

The Kidney-Genetics Documentation

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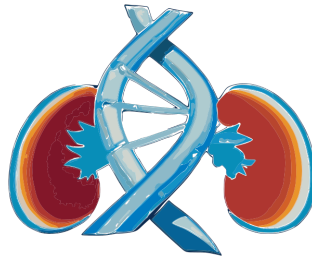
2023-12-20

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Preface

This documentation is intended to describe the Kidney-Genetics¹ project.



Objective

How can we address the lack of a unified and standardized database of kidney disease-associated genes, which hampers diagnosis, treatment, and research comparability in the field of kidney diseases?

Genetic insights are becoming increasingly influential in the understanding and treatment of various kidney diseases (KD). Hundreds of genes associated with monogenic kidney disease have been identified, providing valuable insights into their diagnosis, management, and monitoring. However, the lack of a unified and standardized database of genes assigned to kidney diseases has led to diagnostic blind spots and comparability issues among current studies of kidney genetics. To address this gap, we created the “**Kidney-Genetics**” a regularly updated, automated and publicly accessible database which aims to provide a comprehensive list of all relevant genes associated with kidney disease.

Key issues:

- Create a unified and standardized database of kidney disease-associated genes and provide a valuable resource for the diagnosis, treatment, and monitoring of those diseases
- Allow clinicians and researchers to gain a deeper understanding of the genetic factors underlying different KDs
- Compile, organize and curate important information on the genes to identify novel candidate genes and genetic variants associated with KDs
- Group and sort the genes into different categories, for example into phenotypic groups, the onset, syndromic, etc.
- Establish genotype-phenotype correlations that can be used to assign multiple clinical entities to a single gene in order to improve understanding and treatment choices
- The information can be used to develop personalized treatment strategies and interventions, leading to more effective and targeted therapies for individuals with KD
- Researchers can freely access “Kidney-Genetics” ensuring consistency and comparability across different research projects, which can accelerate scientific progress, foster collaborations, and facilitate the development of new insights and approaches

The scientific literature highlights the need for such a database and emphasizes the importance of genetic research in kidney disease (e.g. [Boulogne et al., 2023]).

In summary, our research question and its approach have the potential to provide a deeper scientific understanding of KD genetics, improve diagnostic accuracy, guide treatment selec-

¹<https://github.com/halbritter-lab/kidney-genetics>

tion, advance precision medicine, and facilitate research collaboration. The establishment of the “**Kidney-Genetics**” database addresses an important gap in the field and provides a valuable resource for researchers, clinicians, and patients involved in the discovery and treatment of KD.

Methods

To create a thorough and standardized database of kidney-related genes, we employed the following methods and compiled kidney disease-associated gene information from various sources:

1. Utilized data from Genomics England and Australia PanelApp [Martin et al., 2019]
2. Conducted a comprehensive literature review of published gene lists
3. Collected information from clinical diagnostic panels for kidney disease
4. Performed a Human Phenotype Ontology (HPO)-based [Köhler et al., 2021] search in rare disease databases (OMIM)
5. Employed a PubTator [Wei et al., 2013] API-based automated literature extraction from PubMed

We also developed an evidence-scoring system to differentiate highly confirmed disease genes from candidate genes. We defined the presence of a certain gene in 3 or more of the 5 resources as highly evident genes. These genes were then manually curated according to predetermined criteria or, in the case of existing ClinGen curation, their data and scores were used. Genes with a score of 2 or less were accordingly more likely to be classified as candidate genes.

Furthermore, we grouped all genes into different categories to later match them in a genotype-phenotype correlation.

To get a more transparent and thus more comprehensive understanding of our several evidence source “pillars”, we listed our different steps below and attached a flowchart for better visualization.

1. We retrieved all kidney disease related panels from both PanelApp UK and PanelApp Australia, meaning all panels that include “renal” or “kidney” in its name. That included xxx different lists. The access date was the xxx.
2. We identified Genes associated with kidney disease in a systematic Literature search using the following search query:
 - (1) “Kidney”[Mesh] OR “Kidney Diseases”[Mesh] OR kidney OR renal AND
 - (2) “Genetic Structures”[Mesh] OR “Genes”[Mesh] OR genetic test OR gene panel OR gene panels OR multigene panel OR targeted panel*

we then screened for published lists and got xxx lists from date to date xxx.

- [Bleyer et al., 2022]
- [Knoers et al., 2022]
- [Alaamery et al., 2022]
- [KDIGO Conference Participants, 2022]
- [Tanudisastro et al., 2021]
- [Devarajan et al., 2022]
- [Rasouly et al., 2019]
- [Elhassan et al., 2022]
- [Cormican et al., 2019]
- [Murray et al., 2020]
- [Claus et al., 2022]
- [Bullich et al., 2018]
- [Ottlewski et al., 2019]

- [Al-Hamed et al., 2016]
 - [Domingo-Gallego et al., 2022]
 - [Jordan et al., 2022]
3. We used ten common diagnostic panels that can be purchased for genome analysis and extracted the screened genes from them. Those included following panels:
 - Centogene nephrology²
 - Cegat kidney diseases³
 - Preventiongenetics comprehensive inherited kidney diseases panel⁴
 - Invitae progressive renal disease panel⁵
 - Invitae expanded renal disease panel⁶
 - Mgz nephrologie⁷
 - Mvz nierenkrankungen⁸
 - Natera renasight comprehensive kidney gene panel⁹
 - MayoCliniclabs renal genetics¹⁰
 - Blueprintgenetics nephrology¹¹
 4. We used common databases (e.g. OMIM) for rare diseases and screened them for kidney disease associated Genes from a Human Phenotype Ontology (HPO) based search query. The most comprehensive HPO term used was “Abnormality of the upper urinary tract” (HP:0010935) and included all subgroup terms. We deliberately chose these to be somewhat broader in order to fully include all relevant kidney diseases such as CAKUT, among others.
 5. We retrieved all kidney disease associated genes from a PubTator API-based automated literature extraction of publications available on PubMed.

Kidney-Genetics Flowchart

Results

The “Kidney-Genetics” database currently contains detailed information on 3025 kidney-associated genes with detailed annotations on gene function, kidney phenotype, incidence, possible syndromic disease expression and genetic variation. To automatically group the genes, we will present the results of phenotypic and functional clustering.

The number of genes extracted from the five analyzed sources of information is as follows: (1) 534, (2) 822, (3) 956, (4) 789, and (5) 2158

Notably, **598** genes (19.8%) of the **total 3025** genes are present in three or more of the analyzed information sources, thus meeting our evidence criteria, indicating high confidence and their potential for diagnostic use. Of these high evidence genes, **526** (88.0%) are present in at least one, and **56** (9.4%) are present in all 10 comprehensive diagnostic laboratory panels.

To ensure currency, Kidney-Genetics will be updated regularly and automatically at XXX week intervals. We will also provide phenotypic and functional clustering results to facilitate gene grouping.

