on human genes (with ‘human’ included as search term) and the titles of search results were reviewed for mention of genes in humans or vertebrate models such that cilia genes which are have been described in model organisms but for which the ortholog has not been well characterised in humans/human cell lines will be omitted. The resulting list is a stringent, high-confidence list of genes involved in ciliogenesis, cilium structure and function with a focus on human cilia and ciliopathy genes. For more comprehensive lists of genes which include candidate genes, likely false positives, and genes which have no ortholog in humans, we direct the reader to CiliaCarta (van Dam et al., 2019) or cildb (Arnaiz et al., 2014).

Materials and Methods

On 1st January 2021 a systematic review of Medline was conducted using the following MESH terms:

\(((cili\ast[Title/Abstract]) \text{ NOT } \text{(ciliary body[Title/Abstract]) AND } ("2013/05/01"[Date - Publication] : "3000"[Date - Publication]) \text{ AND } \text{English}[Language] \text{ AND } \text{Humans}[Mesh]) \text{ NOT } \text{ciliate}[Title/Abstract] \text{ AND } \text{Humans}[Mesh]) \text{ NOT } \text{ciliary muscle}[Title/Abstract] \text{ AND } \text{Humans}[Mesh]) \text{ NOT } \text{Ciliary Neurotrophic Factor Receptor}[Title/Abstract] \text{ AND } \text{Humans}[Mesh]) \text{ NOT } \text{cilioretinal}[Title/Abstract] \text{ AND } \text{Humans}[Mesh]) \text{ NOT } \text{ciliochoroidal}[Title/Abstract] \text{ AND } \text{Humans}[Mesh])\)

This returned 4,548 results. Each title was assessed for mention of gene names, or for the word ‘screen’. Where novel genes or screen results were reported in vertebrates, human cells or human cell lines, abstracts and figures were studied to identify nature of protein function and immunofluorescence or immunogold electron microscopy images showing the localisation of the protein. Official gene symbol, Ensembl gene ID, any associated OMIM ID, curators note, relevant PubMed IDs and localisation were recorded in a spreadsheet.

In addition to the systematic literature search, the 286 genes predicted to be cilia genes in the CiliaCarta(van Dam et al., 2019) study were specifically included in a Medline search using MESH terms cili\ast[Title/Abstract]) \text{ AND } [\text{gene name 1}] \text{ OR } [\text{gene name 2}] \text{... OR } [\text{gene name n}]. \text{ Every paper from this search was studied in depth to identify any reported protein functions in cilia and localisation.}

Once all genes were extracted from this systematic review into a results table, every entry was independently reviewed by a second cilia expert, who entered additional data and annotated the ‘curators note’ column on this table.

If the protein localisation was reported as cilium, axoneme, basal body or part thereof, this gene was scored as a first order cilium gene. If a protein’s localisation was reported as any other cell location,
including centriole, centrosome, centriolar satellite but not explicitly basal body, the gene was scored as a second order cilium gene.

Once finally compiled, Ensembl gene IDs were filtered to identify which we predicted in the SCGSv1 paper, and which were predicted in the CiliaCarta paper.

Gene Ontology enrichment analysis of SCGSv2 was conducted using amiGO (Carbon et al., 2009). Enrichment of gene ontology terms relating to biological processes in SCGSv2 compared to SCGSv1 was conducted using a binomial test, with Bonferroni correction of the p value to account for multiple testing. Ensembl gene IDs were used as input in amiGO.com which accesses the Panther database.

**Table legend**
Table showing all entries in SYSCILIA Gold Standard Version 2 (SCGSv2) with Ensembl gene ID, description of gene, official gene name, any associated OMIM number(s), curators note, associated PubMed ID(s), localisation of the protein product of the gene, whether this is first order (at the cilium or basal body) or second order (elsewhere), whether it was in SCGSv1 or predicted in SCGSv1 or CiliaCarta.

**References**

Arnaiz, O., Cohen, J., Tassin, A.M., and Koll, F. (2014). Remodeling Cildb, a popular database for cilia and links for ciliopathies. Cilia 3, 9-2530-2533-2539. eCollection 2014.

Arnaiz, O., Malinowska, A., Klotz, C., Sperling, L., Dadlez, M., Koll, F., and Cohen, J. (2009). Cildb: a knowledgebase for centrosomes and cilia. Database : the journal of biological databases and curation 2009, bap022.

Ashburner, M., Ball, C.A., Blake, J.A., Botstein, D., Butler, H., Cherry, J.M., Davis, A.P., Dolinski, K., Dwight, S.S., Eppig, J.T., Harris, M.A., Hill, D.P., Issel-Tarver, L., Kasarskis, A., Lewis, S., Matese, J.C., Richardson, J.E., Ringwald, M., Rubin, G.M., and Sherロック, G. (2000). Gene ontology: tool for the unification of biology. The Gene Ontology Consortium. Nat Genet 25, 25-29.

