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The Image Data Resource: A Bioimage Data Integration and Publication Platform

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Abstract

Access to primary research data is vital for the advancement of science. To extend the data types supported by community repositories, we built a prototype Image Data Resource (IDR) that collects and integrates imaging data acquired across many different imaging modalities. IDR links high-content screening, super-resolution microscopy, time-lapse and digital pathology imaging experiments to public genetic or chemical databases, and to cell and tissue phenotypes expressed using controlled ontologies. Using this integration, IDR facilitates the analysis of gene networks and reveals functional interactions that are inaccessible to individual studies. To enable re-analysis, we also established a computational resource based on Jupyter notebooks that allows remote access to the entire IDR. IDR is also an open source platform that others can use to publish their own image data. Thus IDR provides both a novel on-line resource and a software infrastructure that promotes and extends publication and re-analysis of scientific image data.

Much of the published research in the life sciences is based on image datasets that sample 3D space, time, and the spectral characteristics of detected signal (e.g., photons, electrons, proton relaxation, etc.) to provide quantitative measures of cell, tissue and organismal processes and structures. The sheer size of biological image datasets makes data submission, handling and publication extremely challenging. An image-based genome-wide "high-content" screen (HCS) may contain over a million images, and new "virtual slide" and "light sheet" tissue imaging technologies generate individual images that contain gigapixels of data showing tissues or whole organisms at subcellular resolutions. At the same time, published versions of image data often are mere illustrations: they are presented in processed, compressed formats that cannot convey the measurements and multiple dimensions contained in the original image data and that can no longer be easily subjected to re-analysis. Furthermore, conventional publications neither include the metadata that define imaging protocols, biological systems and perturbations nor the processing and analytic outputs that convert the image data into quantitative measurements.

Several public image databases have appeared over the last few years. These provide on-line access to image data, enable browsing and visualization, and in some cases include experimental metadata. The Allen Brain Atlas, the Human Protein Atlas, and the Edinburgh Mouse Atlas all synthesize measurements of gene expression, protein localization and/or other analytic metadata with coordinate systems that place biomolecular localization and concentration into a spatial and biological context[1-3]. Similarly, many other examples of dedicated databases for specific imaging projects exist, each tailored to its aims and its target community[4-8]. There are also a number of public resources that serve as true scientific, structured repositories for image data, i.e., that collect, store and provide persistent identifiers for long-term access to submitted datasets, as well as provide rich functionalities for browsing, search and query. One archetype is the EMDataBank, the definitive community repository for molecular reconstructions recorded by electron microscopy[9]. The *Journal of Cell Biology* has built the JCB DataViewer (http://jcb-dataviewer.rupress.org/), which publishes image datasets associated with its on-line publications. The CELL Image Library publishes several thousand community-submitted images, some of which are linked to publications[10]. FigShare stores 2D pictures derived from image datasets, and can provide links for download of image datasets (http://figshare.com).

The EMDataBank recently has released a prototype repository for 3D tomograms, the EMPIAR resource[11]. Finally, the BioStudies and Dryad archives include support for browsing and downloading image data files linked to studies or publications[12] (https://datadryad.org/). Some of these provide a resource for a specific imaging domain (e.g., EMDataBank) or experiment (Mitocheck), while others archive datasets and provide links to a related publication available at an external journal's website (BioStudies). However, no existing resource links several independent biological imaging datasets to provide an "added value" platform, like the Expression Atlas achieves for a broad set of gene expression datasets[13] and UniProt delivers for protein sequence and function datasets[14].

Inspired by these "added value" resources, we have built a next-generation Image Data Resource (IDR) – an added value platform that combines data from multiple independent imaging experiments and from many different imaging modalities, integrates them into a single resource, and makes the data available for re-analysis in a convenient, scalable form. IDR provides, for the first time, a prototyped resource that supports browsing, search, visualization and computational processing within and across datasets acquired from a wide variety of imaging domains. For each study, metadata related to the experimental design and execution, the acquisition of the image data, and downstream interpretation and analysis are stored in IDR alongside the image data and made available for search and query through a web interface and a single API. Wherever possible, we have mapped the phenotypes determined by dataset authors to a common ontology. For several studies, we have calculated comprehensive sets of image features that can be used by others for re-analysis and the development of phenotypic classifiers. By harmonizing the data from multiple imaging studies into a single system, IDR users can query across studies and identify phenotypic links between different experiments and perturbations.