²<https://www.centogene.com/diagnostics/our-tests/ngs-panels/nephrology>

³<https://cegat.com/diagnostics/rare-diseases/kidney-diseases/>

⁴<https://www.preventiongenetics.com/testInfo?val=Comprehensive-Inherited-Kidney-Diseases-Panel>

⁵<https://www.invitae.com/en/providers/test-catalog/test-75000>

⁶<https://www.invitae.com/en/providers/test-catalog/test-633100>

⁷<https://www.mgz-muenchen.de/gen-panels/section/nephrologie-endokrinologie-und-elektrolyte/tag/14.html>

⁸https://www.medizinische-genetik.de/fileadmin/MVZ-Martinsried/wcck/server/db_dataProvider.php?type=PanelTable&panelid=229

⁹<https://www.natera.com/organ-health/renasight-genetic-testing/gene-conditions-list/>

¹⁰<https://www.mayocliniclabs.com/test-catalog/Overview/618086>

¹¹<https://blueprintgenetics.com/tests/panels/nephrology/>

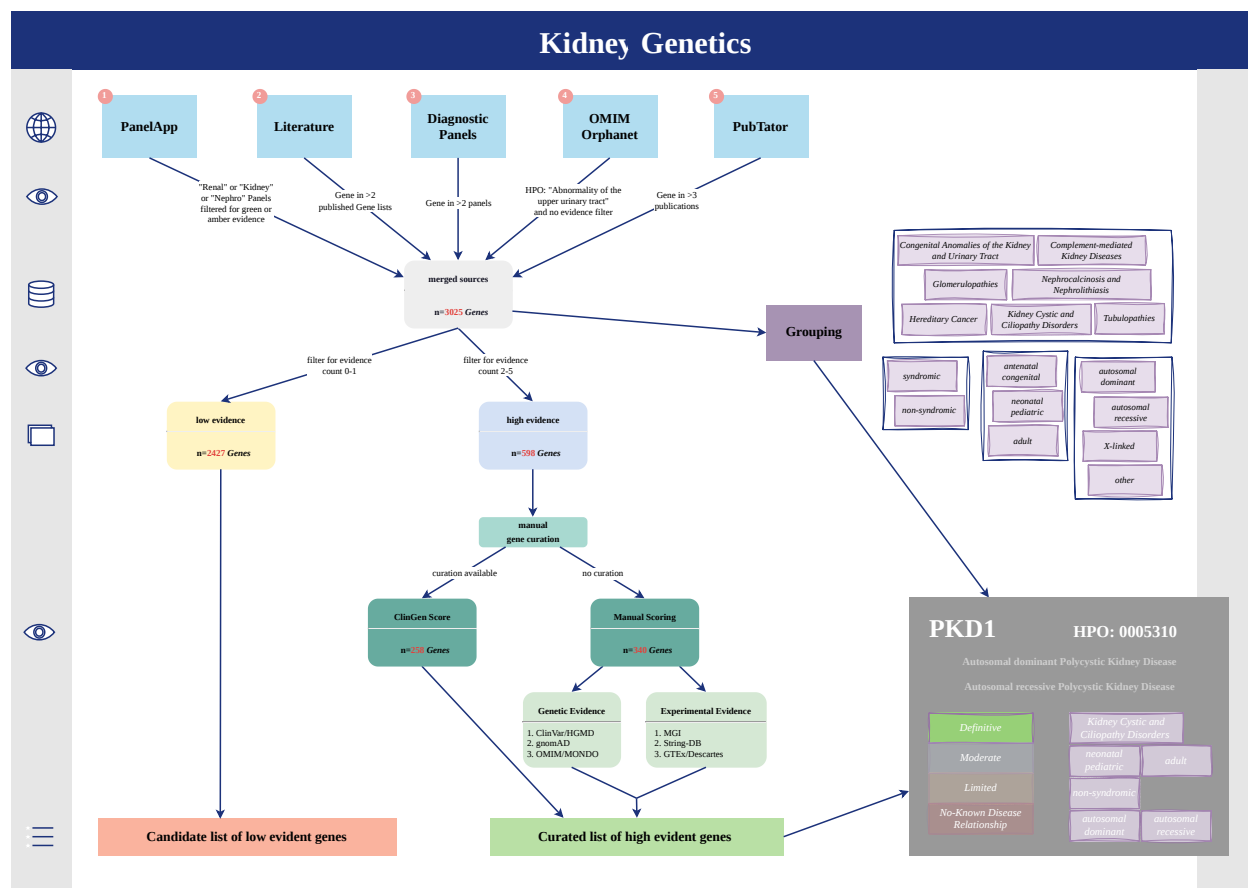


Figure 1: (#fig:curation_flow_diagram)Curation process flow diagram

Conclusion

Kidney-Genetics is a comprehensive, free and publicly accessible database that can be used by researchers to analyze genomic data related to KDs. The database will be routinely updated using an automated system and standardized pipeline to ensure that it is always up-to-date with the latest kidney research and diagnostics.

By utilizing Kidney-Genetics, clinicians, geneticists, and researchers can examine genomic data and improve their understanding of the genetic components of diverse KDs. The code and results are completely available on GitHub. A standardized pipeline and automated system keep our database on the cutting edge of kidney research and diagnostics. Screening efforts toward manual curation (such as through the ClinGen initiative) and assignment of diagnostic genes to nephrologic disease groups (e.g., syndromic vs. isolated; adult vs. pediatric; cystic, nephrotic, etc.) are currently in the development process and our goals for the near future.

Outlook

Future goals include the further manual curation of the high evident genes to acquire a more accurate individual assessment of each gene. For this purpose, we have developed a standardized curation process based on the ClinGen criteria, as previously discussed in the methods section. Furthermore, diagnostic genes will be assigned to certain defined nephrological disease groups, in order to obtain a phenotype-genotype correlation and gain a better clinical understanding.

1 Analyses result tables

1.1 Main table: Merged analyses sources

This table shows the merged results of all analyses files as a wide table with summarized information.

Copy CSV PDF Show entries

Search:

	gene	source_count_percentile
	<input type="text" value="All"/>	<input type="text" value="All"/>
1	ABCG2	1.23662103891279
2	ACE	4.25717405673475
3	ACTA2	1.49410242088822
4	ACTG2	3.00796235157466
5	ACTN4	4.05738833214446
6	ADAMTS13	3.27361542361937
7	ADAMTS9	1.79723624121145
8	ADCY10	2.07142473940403
9	AFF3	1.03909198219274
10	AGK	0.105805243445692

Showing 1 to 10 of 3,025 entries

Previous 2 3 4 5 ...
303 Next

1.2 Result table: PanelApp

This table shows results of the first analysis searching kidney disease associated genes from the PanelApp project in the UK and Australia.

