The Kidney-Genetics Documentation

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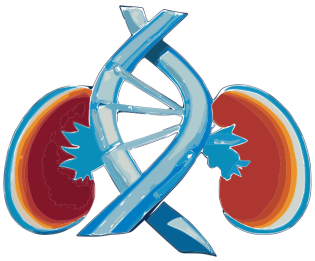
Preface

This documentation is intended to describe the Kidney-Genetics[1] project.

[1] https://github.com/halbritter-lab/kidney-genetics



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?

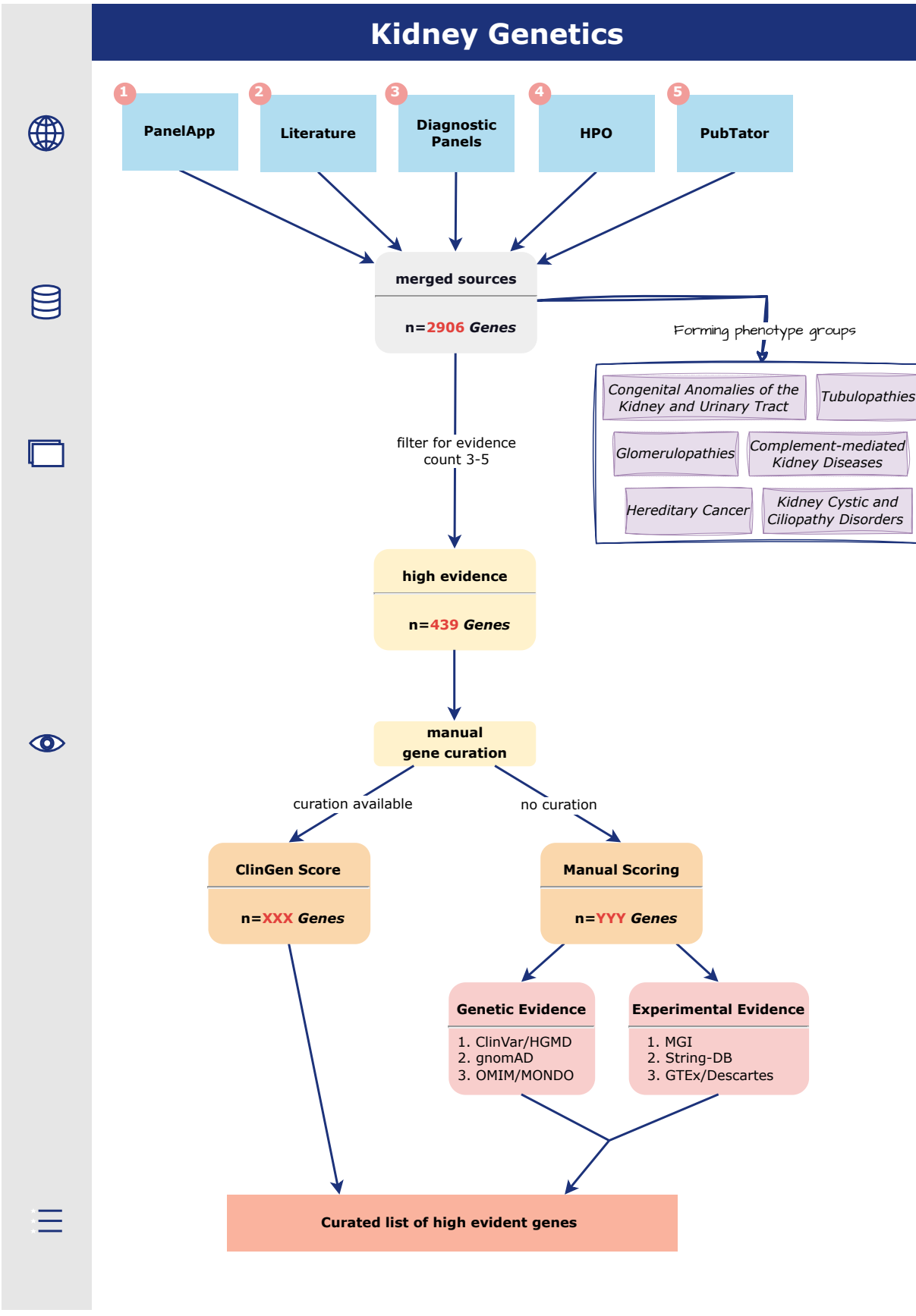
Methods

To create a comprehensive and standardized database of kidney-related genes, we employed the following methods:

1. Utilized data from Genomics England and Australia PanelApp.
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 search in rare disease databases (OMIM, Orphanet).
5. Employed a PubTator API-based automated literature extraction from PubMed.

