Wikidata as a FAIR knowledge graph for the life sciences

Andra Waagmeester^{1,*}, Gregory Stupp^{2,*}, Sebastian Burgstaller-Muehlbacher^{2,¶}, Benjamin M. Good², Malachi Griffith³, Obi Griffith³, Kristina Hanspers⁴, Henning Hermjakob⁵, Kevin Hybiske⁶, Sarah M. Keating⁵, Magnus Manske⁷, Michael Mayers², Elvira Mitraka⁸, Alexander R. Pico⁴, Timothy Putman², Anders Riutta⁴, Núria Queralt-Rosinach², Lynn M. Schriml⁸, Denise Slenter⁹, Ginger Tsueng², Roger Tu², Egon Willighagen⁹, Chunlei Wu², Andrew I. Su^{2,§}

- 1 Micelio, Antwerp 2180, Belgium
- 2 The Scripps Research Institute, La Jolla, CA, USA
- 3 McDonnell Genome Institute, Washington University School of Medicine, St. Louis, MO, USA
- 4 Institute of Data Science and Biotechnology, Gladstone Institutes, San Francisco, CA, USA
- 5 European Molecular Biology Laboratory, European Bioinformatics Institute (EMBL-EBI), Wellcome Trust Genome Campus, CB10 1SD, Hinxton, United Kingdom
- 6 Division of Allergy and Infectious Diseases, Department of Medicine, University of Washington, Seattle, WA, USA
- 7 Wellcome Trust Sanger Institute, Hinxton, Cambridge CB10 1SA, UK
- 8 University of Maryland School of Medicine, Baltimore, Maryland, USA.
- 9 Department of Bioinformatics-BiGCaT, NUTRIM, Maastricht University, 6229 ER Maastricht, The Netherlands
- (*) equal contributions
- (§) Correspondence: asu@scripps.edu
- (¶) Present address: Center for Integrative Bioinformatics Vienna, Max F. Perutz Laboratories, University of Vienna, Medical University Vienna, Austria

ORCID identifiers:

Andra Waagmeester, 0000-0001-9773-4008 Gregory Stupp, 0000-0002-0644-7212 Sebastian Burgstaller-Muehlbacher, 0000-0003-4640-3510 Benjamin M. Good, 0000-0002-7334-7852 Malachi Griffith, 0000-0002-6388-446X Obi Griffith, 0000-0002-0843-4271 Kristina Hanspers 0000-0001-5410-599X Henning Hermjakob, 0000-0001-8479-0262 Kevin Hybiske, 0000-0002-2967-3079 Sarah M. Keating, 0000-0002-3356-3542 Magnus Manske, 0000-0001-5916-0947 Michael Mayers, 0000-0002-7792-0150 Elvira Mitraka, 0000-0003-0719-3485 Alexander R. Pico 0000-0001-5706-2163 Timothy Putman, 0000-0002-4291-0737 Anders Riutta 0000-0002-4693-0591 Núria Queralt-Rosinach, 0000-0003-0169-8159 Lynn M. Schriml, 0000-0001-8910-9851 Denise Slenter, 0000-0001-8949-1318 Ginger Tsueng, 0000-0001-8449-1318 Ginger Tsueng, 0000-0001-9536-9115 Roger Tu, 0000-0002-7899-1604 Egon Willighagen, 0000-0001-7542-0286 Chunlei Wu, 0000-0002-2629-6124 Andrew I. Su, 0000-0002-9859-4104

1 Abstract

2

3 Wikidata is a community-maintained knowledge base that epitomizes the FAIR principles of Findability, 4 Accessibility, Interoperability, and Reusability. Here, we describe the breadth and depth of biomedical 5 knowledge contained within Wikidata, assembled from primary knowledge repositories on genomics, 6 proteomics, genetic variants, pathways, chemical compounds, and diseases. We built a collection of 7 open-source tools that simplify the addition and synchronization of Wikidata with source databases. We furthermore demonstrate several use cases of how the continuously updated, crowd-contributed 8 9 knowledge in Wikidata can be mined. These use cases cover a diverse cross section of biomedical 10 analyses, from crowdsourced curation of biomedical ontologies, to phenotype-based diagnosis of 11 disease, to drug repurposing.

12 Introduction

Integrating data and knowledge is a formidable challenge in biomedical research. Although new
 scientific findings are being discovered at a rapid pace, a large proportion of that knowledge is either

15 locked in data silos (where integration is hindered by differing nomenclature, data models, and licensing

16 terms) [1], or even worse, locked away in free-text. The lack of an integrated and structured version of

biomedical knowledge hinders efficient querying or mining of that information, a limitation that prevents
the full utilization of our accumulated scientific knowledge.

19

Recently, there has been a growing emphasis within the scientific community to ensure all scientific
data are FAIR – Findable, Accessible, Interoperable, and Reusable – and there is a growing consensus
around a concrete set of principles to ensure FAIRness [1,2]. Widespread implementation of these
principles would greatly advance open data efforts to build a rich and heterogeneous network of
scientific knowledge. That knowledge network could, in turn, be the foundation for many computational
tools, applications and analyses.

26

Most data and knowledge integration initiatives fall on either end of a spectrum. At one end, centralized efforts seek to bring all knowledge sources into a single database instance (e.g., [3]). This approach has the advantage of data alignment according to a common data model and of enabling high performance queries. However, centralized resources are very difficult and expensive to maintain and expand [4,5], in large part because of limited bandwidth and resources of the technical team and the bottlenecks that introduces.

33

At the other end of the spectrum, distributed approaches to data integration leave in place a broad landscape of individual resources, focusing on technical infrastructure to query and integrate across them for each query. These approaches lower the barriers to adding new data by enabling anyone to publish data by following community standards. However, performance is often an issue when each query must be sent to many individual databases, and the performance of the system as a whole is highly dependent on the stability and performance of each individual component. In addition, data

1 integration requires harmonizing the differences in the data models and data formats between

- 2 resources, a process that can often require significant skill and effort.
- 3

4 Here we explore the use of Wikidata (https://www.wikidata.org) [6] as a platform for knowledge 5 integration in the life sciences. Wikidata is an openly-accessible knowledge base that is editable by 6 anyone. Like its sister project Wikipedia, the scope of Wikidata is nearly boundless, with items on topics 7 as diverse as books, actors, historical events, and galaxies. Unlike Wikipedia, Wikidata focuses on 8 representing knowledge in a structured format instead of primarily free text. As of September 2019, 9 Wikidata's knowledge graph included over 750 million statements on 61 million items [7]. Wikidata also 10 became the first Wikimedia project that surpassed one billion edits, achieved by its community of 20 thousand active users and 80 active computational 'bots'. Since its inception in 2012, Wikidata has a 11 12 proven track record for leveraging the crowdsourced efforts of engaged users in building a massive 13 knowledge graph [8]. Wikidata is run by the Wikimedia Foundation (https://wikimediafoundation.org), an 14 organization that has a long track record of developing and maintaining web applications at scale. 15

16 As a knowledge integration platform, Wikidata combines several of the key strengths of the centralized 17 and distributed approaches. A large portion of the Wikidata knowledge graph is based on the 18 automated imports of large structured databases via Wikidata bots, thereby breaking down the walls of 19 existing data silos. Since Wikidata is also based on a community-editing model, it harnesses the 20 distributed efforts of a worldwide community of contributors. Anyone is empowered to add new 21 statements, ranging from individual facts to large-scale data imports. Finally, all knowledge in Wikidata 22 is queryable through a SPARQL query interface [9], which enables distributed queries across other 23 Linked Data resources.

24

In previous work, we seeded Wikidata with content from public and authoritative resources on structured knowledge on genes and proteins [10] and chemical compounds [11]. Here, we describe progress on expanding and enriching the biomedical knowledge graph within Wikidata, both by our team and by others in the community [12]. We also describe several representative use cases on how Wikidata can enable new analyses and improve the efficiency of research. Finally, we discuss how researchers can contribute to this effort to build a continuously-updated and community-maintained knowledge graph that epitomizes the FAIR principles.