Show 10 entries		Search		
gene	source	source_count	source_evidence	source_count_percentile
[1]	[2]	[3]	[4]	[5]
1	AB022 Renal tubulopathies (id=202, version=4.17, confidence=Best) Kidneyome SuperPanel (id=275, version=8.40, confidence=Green) Renal superpanel - broad (id=902, version=18.72, confidence=Best) Renal superpanel - narrow (id=903, version=16.60, confidence=Best)	0	false	0.1058052434456929
2	ACE Congenital anomalies of the kidney and urinary tract (CAKUT) Syndrome (id=43, version=0.133, confidence=Green) Unexplained kidney failure in young people (id=136, version=1.117, confidence=Green) Congenital abnormalities of the kidneys and urinary tract (CAKUT) SuperPanel (id=231, version=1.78, confidence=Green) Kidneyome SuperPanel (id=275, version=8.40, confidence=Green) Unexplained young onset and stage renal disease (id=878, version=3.11, confidence=Green) Renal superpanel - broad (id=902, version=18.72, confidence=Green) Renal superpanel - narrow (id=903, version=16.60, confidence=Green)	10	true	0.903558052434457
3	ACTA2 Unexplained kidney failure in young people (id=136, version=1.117, confidence=Best) Unexplained young onset and stage renal disease (id=878, version=3.11, confidence=Best) Renal superpanel - broad (id=902, version=18.72, confidence=Best) Renal superpanel - narrow (id=903, version=16.60, confidence=Best)	0	false	0.1058052434456929
4	ACTG2 Congenital anomalies of the kidney and urinary tract (CAKUT) Syndrome (id=43, version=0.133, confidence=Green) Unexplained kidney failure in young people (id=136, version=1.117, confidence=Green) Congenital abnormalities of the kidneys and urinary tract (CAKUT) SuperPanel (id=231, version=1.78, confidence=Green) Kidneyome SuperPanel (id=275, version=8.40, confidence=Green) Unexplained young onset and stage renal disease (id=878, version=3.11, confidence=Green) Renal superpanel - broad (id=902, version=18.72, confidence=Green) Renal superpanel - narrow (id=903, version=16.60, confidence=Green)	9	true	0.8108614232209738
5	ACTG4 Proximate renal disease (id=106, version=4.3, confidence=Green) Unexplained kidney failure in young people (id=136, version=1.117, confidence=Green) Renal Glomerulop Disease SuperPanel (id=262, version=1.75, confidence=Green) Kidneyome SuperPanel (id=275, version=8.40, confidence=Green) Unexplained young onset and stage renal disease (id=878, version=3.11, confidence=Green) Renal superpanel - broad (id=902, version=18.72, confidence=Green) Renal superpanel - narrow (id=903, version=16.60, confidence=Green)	9	true	0.8108614232209738
6	ADAMTS1 Kidneyome SuperPanel (id=275, version=8.40, confidence=Best) Renal superpanel - broad (id=902, version=18.72, confidence=Best) Renal superpanel - narrow (id=903, version=16.60, confidence=Best)	3	true	0.3941947565543071
7	ADAMTS2 Renal Cystopathies and Nephrocytopenia (id=193, version=1.20, confidence=Best) Renal Cyst Disease SuperPanel (id=263, version=1.49, confidence=Best) Kidneyome SuperPanel (id=275, version=8.40, confidence=Best) Cystic renal disease (id=487, version=7.27, confidence=Best) Tubulointerstitial kidney disease (id=584, version=3.3, confidence=Best) Renal Cystopathies (id=75, version=3.3, confidence=Best) Renal superpanel - broad (id=902, version=18.72, confidence=Best) Renal superpanel - narrow (id=903, version=16.60, confidence=Best)	10	true	0.903558052434457
8	ADCT16 Nephrocalcinosis or nephrocalcinosis (id=149, version=4.11, confidence=Best) Kidneyome SuperPanel (id=275, version=8.40, confidence=Best) Renal (id=902, version=18.72, confidence=Best) Renal superpanel - narrow (id=903, version=16.60, confidence=Best) Renal Tubulopathies and related disorders (id=3993, version=1.9, confidence=Best)	2	true	0.2968164794007491
9	AET2 Congenital anomalies of the kidney and urinary tract (CAKUT) Syndrome (id=43, version=0.133, confidence=Green) Congenital abnormalities of the kidneys and urinary tract (CAKUT) SuperPanel (id=231, version=1.78, confidence=Green) Kidneyome SuperPanel (id=275, version=8.40, confidence=Green)	3	true	0.3941947565543071
10	AGK Nephrocalcinosis or nephrocalcinosis (id=149, version=4.11, confidence=Best) Renal superpanel - broad (id=902, version=18.72, confidence=Best) Renal superpanel - narrow (id=903, version=16.60, confidence=Best)	0	false	0.1058052434456929

1.3 Result table: Literature

This table shows results of the second analysis searching kidney disease associated genes from various publications.

Show entries

Search:

	gene	source	source_count	source_evidence	source_count_percentile
	<input type="text" value="All"/>	<input type="text" value="All"/>	<input type="text" value="All"/>	<input type="text" value="All"/>	<input type="text" value="All"/>
1	ABCC6	PMID_35325889 PMID_30476936	2	true	0.5
2	ABCC8	PMID_35325889	1	false	0.2019464720194647
3	ABCD4	PMID_30476936	1	false	0.2019464720194647
4	ABCG2	PMID_35325889	1	false	0.2019464720194647
5	ACE	PMID_35325889 PMID_34264297 PMID_36035137 PMID_33664247 PMID_30476936 PMID_31509055 PMID_31822006 PMID_31027891 PMID_26862157 PMID_33532864 PMID_35005812	11	true	0.9659367396593674
6	ACP5	PMID_30476936	1	false	0.2019464720194647
7	ACTA2	PMID_34264297 PMID_30476936 PMID_35005812	3	true	0.6295620437956204
8	ACTB	PMID_35325889 PMID_30476936	2	true	0.5
9	ACTG2	PMID_34264297 PMID_30476936 PMID_35005812	3	true	0.6295620437956204
10	ACTN4	PMID_34264297 PMID_36035137 PMID_33664247 PMID_30476936 PMID_31509055 PMID_31822006 PMID_29801666 PMID_31027891 PMID_26862157 PMID_33532864	10	true	0.9190997566909976

Showing 1 to 10 of 822 entries

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1.4 Result table: Diagnostic panels

This table shows results of the third analysis searching kidney disease associated genes from clinical diagnostic panels for kidney disease.

Show entries

Search:

	gene	source	source_count	source_evidence	source_count_percentile
	<input type="text" value="All"/>	<input type="text" value="All"/>	<input type="text" value="All"/>	<input type="text" value="All"/>	<input type="text" value="All"/>
1	ABCB11	centogene_nephrology	1	false	0.2107740585774058
2	ABCB4	centogene_nephrology	1	false	0.2107740585774058
3	ABCC2	centogene_nephrology	1	false	0.2107740585774058
4	ABCC6	invitae_expanded_renal_disease_panel; natera_renasight_comprehensive_kidney_gene_panel; mayocliniclabs_renal_genetics	3	true	0.5993723849372385
5	ABCC8	mgz_nephrologie; natera_renasight_comprehensive_kidney_gene_panel	2	true	0.4911087866108786
6	ACE	centogene_nephrology; cegat_kidney_diseases_genes; preventiongenetics_comprehensive_inherited_kidney_diseases_panel; invitae_progressive_renal_disease_panel; invitae_expanded_renal_disease_panel; mgz_nephrologie; mvz_nierenerkrankungen; natera_renasight_comprehensive_kidney_gene_panel; mayocliniclabs_renal_genetics; blueprintgenetics_nephrology	10	true	0.9712343096234308
7	ACP5	centogene_nephrology	1	false	0.2107740585774058
8	ACTA2	mvz_nierenerkrankungen	1	false	0.2107740585774058
9	ACTB	invitae_progressive_renal_disease_panel; invitae_expanded_renal_disease_panel; natera_renasight_comprehensive_kidney_gene_panel	3	true	0.5993723849372385
10	ACTG1	natera_renasight_comprehensive_kidney_gene_panel	1	false	0.2107740585774058

Showing 1 to 10 of 956 entries

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1.5 Result table: HPO in rare disease databases

This table shows results of the fourth analysis searching kidney disease associated genes from a Human Phenotype Ontology (HPO)-based search in rare disease databases (OMIM, Orphanet).

Show entries

Search:

	gene	source	source_count	source_evidence	source_count_percentile
	<input type="text" value="All"/>	<input type="text" value="All"/>	<input type="text" value="All"/>	<input type="text" value="All"/>	<input type="text" value="All"/>
1	ABCC6	OMIM:264800 (HP:0100817); OMIM:614473 (HP:0000121)	2	true	0.8986058301647655
2	ACE	OMIM:267430 (HP:0008660 HP:0100519)	1	true	0.4201520912547528
3	ACP5	OMIM:607944 (HP:0005576)	1	true	0.4201520912547528
4	ACTG2	OMIM:155310 (HP:0000076 HP:0000126); OMIM:619431 (HP:0000072 HP:0000126)	2	true	0.8986058301647655
5	ACTN4	OMIM:603278 (HP:0003774 HP:0005565 HP:0000097 HP:0004719)	1	true	0.4201520912547528
6	ADA	OMIM:102700 (HP:0001967); OMIM:102700 (HP:0001967); OMIM:102700 (HP:0001967); OMIM:102700 (HP:0001967)	4	true	0.991128010139417
7	ADA2	OMIM:615688 (HP:0033261)	1	true	0.4201520912547528
8	ADAMTS13	OMIM:274150 (HP:0005575 HP:0012211 HP:0002907)	1	true	0.4201520912547528
9	ADCY10	OMIM:143870 (HP:0008672)	1	true	0.4201520912547528
10	ADNP	OMIM:615873 (HP:0000105)	1	true	0.4201520912547528

Showing 1 to 10 of 789 entries

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1.6 Result table: PubTator

This table shows results of the fifth analysis searching kidney disease associated genes from a PubTator API-based automated literature extraction from PubMed.