We also developed an evidence-scoring system to differentiate highly confirmed disease genes from candidate genes.

In order to make our approach more transparent and thus more comprehensible, we have attached our current



workflow as a chart.

Results

The "Kidney-Genetics" database currently includes detailed information on 2,906 kidney-associated genes. Notably, 439 genes (15.1%) are present in three or more of the analyzed information sources, indicating high confidence and their potential for diagnostic use.

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

Conclusion

Kidney-Genetics is a comprehensive and freely accessible database that researchers can use to analyze genomic data related to kidney diseases. The database is regularly updated through a standardized pipeline and an automated system, ensuring it remains up-to-date with the latest advancements in kidney research and diagnostics.

By utilizing Kidney-Genetics, clinicians and researchers can enhance their understanding of the genetic aspects of kidney disorders.

Outlook

Future goals include manual curation and the assignment of diagnostic genes to specific nephrology disease groups, such as syndromic vs. isolated, adult- vs. pediatric-onset, and cystic vs. nephrotic, among others.

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.

approved_symbol	hgnc_id	evidence_count	list_count	01_PanelApp	02_Literature	03_DiagnosticPanels	04_HPO	05_PubTator
All	All	All	All	All	All	All	All	All

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.

approved_symbol	hgnc_id	gene_name_reported	source	source_count	source_evidence
All	All	All	All	All	All

1.3 Result table: Literature

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

approved_symbol	hgnc_id	gene_name_reported	source	source_count	source_evidence
All	All	All	All	All	All

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.

approved_symbol	hgnc_id	gene_name_reported	source	source_count	source_evidence
All	All	All	All	All	All

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).

approved_symbol	hgnc_id	gene_name_reported	source	source_count	source_evidence
All	All	All	All	All	All

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.

approved_symbol	hgnc_id	gene_name_reported	source	source_count	source_evidence
All	All	All	All	All	All

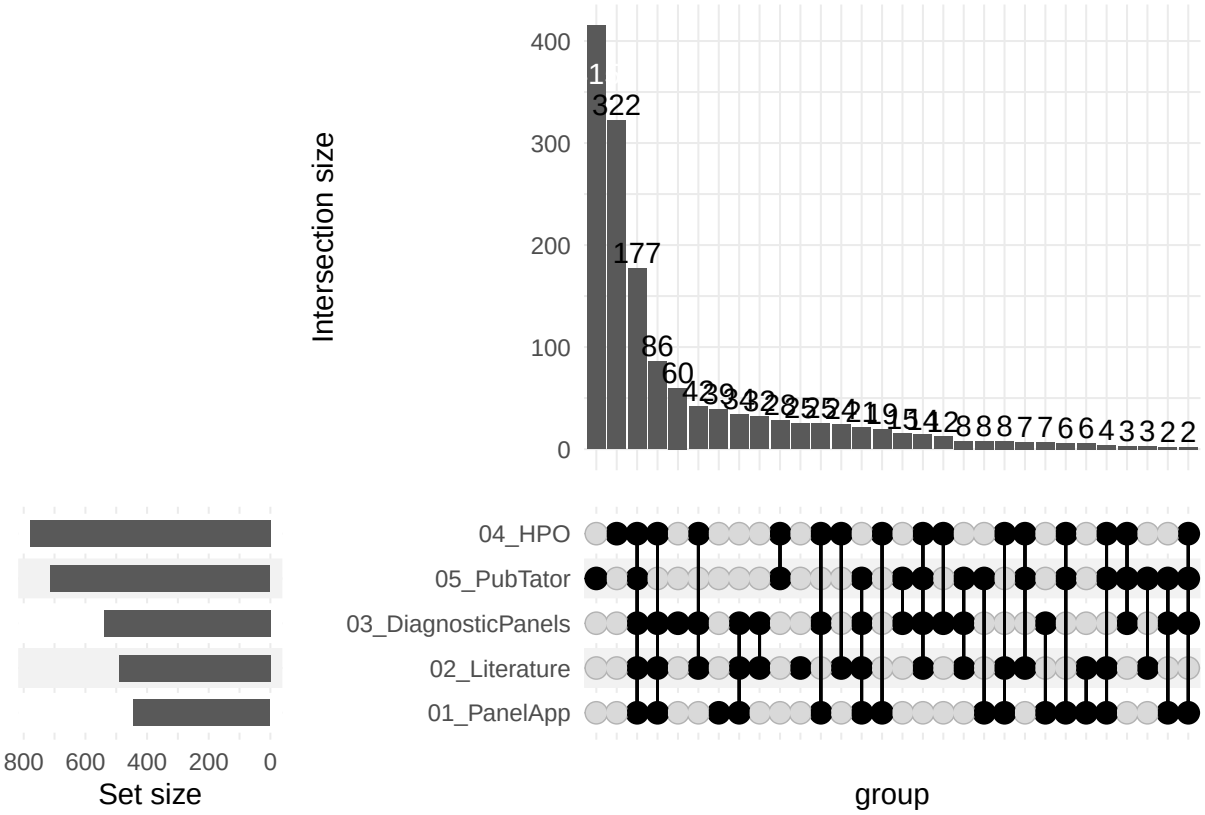
2 Analyses plots

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.