32 Results

33 The Wikidata Biomedical Knowledge Graph

The original effort behind this work focused on creating and annotating Wikidata items for human and mouse genes and proteins [10], and was subsequently expanded to include microbial reference genomes from NCBI RefSeq [13]. Since then, the Wikidata community (including our team) has significantly expanded the depth and breadth of biological information within Wikidata, resulting in a rich, heterogeneous knowledge graph (**Figure 1**). Some of the key new data types and resources are described below.



Figure 1. A class-level diagram of the Wikidata knowledge graph for biomedical entities. Each box represents one type of biomedical entity. The header displays the name of that entity type, as well as the count of Wikidata items of that type. The lower portion of each box displays a partial listing of attributes about each entity type, together with the count of the number of items with that attribute. Edges between boxes represent the number of Wikidata statements corresponding to each combination of subject type, predicate, and object type. For clarity, edges for reciprocal relationships (e.g., "has part" and "part of") are combined into a single edge. All counts of Wikidata items are current as of September 2019. Data are generated using the code in https://github.com/SuLab/genewikiworld.

8 9

10

Genes and proteins. Wikidata contains items for over 1.1 million genes and 940 thousand proteins
from 201 unique taxa. Annotation data on genes and proteins come from several key databases
including NCBI Gene [14], Ensembl [15], UniProt [16], InterPro [17], and the Protein Data Bank (PDB)
[18]. These annotations include information on protein families, gene functions, protein domains,
genomic location, and orthologs, as well as links to related compounds, diseases, and variants.

17 **Genetic variants.** Annotations on genetic variants are primarily drawn from CIViC

(<u>http://www.civicdb.org</u>), an open and community-curated database of cancer variants [19]. Variants are
 annotated with their relevance to disease predisposition, diagnosis, prognosis, and drug efficacy.

20 Wikidata currently contains 1502 items corresponding to human genetic variants, focused on those with 21 a clear clinical or therapeutic relevance.

22

23 Chemical compounds including drugs. Wikidata has items for over 150 thousand chemical compounds, including over 3500 items which are specifically designated as medications. Compound 24 25 attributes are drawn from a diverse set of databases, including PubChem [20], RxNorm [21], IUPHAR 26 Guide to Pharmacology [22–24], NDF-RT [25], and LIPID MAPS [26]. These items typically contain 27 statements describing chemical structure and key physicochemical properties, and links to databases 28 with experimental data (MassBank [27,28], PDB Ligand [29], etc.) and toxicological information (EPA 29 CompTox Dashboard [30]). Additionally, these items contain links to compound classes, disease 30 indications, pharmaceutical products, and protein targets. 31

Pathways. Wikidata has items for almost three thousand human biological pathways, primarily from two established public pathway repositories: Reactome [31] and WikiPathways [32]. The full details of the different pathways remain with the respective primary sources. Our bots enter data for Wikidata properties such as pathway name, identifier, organism, and the list of component genes, proteins, and chemical compounds. Properties for contributing authors (via ORCID properties [33]), descriptions and ontology annotations are also being added for Wikidata pathway entries.

38

Diseases. Wikidata has items for over 16 thousand diseases, the majority of which were created based
 on imports from the Human Disease Ontology [34], with additional disease terms added from the
 Monarch Disease Ontology [3]. Disease attributes include medical classifications, symptoms, relevant
 drugs, as well as subclass relationships to higher-level disease categories. In instances where the
 Human Disease Ontology specifies a related anatomic region and/or a causative organism (for

44 infectious diseases), corresponding statements are also added.

1 References. Whenever practical, the provenance of each statement added to Wikidata was also added

2 in a structured format. References are part of the core data model for a Wikidata statement. References

3 can either cite the primary resource from which the statement was retrieved (including details like

4 version number of the resource), or they can link to a Wikidata item corresponding to a publication as

5 provided by a primary resource (as an extension of the WikiCite project [35]), or both.

6 Bot automation

7 To programmatically upload biomedical knowledge to Wikidata, we developed a series of computer

8 programs, or bots. Bot development began by reaching a consensus on data modeling with the

9 Wikidata community, particularly the Molecular Biology WikiProject [36]. We then coded each bot to
 10 perform data retrieval from a primary resource, data transformation and normalization, and then data

11 upload via the Wikidata **application programming interface (API)**.

12

We generalized the common code modules into a Python library, called **Wikidata Integrator (WDI)**, to simplify the process of creating Wikidata bots [37]. Relative to accessing the API directly, WDI has convenient features that improve the bot development experience. These features include the creation of items for scientific articles as references, basic detection of data model conflicts, automated detection of items needing update, detailed logging and error handling, and detection and preservation of conflicting human edits.

19

20 Just as important as the initial data upload is the synchronization of updates between the primary

21 sources and Wikidata. We utilized Jenkins, an open-source automation server, to automate all our

22 Wikidata bots. This system allows for flexible scheduling, job tracking, dependency management, and

automated logging and notification. Bots are either run on a predefined schedule (for continuously

24 updated resources) or when new versions of original databases are released.

25 Applications

26 Identifier Translation

Translating between identifiers from different databases is one of the most common operations in
bioinformatics analyses. Unfortunately, these translations are most often done by bespoke scripts and
based on entity-specific mapping tables. These translation scripts are repetitively and redundantly
written across our community and are rarely kept up to date.

31

An identifier translation service is a simple and straightforward application of the biomedical content in Wikidata. Based on mapping tables that have been imported, Wikidata items can be mapped to databases that are both widely- and rarely-used in the life sciences community. Because all these mappings are stored in a centralized database and use a systematic data model, generic and reusable

translation scripts can easily be written (Figure 2). These scripts can be used as a foundation for more
 complex Wikidata queries, or the results can be downloaded and used as part of larger scripts or

- 38 analyses.
- 39

- 1 There are a number of other tools that are also aimed at solving the identifier translation use case,
- 2 including the BioThings APIs [38], BridgeDb [39], BioMart [40], UMLS [41], and NCI Thesaurus [42].
- 3 Relative to these tools, Wikidata distinguishes itself with a unique combination of the following:
- 4 5

6

7

8

- an almost limitless scope including all entities in biology, chemistry, and medicine;
- a data model that can represent exact, broader, and narrow matches between items in different identifier namespaces (beyond semantically imprecise "cross-references");
- programmatic access through web services with a track record of high-performance and highavailability
- 9 10

Moreover, Wikidata is also unique as it is the only tool that allows real-time community editing. So while
 Wikidata is certainly not complete with respect to identifier mappings, it can be continually improved
 independent of any centralized effort or curation authority.

14



15

16 Figure 2. Generalizable SPARQL template for identifier translation. This simple example shows how identifiers of any 17 biological type can easily be translated using SPARQL queries. These queries operate on Wikidata properties for gene 18 symbols (wdt:P353) and Entrez Gene IDs (wdt:P351) (top), and RxNorm concept IDs (wdt:P3345) and NDF-RT IDs 19 (wdt:P2115) (bottom). These queries can be submitted to the Wikidata Query Service (WDQS; https://query.wikidata.org/) to 20 get real-time results from Wikidata data. Relatively simple extensions of these gueries can also be added to filter mappings 21 based on the statement references and/or qualifiers. A full list of Wikidata properties can be found at [43]. Note that for 22 translating a large number of identifiers, it is often more efficient to perform a SPARQL query to retrieve all mappings and then 23 perform additional filtering locally.

