http://druggablegenome.net/
http://datascience.unm.edu/

➔ toprea[at]salud.unm.edu ➔

# AN ACADEMIC PERSPECTIVE ON DRUG DISCOVERY & REPOSITIONING FOR COVID-19

Tudor I. Oprea

with contributions from

Sorin Avram, Giovanni Bocci, Cristian Bologa, Steven Bradfute, Lars Juhl Jensen, Praveen Kumar, Jordi Mestres, Douglas J. Perkins, Vishal B. Siramshetty, Anna Waller, Jeremy J. Yang, Gergely Zahoranszky-Kohalmi & many others

**Funding: U24 CA224370, U24 TR002278, U01 CA239108 (NIH)**

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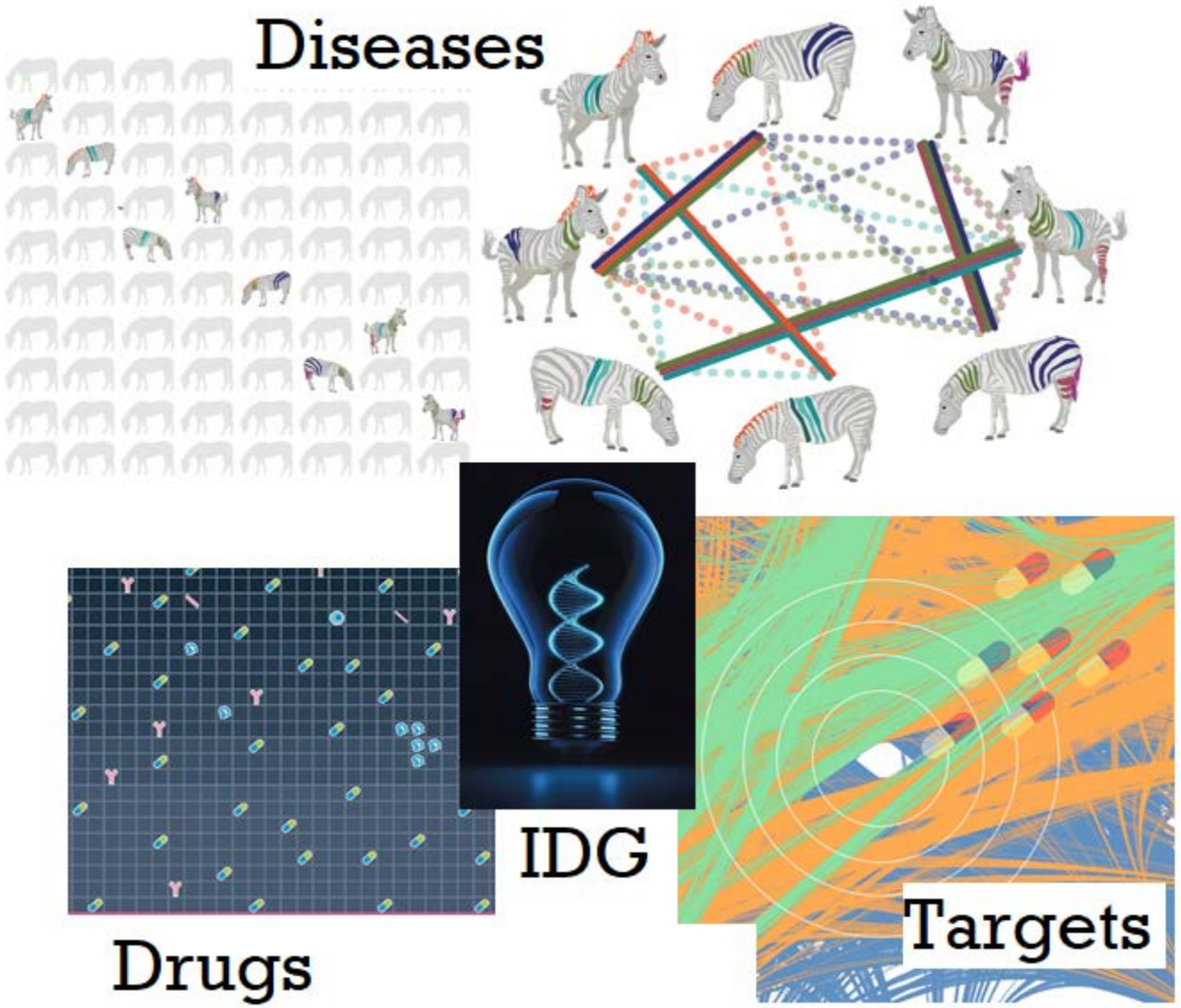
4/23/2020
*XXVI Symposium "Bioinformatics and Computer-Aided Drug Discovery"*
Organized by the V.N. Orekhovich Scientific Research Institute of Biomedical Chemistry --- Updated 4/23/20