Results

Current IDR

IDR is currently populated with 24 imaging studies comprising 35 screens or imaging experiments from the biological imaging community, most of which are related to and linked to published works (Table 1). IDR holds ~42 TB of image data in ~36M image planes and ~1M individual experiments, and includes all associated experimental (e.g., genes, RNAi, chemistry, geographic location), analytic (e.g., submitter-calculated image regions and features), and functional annotations. Datasets in human cells (https://idr.openmicroscopy.org/webclient/?show=well-45407), *Drosophila* (https://idr.openmicroscopy.org/webclient/?show=well-547609) and fungi (https://idr.openmicroscopy.org/webclient/?show=well-590686; https://idr.openmicroscopy.org/webclient/?show=well-469267), super resolution 3DSIM images of centrosomes (https://idr.openmicroscopy.org/webclient/?show=dataset-51); dSTORM images of nuclear pores (https://idr.openmicroscopy.org/webclient/?show=dataset-61), a comprehensive chemical screen in human cells (https://idr.openmicroscopy.org/webclient/?show=plate-4101), a live cell screen in human cells (Mitocheck; https://idr.openmicroscopy.org/webclient/?show=well-771034) and histopathology whole slide images of tissues from several mouse mutants (https://idr.openmicroscopy.org/webclient/?show=dataset-369) are included. Finally, imaging from Tara Oceans, a global survey of plankton and other marine organisms, is also included

(https://idr.openmicroscopy.org/webclient/?show=plate-4751). The current collection of datasets samples a variety of biomedically-relevant biological processes like cell shape, division and adhesion, at scales ranging from nanometer-scale localization of proteins in cells to millimeter-scale structure of tissues from animals.

Genetic, Chemical and Functional Annotation in IDR

To enable querying across the different datasets stored in IDR, we have included annotations describing experimental perturbations (genetic mutants, siRNA targets and reagents, expressed proteins, cell lines, drugs, etc.) and phenotypes declared by the study authors either from quantitative analysis or visual inspection of the image data. Wherever possible, experimental metadata in IDR link to external resources that are the authoritative resource for those metadata (Ensembl, NCBI, PubChem, etc.).

The result is that IDR is a sampling of phenotypes related to experimental perturbations across several independent studies. Many of the studies in IDR perturb gene function by mutation or siRNA depletion. To calculate the sampling of gene orthologues, we used Ensembl's BioMart resource[15] to access a normalized list of gene orthologues. Overall, 19,601 gene orthologues are sampled, and 84.1% of gene orthologues are sampled more than 20 times. 90.3% of gene orthologues are sampled in three or more studies, so even in this early incarnation the phenotypes of perturbations in the majority of known genes are sampled in several different assays and organisms.

We have normalized the phenotypes included in studies submitted to IDR. Functional annotations (e.g., “increased peripheral actin") have been converted to defined terms in the Cellular Microscopy Phenotype Ontology (CMPO)[16], or other ontologies in collaboration with the data submitters (e.g., https://idr.openmicroscopy.org/webclient/?show=image-109846). Overall, 88% of the functional annotations have links to defined, published controlled vocabularies. 158 different ontology-normalized phenotypes (e.g., "increased number of actin filaments", "mitosis arrested") are included in IDR, and 136 are reported by authors in only one study. Nonetheless, these phenotypes are well-sampled-- the mean number of samples per phenotype, across HCS and other imaging datasets is 698 and the median is 144. This skewing occurs because some phenotypes are very common or are over-represented in specific assays, e.g. “protein localized in cytosol phenotype”, (CMPO_0000393; https://idr.openmicroscopy.org/mapr/phenotype/?value=CMPO_0000393). Nonetheless, there are several cases where phenotypes are observed in multiple orthogonal assays. Two examples are the “round cell” phenotype (CMPO_0000118; https://idr.openmicroscopy.org/mapr/phenotype/?value=CMPO_0000118) and the "increased nuclear size" phenotype (CMPO_0000140; https://idr.openmicroscopy.org/mapr/phenotype/?value=CMPO_0000140). Figure 1 summarizes the sampling of phenotypes across the current IDR datasets. Several classes of phenotypes are included, and many cases are sampled in thousands of experiments. In total, IDR includes >1M individual experiments (Table 1), with ~9 % annotated with experimentally observed phenotypes.

Data Visualization in IDR

IDR integrates image data and metadata from several studies into a single resource. The current IDR web user interface (WUI) is based on the open source OMERO.web

application[17] supplemented with a plugin allowing datasets to be viewed by 'Study', 'Genes', 'Phenotypes', 'siRNAs', 'Antibodies', 'Compounds', and 'Organisms' (see Supplementary Note). Using this architecture makes the integrated data resource available for access and re-use in several ways. Image data are viewable as thumbnails for each study (e.g., https://idr.openmicroscopy.org/webclient/?show=plate-4349) and multi-dimensional images can be viewed and browsed (e.g., https://idr.openmicroscopy.org/webclient/?show=well-45501 and https://idr.openmicroscopy.org/webclient/?show=well-93714). Tiled whole slide images used in histopathology are also supported (e.g., https://idr.openmicroscopy.org/webclient/?show=image-1920135). Where identified regions of interest (ROIs) have been submitted with the image data, these have been included and linked, and where possible, made available through the IDR WUI (e.g., https://idr.openmicroscopy.org/webclient/?show=well-590686 and https://idr.openmicroscopy.org/webclient/img_detail/1230005/). IDR images, thumbnails and metadata are accessible through the IDR WUI and web-based API in JSON format (see Supplementary Note). They also can be embedded into other pages using the OMERO.web gateway (e.g., https://www.eurobioimaging-interim.eu/image-data-repository.html).