24

25 Integrative Queries

- 26
- Wikidata contains a much broader set of information than just identifier cross-references. Having
 biomedical data in one centralized data resource facilitates powerful integrative queries that span
 multiple domain areas and data sources. Performing these integrative queries through Wikidata
- 30 obviates the need to perform many time-consuming and error-prone data integration steps.
- 31
- 32 As an example, consider a pulmonologist who is interested in identifying candidate chemical
- compounds for testing in disease models (schematically illustrated in **Figure 3**). She may start by
- identifying genes with a genetic association to any respiratory disease, with a particular interest in
- 35 genes that encode membrane-bound proteins (for ease in cell sorting). She may then look for chemical

- 1 compounds that either directly inhibit those proteins, or finding none, compounds that inhibit another
- 2 protein in the same pathway. Because she has collaborators with relevant expertise, she may
- 3 specifically filter for proteins containing a serine-threonine kinase domain.
- 4
- 5 Almost any competent informatician can perform the query described above by integrating cell
- 6 localization data from Gene Ontology annotations, genetic associations from GWAS Catalog, disease
- 7 subclass relationships from the Human Disease Ontology, pathway data from WikiPathways and
- 8 Reactome, compound targets from the IUPHAR Guide to Pharmacology, and protein domain
- 9 information from InterPro. However, actually performing this data integration is a time-consuming and
- 10 error-prone process. At the time of publication of this manuscript, this Wikidata query completed in less
- 11 than 10 seconds and reported 31 unique compounds. Importantly, the results of that query will always
- 12 be up-to-date with the latest information in Wikidata.
- 13
- 14 This query, and other example SPARQL queries that take advantage of the rich, heterogeneous
- 15 knowledge network in Wikidata are available at
- 16 <u>https://www.wikidata.org/wiki/User:ProteinBoxBot/SPARQL_Examples</u>. That page additionally
- 17 demonstrates federated SPARQL queries that perform complex queries across other biomedical
- 18 SPARQL endpoints. Federated queries are useful for accessing data that cannot be included in
- 19 Wikidata directly due to limitations in size, scope, or licensing.
- 20



21 22

Figure 3. A representative SPARQL query that integrates data from multiple data resources and annotation types.
 This query incorporates data on genetic associations to disease, Gene Ontology annotations for cellular compartment, protein target information for compounds, pathway data, and protein domain information. More context is provided in the text. Real-time query results can be viewed at https://w.wiki/6pZ.

27 Crowdsourced Curation

28 Ontologies are essential resources for structuring biomedical knowledge. However, even after the initial

effort in creating an ontology is finalized, significant resources must be devoted to maintenance and

30 further development. These tasks include cataloging cross references to other ontologies and

- 31 vocabularies, and modifying the ontology as current knowledge evolves. Community curation has been
- 32 explored in a variety of tasks in ontology curation and annotation (e.g., [13,44–47]). While community

curation offers the potential of distributing these responsibilities over a wider set of scientists, it also has
 the potential to introduce errors and inconsistencies.

3

Here, we examined how a crowd-based curation model through Wikidata works in practice. We
designed a system to monitor, filter, and prioritize changes made by Wikidata contributors to items in
the Human Disease Ontology. We initially seeded Wikidata with disease items from the Disease
Ontology (DO) starting in late 2015. Beginning in 2018, we compared the disease data in Wikidata to
the most current DO release on a monthly basis.

9

10 In our first comparison between Wikidata and the official DO release, we found that Wikidata users added a total of 2030 new cross references to GARD [48] and MeSH [49]. Each cross reference was 11 12 manually reviewed by DO curators, and 98.9% of these mappings were deemed correct and therefore 13 added to the ensuing DO release. Each subsequent monthly report included a smaller number of added 14 cross references to GARD and MeSH, as well as ORDO [50], and OMIM [51,52], and these entries 15 were incorporated after expert review at a high approval rate (>90%). Wikidata users also suggested 16 numerous refinements to the ontology structure, including changes to the subclass relationships and 17 the addition of new disease terms. While these structural changes were rarely incorporated into DO 18 releases with no modifications, they often prompted further review and refinement by DO curators in 19 specific subsections of the ontology.

20

The Wikidata crowdsourcing curation model is generalizable to any other external resource that is automatically synced to Wikidata. The code to detect changes and assemble reports is tracked online [53] and can easily be adapted to other domain areas. This approach offers a novel solution for integrating new knowledge into a biomedical ontology through distributed crowdsourcing while preserving control over the expert curation process. Incorporation into Wikidata also enhances exposure and visibility of the resource by engaging a broader community of users and curators.

27 Interactive Pathway Pages

In addition to its use as a repository for data, we explored the use of Wikidata as a primary access and visualization endpoint for pathway data. We used Scholia, a web app for displaying scholarly profiles for a variety of Wikidata entries, including individual researchers, research topics, chemicals, and proteins [11]. Scholia provides a more user-friendly view of Wikidata content with context and interactivity that is tailored to the entity type.

33

34 We contributed a Scholia profile template specifically for biological pathways [54,55]. In addition to 35 essential items such as title and description, these pathway pages include an interactive view of the 36 pathway diagram collectively drawn by contributing authors. The WikiPathways identifier property in 37 Wikidata informs the Scholia template to source a *pathway-viewer* widget from Toolforge [56] that in 38 turn retrieves the corresponding interactive pathway image. Embedded into the Scholia pathway page, 39 the widget provides pan and zoom, plus links to gene, protein and chemical Scholia pages for every 40 clickable molecule on the pathway diagram (see for example [57]). Each pathway page also includes 41 information about the pathway authors. The Scholia template also generates a participants table that 42 shows the genes, proteins, metabolites, and chemical compounds that play a role in the pathway, as 43 well as citation information in both tabular and chart formats.

1

2 With Scholia template views of Wikidata, we are able to generate interactive pathway pages with

- 3 comparable content and functionality to that of dedicated pathway databases. Wikidata provides a
- 4 powerful interface to access these biological pathway data in the context of other biomedical
- 5 knowledge, and Scholia templates provide rich, dynamic views of Wikidata that are relatively simple to
- 6 develop and maintain.

7 Phenotype-based disease diagnosis

- 8 Phenomizer is a web application that suggests clinical diagnoses based on an array of patient
- 9 phenotypes. Phenomizer takes as input a list of phenotypes (using the Human Phenotype Ontology
- 10 (HPO) [58]) and an association file between phenotypes and diseases, and the Phenomizer algorithm
- 11 suggests disease diagnoses based on semantic similarity [59]. Here, we studied whether phenotype-
- 12 disease associations from Wikidata could improve Phenomizer's ability to make differential diagnoses
- 13 for certain sets of phenotypes. We modified the Phenomizer codebase to accept arbitrary inputs and to
- 14 be able to run from the command line [60] and also wrote a script to extract and incorporate the
- 15 phenotype-disease annotations in Wikidata [61].
- 16

17 As of September 2019, there were 273 phenotype-disease associations in Wikidata that were not in the 18 HPO's annotation file (which contained a total of 172,760 associations). Based on parallel biocuration 19 work by our team, many of these new associations were related to the disease Congenital Disorder of 20 Deglycosylation (CDDG; also known as NGLY-1 deficiency). To see if the Wikidata-sourced 21 annotations improved the ability of Phenomizer to diagnose CDDG, we ran our modified version using 22 the phenotypes taken from a publication describing two siblings with suspected cases of CDDG [62]. 23 Using these phenotypes and the annotation file supplemented with Wikidata-derived associations, 24 Phenomizer returned a much stronger semantic similarity to CDDG relative to the HPO annotation file 25 alone (Figure 4). Analyses with the combined annotation file reported CDDG as the top result for each 26 of the past 14 releases of the HPO annotation file, whereas CDDG was never the top result when run 27 without the Wikidata-derived annotations. This result demonstrated an example scenario in which

- 28 Wikidata-derived annotations could be a useful complement to expert curation.
- 29



Figure 4. Phenomizer analysis of suspected cases of CDDG. Clinical phenotypes from two cases of suspected CDDG patients were extracted from a published case report [62]. These phenotypes were run through the Phenomizer tool using phenotype-disease annotations from HPO alone, or from a combination of HPO and Wikidata. The semantic similarity score for CDDG is reported on the y-axis.

1 Drug Repurposing

2 The mining of graphs for latent edges has been an area of interest in a variety of contexts from

3 predicting friend relationships in social media platforms to suggesting movies based on past viewing

4 history. A number of groups have explored the mining of knowledge graphs to reveal biomedical

5 insights, with the open source Rephetio effort for drug repurposing as one example [63]. Rephetio uses

6 logistic regression, with features based on graph metapaths, to predict drug repurposing candidates.