Avolio, R., Järvelin, A.I., Mohammed, S., Agliarulo, I., Condelli, V., Zoppoli, P., Calice, G., Sarnataro, D., Bechara, E., Tartaglia, G.G., Landriscina, M., Castello, A., Esposito, F., and Matassa, D.S. (2018). Protein Syndesmos is a novel RNA-binding protein that regulates primary cilia formation. Nucleic Acids Res 46, 12067-12086.

Blacque, O.E., Perens, E.A., Boroevich, K.A., Inglis, P.N., Li, C.M., Warner, A., Khattria, J., Holt, R.A., Ou, G.S., Mah, A.K., McKay, S.J., Huang, P., Swoboda, P., Jones, S.J.M., Marra, M.A., Baillie, D.L., Moerman, D.G., Shaham, S., and Leroux, M.R. (2005). Functional genomics of the cilium, a sensory organelle. Current Biology 15, 935-941.

Boldt, K., van Reeuwijk, J., Lu, Q., Koutroumpas, K., Nguyen, T.M., Texier, Y., van Beersum, S.E., Horn, N., Willer, J.R., Mans, D.A., Dougherty, G., Lamers, I.J., Coene, K.L., Arts, H.H., Betts, M.J., Beyer, T., Bolat, E., Gloeckner, C.J., Haidari, K., Hettersonschijt, L., Iaconis, D., Jenkins, D., Klose, F., Knapp, B., Latour, B., Letteboer, S.J., Marcelis, C.L., Mitic, D., Morleo, M., Oud, M.M., Riemersma, M., Rix, S., Terhal, P., Toedt, G., van Dam, T.J., de Vrieze, E., Wissinger, Y., Wu, K.M., Apic, G., Beales, P.L., Blacque, O.E., Gibson, T.J., Huynen, M.A., Katsanis, N., Kremer, H., Omran, H., van Wijk, E., Wolfrum, U., Kepes, F., Davis, E.E., Franco, B., Giles, R.H., Ueffing, M., Russell, R.B., Roepman, R., and Group, U.K.R.D. (2016). An organelle-specific protein landscape identifies novel diseases and molecular mechanisms. Nature communications 7, 11491.
Boskovski, M.T., Yuan, S., Pedersen, N.B., Goth, C.K., Makova, S., Clausen, H., Brueckner, M., and Khokha, M.K. (2013). The heterotaxy gene GALNT11 glycosylates Notch to orchestrate cilia type and laterality. Nature 504, 456-459.

Boukhalfa, A., Nascimbeni, A.C., Ramel, D., Dupont, N., Hirsch, E., Gayral, S., Laffargue, M., Codogno, P., and Morel, E. (2020). PI3KC2alpha-dependent and VPS34-independent generation of PI3P controls primary cilium-mediated autophagy in response to shear stress. Nat Commun 11, 294.

Bozal-Basterra, L., Martín-Ruíz, I., Pirone, L., Liang, Y., Sigurðsson, J.O., Gonzalez-Santamarta, M., Giordano, I., Gabicagogeasceoa, E., de Luca, A., Rodríguez, J.A., Wilkie, A.O.M., Kohlhase, J., Eastwood, D., Yale, C., Olsen, J.V., Rauchman, M., Anderson, K.V., Sutherland, J.D., and Barrio, R. (2018). Truncated SALL1 Impedes Primary Cilia Function in Townes-Brocks Syndrome. Am J Hum Genet 102, 249-265.

Broadhead, R., Dawe, H.R., Farr, H., Griffiths, S., Hart, S.R., Portman, N., Shaw, M.K., Ginger, M.L., Gaskell, S.J., McKean, P.G., and Gull, K. (2006). Flagellar motility is required for the viability of the bloodstream trypanosome. Nature 440, 224-227.

Bujakowska, K.M., Liu, Q., and Pierce, E.A. (2017). Photoreceptor Cilia and Retinal Ciliopathies. Cold Spring Harbor perspectives in biology 9, 10.1101/cshperspect.a028274.

Buskin, A., Zhu, L., Chichagova, V., Basu, B., Mozaffari-Jovin, S., Dolan, D., Droop, A., Collin, J., Bronstein, R., Mehrrotra, S., Farkas, M., Hilgen, G., White, K., Pan, K.T., Treumann, A., Hallam, D., Bialas, K., Chung, G., Mellough, C., Ding, Y., Krasnogor, N., Przyborski, S., Zwolinski, S., Al-Aama, J., Alharthi, S., Xu, Y., Wheway, G., Szymanska, K., McKidbin, M., Inglehearn, C.F., Elliott, D.J., Lindsay, S., Ali, R.R., Steel, D.H., Armstrong, L., Sernagor, E., Urlaub, H., Pierce, E., Luhrmann, R., Grellscheid, S.N., Johnson, C.A., and Lako, M. (2018). Disrupted alternative splicing for genes implicated in splicing and ciliogenesis causes PRPF31 retinitis pigmentosa. Nat Commun 9, 4234.