Show entriesSearch:

	gene	source	source_count	source_evidence	source_count_percentile
	<input type="text" value="All"/>	<input type="text" value="All"/>	<input type="text" value="All"/>	<input type="text" value="All"/>	<input type="text" value="All"/>
1	A2M	PMID_33107589 PMID_30624993	2	false	0.5479610750695088
2	A4GALT	PMID_37301502 PMID_32274449 PMID_29618309 PMID_27438980	4	true	0.7680722891566265
3	AATF	PMID_22178801	1	false	0.2247451343836886
4	ABCA1	PMID_36496495 PMID_35547199 PMID_31929604 PMID_29046474 PMID_26546829 PMID_19056482 PMID_17332731	9	true	0.8922613531047267
5	ABCB1	PMID_37629712 PMID_34740465 PMID_33923087 PMID_33785019 PMID_27841150 PMID_24262617 PMID_24309308 PMID_18518855 PMID_18518969 PMID_17376299 PMID_17043887	18	true	0.943466172381835
6	ABCB11	PMID_25771912	1	false	0.2247451343836886
7	ABCC1	PMID_28891970	1	false	0.2247451343836886
8	ABCC2	PMID_18518855	1	false	0.2247451343836886
9	ABCC4	PMID_36923356 PMID_30382560	2	false	0.5479610750695088
10	ABCC6	PMID_31861118 PMID_29991491 PMID_28891970 PMID_18791038	5	true	0.8127896200185357

Showing 1 to 10 of 2,158 entries

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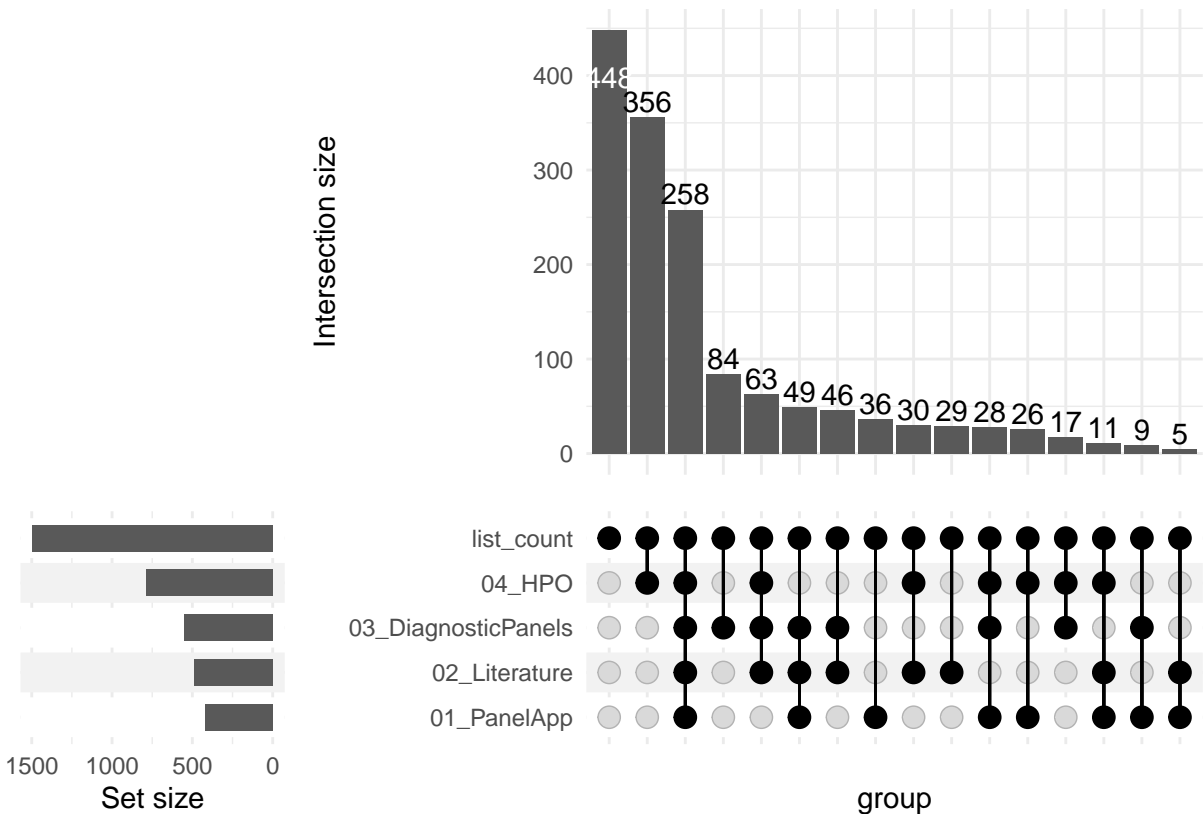
2 Analyses plots

2.1 UpSet plot of merged analyses sources

Below you can see a UpSet plot of the merged analyses.

In the lower left corner you can see the number of Genes originating from each of the different resources, after that resources are sorted on the right side. UpSet plots generally represent the intersections of a data set in the form of a matrix, as can be seen in the graph below.

- Each column corresponds to a set, and the bar graphs at the top show the size of the set.
- Each row corresponds to a possible intersection: the dark filled circles show which set is part of an intersection.
- For example, the first column shows that most of the genes found in only one of the five sources are derived from the PubTator query, and in the third column you can see that **177 Genes** are found in all five sources.



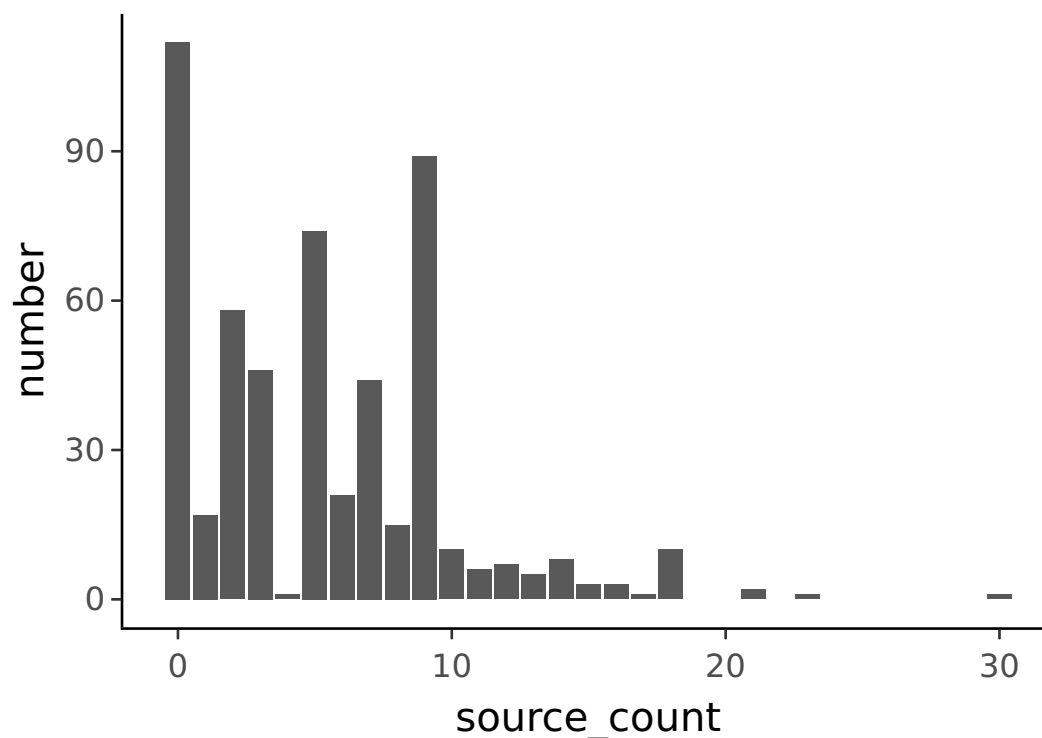
2.2 Bar plot of PanelApp results

Below you can see a Bar plot of the PanelApp analysis.