7

8 The knowledge graph that served as the foundation for Rephetio was manually assembled from many 9 different resources into a heterogeneous knowledge network. Here, we explored whether the Rephetio 10 algorithm could successfully predict drug indications on the Wikidata knowledge graph. Based on the 11 class diagram in Figure 1, we extracted a biomedically-focused subgraph of Wikidata with 19 node 12 types and 41 edge types. We performed five-fold cross validation on drug indications within Wikidata and found that Rephetio substantially enriched for the true indications in the hold-out set. We then 13 downloaded historical Wikidata versions from 2017 and 2018, and observed marked improvements in 14 15 performance over time (Figure 6). We also performed this analysis using an external test set based on

Drug Central, which showed a similar improvement in Rephetio results over time (Supplemental
 Figure 1).

17 **Fig** 18

19 This analysis demonstrates the value of a community-maintained, centralized knowledge base to which

20 many researchers are contributing. It suggests that scientific analyses based on Wikidata may

21 continually improve irrespective of any changes to the underlying algorithms, but simply based on

22 progress in curating knowledge through the distributed, and largely uncoordinated efforts of the

- 23 Wikidata community.
- 24



25 26

Figure 5. Drug repurposing using the Wikidata knowledge graph. We analyzed three snapshots of Wikidata using
 Rephetio, a graph-based algorithm for predicting drug repurposing candidates [63]. We evaluated the performance of the
 Rephetio algorithm on three historical versions of the Wikidata knowledge graph, quantified based on the area under the
 receiver operator characteristic curve (AUC). This analysis demonstrated that the performance of Rephetio in drug
 repurposing improved over time based only on improvements to the underlying knowledge graph. Details of this analysis can
 be found at https://github.com/SuLab/WD-rephetio-analysis.



1 2 3 Supplemental Figure 1. Drug repurposing using the Wikidata knowledge graph, evaluated using an external test set. Whereas the analysis in Figure 5 was based on a cross-validation of indications that were present in Wikidata, we also ran our 4 time-resolved analysis using an external gold standard set of indications from Drug Central [64].

Discussion 5

6 We believe that Wikidata is among the most FAIR biomedical resources available (a view that is also 7 shared among some funding bodies [65]).

- 9 Findable: Wikidata items are assigned globally unique identifiers with direct cross-links into the • 10 massive online ecosystem of Wikipedias. Wikidata also has broad visibility within the Linked 11 Data community and listed in the life science registries FAIRsharing [66] and Identifiers.org [67]. 12 Wikidata has already attracted a robust, global community of contributors and consumers.
- 13 Accessible: Wikidata provides access to its underlying knowledge graph via both an online • 14 graphical user interface and an API, and access includes both read- and write-privileges. 15 Wikidata also provides database dumps at least weekly [68], ensuring the long-term accessibility of the Wikidata knowledge graph independent of the organization and web 16 17 application.
- 18 Interoperable: Wikidata items are extensively cross-linked to other biomedical resources using • 19 Universal Resource Identifiers (URIs), which unambiguously anchor these concepts in the Linked Open Data cloud [69]. Wikidata is also available in many standard formats in computer programming and knowledge management, including JSON, XML, and RDF.
- 22 **Reusable:** Data provenance is directly tracked in the reference section of the Wikidata 23 statement model. The Wikidata knowledge graph is released under the Creative Commons Zero 24 (CC0) Public Domain Declaration, which explicitly declares that there are no restrictions on 25 downstream reuse and redistribution [70].
- 26

20 21

8

27 The open data licensing of Wikidata is particularly notable. The use of data licenses in biomedical research has rapidly proliferated, presumably in an effort to protect intellectual property and/or justify 28 29 long-term grant funding (e.g. [71]). However, even seemingly innocuous license terms (like 30 requirements for attribution) still impose legal requirements and therefore expose consumers to legal

31 liability. This liability is especially problematic for data integration efforts, in which the license terms of

1 all resources (dozens or hundreds or more) must be independently tracked and satisfied (a

2 phenomenon referred to as "license stacking"). Because it is released under CC0, Wikidata can be

3 freely and openly used in any other resource without any restriction. This freedom greatly simplifies and

4 5 encourages downstream use.

6 In addition to simplifying data licensing, Wikidata offers significant advantages in centralizing the data 7 harmonization process. Consider the use case of trying to get a comprehensive list of disease 8 indications for the drug bupropion. The National Drug File - Reference Terminology (NDF-RT) reported that bupropion may treat nicotine dependence and attention deficit hyperactivity disorder, the Inxight 9 10 database listed major depressive disorder, and the FDA Adverse Event Reporting System (FAERS) 11 listed anxiety and bipolar disorder. While no single database listed all these indications, Wikidata 12 provided an integrated view that enabled seamless guery and access across resources. Integrating 13 drug indication data from these individual data resources was not a trivial process. Both Inxight and 14 NDF-RT mint their own identifiers for both drugs and diseases. FAERS uses Medical Dictionary for 15 Regulatory Activities (MedDRA) names for diseases and free-text names for drugs [72]. By harmonizing 16 and integrating all resources in the context of Wikidata, we ensure that those data are immediately 17 usable by others without having to repeat the normalization process. Moreover, by harmonizing data at 18 the time of data loading, consumers of that data do not need to perform the repetitive and redundant 19 work at the point of querying and analysis.

20

As the biomedical data within Wikidata continues to grow, we believe that its unencumbered use will spur the development of many new innovative tools and analyses. These innovations will undoubtedly include the machine learning-based mining of the knowledge graph to predict new relationships (also referred to as knowledge graph reasoning [73–75]).

25

26 For those who subscribe to this vision for cultivating a FAIR and open graph of biomedical knowledge, 27 there are two simple ways to contribute to Wikdiata. First, owners of data resources can release their 28 data using the CC0 declaration. Because Wikidata is released under CC0, it also means that all data 29 imported in Wikidata must also use CC0-compatible terms (e.g., be in the public domain). For 30 resources that currently use a restrictive data license primarily for the purposes of enforcing attribution 31 or citation, we encourage the transition to "CC0 (+BY)", a model that "[pairs] a permissive license with a 32 strong moral entreaty" [76]. For resources that must retain data license restrictions, consider releasing 33 a subset of data or older versions of data using CC0. Many biomedical resources were created under 34 or transitioned to CC0 (in part or in full) in recent years [77], including the Disease Ontology [34], Pfam [78], Bgee [79], WikiPathways [32], Reactome [31], ECO [80], and CIViC [19]. 35

36

Second, informaticians can contribute to Wikidata by adding the results of data parsing and integration efforts to Wikidata. Currently, the useful lifespan of data integration code typically does not extend beyond the immediate project-specific use. As a result, that same data integration process is likely being done repetitively and redundantly by other informaticians elsewhere. If every informatician contributed the output of their effort to Wikidata, the resulting knowledge graph would be far more useful than the stand-alone contribution of any single individual, and it would continually improve in both breadth and depth over time.

- 1 FAIR and open access to the sum total of biomedical knowledge will improve the efficiency of
- 2 biomedical research. Capturing that information in a centralized knowledge graph is useful for
- 3 experimental researchers, informatics tool developers and biomedical data scientists. As a
- 4 continuously-updated and collaboratively-maintained community resource, we believe that Wikidata has
- 5 made significant strides toward achieving this ambitious goal.
- 6

7 Acknowledgments

8 The authors thank the thousands of Wikidata contributors for curating knowledge, both directly related 9 and unrelated to this work. The authors also thank the Wikimedia Foundation developers and 10 administrators for maintaining Wikidata as a community resource. This work has been supported by 11 grants from the National Institute for General Medical Science (NIGMS) under awards R01 GM089820 to AS, U54 GM114833 to AS and HH, and R01 GM100039 to AP. MG is supported by the National 12 13 Human Genome Research Institute (NHGRI) of the NIH under Award Number R00HG007940, the 14 National Cancer Institute under Award Number U24CA237719 and the V Foundation for Cancer 15 Research under Award Number V2018-007. KH was supported by the National Institute of Allergy and 16 Infectious Diseases (NIAID) under award R01 AI126785 Additional support was provided by the 17 National Center for Advancing Translational Sciences (NCATS) under award UL1 TR002550.