Standardized Interfaces for Imaging Metadata

IDR integrates imaging data from many different, independent studies. These data were acquired using several different imaging modalities, in the absence of any over-arching standards for experimental, imaging or analytic metadata. While efforts like MIACA (http://miaca.sourceforge.net/), NeuroVault[18], MULTIMOT[19] and several other projects have proposed data standards in specific imaging subdomains, there is not yet a metadata standard that crosses all of the imaging domains potentially served by IDR. We therefore sought to adopt lightweight methods from other communities that have had broad acceptance[20] and converted metadata submitted in custom formats – spreadsheets, PDFs, MySQL databases, and Microsoft Word documents -- into a consistent tabular format inspired by the MAGE-TAB and ISA-TAB specifications[21, 22] that could then be used for importing semi-structured metadata like gene and ontology identifiers into OMERO[23]. We also used the Bio-Formats software library to identify and convert well-defined, semantically-typed elements that describe the imaging metadata (e.g., image pixel size) as specified in the OME Data Model[24, 25]. The resulting translation scripts were used to integrate datasets from multiple distinct studies and imaging modalities into a single resource. The scripts are publicly available (see Online Methods) and thus comprise a framework for recognizing and reading a range of metadata types across several imaging domains into a common, open specification.

Added Value of IDR

Because IDR links gene names and phenotypes, query results that combine genes and phenotypes across multiple studies are possible through simple text-based search. Searching for the gene *SGOL1* (https://idr.openmicroscopy.org/mapr/gene/?value=SGOL1) returns a range of phenotypes from four separate studies associated with mitotic defects (for example, CMPO_0000118, CMPO_0000305, CMPO_0000212, CMPO_0000344, etc.)[4, 26] but also an accelerated secretion phenotype (CMPO_0000246) in a screen for defects in protein secretion[27]. A second example is provided in a histopathology study of tissue phenotypes in a series of mouse mutants. Knockout of carbonic anhydrase 4 (Car4; https://idr.openmicroscopy.org/mapr/gene/?value=Car4) in mouse results in a range of defects in homeostasis in the brain, rib growth and male fertility[28-30]. Data held in IDR show

abnormal nuclear phenotypes in several tissues from Car4-/- mice (e.g., GI: https://idr.openmicroscopy.org/webclient/?show=dataset-153; liver: https://idr.openmicroscopy.org/webclient/?show=image-1918940; male reproductive tract: https://idr.openmicroscopy.org/webclient/?show=image-1918953). The human orthologue, *CA4*, is involved in certain forms of retinitis pigmentosa[31, 32]. Data presented in IDR from the Mitocheck study show that siRNA depletion of CA4 in HeLa cells[4] also results in abnormally shaped nuclei (https://idr.openmicroscopy.org/webclient/?show=well-828419) consistent with a defect in some aspect of the cell division cycle.

Phenotypes across distinct studies can also be used to build novel representations of gene networks. Figure 2A shows the gene network created when the gene knockouts or knockdowns that caused an elongated cell phenotype (CMPO_0000077) in studies in *S. pombe* and human cells are linked by queries to String DB[33] and visualized in Cytoscape[34] (see Supplementary Note and Supplementary Table 1). The genes discovered in the three studies form interconnected, non-overlapping, complementary networks that connect specific macromolecular complexes to the elongated cell phenotype. For example, HELZ2, MED30, MED18 and MED20 are all part of the Mediator Complex, but were identified as "elongated cell" hits in separate studies using different biological models (idr0001-A, idr0008-B, idr0012-A, Figure 2B). POLR2G (from idr0012-A), PAF1 (from idr0001-A) and SUPT16H (from idr0008-B) were scored as elongated cell hits in these studies and are all part of the Elongation complex in the RNA Polymerase II transcription pathway. Finally, ASH2L ("elongated cell phenotype" in idr0012-A), associates with SETD1A and SETD1B ("elongated cell phenotype" in idr0001-A) to form the Set1 histone methyltransferase (HMT). These examples demonstrate that these individual hits are probably not due to off-target effects or characteristics of individual biological models but arise through conserved, specific functions of large macromolecular complexes. This shows the utility and importance of combining phenotypic data of studies from different organisms and scales, and of integrating metadata from independent studies, to generate added value that can enhance the understanding of biological mechanisms and lead to new mechanistic hypothesis and predictions.