Carbon, S., Ireland, A., Mungall, C.J., Shu, S., Marshall, B., Lewis, S., Hub, A., and Group, W.P.W. (2009). AmiGO: online access to ontology and annotation data. Bioinformatics 25, 288-289.

Carroll, B., and Korolchuk, V.I. (2018). Nutrient sensing, growth and senescence. FEBS J 285, 1948-1958.

Carroll, B., Nelson, G., Rabanal-Ruiz, Y., Kucheryavenko, O., Dunhill-Turner, N.A., Chesterman, C.C., Zahari, Q., Zhang, T., Conduit, S.E., Mitchell, C.A., Maddocks, O.D.K., Lovat, P., von Zglinicki, T., and Korolchuk, V.I. (2017). Persistent mTORC1 signaling in cell senescence results from defects in amino acid and growth factor sensing. J Cell Biol 216, 1949-1957.

Casar Tena, T., Maerz, L.D., Szafranski, K., Groth, M., Blätte, T.J., Donow, C., Matysik, S., Walther, P., Jeggo, P.A., Burkhalter, M.D., and Philipp, M. (2019). Resting cells rely on the DNA helicase component MCM2 to build cilia. Nucleic Acids Res 47, 134-151.

Chang, C.H., Zanini, M., Shirvani, H., Cheng, J.S., Yu, H., Feng, C.H., Mercier, A.L., Hung, S.Y., Forget, A., Wang, C.H., Cigna, S.M., Lu, I.L., Chen, W.Y., Leboucher, S., Wang, W.J., Ruat, M., Spassky, N., Tsai, J.W., and Ayrault, O. (2019). Atoh1 Controls Primary Cilia Formation to Allow for SHH-Triggered Granule Neuron Progenitor Proliferation. Dev Cell 48, 184-199.e185.

Chen, N., Mah, A., Blacque, O.E., Chu, J., Phgora, K., Bakhoum, M.W., Newbury, C.R., Khattra, J., Chan, S., Go, A., Efimenko, E., Johnsen, R., Phirke, P., Swoboda, P., Marra, M., Moerman, D.G., Leroux, M.R., Baillie, D.L., and Stein, L.D. (2006). Identification of ciliary
ciliopathy genes in Caenorhabditis elegans through comparative genomics. Genome Biol 7, R126.
Chung, M.I., Kwon, T., Tu, F., Brooks, E.R., Gupta, R., Meyer, M., Baker, J.C., Marcotte, E.M., and Wallingford, J.B. (2014). Coordinated genomic control of ciliogenesis and cell movement by RFX2. Elife 3, e01439.
Clement, C.A., Ajbro, K.D., Koefoed, K., Vestergaard, M.L., Veland, I.R., Henriques de Jesus, M.P., Pedersen, L.B., Benmerah, A., Andersen, C.Y., Larsen, L.A., and Christensen, S.T. (2013). TGF-β signaling is associated with endocytosis at the pocket region of the primary cilium. Cell Rep 3, 1806-1814.
Cloonan, S.M., Lam, H.C., Ryter, S.W., and Choi, A.M. (2014). "Ciliophagy": The consumption of cilia components by autophagy. Autophagy 10, 532-534.
Efimenko, E., Bubb, K., Mak, H.Y., Holzman, T., Leroux, M.R., Ruvkun, G., Thomas, J.H., and Swoboda, P. (2005). Analysis of xbx genes in C. elegans. Development 132, 1923-1934.
Gheiratmand, L., Coyaud, E., Gupta, G.D., Gonçalves, J., Raught, B., and Pelletier, L. (2019). Spatial and proteomic profiling reveals centrosome-independent features of centriolar satellites. EMBO J 38, e101109.
Gherman, A., Davis, E.E., and Katsanis, N. (2006). The ciliary proteome database: an integrated community resource for the genetic and functional dissection of cilia. Nature genetics 38, 961-962.
Gijis, H.L., Willemarck, N., Vanderhoydonc, F., Khan, N.A., Dehairs, J., Derua, R., Waelkens, E., Taketomi, Y., Murakami, M., Agostinis, P., Annaert, W., and Swinnen, J.V. (2015). Primary cilium suppression by SREBP1c involves distortion of vesicular trafficking by PLA2G3. Mol Biol Cell 26, 2321-2332.
Gupta, G.D., Coyaud, E., Gonçalves, J., Mojarad, B.A., Liu, Y., Wu, Q., Gheiratmand, L., Comartin, D., Tkach, J.M., Cheung, S.W., Bashkurov, M., Hasegan, M., Knit, J.D., Lin, Z.Y., Schueler, M., Hildebrandt, F., Moffat, J., Gingras, A.C., Raught, B., and Pelletier, L. (2015). A Dynamic Protein Interaction Landscape of the Human Centrosome-Cilium Interface. Cell 163, 1484-1499.
Hsiao, C.J., Chang, C.H., Ibrahim, R.B., Lin, I.H., Wang, C.H., Wang, W.J., and Tsai, J.W. (2018). Gli2 modulates cell cycle re-entry through autophagy-mediated regulation of the length of primary cilia. J Cell Sci 131.
Huangfu, D.W., Liu, A.M., Rakeman, A.S., Murcia, N.S., Niswander, L., and Anderson, K.V. (2003). Hedgehog signalling in the mouse requires intraflagellar transport proteins. Nature 426, 83-87.
Inglis, P.N., Boroevich, K.A., and Leroux, M.R. (2006). Piecing together a ciliome. Trends Genet 22, 491-500.
Jang, J., Wang, Y., Lalli, M.A., Guzman, E., Godshalk, S.E., Zhou, H., and Kosik, K.S. (2016). Primary Cilium-Autophagy-Nrf2 (PAN) Axis Activation Commits Human Embryonic Stem Cells to a Neuroectoderm Fate. Cell 165, 410-420.
Jeffries, E.P., Di Filippo, M., and Galbiati, F. (2019). Failure to reabsorb the primary cilium induces cellular senescence. FASEB J 33, 4866-4882.
Jin, D., Ni, T.T., Sun, J., Wan, H., Amack, J.D., Yu, G., Fleming, J., Chiang, C., Li, W., Papierniak, A., Cheepala, S., Conseil, G., Cole, S.P.C., Zhou, B., Drummond, I.A., Schuetz, J.D., Malicki, J., and Zhong, T.P. (2014). Prostaglandin signalling regulates ciliogenesis by modulating intraflagellar transport. Nature Cell Biology 16, 841.
Keller, L.C., Romijn, E.P., Zamora, I., Yates III, J.R., and Marshall, W.F. (2005). Proteomic Analysis of Isolated Chlamydomonas Centrioles Reveals Orthologs of Ciliary-Disease Genes. Current Biology 15, 1090-1098.