18

19 Competing interests

20 The authors have no competing interests.

References

- Wilkinson MD, Dumontier M, Aalbersberg IJJ, Appleton G, Axton M, Baak A, Blomberg N, Boiten J-W, da Silva Santos LB, Bourne PE, Bouwman J, Brookes AJ, Clark T, Crosas M, Dillo I, Dumon O, Edmunds S, Evelo CT, Finkers R, Gonzalez-Beltran A, Gray AJG, Groth P, Goble C, Grethe JS, Heringa J, 't Hoen PAC, Hooft R, Kuhn T, Kok R, Kok J, Lusher SJ, Martone ME, Mons A, Packer AL, Persson B, Rocca-Serra P, Roos M, van Schaik R, Sansone S-A, Schultes E, Sengstag T, Slater T, Strawn G, Swertz MA, Thompson M, van der Lei J, van Mulligen E, Velterop J, Waagmeester A, Wittenburg P, Wolstencroft K, Zhao J, Mons B. The FAIR Guiding Principles for scientific data management and stewardship. Sci Data. 2016 Mar 15;3:160018. PMCID: PMC4792175
- Evaluating FAIR Maturity Through a Scalable, Automated, Community-Governed Framework | bioRxiv [Internet]. [cited 2019 Jul 31]. Available from: https://www.biorxiv.org/content/10.1101/649202v1
- Mungall CJ, McMurry JA, Köhler S, Balhoff JP, Borromeo C, Brush M, Carbon S, Conlin T, Dunn N, Engelstad M, Foster E, Gourdine JP, Jacobsen JOB, Keith D, Laraway B, Lewis SE, NguyenXuan J, Shefchek K, Vasilevsky N, Yuan Z, Washington N, Hochheiser H, Groza T, Smedley D, Robinson PN, Haendel MA. The Monarch Initiative: an integrative data and analytic platform connecting phenotypes to genotypes across species. Nucleic Acids Res. 2017 04;45(D1):D712–D722. PMCID: PMC5210586
- 4. Gabella C, Durinx C, Appel R. Funding knowledgebases: Towards a sustainable funding model for the UniProt use case. F1000Research [Internet]. 2018 Mar 22 [cited 2019 Aug 26];6. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5747334/ PMCID: PMC5747334
- Chandras C, Weaver T, Zouberakis M, Smedley D, Schughart K, Rosenthal N, Hancock JM, Kollias G, Schofield PN, Aidinis V. Models for financial sustainability of biological databases and resources. Database [Internet]. 2009 Jan 1 [cited 2019 Aug 26];2009. Available from: https://academic.oup.com/database/article/doi/10.1093/database/bap017/357253
- Vrandečić D. Wikidata: A New Platform for Collaborative Data Collection. Proc 21st Int Conf World Wide Web [Internet]. New York, NY, USA: ACM; 2012 [cited 2019 Aug 1]. p. 1063–1064. Available from: http://doi.acm.org/10.1145/2187980.2188242
- 7. Wikidata Statistics [Internet]. [cited 2019 Sep 11]. Available from: https://tools.wmflabs.org/wikidata-todo/stats.php
- 8. Mora-Cantallops M, Sánchez-Alonso S, García-Barriocanal E. A systematic literature review on Wikidata. Data Technol Appl [Internet]. 2019 Jul 1 [cited 2019 Sep 6]; Available from: https://www.emerald.com/insight/content/doi/10.1108/DTA-12-2018-0110/full/html
- 9. Wikidata Query Service [Internet]. [cited 2019 Jul 31]. Available from: https://query.wikidata.org/
- 10. Burgstaller-Muehlbacher S, Waagmeester A, Mitraka E, Turner J, Putman T, Leong J, Naik C, Pavlidis P, Schriml L, Good BM, Su AI. Wikidata as a semantic framework for the Gene Wiki initiative. Database J Biol Databases Curation. 2016;2016. PMCID: PMC4795929
- 11. Willighagen E, Slenter D, Mietchen D, Evelo C, Nielsen F. Wikidata and Scholia as a hub linking chemical knowledge [Internet]. 2018 [cited 2019 Aug 23]. Available from:

https://figshare.com/articles/Wikidata_and_Scholia_as_a_hub_linking_chemical_knowledge/6356 027

- 12. Turki H, Shafee T, Taieb MAH, Aouicha MB, Vrandečić D, Das D, Hamdi H. Wikidata: A largescale collaborative ontological medical database. J Biomed Inform. 2019 Sep 23;103292.
- 13. Putman TE, Lelong S, Burgstaller-Muehlbacher S, Waagmeester A, Diesh C, Dunn N, Munoz-Torres M, Stupp GS, Wu C, Su AI, Good BM. WikiGenomes: an open web application for community consumption and curation of gene annotation data in Wikidata. Database J Biol Databases Curation. 2017 01;2017(1). PMCID: PMC5467579
- 14. NCBI Resource Coordinators. Database resources of the National Center for Biotechnology Information. Nucleic Acids Res. 2018 04;46(D1):D8–D13. PMCID: PMC5753372
- 15. Zerbino DR, Achuthan P, Akanni W, Amode MR, Barrell D, Bhai J, Billis K, Cummins C, Gall A, Girón CG, Gil L, Gordon L, Haggerty L, Haskell E, Hourlier T, Izuogu OG, Janacek SH, Juettemann T, To JK, Laird MR, Lavidas I, Liu Z, Loveland JE, Maurel T, McLaren W, Moore B, Mudge J, Murphy DN, Newman V, Nuhn M, Ogeh D, Ong CK, Parker A, Patricio M, Riat HS, Schuilenburg H, Sheppard D, Sparrow H, Taylor K, Thormann A, Vullo A, Walts B, Zadissa A, Frankish A, Hunt SE, Kostadima M, Langridge N, Martin FJ, Muffato M, Perry E, Ruffier M, Staines DM, Trevanion SJ, Aken BL, Cunningham F, Yates A, Flicek P. Ensembl 2018. Nucleic Acids Res. 2018 04;46(D1):D754–D761. PMCID: PMC5753206
- 16. UniProt: a worldwide hub of protein knowledge. Nucleic Acids Res. 2019 Jan 8;47(D1):D506– D515.
- 17. Mitchell AL, Attwood TK, Babbitt PC, Blum M, Bork P, Bridge A, Brown SD, Chang H-Y, El-Gebali S, Fraser MI, Gough J, Haft DR, Huang H, Letunic I, Lopez R, Luciani A, Madeira F, Marchler-Bauer A, Mi H, Natale DA, Necci M, Nuka G, Orengo C, Pandurangan AP, Paysan-Lafosse T, Pesseat S, Potter SC, Qureshi MA, Rawlings ND, Redaschi N, Richardson LJ, Rivoire C, Salazar GA, Sangrador-Vegas A, Sigrist CJA, Sillitoe I, Sutton GG, Thanki N, Thomas PD, Tosatto SCE, Yong S-Y, Finn RD. InterPro in 2019: improving coverage, classification and access to protein sequence annotations. Nucleic Acids Res. 2019 Jan 8;47(D1):D351–D360.
- 18. Burley SK, Berman HM, Bhikadiya C, Bi C, Chen L, Costanzo LD, Christie C, Duarte JM, Dutta S, Feng Z, Ghosh S, Goodsell DS, Green RK, Guranovic V, Guzenko D, Hudson BP, Liang Y, Lowe R, Peisach E, Periskova I, Randle C, Rose A, Sekharan M, Shao C, Tao Y-P, Valasatava Y, Voigt M, Westbrook J, Young J, Zardecki C, Zhuravleva M, Kurisu G, Nakamura H, Kengaku Y, Cho H, Sato J, Kim JY, Ikegawa Y, Nakagawa A, Yamashita R, Kudou T, Bekker G-J, Suzuki H, Iwata T, Yokochi M, Kobayashi N, Fujiwara T, Velankar S, Kleywegt GJ, Anyango S, Armstrong DR, Berrisford JM, Conroy MJ, Dana JM, Deshpande M, Gane P, Gáborová R, Gupta D, Gutmanas A, Koča J, Mak L, Mir S, Mukhopadhyay A, Nadzirin N, Nair S, Patwardhan A, Paysan-Lafosse T, Pravda L, Salih O, Sehnal D, Varadi M, Vařeková R, Markley JL, Hoch JC, Romero PR, Baskaran K, Maziuk D, Ulrich EL, Wedell JR, Yao H, Livny M, Ioannidis YE. Protein Data Bank: the single global archive for 3D macromolecular structure data. Nucleic Acids Res. 2019 Jan 8;47(D1):D520–D528.
- Griffith M, Spies NC, Krysiak K, McMichael JF, Coffman AC, Danos AM, Ainscough BJ, Ramirez CA, Rieke DT, Kujan L, Barnell EK, Wagner AH, Skidmore ZL, Wollam A, Liu CJ, Jones MR, Bilski RL, Lesurf R, Feng Y-Y, Shah NM, Bonakdar M, Trani L, Matlock M, Ramu A, Campbell KM, Spies GC, Graubert AP, Gangavarapu K, Eldred JM, Larson DE, Walker JR, Good BM, Wu C, Su