The integration of experimental, image and analytic metadata also provides an opportunity to include new functionalities for more advanced visualization and analytics of imaging data and metadata, bringing further added value to the original studies and datasets. We have added the data analytics tool Mineotaur[35] to one of IDR's datasets (https://idr.openmicroscopy.org/mineotaur/). This allows visual querying and analysis of quantitative feature data. For instance, having shown that components of the Set1 HMT function in controlling cell morphology in *S. pombe* and human cells, we noticed that genes like *ASH2L* were in the "elongated cell" network based on human cell data (idr0012-A) but not *S. pombe* data, where *ash2*, the *S. pombe ASH2L* orthologue, was not annotated as a cell elongation "hit". We first noted that ash2 has a microtubule cytoskeleton phenotype (https://idr.openmicroscopy.org/webclient/?show=well-592371). We then queried the criteria previously used for cell shape hits in the Sysgro screen (idr0001-A) and found that *ash2* fell just below the cutoff originally used in this study to define phenotypic hits for cell shape (Supplementary Note). When combined with results on *ASH2L* from HeLa cells (Figure 2B) these results suggest that the Set1 HMT has a strongly conserved role in controlling cell shape and the cytoskeleton in unicellular and multicellular organisms.

Data Integration and Access

Like most modern on-line resources IDR makes data available through a web user-interface as well as a web-based JSON API. This encourages third-parties to make use of IDR in their own sites. For example, image data in IDR has been linked to study data in BioStudies, thereby extending the linkage of study and image metadata (e.g., https://www.ebi.ac.uk/biostudies/studies/S-EPMC4704494), and to PhenoImageShare[36], an on-line phenotypic repository (e.g., http://www.phenoimageshare.org/search/?term=&hostName=Image+Data+Repository+(IDR)). These are examples of use of IDR as a service that delivers data for other applications to integrate and reuse.

To add further value and extend the possibilities for reuse of IDR data, we are calculating comprehensive sets of feature vectors of IDR image data using the open source tool WND-CHARM[37]. To date full WND-CHARM features have been calculated for images in idr0002-A, idr0005-A, idr0008-B, idr0009-A, idr0009-B, idr0012-A, and parts of idr0013-A and idr0013-B. Feature calculations for other IDR datasets are in progress. Features are stored in IDR using OMERO's HDF5-based data store and available through the OMERO API (see Supplementary Note).

The integration of image-based phenotypes and calculated features makes IDR an attractive candidate for computational re-analysis. To ease the access to IDR's TB-scale datasets, we have connected IDR to a Jupyter notebook-based computational resource (https://idr.openmicroscopy.org/jupyter) that exposes IDR datasets via an API (https://idr.openmicroscopy.org/about/api.html). We include exemplar notebooks that provide visualization of image features using PCA, access to images annotated with CMPO phenotypes, calculation of gene networks, calculation of WND-CHARM features for individual images and recreation of Figures 1 and 2 from IDR data. Alternatively, users can run their own analyses using notebooks stored in GitHub (https://github.com/IDR/idr-notebooks). To allow re-use of IDR metadata locally, we have made all IDR databases, metadata and thumbnails available for download and have built Ansible scripts that automate the deployment of the IDR software stack (original image data are not included; see Supplementary Note).

Discussion

Making data public and available is a critical part of the scientific enterprise[38] (https://wellcome.ac.uk/what-we-do/our-work/expert-advisory-group-data-access) (https://royalsociety.org/topics-policy/projects/science-public-enterprise/report/). To take the next step in facilitating the reuse and meta-analysis of image datasets we have built IDR, a next-generation data technology that integrates and publishes image data and metadata from a wide range of imaging modalities and scales in a consistent format. IDR integrates experimental, imaging, phenotypic and analytic metadata from several independent studies into a single resource, allowing new modes of biological Big Data querying and analysis. As more datasets are added to IDR, they will potentiate and catalyze the generation of new biological hypotheses and discoveries.

In IDR, we have linked image metadata from several independent studies. Experimental, imaging phenotypic and analytic metadata are recorded in a consistent format. Rather than

declaring and attempting to enforce a strict imaging data standard, IDR provides tools for supporting community formats and releases these as a framework that facilitates data reuse. We hope that the availability of this framework will provide incentives for others to structure their metadata in shareable formats that can be read into IDR or other applications, whether based on OMERO or not. In the future, we can imagine that these and other capabilities could be extended in IDR - or similar repositories that link to IDR - to enable systematic integration, visualization and analytics across imaging studies, thereby helping to harness and capitalize on the exponentially increasing amounts of bio-imaging data that the community generates.

As of this writing, IDR has published 35 reference image datasets grouped into 24 studies (Table 1) and, utilizing EMBL-EBI's Embassy Cloud, has capacity to receive and publish many more. Authors of scientific publications that are already published or under submission can submit accompanying image datasets for publication in IDR, using the metadata specifications and formats we have built. Once published, the datasets can be browsed and viewed through IDR's WUI, or queried and re-analyzed using the IDR computational resource. Details about the submission process are available (https://idr.openmicroscopy.org/about/submission.html).

IDR software and technology is open source, so it can be accessed and built into other image data publication systems. This supports the building of technology and installations that integrate and publish bio-image data for the scientific community, allowing discoveries and predictions similar to what we have shown in Figure 2. IDR therefore functions both as a resource for image data publication and as a technology platform that supports the creation of on-line scientific image databases and services. In the future, those databases and services may ultimately amalgamate to form resources analogous to the genomic resources that are the foundation of much of modern biology.