# THREE PILLARS OF DRUG DISCOVERY




- There are 3 main pillars at the root of successful drug discovery programs.
- Informatics, Data Science and Machine Learning ("AI" according to the hype cycle) are successfully used, as follows:
- **Diseases:** Significant improvements in EMR processing, nosology, ontology, and EMR-based ML for Dx & mechanisms
- **Targets:** Knowledge graph methods, coupled with ML, for biological discovery, target selection & validation
- **Drugs:** From virtual screening to vaccine design, therapeutic modalities benefit from predictive methods across the board
- **IDG** is developing methods applicable to each of these 3 areas

Diseases image credit: Julie McMurry, Melissa Haendel (OHSU).
All other images credit: Nature Reviews Drug Discovery

2/5/20 revision

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# A COMPREHENSIVE MAP OF MOLECULAR DRUG TARGETS

We curated 667 human genome-derived proteins and 226 pathogen-derived biomolecules through which 1,578 US FDA-approved drugs act.

This set included 1004 orally formulated drugs as well as 530 injectable drugs (approved through June 2016).

Data captured in DrugCentral (link)

R. Santos et al., *Nature Rev. Drug Discov.* **2017**, 16:19-34 link

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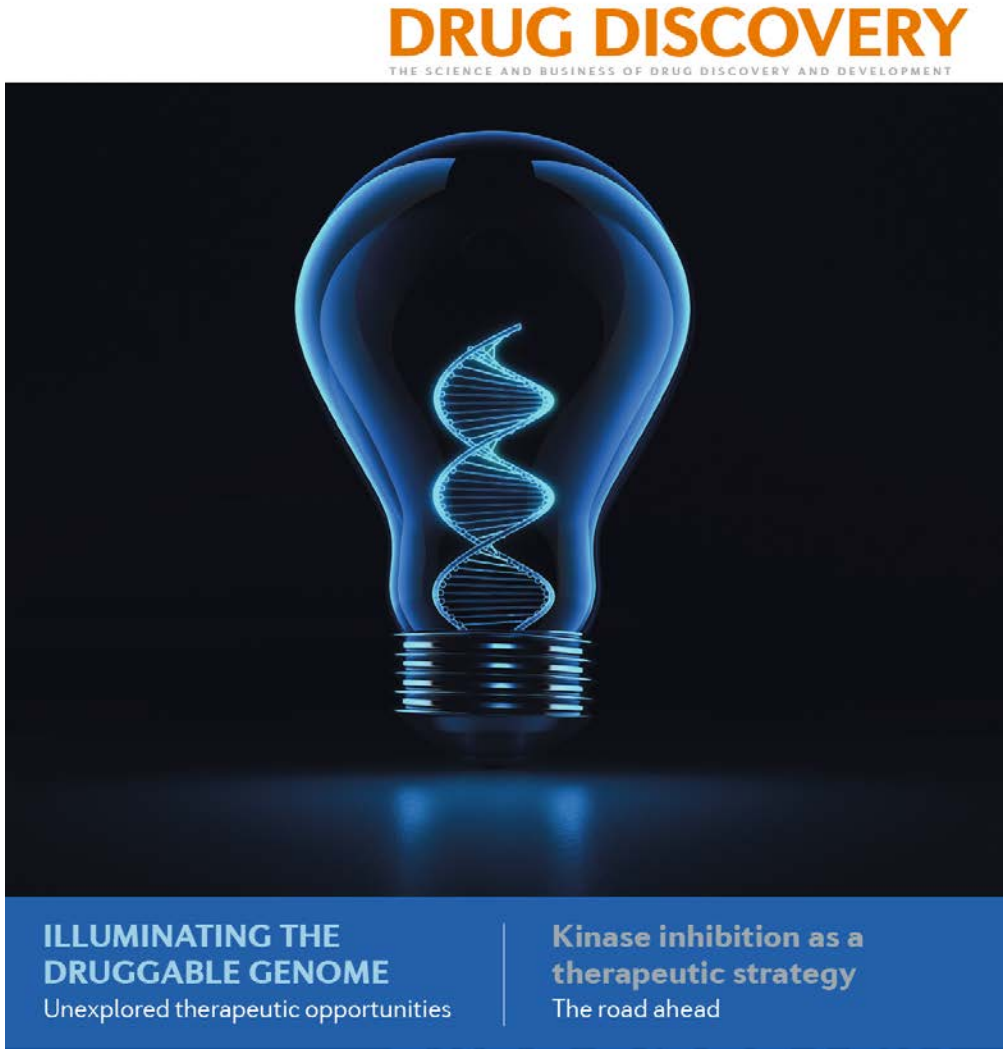
# ILLUMINATING THE DRUGGABLE GENOME