We retrieved all kidney disease related panels from both PanelApp UK and PanelApp Australia, meaning all panels that include “renal” or “kidney” in its name.

- The y axis shows the number of Genes in the different panels, which is also visualized by the height of the bars.

- The x axis displays the number of panels (source_count), i.e. in how many different panels a single Gene occurred.
- For example **38 Genes** occurred in just one panel and **2 Genes** were present in all thirty different panels.



2.3 Bar plot of Literature results

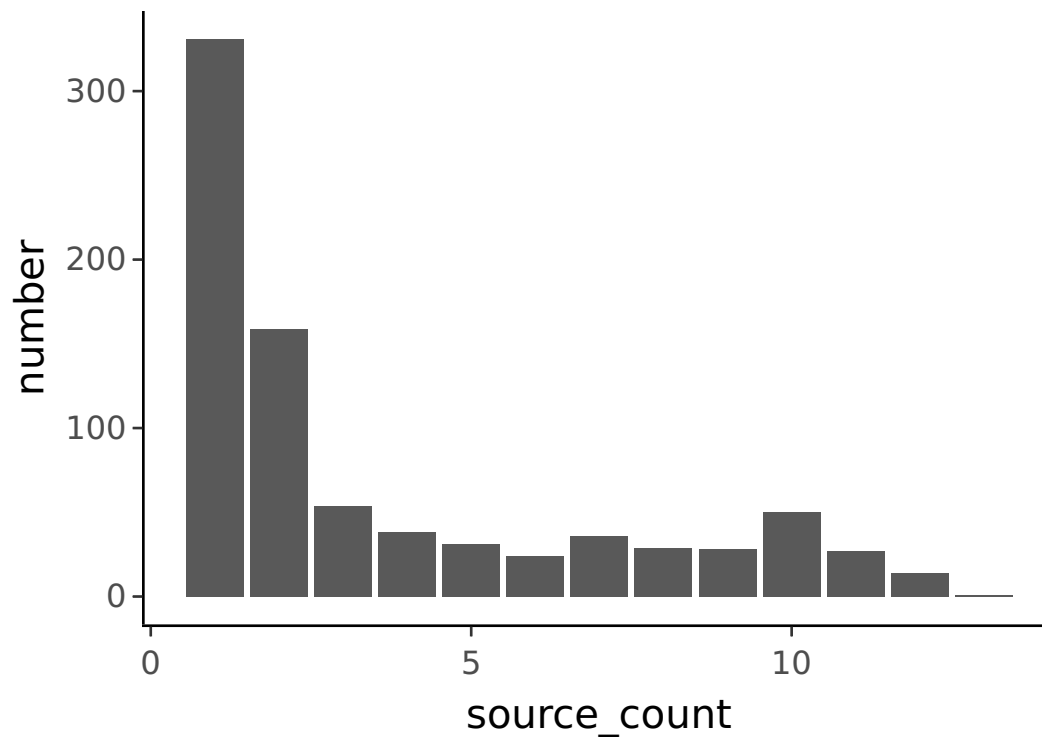
Below you can see a Bar plot of the Literature analysis.

We identified Genes associated with kidney disease in a systematic Literature search using the following search query:

(1) *“Kidney”[Mesh] OR “Kidney Diseases”[Mesh] OR kidney OR renal* AND

(2) *“Genetic Structures”[Mesh] OR “Genes”[Mesh] OR genetic test OR gene panel OR gene panels OR multigene panel OR targeted panel**

- The y axis shows the number of Genes in different publications, which is also visualized by the height of the bars.
- The x axis displays the number of publications (source_count), i.e. in how many different publications a single Gene occurred.
- For example **331 Genes** occurred in just one of the publications and **1 Gene** was present in all 13 different publications.

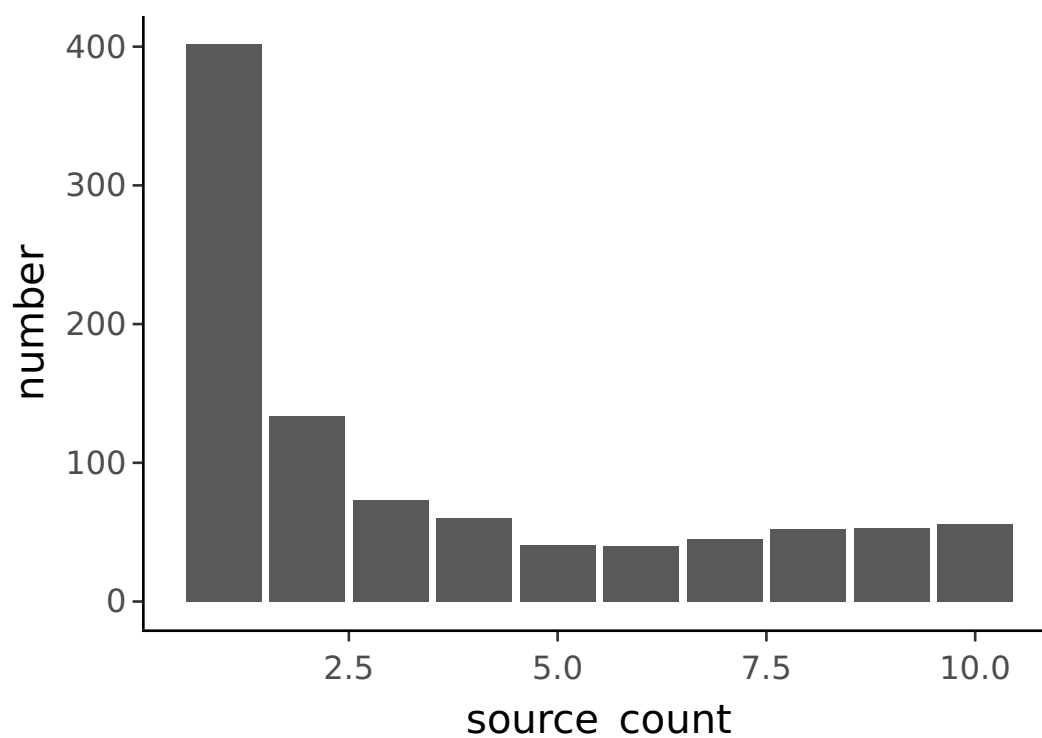


2.4 Bar plot of Diagnostic panels results

Below you can see a Bar plot of the Diagnostic panels analysis.

We used ten common diagnostic panels that can be purchased for genome analysis and extracted the screened Genes from them.

- The y axis shows the number of Genes in the different diagnostic panels, which is also visualized by the height of the bars.
- The x axis displays the number of panels (source_count), i.e. in how many different panels a single Gene occurred.
- For example **371 Genes** occurred in just one panel and **56 Genes** were present in all ten different panels.