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Author Contributions

J.R.S., A.B. and R.E.C.S conceived and funded the project which was overseen by J.R.S. J.M., S.W.L, A.T., S.L. and E.W. built the IDR software stack: J.M. designed the software architecture and managed the software development team; S.W.L. built all the tools for deploying IDR in the OpenStack cloud and ran all the IDR systems; A.T. built Mapr, the metadata querying application; S.L. updated Bio-Formats to read the incoming datasets; E.W. performed all data curation and annotation. G.R., S.W.L. and E.W. sourced and received the datasets. A.C. analyzed features of the integrated datasets. B.A. helped with the IDR/Mineotaur integration. R.K.F. designed the updates to the OMERO UI. U.S. helped with the integration of IDR datasets into BioStudies.

Competing Financial Interests

J. R. S is affiliated with Glencoe Software, Inc., an open-source US-based commercial company that provides commercial licenses for OME software.

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Figure Legends

Figure 1. Sampling of Phenotypes in the IDR.

The numbers of samples per phenotype. Each sample represents a well from a micro-well plate in a screen or image from a dataset. Wells annotated as controls were not included. User submitted phenotype terms were mapped to the CMPO terms shown here. Colors represent higher-level groupings of phenotype terms. Point size shows the number of studies (group of related screens) each phenotype is linked to points of increasing size representing 1, 2, 3 or 4 studies respectively.

Figure 2. Network Analysis of Genes Linked to the Elongated Cell Phenotype in the IDR.

A. Protein-protein interaction network based on the genes linked to the elongated cell phenotype (CMPO_0000077) in three distinct IDR studies. Genes from *S. pombe* (green, idr0001-A[5]), HeLa cell morphology (blue, idr0012-A[39]) and HeLa Actinome (red, idr0008-B[40]) are displayed with linkages (gray) from StringDB[33]. To enable comparisons in Cytoscape, the human orthologues of *S. pombe* genes are used for the genes identified in idr0001-A. For more information, see Supplementary Note.

B. Zoomed view of network in A, with gene names. See Supplementary Note for the list of gene names used in the figure.

Table 1. List of Datasets in IDR

The phenotype column contains the number of submitted phenotypes. The number of genes, compounds or proteins identified as targets for analysis is listed in the Targets column and the 'Experiments' column lists the number of individual wells in HCS studies or imaging experiments in non-screen datasets.

Study	Species	Type	No. of screens or experi-ments	5D Images	Size (TB)	Pheno-types	Targets	Experi-ments	Reference
idr0001-graml-sysgro	*S. pombe*	gene deletion screen	1	109,728	10.06	19	3,005	18,432	[5]
idr0002-heriche-condensation	Human	RNAi screen	1	1,152	2.10	2	102	1,152	[26]
idr0003-breker-plasticity	*S. cerevisiae*	protein screen	1	97,920	0.20	14	6,234	32,640	[41]
idr0004-thorpe-rad52	*S. cerevisiae*	gene deletion screen	1	3,765	0.17	1	4,195	4,512	[42]
idr0005-toret-adhesion	*D. melanogaster*	RNAi screen	2	45, 792	0.14	1	13,035	15,264	[43]
idr0006-fong-nuclearbodies	Human	protein localization screen	1	240,848	1.40	8	12,743	16,224	[44]
idr0007-srikumar-sumo	*S. cerevisiae*	protein localization screen	1	3,456	0.02	23	377	1,152	[45]
idr0008-rohn-actinome	*D. melanogaster,* Human	RNAi screen	2	55,944	0.12	46	12,826	26,496	[40]
idr0009-simpson-secretion	Human	RNAi screen	2	397, 056	3.25	3	17,960	397,056	[27]
idr0010-doil-dnadamage	Human	RNAi screen	1	56,832	0.08	2	18,675	56,832	[46]
idr0011-ledesmafernandez-dad4	*S. cerevisiae*	gene deletion screen	5	8,957	0.4	1	5209	8736	Under review

idr0012-fuchs-cellmorph	Human	RNAi screen	1	45,692	0.38	18	16,701	26,112	[39]
idr0013-neumann-mitocheck	Human	RNAi screen	2	200,995	14.54	18	18,393	206,592	[4]
idr0015-UNKNOWN-taraoceans	multi-species	geographic screen	1	32,776	2.49	0	84	84	[47]
idr0016-wawer-bioactivecompoundprofiling	Human	small molecule screen	1	869,820	3.19	2	29,542	144,000	[48]
idr0017-breinig-drugscreen	Human	small molecule screen	1	147,456	2.48	0	1,281	36,864	[49]
idr0018-neff-histopathology	*Mus musculus*	histopathology of gene knockouts	1	899	0.27	48	9	248	---
idr0019-sero-nfkappab	Human	HCS image analysis	1	25,872	0.03	0	198	2,156	[50]
idr0020-barr-chtog	Human	RNAi screen	1	36,960	0.03	2	241	1,232	[51]
idr0021-lawo-pericentriolarmaterial	Human	protein localization using 3D-SIM	1	414	0.0003	1	9	414	[52]
idr0023-szymborska-nuclearpore	Human	protein localization using dSTORM	1	524	0.0005	1	7	359	[53]
idr0027-dickerson-chromatin	*S. cerevisiae*	3D-tracking of tagged chromatin loci	1	229	0.03	0	8	112	[54]
idr0028-pascualvargas-rhogtpases	Human	RNAi screen	4	155,332	0.18	9	170	5544	[55]
idr0032-yang-meristem	*A. thaliana*	*in situ* hybridization	1	458	0.003	5	115	115	[56]
Sum			**35**	**2,538,777**	**42**	**224**	**161,119**	**1,002,328**	
Average				**105,782**	**1.73**	**9**	**6,713**	**41,764**	