| | | |
|---|---|---|
| RFA-RM-16-026 (DRGC) | GPCRs | U24 DK116195:<br>Bryan Roth, M.D., Ph.D. (UNC)<br>Brian Shoichet, Ph.D. (UCSF) |
| | Ion Channels | U24 DK116214:<br>Lily Jan, Ph.D. (UCSF)<br>Michael T. McManus, Ph.D. (UCSF) |
| | Kinases | U24 DK116204:<br>Gary L. Johnson, Ph.D. (UNC) |
| RFA-RM-16-025 (RDOC) | Outreach | U24 TR002278:<br>Stephan C. Schürer, Ph.D. (UMiami)<br>Tudor Oprea, M.D., Ph.D. (UNM)<br>Larry A. Sklar, Ph.D. (UNM) |
| RFA-RM-16-024 (KMC) | Data | U24 CA224260:<br>Avi Ma'ayan, Ph.D. (ISMMS)<br>U24 CA224370:<br>Tudor Oprea, M.D., Ph.D. (UNM) |
| RFA-RM-18-011 (CEIT) | Tools | U01 CA239106: N Kannan, PhD & KJ Kochut (UGA)<br>U01 CA239108: PN Robinson, MD PhD (JAX), CJ Mungall (LBL), T Oprea (UNM)<br>U01 CA239069: G Wu, PhD (OHSU), PG D'Eustachio PhD (NYU), Lincoln D Stein, PhD (OICR) |