Kilburn, C.L., Pearson, C.G., Romijn, E.P., Meehl, J.B., Giddings, T.H., Jr., Culver, B.P., Yates, J.R., 3rd, and Winey, M. (2007). New Tetrahymena basal body protein components identify basal body domain structure. J Cell Biol 178, 905-912.

Kim, J., Jo, H., Hong, H., Kim, M.H., Kim, J.M., Lee, J.K., and Heo, W.D. (2015). Actin remodelling factors control ciliogenesis by regulating YAP/TAZ activity and vesicle trafficking. Nat Commun 6, 6781.

Kunova Bosakova, M., Nita, A., Gregor, T., Varecha, M., Gudernova, I., Fafilek, B., Barta, T., Basheer, N., Abraham, S.P., Balek, L., Tomanova, M., Fialova Kucerova, J., Bosak, J., Potesil, D., Zieba, J., Song, J., Konik, P., Park, S., Duran, I., Zdrahal, Z., Smajs, D., Jansen, G., Fu, Z., Ko, H.W., Hampl, A., Trantirek, L., Krakow, D., and Krejci, P. (2019). Fibroblast growth factor receptor influences primary cillum length through an interaction with intestinal cell kinase. Proc Natl Acad Sci U S A 116, 4316-4325.

Lambacher, N.J., Bruel, A.L., van Dam, T.J., Szymańska, K., Slaats, G.G., Kuhns, S., McManus, G.J., Kennedy, J.E., Gaff, K., Wu, K.M., van der Lee, R., Burglen, L., Doummar, D., Rivière, J.B., Faivre, L., Attié-Bitach, T., Saunier, S., Curd, A., Peckham, M., Giles, R.H., Johnson, C.A., Huynen, M.A., Thauvin-Robinet, C., and Blacque, O.E. (2016). TMEM107 recruits ciliopathy proteins to subdomains of the ciliary transition zone and causes Joubert syndrome. Nat Cell Biol 18, 122-131.

Laurençon, A., Dubruille, R., Efimenko, E., Grenier, G., Bissett, R., Cortier, E., Rolland, V., Swoboda, P., and Durand, B. (2007). Identification of novel regulatory factor X (RFX) target genes by comparative genomics in Drosophila species. Genome Biol 8, R195.