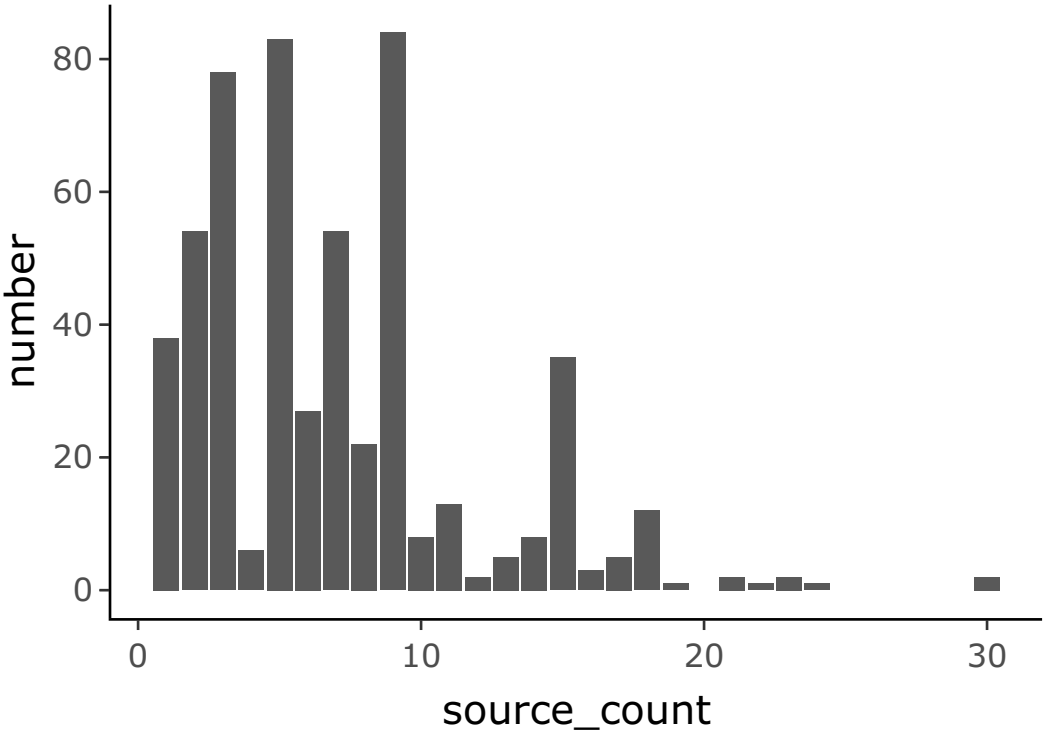


2.2 Bar plot of PanelApp results

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.