T. Oprea et al., *Nature Rev. Drug Discov.* **2018,** 17:317-332 link

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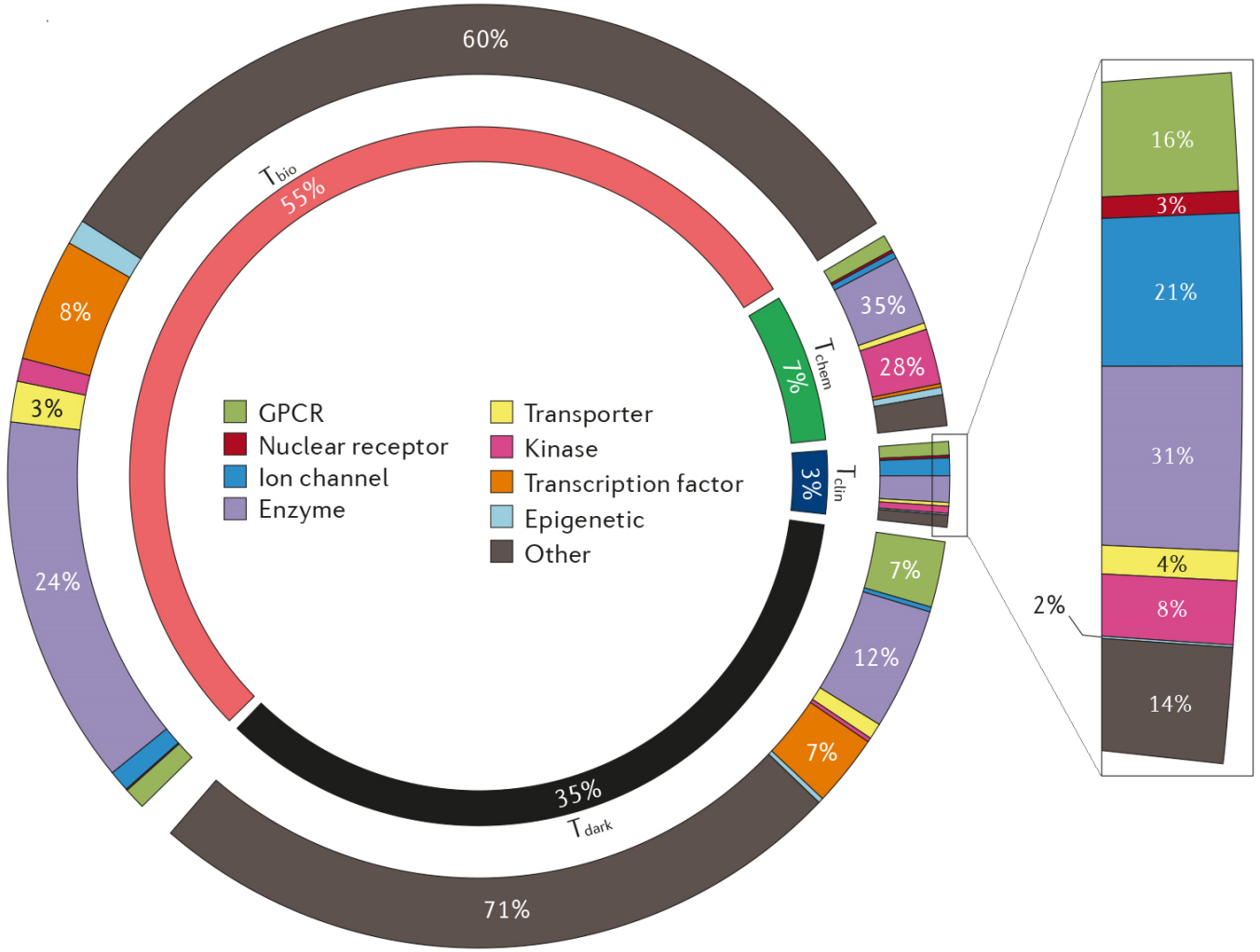
# TARGET DEVELOPMENT LEVELS




- Most protein classification schemes are based on structural and functional criteria.
- For therapeutic development, it is useful to understand how much and what types of data are available for a given protein, thereby highlighting well-studied and understudied targets.
- **Tclin:** Proteins annotated as drug targets
- **Tchem:** Proteins for which *potent* small molecules are known
- **Tbio:** Proteins for which biology is better understood
- **Tdark:** These proteins lack antibodies, publications or Gene RIFs