Legendre, M., Zaragosi, L.E., and Mitchison, H.M. (2021). Motile cilia and airway disease. Semin Cell Dev Biol 110, 19-33.

Li, Y., Klena, N.T., Gabriel, G.C., Liu, X., Kim, A.J., Lemke, K., Chen, Y., Chatterjee, B., Devine, W., Damerla, R.R., Chang, C., Yagi, H., San Agustin, J.T., Thahir, M., Anderton, S., Lawhead, C., Vescovi, A., Pratt, H., Morgan, J., Haynes, L., Smith, C.L., Eppig, J.T., Reinholdt, L., Francis, R., Leatherbury, L., Ganapathiraju, M.K., Tobita, K., Pazour, G.J., and Lo, C.W. (2015). Global genetic analysis in mice unveils central role for cilia in congenital heart disease. Nature 521, 520.

Liu, Z.-Q., Lee, J.N., Son, M., Lim, J.-Y., Dutta, R.K., Maharjan, Y., Kwak, S., Oh, G.T., Byun, K., Choe, S.-K., and Park, R. (2018). Ciliogenesis is reciprocally regulated by PPARA and NR1H4/FXR through controlling autophagy in vitro and in vivo. Autophagy 14, 1011-1027.

Lu, D., Rauhauser, A., Li, B., Ren, C., McEnery, K., Zhu, J., Chaki, M., Vadnagara, K., Elhadi, S., Jetten, A.M., Igarashi, P., and Attanasio, M. (2016). Loss of Glis2/NPHP7 causes kidney epithelial cell senescence and suppresses cyst growth in the Kif3a mouse model of cystic kidney disease. Kidney Int 89, 1307-1323.

Ma, G., Li, S., Han, Y., Li, S., Yue, T., Wang, B., and Jiang, J. (2016). Regulation of Smoothened Trafficking and Hedgehog Signaling by the SUMO Pathway. Dev Cell 39, 438-451.

Manojlovic, Z., Earwood, R., Kato, A., Stefanovic, B., and Kato, Y. (2014). RFX7 is required for the formation of cilia in the neural tube. Mech Dev 132, 28-37.

Massa, F., Tammaro, R., Prado, M.A., Cesana, M., Lee, B.H., Finley, D., Franco, B., and Morleo, M. (2019). The deubiquitinating enzyme Usp14 controls ciliogenesis and Hedgehog signaling. Hum Mol Genet 28, 764-777.
Nauli, S.M., Alenghat, F.J., Luo, Y., Williams, E., Vassilev, P., Li, X., Elia, A.E., Lu, W., Brown, E.M., Quinn, S.J., Inger, D.E., and Zhou, J. (2003). Polycystins 1 and 2 mediate mechanosensation in the primary cilium of kidney cells. Nature genetics 33, 129-137.

Nevers, Y., Prasad, M.K., Poidevin, L., Chennen, K., Allot, A., Kress, A., Ripp, R., Thompson, J.D., Dollfus, H., Poch, O., and Lecompte, O. (2017). Insights into Ciliary Genes and Evolution from Multi-Level Phylogenetic Profiling. Mol Biol Evol 34, 2016-2034.

Nogales-Cadenas, R., Abascal, F., Díez-Pérez, J., Carazo, J.M., and Pascual-Montano, A. (2009). CentrosomeDB: a human centrosomal proteins database. Nucleic Acids Res 37, D175-180.

Nonaka, S., Tanaka, Y., Okada, Y., Takeda, S., Harada, A., Kanai, Y., Kido, M., and Hirokawa, N. (1998). Randomization of Left-Right Asymmetry due to Loss of Nodal Cilia Generating Leftward Flow of Extraembryonic Fluid in Mice Lacking KIF3B Motor Protein. Cell 95, 829-837.

Norris, D.P., and Grimes, D.T. (2012). Mouse models of ciliopathies: the state of the art. Dis Model Mech 5, 299-312.

Ong, A.C., and Wheatley, D.N. (2003). Polycystic kidney disease--the ciliary connection. Lancet 361, 774-776.

Orhon, I., Dupont, N., Zaidan, M., Boitez, V., Burtin, M., Schmitt, A., Capiod, T., Viau, A., Beau, I., Kuehn, E.W., Friedlander, G., Terzi, F., and Codogno, P. (2016). Primary-cilium-dependent autophagy controls epithelial cell volume in response to fluid flow. Nat Cell Biol 18, 657-667.

Oud, M.M., Lamers, I.J., and Arts, H.H. (2017). Ciliopathies: Genetics in Pediatric Medicine. Journal of pediatric genetics 6, 18-29.