Online Methods

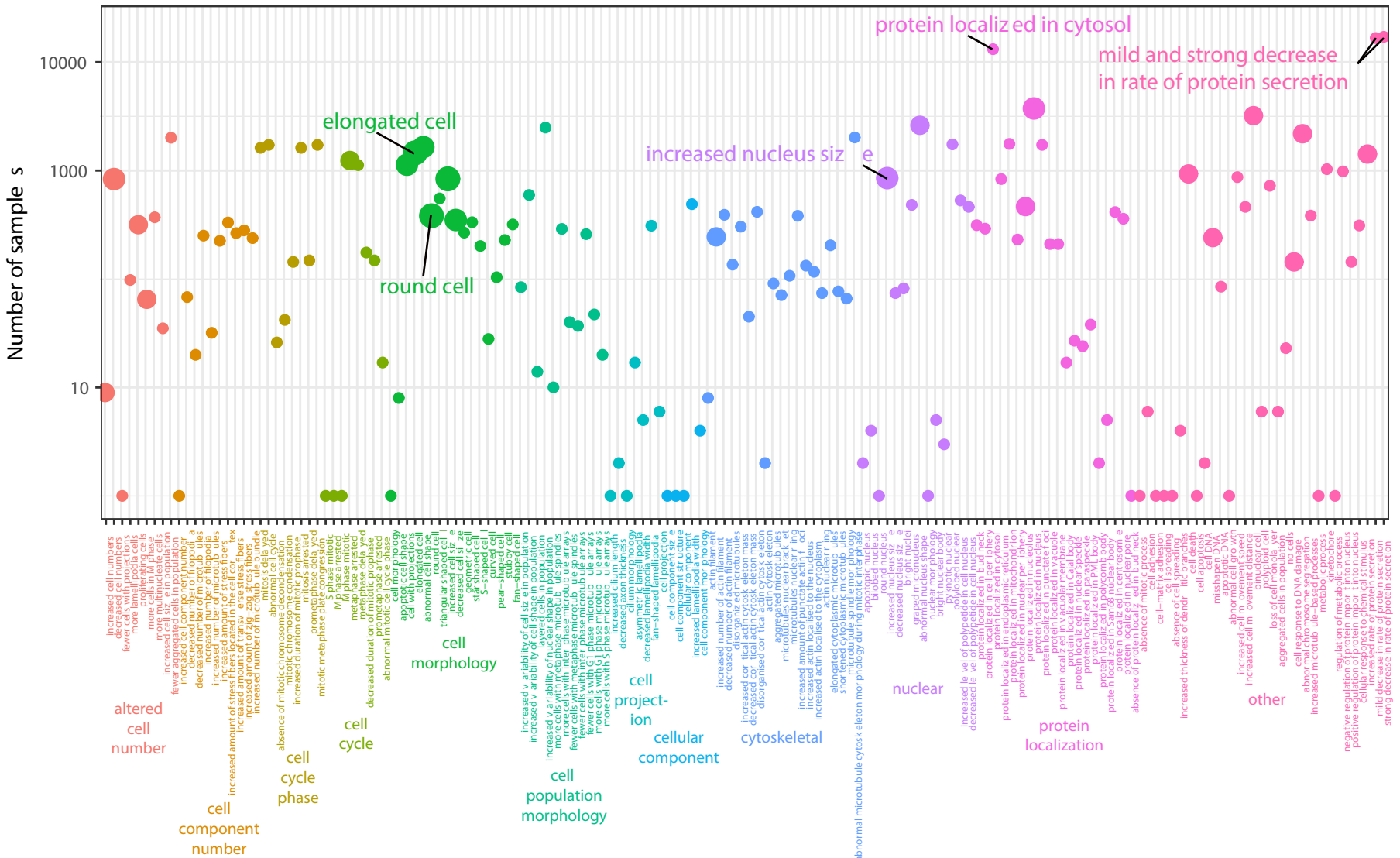
Architecture and Population of IDR

IDR (https://idr.openmicroscopy.org) was built using open-source OMERO[17] and Bio-Formats[24] as a foundation. Deployments are managed by Ansible playbooks along with re-usable roles on an OpenStack-based cloud contained within the EMBL-EBI Embassy resource. Datasets (Table 1) were collected by shipped USB-drive or transferred by Aspera. Included datasets were selected according to the criteria defined by the Euro-BioImaging/Elixir Data Strategy concept of "reference images" (http://www.eurobioimaging.eu/content-news/euro-bioimaging-elixir-image-data-strategy), which states that image datasets for publication should be related to published studies, linked as much as possible to other resources and be candidates for re-use, re-analysis, and/or integration with other studies.