**2020 Update:** Tdark 31.2%; Tbio 57.7%; Tchem 8%; Tclin 3.1%

T. Oprea et al., *Nature Rev. Drug Discov.* **2018,** 17:317-332 link

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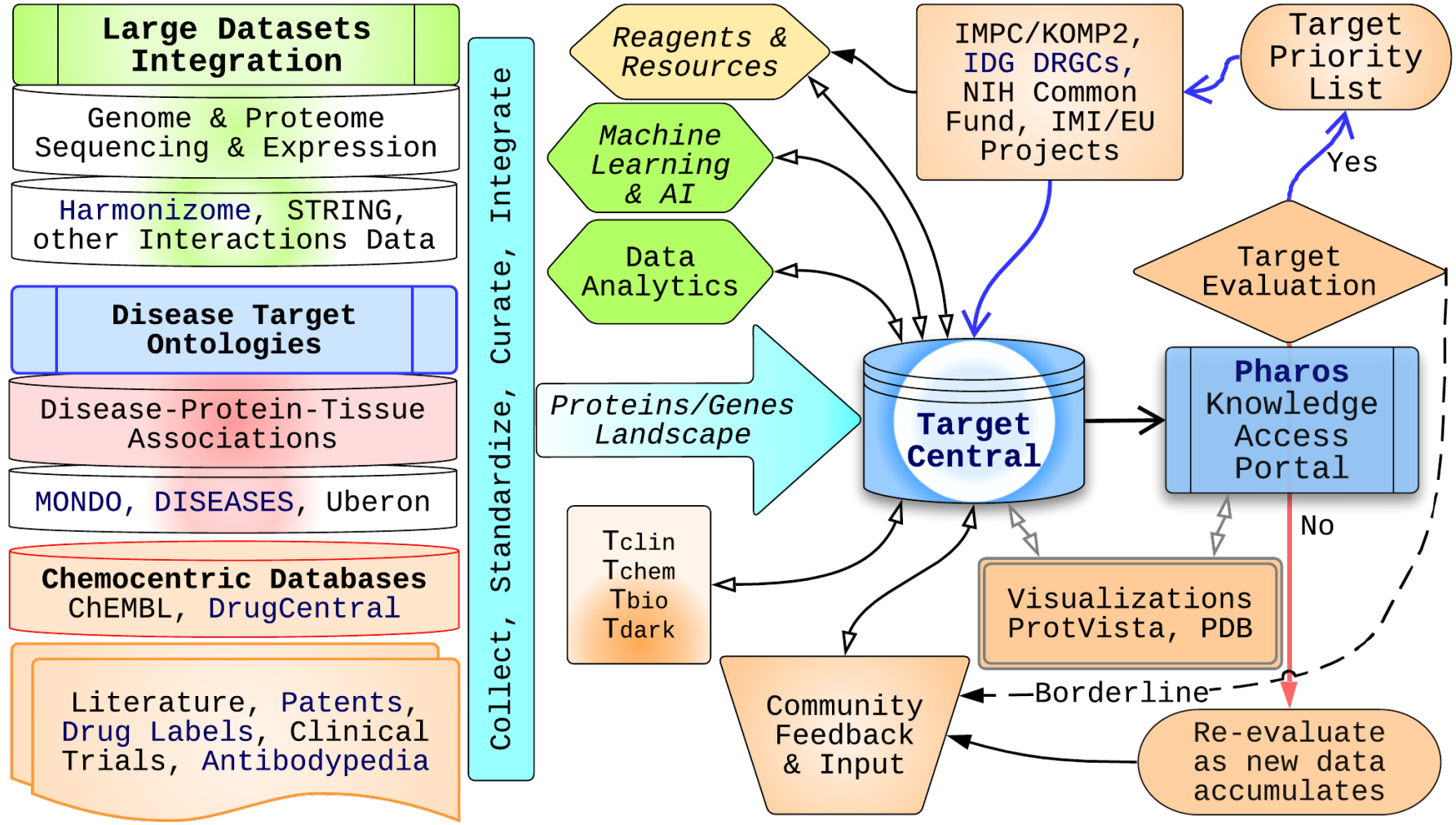
# IDG KMC ANNOTATION PROCESS

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URL: https://pharos.nih.gov/