Park, S.M., Lim, J.S., Ramakrishina, S., Kim, S.H., Kim, W.K., Lee, J., Kang, H.C., Reiter, J.F., Kim, D.S., Kim, H.H., and Lee, J.H. (2018). Brain Somatic Mutations in MTOR Disrupt Neuronal Ciliogenesis, Leading to Focal Cortical Dyslamination. Neuron 99, 83-97.e87.

Pazour, G.J., Agrin, N., Leszyk, J., and Witman, G.B. (2005). Proteomic analysis of a eukaryotic cilium. Journal of Cell Biology 170, 103-113.

Pazour, G.J., Dickert, B.L., Vucica, Y., Seeley, E.S., Rosenbaum, J.L., Witman, G.B., and Cole, D.G. (2000). Chlamydomonas IFT88 and its mouse homologue, polycystic kidney disease gene tg737, are required for assembly of cilia and flagella. The Journal of cell biology 151, 709-718.

Pusapati, G.V., Kong, J.H., Patel, B.B., Krishnan, A., Sagner, A., Kinnebrew, M., Briscoe, J., Aravind, L., and Rohatgi, R. (2018). CRISPR Screens Uncover Genes that Regulate Target Cell Sensitivity to the Morphogen Sonic Hedgehog. Dev Cell 44, 271.

Rao, V.G., and Kulkarni, S.S. (2021). Xenopus to the rescue: A model to validate and characterize candidate ciliopathy genes. Genesis 59, e23414.

Reiter, J.F., and Leroux, M.R. (2017). Genes and molecular pathways underpinning ciliopathies. Nat Rev Mol Cell Biol 18, 533-547.

Roosning, S., Hofree, M., Kim, S., Scott, E., Copeland, B., Romani, M., Silhavy, J.L., Rosti, R.O., Schroth, J., Mazza, T., Miccinilli, E., Zaki, M.S., Swoboda, K.J., Milisa-Drautz, J., Dobyns, W.B., Mikati, M.A., Inceci, F., Azam, M., Borgatti, R., Romaniello, R., Boustany, R.M., Clericuzio, C.L., D’Arrigo, S., Strømme, P., Boltshauser, E., Stanzial, F., Mirabelli-Badenier, M., Moroni, I., Bertini, E., Emma, F., Steinlin, M., Hildebrandt, F., Johnson, C.A., Freilinger, M., Vaux, K.K., Gabriel, S.B., Aza-Blanc, P., Heynen-Genel, S., Ideker, T., Dynlacht, B.D., Lee, J.E., Valente, E.M., Kim, J., and Gleeson, J.G. (2015). Functional genome-wide siRNA screen identifies KIAA0586 as mutated in Joubert syndrome. Elife 4, e06602.
Schneider, L., Clement, C.A., Teilmann, S.C., Pazour, G.J., Hoffmann, E.K., Satir, P., and Christensen, S.T. (2005). PDGFR alpha alpha signaling is regulated through the primary cilium in fibroblasts. Current Biology 15, 1861-1866.

Scott, C.A., Marsden, A.N., Rebagliati, M.R., Zhang, Q., Chamling, X., Searby, C.C., Baye, L.M., Sheffield, V.C., and Slusarski, D.C. (2017). Nuclear/cytoplasmic transport defects in BBS6 underlie congenital heart disease through perturbation of a chromatin remodeling protein. PLoS Genet 13, e1006936.

Shaheen, R., Szymanska, K., Basu, B., Patel, N., Ewida, N., Faeqih, E., Al Hashem, A., Derar, N., Alsharif, H., Aldahmesh, M.A., Alazami, A.M., Hashem, M., Ibrahim, N., Abdulwahab, F.M., Sonbul, R., Alkuraya, H., Alnemer, M., Al Tala, S., Al-Husain, M., Morsy, H., Seidahmed, M.Z., Meriki, N., Al-Owain, M., AlShahwan, S., Tabarki, B., Salih, M.A., Ciliopathy, W., Faquih, T., El-Kalioby, M., Ueffing, M., Boldt, K., Logan, C.V., Parry, D.A., Al Tassan, N., Monies, D., Megarbane, A., Abouelhoda, M., Halees, A., Johnson, C.A., and Alkuraya, F.S. (2016). Characterizing the morbid genome of ciliopathies. Genome biology 17, 242.

Shim, H., Kim, J.H., Kim, C.Y., Hwang, S., Kim, H., Yang, S., Lee, J.E., and Lee, I. (2016). Function-driven discovery of disease genes in zebrafish using an integrated genomics big data resource. Nucleic Acids Res 44, 9611-9623.

Shulman, A.S., and Tsou, M.F. (2017). Probing Cilia-Associated Signaling Proteomes in Animal Evolution. Dev Cell 43, 653-655.