Experimental and analytic metadata were submitted in either spreadsheets (CSV, XLS), PDF or HDF5 files or a MySQL database, each using its own custom format. We converted these custom formats to a consistent tabular format inspired by the MAGE and ISA-TAB specifications[21, 22] and combined into a single CSV file using a custom script (available in https://github.com/IDR/idr-metadata) and imported into OMERO. Imaging metadata and binary data were imported into OMERO using Bio-Formats. Experimental and analytic metadata were stored using OMERO.tables, an HDF5-backed tabular data store used by OMERO. For each dataset, metadata that were valuable for querying and search were copied to OMERO's key-value-based Map Annotation facility[23]. This means that different metadata types and elements can be accessed using different parts of the OMERO API, depending on the search and querying capabilities they require. For more information on the construction of queries, see Supplementary Note.

Data Availability

All datasets described in Table 1 and in this paper are available at https://idr.openmicroscopy.org. All software for building and running the IDR and reading metadata of the IDR datasets is open source and available at https://github.com/IDR and https://github.com/openmicroscopy.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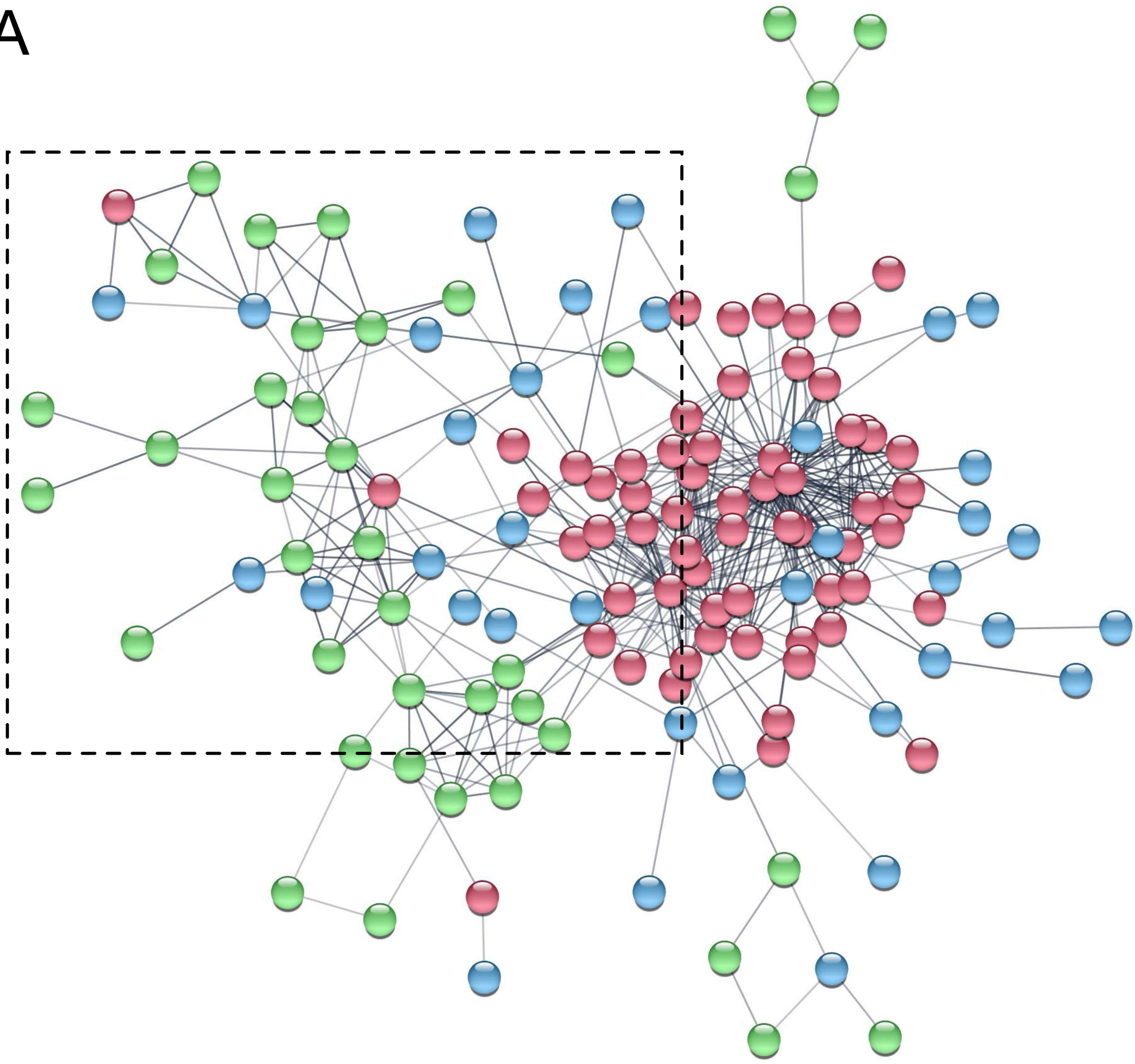