AI, Dienstmann R, Margolin AA, Tamborero D, Lopez-Bigas N, Jones SJM, Bose R, Spencer DH, Wartman LD, Wilson RK, Mardis ER, Griffith OL. CIViC is a community knowledgebase for expert crowdsourcing the clinical interpretation of variants in cancer. Nat Genet. 2017 Jan 31;49(2):170–174. PMCID: PMC5367263

- Wang Y, Xiao J, Suzek TO, Zhang J, Wang J, Bryant SH. PubChem: a public information system for analyzing bioactivities of small molecules. Nucleic Acids Res. 2009 Jul 1;37(suppl_2):W623– W633.
- 21. Nelson SJ, Zeng K, Kilbourne J, Powell T, Moore R. Normalized names for clinical drugs: RxNorm at 6 years. J Am Med Inform Assoc. 2011 Jul 1;18(4):441–448.
- 22. Harding SD, Sharman JL, Faccenda E, Southan C, Pawson AJ, Ireland S, Gray AJG, Bruce L, Alexander SPH, Anderton S, Bryant C, Davenport AP, Doerig C, Fabbro D, Levi-Schaffer F, Spedding M, Davies JA, NC-IUPHAR. The IUPHAR/BPS Guide to PHARMACOLOGY in 2018: updates and expansion to encompass the new guide to IMMUNOPHARMACOLOGY. Nucleic Acids Res. 2018 04;46(D1):D1091–D1106. PMCID: PMC5753190
- 23. Southan C, Sharman JL, Benson HE, Faccenda E, Pawson AJ, Alexander SPH, Buneman OP, Davenport AP, McGrath JC, Peters JA, Spedding M, Catterall WA, Fabbro D, Davies JA, NC-IUPHAR. The IUPHAR/BPS Guide to PHARMACOLOGY in 2016: towards curated quantitative interactions between 1300 protein targets and 6000 ligands. Nucleic Acids Res. 2016 Jan 4;44(D1):D1054-1068. PMCID: PMC4702778
- 24. Pawson AJ, Sharman JL, Benson HE, Faccenda E, Alexander SPH, Buneman OP, Davenport AP, McGrath JC, Peters JA, Southan C, Spedding M, Yu W, Harmar AJ, NC-IUPHAR. The IUPHAR/BPS Guide to PHARMACOLOGY: an expert-driven knowledgebase of drug targets and their ligands. Nucleic Acids Res. 2014 Jan;42(Database issue):D1098-1106. PMCID: PMC3965070
- 25. UMLS Metathesaurus NDFRT (National Drug File Reference Terminology) Synopsis [Internet]. [cited 2019 Sep 9]. Available from: https://www.nlm.nih.gov/research/umls/sourcereleasedocs/current/NDFRT/index.html
- 26. Sud M, Fahy E, Cotter D, Brown A, Dennis EA, Glass CK, Merrill AH, Murphy RC, Raetz CRH, Russell DW, Subramaniam S. LMSD: LIPID MAPS structure database. Nucleic Acids Res. 2007 Jan 1;35(suppl_1):D527–D532.
- 27. Horai H, Arita M, Kanaya S, Nihei Y, Ikeda T, Suwa K, Ojima Y, Tanaka K, Tanaka S, Aoshima K, Oda Y, Kakazu Y, Kusano M, Tohge T, Matsuda F, Sawada Y, Hirai MY, Nakanishi H, Ikeda K, Akimoto N, Maoka T, Takahashi H, Ara T, Sakurai N, Suzuki H, Shibata D, Neumann S, Iida T, Tanaka K, Funatsu K, Matsuura F, Soga T, Taguchi R, Saito K, Nishioka T. MassBank: a public repository for sharing mass spectral data for life sciences. J Mass Spectrom. 2010;45(7):703–714.
- Wohlgemuth G, Mehta SS, Mejia RF, Neumann S, Pedrosa D, Pluskal T, Schymanski EL, Willighagen EL, Wilson M, Wishart DS, Arita M, Dorrestein PC, Bandeira N, Wang M, Schulze T, Salek RM, Steinbeck C, Nainala VC, Mistrik R, Nishioka T, Fiehn O. SPLASH, a hashed identifier for mass spectra. Nat Biotechnol. 2016 Nov 8;34:1099–1101.

- 29. Shin J-M, Cho D-H. PDB-Ligand: a ligand database based on PDB for the automated and customized classification of ligand-binding structures. Nucleic Acids Res. 2005 Jan 1;33(suppl_1):D238–D241.
- 30. Williams AJ, Grulke CM, Edwards J, McEachran AD, Mansouri K, Baker NC, Patlewicz G, Shah I, Wambaugh JF, Judson RS, Richard AM. The CompTox Chemistry Dashboard: a community data resource for environmental chemistry. J Cheminformatics. 2017 Nov 28;9(1):61.
- Fabregat A, Jupe S, Matthews L, Sidiropoulos K, Gillespie M, Garapati P, Haw R, Jassal B, Korninger F, May B, Milacic M, Roca CD, Rothfels K, Sevilla C, Shamovsky V, Shorser S, Varusai T, Viteri G, Weiser J, Wu G, Stein L, Hermjakob H, D'Eustachio P. The Reactome Pathway Knowledgebase. Nucleic Acids Res. 2018 Jan 4;46(D1):D649–D655. PMCID: PMC5753187
- 32. Slenter DN, Kutmon M, Hanspers K, Riutta A, Windsor J, Nunes N, Mélius J, Cirillo E, Coort SL, Digles D, Ehrhart F, Giesbertz P, Kalafati M, Martens M, Miller R, Nishida K, Rieswijk L, Waagmeester A, Eijssen LMT, Evelo CT, Pico AR, Willighagen EL. WikiPathways: a multifaceted pathway database bridging metabolomics to other omics research. Nucleic Acids Res. 2018 Jan 4;46(D1):D661–D667. PMCID: PMC5753270
- 33. Sprague ER. ORCID. J Med Libr Assoc JMLA. 2017 Apr;105(2):207–208. PMCID: PMC5370620
- Schriml LM, Mitraka E, Munro J, Tauber B, Schor M, Nickle L, Felix V, Jeng L, Bearer C, Lichenstein R, Bisordi K, Campion N, Hyman B, Kurland D, Oates CP, Kibbey S, Sreekumar P, Le C, Giglio M, Greene C. Human Disease Ontology 2018 update: classification, content and workflow expansion. Nucleic Acids Res. 2019 Jan 8;47(D1):D955–D962.
- Ayers P, Mietchen D, Orlowitz J, Proffitt M, Rodlund S, Seiver E, Taraborelli D, Vershbow B. WikiCite 2018-2019: Citations for the sum of all human knowledge [Internet]. 2019 [cited 2019 Sep 6]. Available from: https://figshare.com/articles/WikiCite_2018-2019_Citations_for_the_sum_of_all_human_knowledge/8947451
- 36. Wikidata:WikiProject Molecular biology Wikidata [Internet]. [cited 2019 Jul 29]. Available from: https://www.wikidata.org/wiki/Wikidata:WikiProject_Molecular_biology
- 37. A Wikidata Python module integrating the MediaWiki API and the Wikidata SPARQL endpoint: SuLab/WikidataIntegrator [Internet]. Su Lab; 2019 [cited 2019 Jul 23]. Available from: https://github.com/SuLab/WikidataIntegrator
- Xin J, Afrasiabi C, Lelong S, Adesara J, Tsueng G, Su AI, Wu C. Cross-linking BioThings APIs through JSON-LD to facilitate knowledge exploration. BMC Bioinformatics. 2018 01;19(1):30. PMCID: PMC5796402
- 39. van Iersel MP, Pico AR, Kelder T, Gao J, Ho I, Hanspers K, Conklin BR, Evelo CT. The BridgeDb framework: standardized access to gene, protein and metabolite identifier mapping services. BMC Bioinformatics. 2010 Jan 4;11(1):5.
- 40. Smedley D, Haider S, Durinck S, Pandini L, Provero P, Allen J, Arnaiz O, Awedh MH, Baldock R, Barbiera G, Bardou P, Beck T, Blake A, Bonierbale M, Brookes AJ, Bucci G, Buetti I, Burge S, Cabau C, Carlson JW, Chelala C, Chrysostomou C, Cittaro D, Collin O, Cordova R, Cutts RJ, Dassi E, Genova AD, Djari A, Esposito A, Estrella H, Eyras E, Fernandez-Banet J, Forbes S, Free RC, Fujisawa T, Gadaleta E, Garcia-Manteiga JM, Goodstein D, Gray K, Guerra-Assunção JA,