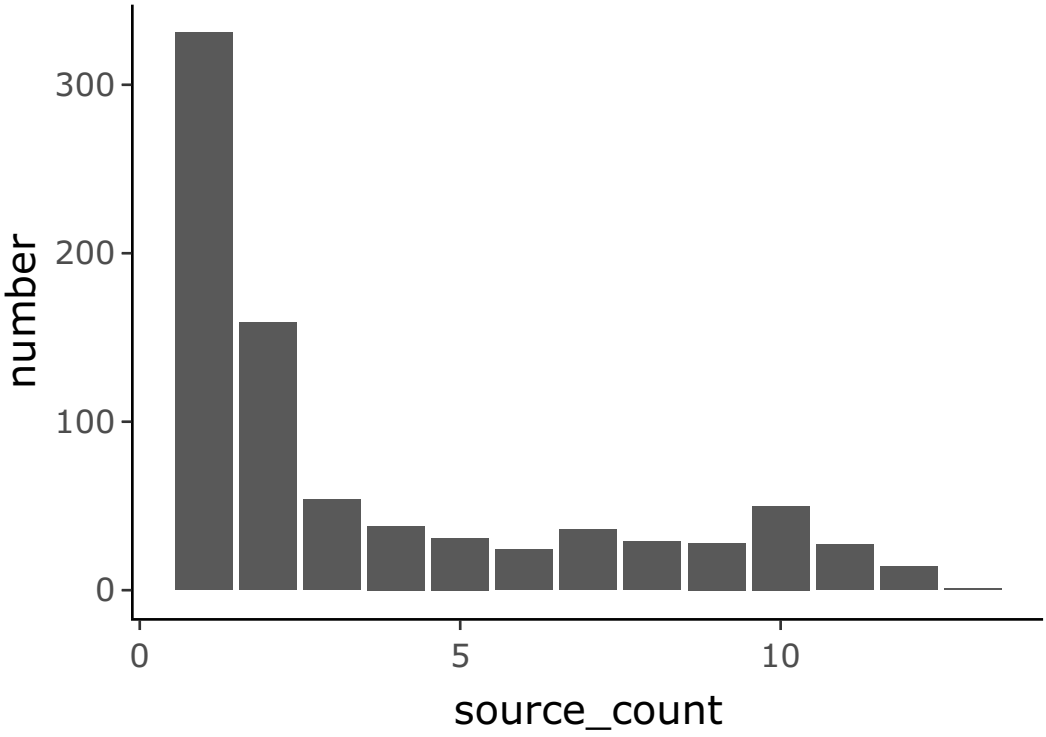


2.3 Bar plot of Literature results

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.

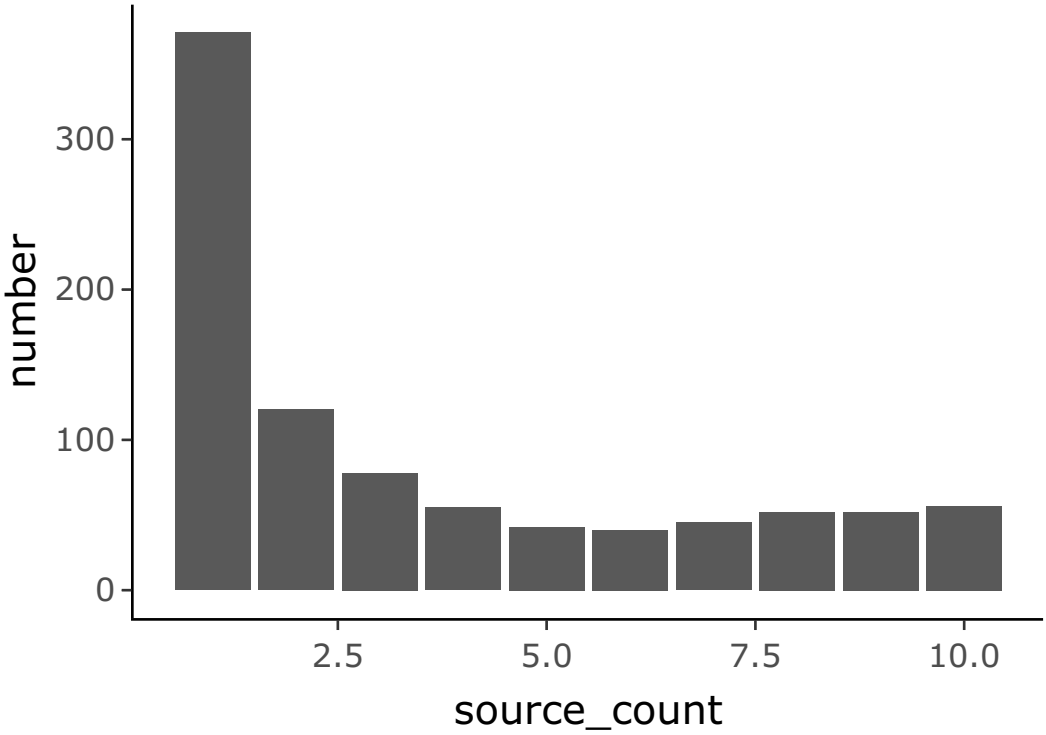


2.4 Bar plot of Diagnostic panels results

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.