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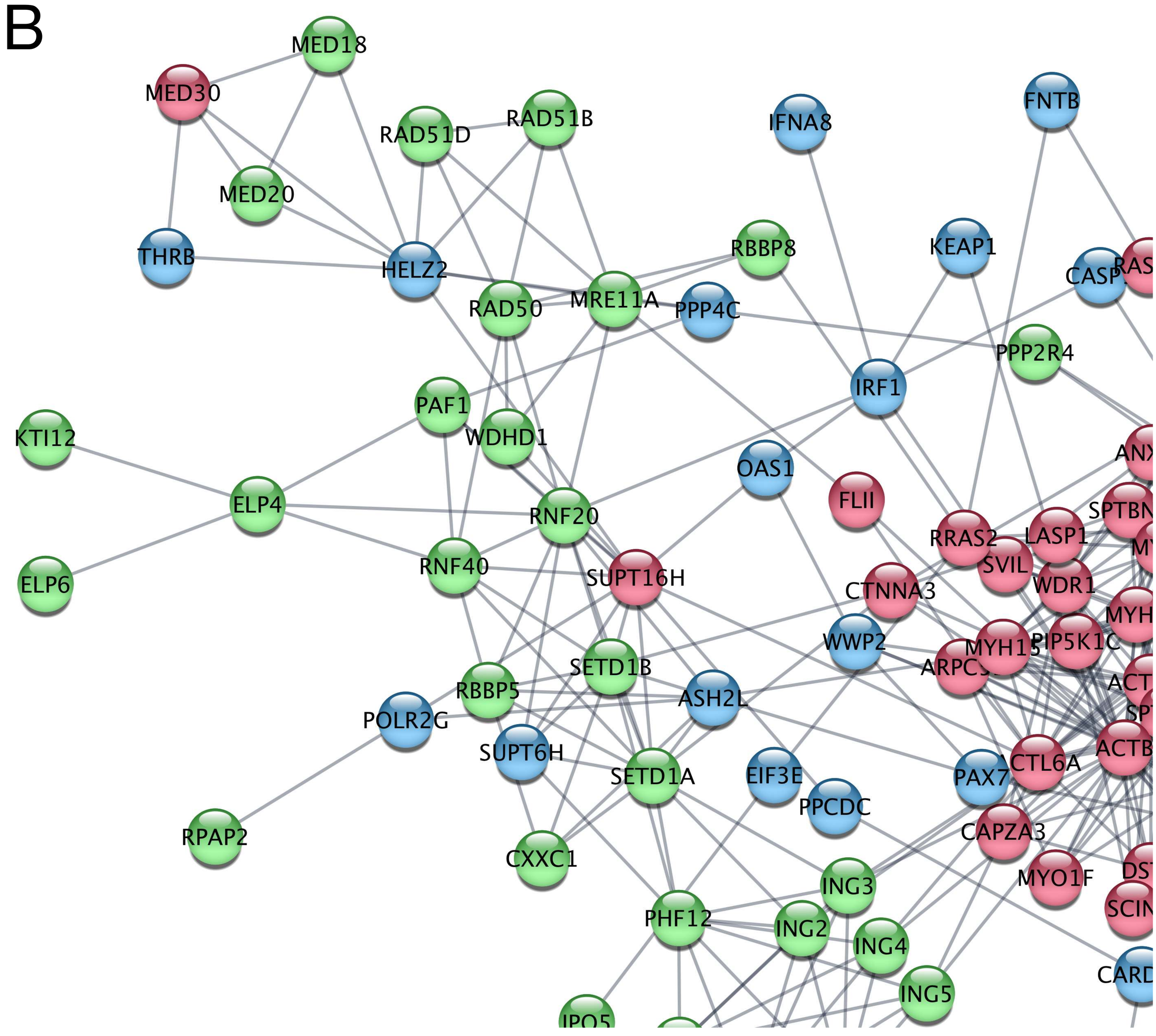
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RAD51B
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PPP4C
PPP2R4
IRF1
PAF1
WDHD1
KTI12
OAS1
FLII
ELP4
RNF20
SPTBN
RRAS2
LASP1
RNF40
SUPT16H
SVIL
WDR1
ELP6
CTNNA3
MYH
WWP2
MYH15
PIP5K1C
ARPC3
ACT
SETD1B
RBBP5
ASH2L
POLR2G
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EIF3E
PPCDC
CAPZA3
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ING3
PHF12
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ING5
CARD
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