Haggarty B, Han D-J, Han BW, Harris T, Harshbarger J, Hastings RK, Hayes RD, Hoede C, Hu S, Hu Z-L, Hutchins L, Kan Z, Kawaji H, Keliet A, Kerhornou A, Kim S, Kinsella R, Klopp C, Kong L, Lawson D, Lazarevic D, Lee J-H, Letellier T, Li C-Y, Lio P, Liu C-J, Luo J, Maass A, Mariette J, Maurel T, Merella S, Mohamed AM, Moreews F, Nabihoudine I, Ndegwa N, Noirot C, Perez-Llamas C, Primig M, Quattrone A, Quesneville H, Rambaldi D, Reecy J, Riba M, Rosanoff S, Saddiq AA, Salas E, Sallou O, Shepherd R, Simon R, Sperling L, Spooner W, Staines DM, Steinbach D, Stone K, Stupka E, Teague JW, Dayem Ullah AZ, Wang J, Ware D, Wong-Erasmus M, Youens-Clark K, Zadissa A, Zhang S-J, Kasprzyk A. The BioMart community portal: an innovative alternative to large, centralized data repositories. Nucleic Acids Res. 2015 Jul 1;43(W1):W589–W598.

- 41. Bodenreider O. The Unified Medical Language System (UMLS): integrating biomedical terminology. Nucleic Acids Res. 2004 Jan 1;32(Database issue):D267-270. PMCID: PMC308795
- 42. de Coronado S, Wright LW, Fragoso G, Haber MW, Hahn-Dantona EA, Hartel FW, Quan SL, Safran T, Thomas N, Whiteman L. The NCI Thesaurus quality assurance life cycle. J Biomed Inform. 2009 Jun;42(3):530–539. PMID: 19475726
- 43. List of Properties Wikidata [Internet]. [cited 2019 Aug 23]. Available from: https://www.wikidata.org/wiki/Special:ListProperties
- 44. Gil Y, Garijo D, Ratnakar V, Khider D, Emile-Geay J, McKay N. A Controlled Crowdsourcing Approach for Practical Ontology Extensions and Metadata Annotations. In: d'Amato C, Fernandez M, Tamma V, Lecue F, Cudré-Mauroux P, Sequeda J, Lange C, Heflin J, editors. Semantic Web – ISWC 2017. Springer International Publishing; 2017. p. 231–246.
- 45. Bunt SM, Grumbling GB, Field HI, Marygold SJ, Brown NH, Millburn GH, FlyBase Consortium. Directly e-mailing authors of newly published papers encourages community curation. Database J Biol Databases Curation. 2012;2012:bas024. PMCID: PMC3342516
- 46. Wang M, Carver JJ, Phelan VV, Sanchez LM, Garg N, Peng Y, Nguyen DD, Watrous J, Kapono CA, Luzzatto-Knaan T, Porto C, Bouslimani A, Melnik AV, Meehan MJ, Liu W-T, Crüsemann M, Boudreau PD, Esquenazi E, Sandoval-Calderón M, Kersten RD, Pace LA, Quinn RA, Duncan KR, Hsu C-C, Floros DJ, Gavilan RG, Kleigrewe K, Northen T, Dutton RJ, Parrot D, Carlson EE, Aigle B, Michelsen CF, Jelsbak L, Sohlenkamp C, Pevzner P, Edlund A, McLean J, Piel J, Murphy BT, Gerwick L, Liaw C-C, Yang Y-L, Humpf H-U, Maansson M, Keyzers RA, Sims AC, Johnson AR, Sidebottom AM, Sedio BE, Klitgaard A, Larson CB, Boya P CA, Torres-Mendoza D, Gonzalez DJ, Silva DB, Marques LM, Demarque DP, Pociute E, O'Neill EC, Briand E, Helfrich EJN, Granatosky EA, Glukhov E, Ryffel F, Houson H, Mohimani H, Kharbush JJ, Zeng Y, Vorholt JA, Kurita KL, Charusanti P, McPhail KL, Nielsen KF, Vuong L, Elfeki M, Traxler MF, Engene N, Koyama N, Vining OB, Baric R, Silva RR, Mascuch SJ, Tomasi S, Jenkins S, Macherla V, Hoffman T, Agarwal V, Williams PG, Dai J, Neupane R, Gurr J, Rodríguez AMC, Lamsa A, Zhang C, Dorrestein K, Duggan BM, Almaliti J, Allard P-M, Phapale P, Nothias L-F, Alexandrov T, Litaudon M, Wolfender J-L, Kyle JE, Metz TO, Peryea T, Nguyen D-T, VanLeer D, Shinn P, Jadhav A, Müller R, Waters KM, Shi W, Liu X, Zhang L, Knight R, Jensen PR, Palsson BØ, Pogliano K, Linington RG, Gutiérrez M, Lopes NP, Gerwick WH, Moore BS, Dorrestein PC, Bandeira N. Sharing and community curation of mass spectrometry data with Global Natural Products Social Molecular Networking. Nat Biotechnol. 2016 Aug;34(8):828-837.