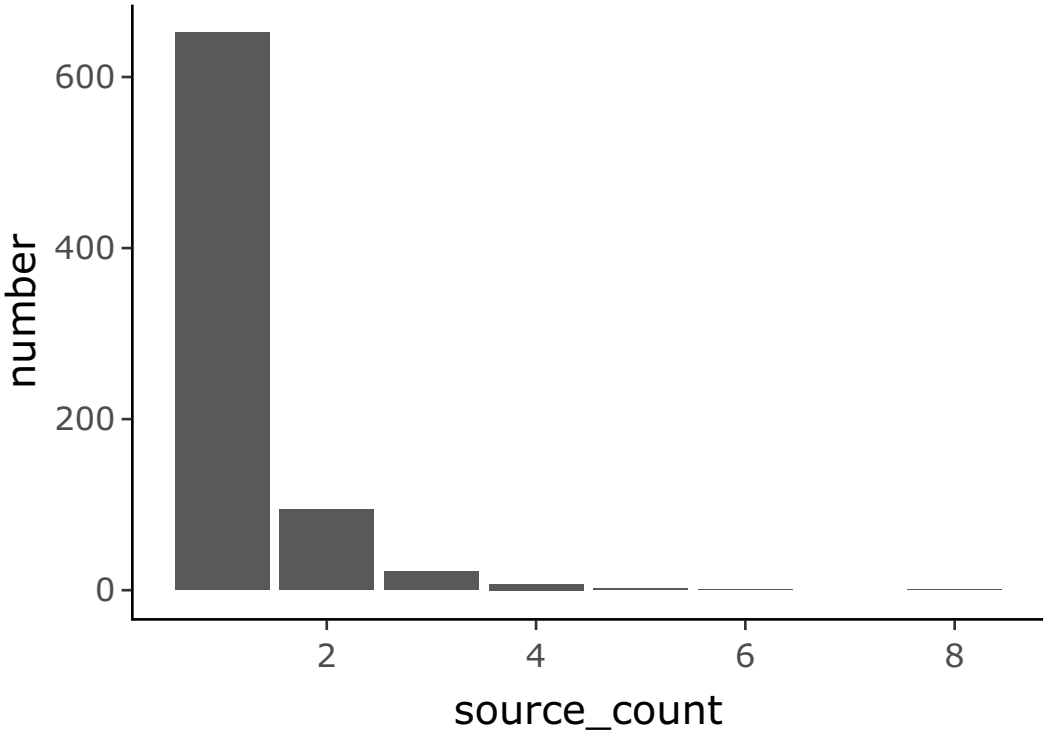


2.5 Bar plot of HPO in rare disease databases results

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.

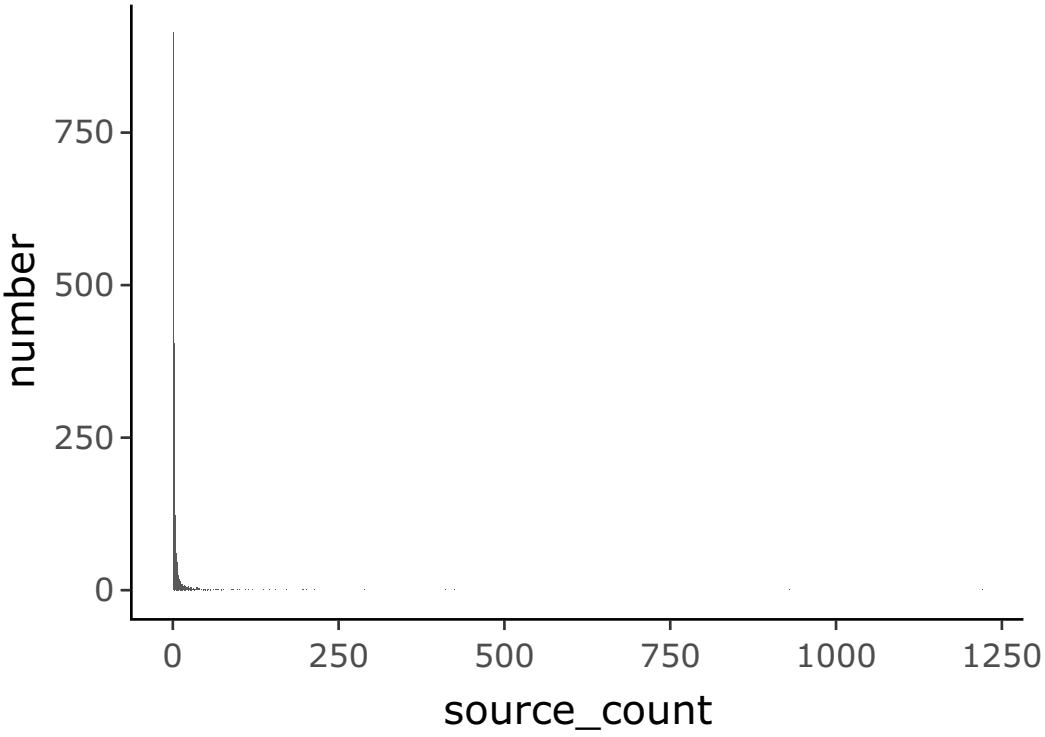


2.6 Bar plot of PubTator results

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.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250
500
750
1000
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source_count