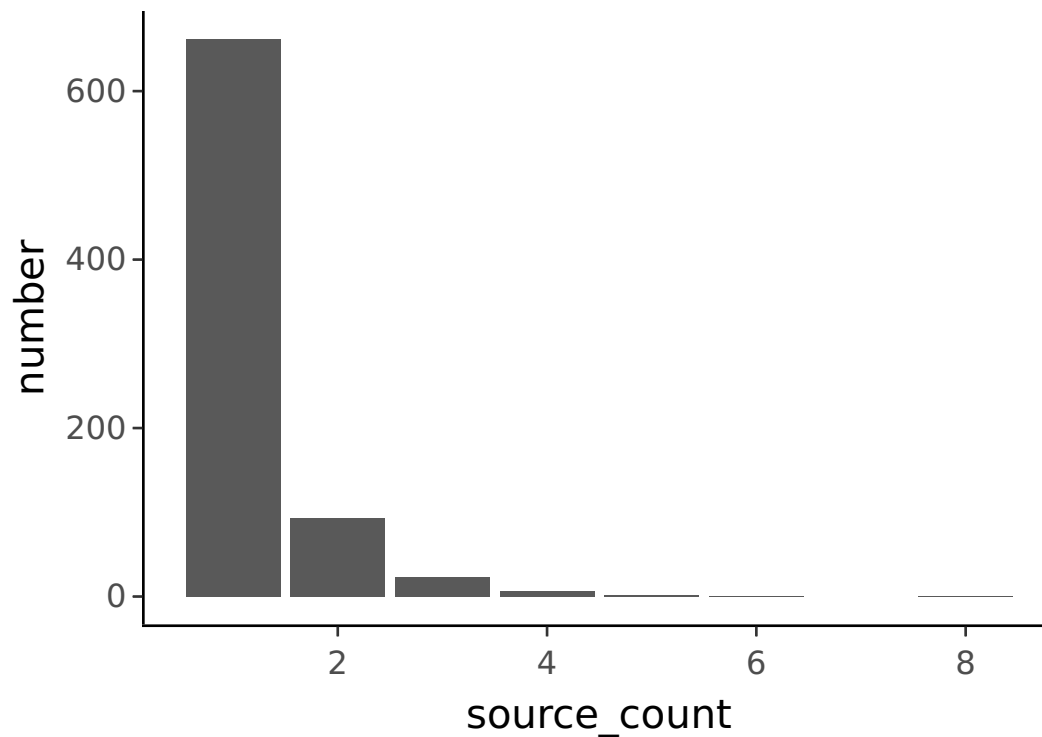


2.5 Bar plot of HPO in rare disease databases results

Below you can see a Bar plot of the HPO-term based query in rare disease databases (OMIM, Orphanet).

We used eight common databases for rare diseases and screened them for kidney disease associated Genes from a Human Phenotype Ontology (HPO) based search query. The most comprehensive HPO term used was “*Abnormality of the upper urinary tract*” (HP:0010935) and included all sub group terms. We deliberately chose these to be somewhat broader in order to fully include all relevant kidney diseases such as CAKUT, among others.

- The y axis shows the number of Genes in the different rare disease databases, which is also visualized by the height of the bars.
- The x axis displays the number of databases (source_count), i.e. in how many different databases a single Gene occurred.
- For example **652 Genes** occurred in just one database and **1 Gene** was present in all eight different databases.

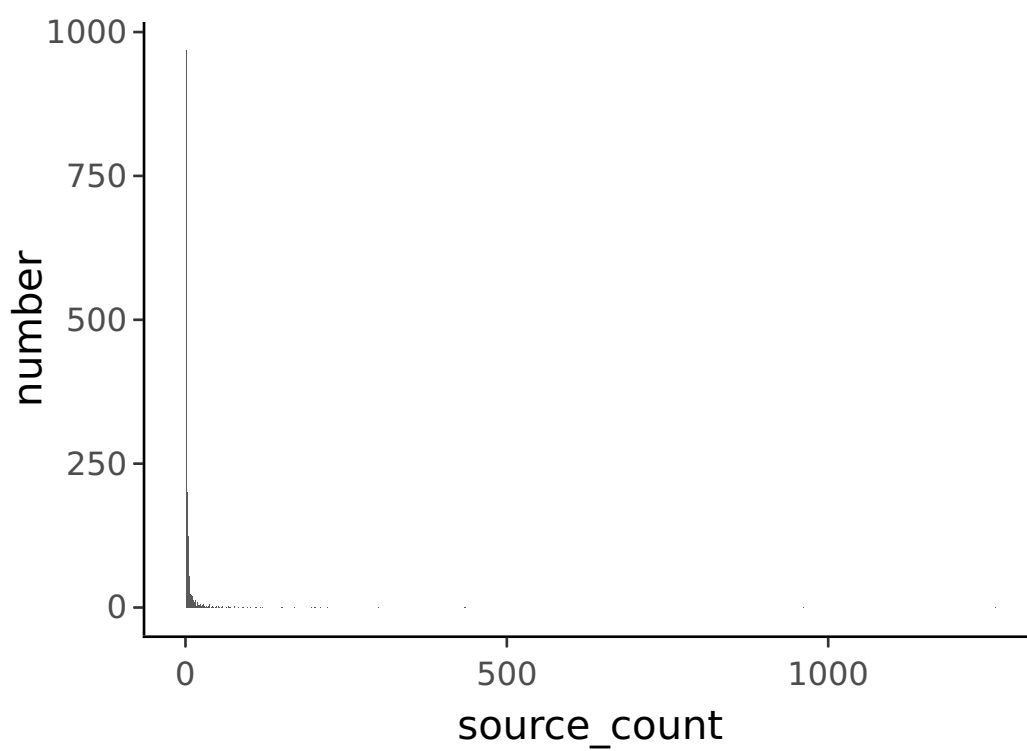


2.6 Bar plot of PubTator results

Below you can see a Bar plot of the PubTator analysis.

We retrieved all kidney disease associated Genes from a PubTator API-based automated literature extraction of publications available on PubMed.

- The y axis shows the number of Genes in the different publications, which is also visualized by the height of the bars.
- The x axis displays the number of publications (source_count), i.e. in how many different publications a single Gene occurred.
- For example **914 Genes** occurred in just one publication and **1 Gene** was present in **1221** different publications.



Copy

CSV

PDF

Show

10

entries

Search:

gene

evidence_count

All

All

1	ACE	5
---	---------------------	---

2	ACTG2	4
---	-----------------------	---

3	ACTN4	5
---	-----------------------	---

4	ADAMTS13	5
---	--------------------------	---

5	ADAMTS9	2
---	-------------------------	---

6	ADCY10	4
---	------------------------	---

7	AFF3	2
---	----------------------	---

8	AGT	5
---	---------------------	---

9	AGTR1	5
---	-----------------------	---

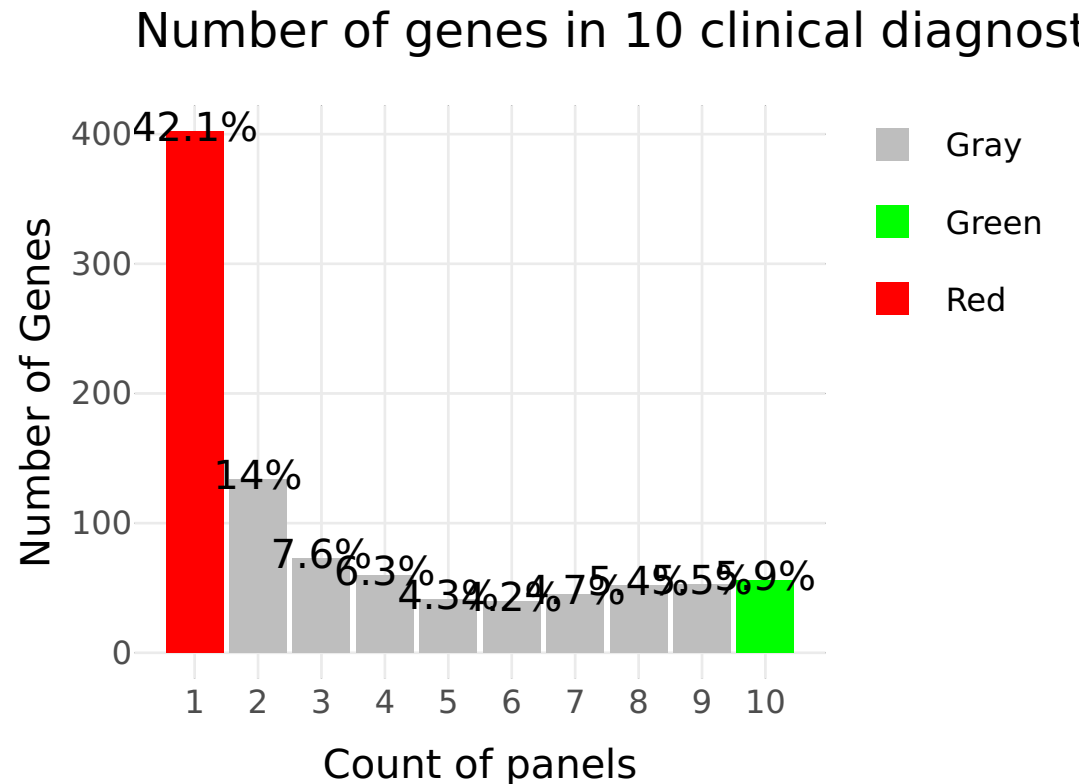
10	AGXT	5
----	----------------------	---

4 Additional analyses

4.1 Diagnostic panels content overlap

Below you can see a bar plot of the diagnostic panels content overlap.