Simons, M., Gloy, J., Ganner, A., Bullerkotte, A., Bashkurov, M., Kronig, C., Schermer, B., Benzing, T., Cabello, O.A., Jenny, A., Mlodzik, M., Polok, B., Driever, W., Obara, T., and Walz, G. (2005). Inversin, the gene product mutated in nephronophthisis type II, functions as a molecular switch between Wnt signaling pathways. Nature genetics 37, 537-543.

Slaats, G.G., Wheway, G., Foletto, V., Szymanska, K., van Balkom, B.W., Logister, I., Den Ouden, K., Keijzer-Veen, M.G., Lilien, M.R., Knoers, N.V., Johnson, C.A., and Giles, R.H. (2015). Screen-based identification and validation of four new ion channels as regulators of renal ciliogenesis. Journal of cell science 128, 4550-4559.

Smith, J.C., Northey, J.G., Garg, J., Pearlman, R.E., and Siu, K.W. (2005). Robust method for proteome analysis by MS/MS using an entire translated genome: demonstration on the ciliome of Tetrahymena thermophila. J Proteome Res 4, 909-919.

Song, Z., Zhang, X., Jia, S., Yelick, P.C., and Zhao, C. (2016). Zebrafish as a Model for Human Ciliopathies. J Genet Genomics 43, 107-120.

Struchtrup, A., Wiegering, A., Stork, B., Ruther, U., and Gerhardt, C. (2018). The ciliary protein RPGRIP1L governs autophagy independently of its proteasome-regulating function at the ciliary base in mouse embryonic fibroblasts. Autophagy 14, 567-583.

Tan, F.E., Vladar, E.K., Ma, L., Fuentealba, L.C., Hoh, R., Espinoza, F.H., Axelrod, J.D., Alvarez-Buylla, A., Stearns, T., Kintner, C., and Krasnow, M.A. (2013). Myb promotes centriole amplification and later steps of the multiciliogenesis program. Development 140, 4277-4286.

Tang, Z., Lin, M.G., Stowe, T.R., Chen, S., Zhu, M., Stearns, T., Franco, B., and Zhong, Q. (2013). Autophagy promotes primary ciliogenesis by removing OFD1 from centriolar satellites. Nature 502, 254-257.

Toomer, K.A., Yu, M., Fulmer, D., Guo, L., Moore, K.S., Moore, R., Drayton, K.D., Glover, J., Peterson, N., Ramos-Ortiz, S., Drohan, A., Catching, B.J., Stairley, R., Wessels, A., Lipschutz, J.H., Delling, F.N., Jeunemaitre, X., Dina, C., Collins, R.L., Brand, H., Talkowski, M.E., Del...
Monte, F., Mukherjee, R., Awgulewitsch, A., Body, S., Hardiman, G., Hazard, E.S., da Silveira, W.A., Wang, B., Leyne, M., Durst, R., Markwald, R.R., Le Scouarnec, S., Hagege, A., Le Tourneau, T., Kohl, P., Rog-Zielinski, E.A., Ellinor, P.T., Levine, R.A., Milan, D.J., Schott, J.J., Bouatia-Naji, N., Slaugenhaupt, S.A., and Norris, R.A. (2019). Primary cilia defects causing mitral valve prolapse. Sci Transl Med 11.

Troilo, A., Alexander, I., Muehl, S., Jaramillo, D., Knobeloch, K.P., and Krek, W. (2014). HIF1alpha deubiquitination by USP8 is essential for ciliogenesis in normoxia. EMBO Rep 15, 77-85.

van Dam, T.J., Wheway, G., Slaats, G.G., Group, S.S., Huynen, M.A., and Giles, R.H. (2013). The SYSCILIA gold standard (SCGSv1) of known ciliary components and its applications within a systems biology consortium. Cilia 2, 7-2530-2532-2537.

van Dam, T.J.P., Kennedy, J., van der Lee, R., de Vrieze, E., Wunderlich, K.A., Rix, S., Dougherty, G.W., Lambacher, N.J., Li, C., Jensen, V.L., Leroux, M.R., Hjeij, R., Horn, N., Texier, Y., Wissinger, Y., van Reeuwijk, J., Wheway, G., Knapp, B., Scheel, J.F., Franco, B., Mans, D.A., van Wijk, E., Kepes, F., Slaats, G.G., Toedt, G., Kremer, H., Omran, H., Szymanska, K., Koutroumpas, K., Ueffing, M., Nguyen, T.T., Letteboer, S.J.F., Oud, M.M., van Beersum, S.E.C., Schmidts, M., Beales, P.L., Lu, Q., Giles, R.H., Szklarczyk, R., Russell, R.B., Gibbons, T.J., Johnson, C.A., Blacque, O.E., Wolfrum, U., Boldt, K., Roepman, R., Hernandez-Hernandez, V., and Huynen, M.A. (2019). CiliaCarta: An integrated and validated compendium of ciliary genes. PLoS One 14, e0216705.