- 47. Putman T, Hybiske K, Jow D, Afrasiabi C, Lelong S, Cano MA, Stupp GS, Waagmeester A, Good BM, Wu C, Su AI. ChlamBase: a curated model organism database for the Chlamydia research community. Database J Biol Databases Curation. 2019 01;2019. PMCID: PMC6580685
- 48. Lewis J, Snyder M, Hyatt-Knorr H. Marking 15 years of the Genetic and Rare Diseases Information Center. Transl Sci Rare Dis. 2017 May 25;2(1–2):77–88. PMCID: PMC5685198
- 49. Medical Subject Headings Home Page [Internet]. [cited 2019 Aug 27]. Available from: https://www.nlm.nih.gov/mesh/meshhome.html
- Maiella S, Olry A, Hanauer M, Lanneau V, Lourghi H, Donadille B, Rodwell C, Köhler S, Seelow D, Jupp S, Parkinson H, Groza T, Brudno M, Robinson PN, Rath A. Harmonising phenomics information for a better interoperability in the rare disease field. Eur J Med Genet. 2018 Nov;61(11):706–714. PMID: 29425702
- Amberger JS, Hamosh A. Searching Online Mendelian Inheritance in Man (OMIM): A Knowledgebase of Human Genes and Genetic Phenotypes. Curr Protoc Bioinforma. 2017 27;58:1.2.1-1.2.12. PMCID: PMC5662200
- 52. McKusick VA. Mendelian Inheritance in Man and its online version, OMIM. Am J Hum Genet. 2007 Apr;80(4):588–604. PMCID: PMC1852721
- 53. GeneWiki Scheduled Bots. Contribute to SuLab/scheduled-bots development by creating an account on GitHub [Internet]. Su Lab; 2019 [cited 2019 Aug 23]. Available from: https://github.com/SuLab/scheduled-bots
- 54. fnielsen/scholia [Internet]. GitHub. [cited 2019 Sep 27]. Available from: https://github.com/fnielsen/scholia
- 55. Scholia [Internet]. [cited 2019 Oct 1]. Available from: https://tools.wmflabs.org/scholia/pathway/
- 56. Tool information: pathway-viewer Wikimedia Toolforge [Internet]. [cited 2019 Sep 27]. Available from: https://tools.wmflabs.org/admin/tool/pathway-viewer
- 57. Scholia, ACE Inhibitor Pathway [Internet]. Available from: https://tools.wmflabs.org/scholia/pathway/Q29892242
- 58. Köhler S, Vasilevsky NA, Engelstad M, Foster E, McMurry J, Aymé S, Baynam G, Bello SM, Boerkoel CF, Boycott KM, Brudno M, Buske OJ, Chinnery PF, Cipriani V, Connell LE, Dawkins HJS, DeMare LE, Devereau AD, de Vries BBA, Firth HV, Freson K, Greene D, Hamosh A, Helbig I, Hum C, Jähn JA, James R, Krause R, F. Laulederkind SJ, Lochmüller H, Lyon GJ, Ogishima S, Olry A, Ouwehand WH, Pontikos N, Rath A, Schaefer F, Scott RH, Segal M, Sergouniotis PI, Sever R, Smith CL, Straub V, Thompson R, Turner C, Turro E, Veltman MWM, Vulliamy T, Yu J, von Ziegenweidt J, Zankl A, Züchner S, Zemojtel T, Jacobsen JOB, Groza T, Smedley D, Mungall CJ, Haendel M, Robinson PN. The Human Phenotype Ontology in 2017. Nucleic Acids Res. 2017 Jan 4;45(D1):D865–D876.
- Köhler S, Schulz MH, Krawitz P, Bauer S, Dölken S, Ott CE, Mundlos C, Horn D, Mundlos S, Robinson PN. Clinical diagnostics in human genetics with semantic similarity searches in ontologies. Am J Hum Genet. 2009 Oct;85(4):457–464. PMCID: PMC2756558

- 60. Bayesian ontology querying from Bauer et al. Contribute to SuLab/boqa development by creating an account on GitHub [Internet]. Su Lab; 2018 [cited 2019 Jul 23]. Available from: https://github.com/SuLab/boqa
- 61. Incorporate wikidata statements into phenomizer. Contribute to SuLab/Wikidata-phenomizer development by creating an account on GitHub [Internet]. Su Lab; 2019 [cited 2019 Jul 23]. Available from: https://github.com/SuLab/Wikidata-phenomizer
- Caglayan AO, Comu S, Baranoski JF, Parman Y, Kaymakçalan H, Akgumus GT, Caglar C, Dolen D, Erson-Omay EZ, Harmanci AS, Mishra-Gorur K, Freeze HH, Yasuno K, Bilguvar K, Gunel M. NGLY1 mutation causes neuromotor impairment, intellectual disability, and neuropathy. Eur J Med Genet. 2015 Jan;58(1):39–43. PMCID: PMC4804755
- 63. Himmelstein DS, Lizee A, Hessler C, Brueggeman L, Chen SL, Hadley D, Green A, Khankhanian P, Baranzini SE. Systematic integration of biomedical knowledge prioritizes drugs for repurposing. eLife. 2017 22;6. PMCID: PMC5640425
- 64. Ursu O, Holmes J, Knockel J, Bologa CG, Yang JJ, Mathias SL, Nelson SJ, Oprea TI. DrugCentral: online drug compendium. Nucleic Acids Res. 2017 Jan 4;45(D1):D932–D939.
- 65. Union PO of the E. Turning FAIR into reality : final report and action plan from the European Commission expert group on FAIR data. [Internet]. 2018 [cited 2019 Aug 23]. Available from: https://publications.europa.eu/en/publication-detail/-/publication/7769a148-f1f6-11e8-9982-01aa75ed71a1/language-en/format-PDF
- Sansone S-A, McQuilton P, Rocca-Serra P, Gonzalez-Beltran A, Izzo M, Lister AL, Thurston M. FAIRsharing as a community approach to standards, repositories and policies. Nat Biotechnol. 2019 Apr;37(4):358–367.
- 67. Wimalaratne SM, Juty N, Kunze J, Janée G, McMurry JA, Beard N, Jimenez R, Grethe JS, Hermjakob H, Martone ME, Clark T. Uniform resolution of compact identifiers for biomedical data. Sci Data. 2018 May 8;5:180029.
- 68. Wikidata:Database download Wikidata [Internet]. [cited 2019 Aug 8]. Available from: https://www.wikidata.org/wiki/Wikidata:Database_download
- 69. Jacobsen A. Wikidata as an intuitive resource towards semantic data modeling in data FAIRification. 2018; Available from: http://ceur-ws.org/Vol-2275/short1.pdf
- 70. Creative Commons CC0 1.0 Universal [Internet]. [cited 2019 Aug 8]. Available from: https://creativecommons.org/publicdomain/zero/1.0/
- Reiser L, Berardini TZ, Li D, Muller R, Strait EM, Li Q, Mezheritsky Y, Vetushko A, Huala E. Sustainable funding for biocuration: The Arabidopsis Information Resource (TAIR) as a case study of a subscription-based funding model. Database J Biol Databases Curation. 2016;2016. PMCID: PMC4795935
- 72. Stupp GS, Su AI. Drug Indications Extracted from FAERS [Internet]. Zenodo; 2018 [cited 2019 Jun 27]. Available from: https://zenodo.org/record/1436000#.XRVY5-hKguU

- 73. Das R, Dhuliawala S, Zaheer M, Vilnis L, Durugkar I, Krishnamurthy A, Smola A, McCallum A. Go for a Walk and Arrive at the Answer: Reasoning Over Paths in Knowledge Bases using Reinforcement Learning. ArXiv171105851 Cs [Internet]. 2017 Nov 15 [cited 2019 May 6]; Available from: http://arxiv.org/abs/1711.05851
- 74. Xiong W, Hoang T, Wang WY. DeepPath: A Reinforcement Learning Method for Knowledge Graph Reasoning. ArXiv170706690 Cs [Internet]. 2017 Jul 20 [cited 2019 May 6]; Available from: http://arxiv.org/abs/1707.06690
- 75. Lin XV, Socher R, Xiong C. Multi-Hop Knowledge Graph Reasoning with Reward Shaping. ArXiv180810568 Cs [Internet]. 2018 Aug 30 [cited 2019 May 6]; Available from: http://arxiv.org/abs/1808.10568
- 76. CC0 (+BY) Dan Cohen [Internet]. [cited 2019 Aug 8]. Available from: https://dancohen.org/2013/11/26/cc0-by/
- 77. FAIRsharing [Internet]. [cited 2019 Jan 25]. Available from: https://fairsharing.org/
- 78. El-Gebali S, Mistry J, Bateman A, Eddy SR, Luciani A, Potter SC, Qureshi M, Richardson LJ, Salazar GA, Smart A, Sonnhammer ELL, Hirsh L, Paladin L, Piovesan D, Tosatto SCE, Finn RD. The Pfam protein families database in 2019. Nucleic Acids Res. 2019 Jan 8;47(D1):D427–D432.
- 79. Bastian F, Parmentier G, Roux J, Moretti S, Laudet V, Robinson-Rechavi M. Bgee: Integrating and Comparing Heterogeneous Transcriptome Data Among Species. In: Bairoch A, Cohen-Boulakia S, Froidevaux C, editors. Data Integr Life Sci. Springer Berlin Heidelberg; 2008. p. 124–131.
- Chibucos MC, Mungall CJ, Balakrishnan R, Christie KR, Huntley RP, White O, Blake JA, Lewis SE, Giglio M. Standardized description of scientific evidence using the Evidence Ontology (ECO). Database [Internet]. 2014 Jan 1 [cited 2019 Aug 8];2014. Available from: https://academic.oup.com/database/article/doi/10.1093/database/bau075/2634798