We used ten common diagnostic panels that can be ordered for kidney disease analysis and extracted the screened genes from them. Here we show the overlap of the genes in the different panels.



5 Visualizations

This section provides a comprehensive overview of presentations and posters related to the Kidney Genetics project. As an essential part of our approach to transparency, we have assembled a collection of materials, presented at various conferences and meetings to illustrate the milestones in the project's development.

5.1 Objectives

1. **Project Progress Tracking:** By organizing presentations and posters chronologically, this section serves as a dynamic timeline to track the progress and evolution of the project.
2. **Event-specific Insights:** Each entry includes details about the date and event where the presentation or poster was showcased.

5.2 Presentations

Below you can explore the list of Presentations:

2023-12-05 / This is the presentation of our project presented at our monthly AG-Halbritter Working Group Meeting as a progress report.

2023-10-07 / This is the presentation of our project presented by Nina Rank as a pitch talk at the annual congress of the German Society of Nephrology - DGfN in Berlin.

2023-07-05 / This is one of the first presentations at the beginning of this project with some initial ideas presented at our weekly AG-Halbritter Working Group Meeting.

5.3 Posters

Below you can explore the list of Posters:

2023-09-28 / This is our first Poster presented at the inaugural Symposium of the Max Rubner Center for Cardiovascular-Metabolic-Renal-Research.

References

- Mohamed H. Al-Hamed, Wesam Kurdi, Nada Alsahan, Zainab Alabdullah, Rania Abudraz, Maha Tulbah, Maha Alnemer, Rubina Khan, Haya Al-Jurayb, Ahmed Alahmed, Asma I. Tahir, Dania Khalil, Noel Edwards, Basma Al Abdulaziz, Faisal S. Binhumaid, Salma Majid, Tariq Faquih, Mohamed El-Kalioby, Mohamed Abouelhoda, Nada Altassan, Dorota Monies, Brian Meyer, John A. Sayer, and Mamdouh Albaqumi. Genetic spectrum of Saudi Arabian patients with antenatal cystic kidney disease and ciliopathy phenotypes using a targeted renal gene panel. *Journal of Medical Genetics*, 53(5):338–347, May 2016. ISSN 1468-6244. doi: 10.1136/jmedgenet-2015-103469.
- Manal Alaamery, Jahad Alghamdi, Salam Massadeh, Mona Alsawaji, Nora Aljawini, Nour Albeshir, Bader Alghamdi, Mansour Almutairi, Fayez Hejaili, Majid Alfadhel, Batoul Baz, Bader Almuzzaini, Adel F. Almutairi, Mubarak Abdullah, Francisco J. Quintana, and Abdullah Sayyari. Analysis of chronic kidney disease patients by targeted next-generation sequencing identifies novel variants in kidney-related genes. *Frontiers in Genetics*, 13:886038, 2022. ISSN 1664-8021. doi: 10.3389/fgene.2022.886038.
- Anthony J. Bleyer, Maggie Westemeyer, Jing Xie, Michelle S. Bloom, Katya Brossart, Jason J. Eckel, Frederick Jones, Miklos Z. Molnar, Wayne Kotzker, Prince Anand, Stanislav Kmoch, Yuan Xue, Samuel Strom, Sumit Punj, Zachary P. Demko, Hossein Tabriziani, Paul R. Billings, and Trudy McKanna. Genetic Etiologies for Chronic Kidney Disease Revealed through Next-Generation Renal Gene Panel. *American Journal of Nephrology*, 53(4):297–306, 2022. ISSN 1421-9670. doi: 10.1159/000522226.
- Florianne Boulogne, Laura R. Claus, Henry Wiersma, Roy Oelen, Floor Schukking, Niek de Klein, Shuang Li, Harm-Jan Westra, Bert van der Zwaag, Franka van Reekum, Genomics England Research Consortium, Dana Sierks, Ria Schönauer, Zhigui Li, Emilia K. Bijlsma, Willem Jan W. Bos, Jan Halbritter, Nine V. A. M. Knoers, Whitney Besse, Patrick Deelen, Lude Franke, and Albertien M. van Eerde. KidneyNetwork: using kidney-derived gene expression data to predict and prioritize novel genes involved in kidney disease. *European journal of human genetics: EJHG*, February 2023. ISSN 1476-5438. doi: 10.1038/s41431-023-01296-x.
- Gemma Bullich, Andrea Domingo-Gallego, Iván Vargas, Patricia Ruiz, Laura Lorente-Grandoso, Mónica Furlano, Gloria Fraga, Álvaro Madrid, Gema Ariceta, Mar Borregán, Juan Alberto Piñero-Fernández, Lidia Rodríguez-Peña, Maria Juliana Ballesta-Martínez, Isabel Llano-Rivas, Mireia Aguirre Meñica, José Ballarín, David Torrents, Roser Torra, and Elisabet Ars. A kidney-disease gene panel allows a comprehensive genetic diagnosis of cystic and glomerular inherited kidney diseases. *Kidney International*, 94(2): 363–371, August 2018. ISSN 1523-1755. doi: 10.1016/j.kint.2018.02.027.
- Laura R. Claus, Rozemarijn Snoek, Nine V. A. M. Knoers, and Albertien M. van Eerde. Review of genetic testing in kidney disease patients: Diagnostic yield of single nucleotide variants and copy number variations evaluated across and within kidney phenotype groups. *American Journal of Medical Genetics. Part C, Seminars in Medical Genetics*, 190(3):358–376, September 2022. ISSN 1552-4876. doi: 10.1002/ajmg.c.31995.
- S. Cormican, D. M. Connaughton, C. Kennedy, S. Murray, M. Živná, S. Kmoch, N. K. Fennelly, P. O’Kelly, K. A. Benson, E. T. Conlon, G. Cavalleri, C. Foley, B. Doyle, A. Dorman, M. A. Little, P. Lavin, K. Kidd,