Villumsen, B.H., Danielsen, J.R., Povlsen, L., Sylvestersen, K.B., Merdes, A., Beli, P., Yang, Y.G., Choudhary, C., Nielsen, M.L., Mailand, N., and Bekker-Jensen, S. (2013). A new cellular stress response that triggers centriolar satellite reorganization and ciliogenesis. Embo j 32, 3029-3040.

Vincensini, L., Blisnick, T., and Bastin, P. (2011). 1001 Model Organisms to Study Cilia and Flagella. Biology of the cell 103, 109-130.

Wang, P., Xia, J., Zhang, L., Zhao, S., Li, S., Wang, H., Cheng, S., Li, H., Yin, W., Pei, D., and Shu, X. (2019). SNX17 Recruits USP9X to Antagonize MIB1-Mediated Ubiquitination and Degradation of PCM1 during Serum-Starvation-Induced Ciliogenesis. Cells 8.

Wang, Z., Plasschaert, L.W., Aryal, S., Renaud, N.A., Yang, Z., Choo-Wing, R., Pessotti, A., D. Kirkpatrick, N.D., Cochrans, N.R., Carbone, W., Maher, R., Lindeman, A., Russ, C., Reece-Hoyes, J., McAllister, G., Hoffman, G.R., Roma, G., and Jaffe, A.B. (2018). TRRAP is a central regulator of human multiciliated cell formation. J Cell Biol 217, 1941-1955.

Wheway, G., Nazlamova, L., and Hancock, J.T. (2018). Signaling through the Primary Cilium. Frontiers in cell and developmental biology 6, 8.

Wheway, G., Schmidts, M., Mans, D.A., Szymanska, K., Nguyen, T.M., Racher, H., Phelps, I.G., Toedt, G., Kennedy, J., Wunderlich, K.A., Sorusch, N., Abdelhamed, Z.A., Natarajan, S., Herridge, W., van Reeuwijk, J., Horn, N., Boldt, K., Parry, D.A., Letteboer, S.J., Roosin, S., Adams, M., Bell, S.M., Bond, J., Higgins, J., Morrison, E.E., Tomlinson, D.C., Slaats, G.G., van Dam, T.J., Huang, L., Kessler, K., Giessl, A., Logan, C.V., Boyle, E.A., Shendure, J., Anazi, S., Aldahmesh, M., Al Hazzaa, S., Hegele, R.A., Ober, C., Froak, P., Mhanni, A.A., Chodirker, B.N., Chudley, A.E., Lamont, R., Bernier, F.P., Beaumel, C.L., Gordon, P., Pon, R.T., Donahue, C., Barkovich, A.J., Wolf, L., Toomes, C., Thiel, C.T., Boycott, K.M., McKibbin, M., Ingleharn, C.F., Consortium, U.K., University of Washington Center for Mendelian, G., Stewart, F., Omran, H., Huynen, M.A., Sergouniotis, P.I., Alkuraya, F.S., Parboosingh, J.S., Innis, A.M., Willoughby, C.E., Giles, R.H., Webster, A.R., Ueffing, M., Blacque, O., Gleeson, J.G., Wolfrum, U., Beales, P.L., Gibson, T., Doherty, D., Mitchison, H.M., Roepman, R., and Johnson, C.A.
(2015). An siRNA-based functional genomics screen for the identification of regulators of ciliogenesis and ciliopathy genes. Nature cell biology 17, 1074-1087.

Yeh, C., Li, A., Chuang, J.Z., Saito, M., Cáceres, A., and Sung, C.H. (2013). IGF-1 activates a cilium-localized noncanonical Gβγ signaling pathway that regulates cell-cycle progression. Dev Cell 26, 358-368.

Yeyati, P.L., Schiller, R., Mali, G., Kasioulis, I., Kawamura, A., Adams, I.R., Playfoot, C., Gilbert, N., van Heyningen, V., Wills, J., von Kriegsheim, A., Finch, A., Sakai, J., Schofield, C.J., Jackson, I.J., and Mill, P. (2017). KDM3A coordinates actin dynamics with intraflagellar transport to regulate cilia stability. J Cell Biol 216, 999-1013.

Yoder, B.K., Hou, X.Y., and Guay-Woodford, L.M. (2002). The polycystic kidney disease proteins, polycystin-1, polycystin-2, polars, and cystin, are co-localized in renal cilia. Journal of the American Society of Nephrology 13, 2508-2516.

Zhong, M., Zhao, X., Li, J., Yuan, W., Yan, G., Tong, M., Guo, S., Zhu, Y., Jiang, Y., and Liu, Y. (2016). Tumor Suppressor Folliculin Regulates mTORC1 through Primary Cilia. J Biol Chem 291, 11689-11697.