- A. J. Bleyer, and P. J. Conlon. Autosomal dominant tubulointerstitial kidney disease (ADTKD) in Ireland. *Renal Failure*, 41(1):832–841, November 2019. ISSN 1525-6049. doi: 10.1080/0886022X.2019.1655452.
- Prasad Devarajan, Glenn M. Chertow, Katalin Susztak, Adeera Levin, Rajiv Agarwal, Peter Stenvinkel, Arlene B. Chapman, and Bradley A. Warady. Emerging Role of Clinical Genetics in CKD. *Kidney Medicine*, 4(4):100435, April 2022. ISSN 2590-0595. doi: 10.1016/j.xkme.2022.100435.
- Andrea Domingo-Gallego, Marc Pybus, Gemma Bullich, Mónica Furlano, Laia Ejarque-Vila, Laura Lorente-Grandoso, Patricia Ruiz, Gloria Fraga, Mercedes López González, Juan Alberto Piñero-Fernández, Lidia Rodríguez-Peña, Isabel Llano-Rivas, Raquel Sáez, Anna Bujons-Tur, Gema Ariceta, Lluís Guirado, Roser Torra, and Elisabet Ars. Clinical utility of genetic testing in early-onset kidney disease: seven genes are the main players. *Nephrology, Dialysis, Transplantation: Official Publication of the European Dialysis and Transplant Association - European Renal Association*, 37(4):687–696, March 2022. ISSN 1460-2385. doi: 10.1093/ndt/gfab019.
- Elhussein A. E. Elhassan, Susan L. Murray, Dervla M. Connaughton, Claire Kennedy, Sarah Cormican, Cliona Cowhig, Caragh Stapleton, Mark A. Little, Kendrah Kidd, Anthony J. Bleyer, Martina Živná, Stanislav Kmoch, Neil K. Fennelly, Brendan Doyle, Anthony Dorman, Matthew D. Griffin, Liam Casserly, Peter C. Harris, Friedhelm Hildebrandt, Gianpiero L. Cavalleri, Katherine A. Benson, and Peter J. Conlon. The utility of a genetic kidney disease clinic employing a broad range of genomic testing platforms: experience of the Irish Kidney Gene Project. *Journal of Nephrology*, 35(6):1655–1665, July 2022. ISSN 1724-6059. doi: 10.1007/s40620-021-01236-2.
- Penelope Jordan, Guillaume Dorval, Christelle Arrondel, Vincent Morinière, Carole Tournant, Marie-Pierre Audrezet, Laurence Michel-Calemard, Audrey Putoux, Gaëthan Lesca, Audrey Labalme, Sandra Whalen, Laurence Loeuillet, Jelena Martinovic, Tania Attie-Bitach, Bettina Bessières, Elise Schaefer, Sophie Scheidecker, Laetitia Lambert, Claire Beneteau, Olivier Patat, Odile Boute-Benejean, Arnaud Molin, Fabien Guimiot, Nicolas Fontanarosa, Mathilde Nizon, Mathilde Lefebvre, Cécile Jeanpierre, Sophie Saunier, and Laurence Heidet. Targeted next-generation sequencing in a large series of fetuses with severe renal diseases. *Human Mutation*, 43(3):347–361, March 2022. ISSN 1098-1004. doi: 10.1002/humu.24324.
- KDIGO Conference Participants. Genetics in chronic kidney disease: conclusions from a Kidney Disease: Improving Global Outcomes (KDIGO) Controversies Conference. *Kidney International*, 101(6):1126–1141, June 2022. ISSN 1523-1755. doi: 10.1016/j.kint.2022.03.019.
- Nine Knoers, Corinne Antignac, Carsten Bergmann, Karin Dahan, Sabrina Giglio, Laurence Heidet, Beata S. Lipska-Ziętkiewicz, Marina Noris, Giuseppe Remuzzi, Rosa Vargas-Poussou, and Franz Schaefer. Genetic testing in the diagnosis of chronic kidney disease: recommendations for clinical practice. *Nephrology, Dialysis, Transplantation: Official Publication of the European Dialysis and Transplant Association - European Renal Association*, 37(2):239–254, January 2022. ISSN 1460-2385. doi: 10.1093/ndt/gfab218.
- Sebastian Köhler, Michael Gargano, Nicolas Matentzoglou, Leigh C Carmody, David Lewis-Smith, Nicole A Vasilevsky, Daniel Danis, Ganna Balagura, Gareth Baynam, Amy M Brower, Tiffany J Callahan, Christopher G Chute, Johanna L Est, Peter D Galer, Shiva Ganesan, Matthias Griesse, Matthias Haimel, Julia Pazmandi, Marc Hanauer, Nomi L Harris, Michael J Hartnett, Maximilian Hastreiter, Fabian Hauck, Yongqun He, Tim Jeske, Hugh Kearney, Gerhard Kindle, Christoph Klein, Katrin Knoflach, Roland Krause, David Lagorce, Julie A McMurphy, Jillian A Miller, Monica C Munoz-Torres, Rebecca L Peters, Christina K Rapp, Ana M Rath, Shahmir A Rind, Avi Z Rosenberg, Michael M Segal, Markus G Seidel, Damian Smedley, Tomer Talmy, Yarlalu Thomas, Samuel A Wiafe, Julie Xian, Zafer Yüksel, Ingo Helbig, Christopher J Mungall, Melissa A Haendel, and Peter N Robinson. The Human Phenotype Ontology in 2021. *Nucleic Acids Research*, 49(D1):D1207–D1217, January 2021. ISSN 0305-1048, 1362-4962. doi: 10.1093/nar/gkaa1043. URL <https://academic.oup.com/nar/article/49/D1/D1207/6017351>.
- Antonio Rueda Martin, Eleanor Williams, Rebecca E. Foulger, Sarah Leigh, Louise C. Daugherty, Olivia Niblock, Ivone U. S. Leong, Katherine R. Smith, Oleg Gerasimenko, Eik Haraldsdottir, Ellen Thomas, Richard H. Scott, Emma Baple, Arianna Tucci, Helen Brittain, Anna De Burca, Kristina Ibañez, Dalia Kasperaviciute, Damian Smedley, Mark Caulfield, Augusto Rendon, and Ellen M. McDonagh. PanelApp crowdsources expert knowledge to establish consensus diagnostic gene panels. *Nature Genetics*, 51(11):

- 1560–1565, November 2019. ISSN 1061-4036, 1546-1718. doi: 10.1038/s41588-019-0528-2. URL <https://www.nature.com/articles/s41588-019-0528-2>.
- Susan L. Murray, Anthony Dorman, Katherine A. Benson, Dervla M. Connaughton, Caragh P. Stapleton, Neil K. Fennelly, Claire Kennedy, Ciara A. McDonnell, Kendrah Kidd, Sarah M. Cormican, Louise A. Ryan, Peter Lavin, Mark A. Little, Anthony J. Bleyer, Brendan Doyle, Gianpiero L. Cavalleri, Friedhelm Hildebrandt, and Peter J. Conlon. Utility of Genomic Testing after Renal Biopsy. *American Journal of Nephrology*, 51(1):43–53, 2020. ISSN 1421-9670. doi: 10.1159/000504869.
- Isabel Ottlewski, Johannes Münch, Timo Wagner, Ria Schönauer, Anette Bachmann, Antje Weimann, Julia Hentschel, Tom H. Lindner, Daniel Seehofer, Carsten Bergmann, Rami Abou Jamra, and Jan Halbritter. Value of renal gene panel diagnostics in adults waiting for kidney transplantation due to undetermined end-stage renal disease. *Kidney International*, 96(1):222–230, July 2019. ISSN 1523-1755. doi: 10.1016/j.kint.2019.01.038.
- Hila Milo Rasouly, Emily E. Groopman, Reuben Heyman-Kantor, David A. Fasel, Adele Mitrotti, Rik Westland, Louise Bier, Chunhua Weng, Zhong Ren, Brett Copeland, Priya Krithivasan, Wendy K. Chung, Simone Sanna-Cherchi, David B. Goldstein, and Ali G. Gharavi. The Burden of Candidate Pathogenic Variants for Kidney and Genitourinary Disorders Emerging From Exome Sequencing. *Annals of Internal Medicine*, 170(1):11–21, January 2019. ISSN 1539-3704. doi: 10.7326/M18-1241.
- Hope A. Tanudisastro, Katherine Holman, Gladys Ho, Elizabeth Farnsworth, Katrina Fisk, Thet Gayagay, Emma Hackett, Gemma Jenkins, Rahul Krishnaraj, Tiffany Lai, Karen Wong, Chirag Patel, Amali Mallawaarachchi, Andrew J. Mallett, Bruce Bennetts, Stephen I. Alexander, and Hugh J. McCarthy. Australia and New Zealand renal gene panel testing in routine clinical practice of 542 families. *NPJ genomic medicine*, 6(1):20, March 2021. ISSN 2056-7944. doi: 10.1038/s41525-021-00184-x.
- Chih-Hsuan Wei, Hung-Yu Kao, and Zhiyong Lu. PubTator: a web-based text mining tool for assisting biocuration. *Nucleic Acids Research*, 41(W1):W518–W522, July 2013. ISSN 1362-4962, 0305-1048. doi: 10.1093/nar/gkt441. URL <http://academic.oup.com/nar/article/41/W1/W518/1105731/PubTator-a-webbased-text-mining-tool-for-assisting>.