**IDG databases are interfaced in UniProt**

https://www.uniprot.org/news/2019/09/18/release

**GTEx, LINCS, IMPC:** Data from 3 CommonFund programs is already in Pharos

T. Oprea, *Mammalian Genome*, **2019**, 30:192-200 https://bit.ly/2NUK0BK

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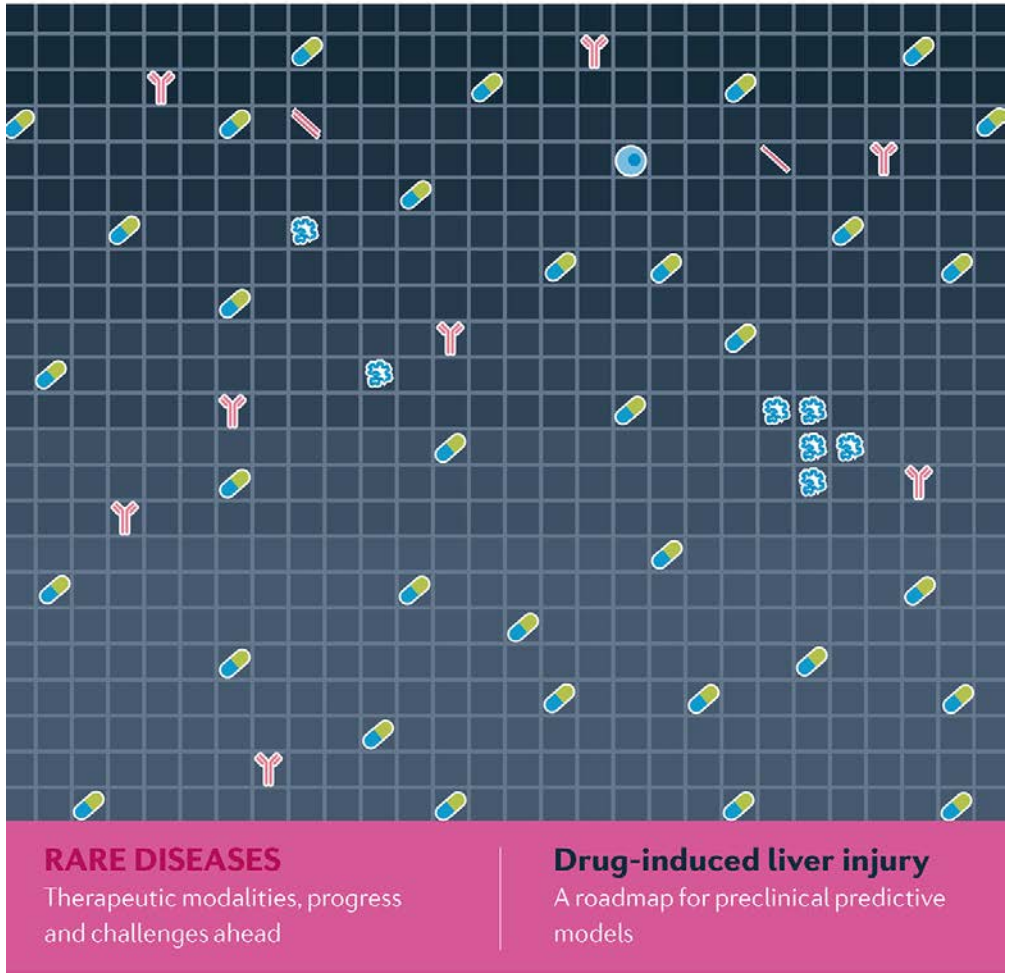
February 2020 volume 19 no. 2
www.nature.com/nrd

nature reviews
drug discovery




# RARE DISEASES: AN INFORMATICS SURVEY

- *We revised the number of RDs from ~7,000 to 10,393* using Disease Ontology, OrphaNet, GARD, NCIT, OMIM and the Monarch Initiative MONDO system
- We also pointed out the lack of a uniform definition for rare diseases, and called for coordinated efforts to precisely define them
- We surveyed therapeutic modalities (link) available to translate advances in the scientific understanding of rare diseases into therapies, and discussed overarching issues in drug development for rare diseases.

Haendel M, et al. *Nature Rev. Drug Discov.* **2020** 19:77-78 link

2/4/20 revision

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# TAKE HOME MESSAGE

# THERE IS A KNOWLEDGE DEFICIT

~31% of the proteins remain understudied (Tdark, ignorome)
*that number is steadily decreasing*

~11.1% of the Proteome (Tclin & Tchem) are currently targeted by small molecule probes and drugs – *that number is slowly increasing*

With help from rare disease patient advocacy groups, rare disease research is likely to witness a significant increase in translation



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# COVID-19 CLINICAL TRIALS

- To date, no drug is expressly approved for SARS-CoV-2 infections except the emergency authorization for (hydroxyl)chloroquine.
- Until such time that effective vaccines and/or therapeutics are approved, our "best guess" is "drug repositioning" (aka drug repurposing) followed by drug discovery
- As of 4/15/20, there were 585 clinical trials for "COVID-19".
- Of these 585 clinical trials, 274 listed a "drug" intervention; of these, 259 reference an actual medicine; 230 are "interventional".
- Examples of non-medicine "drug" entries: BCG vaccine; gargle/mouthwash…

https://clinicaltrials.gov/ct2/results?cond=COVID-19

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# CURATING COVID-19 CLINICAL TRIALS

- Manual curation (by intervention), e.g., identify experimental (novel) drug vs. already approved drug; reconcile spelling errorls (e.g., hidroxicloroquin; abidol)
- Five general categories: Placebo (69), Antiviral (54), Experimental (29), Repurposed (201), Biologic (50)
- Twenty-one "specific" categories: HCQ (76/23), CQ (11), Azithromycin (25/23), -navir (18), Oseltamivir (4), Favipiravir (3), Umifenovir (4), Remdesivir (7), -tinib (10), RAS drugs (12), NSAIDs (4), Steroid (17), TMPRSS2 (4), Traditional Chinese (5), Colchicine (4), Gases (10), Tocilizumab (15), Anakinra (4), IFN (11), Ig-based (4), Supplements (6)

https://clinicaltrials.gov/ct2/results?cond=COVID-19

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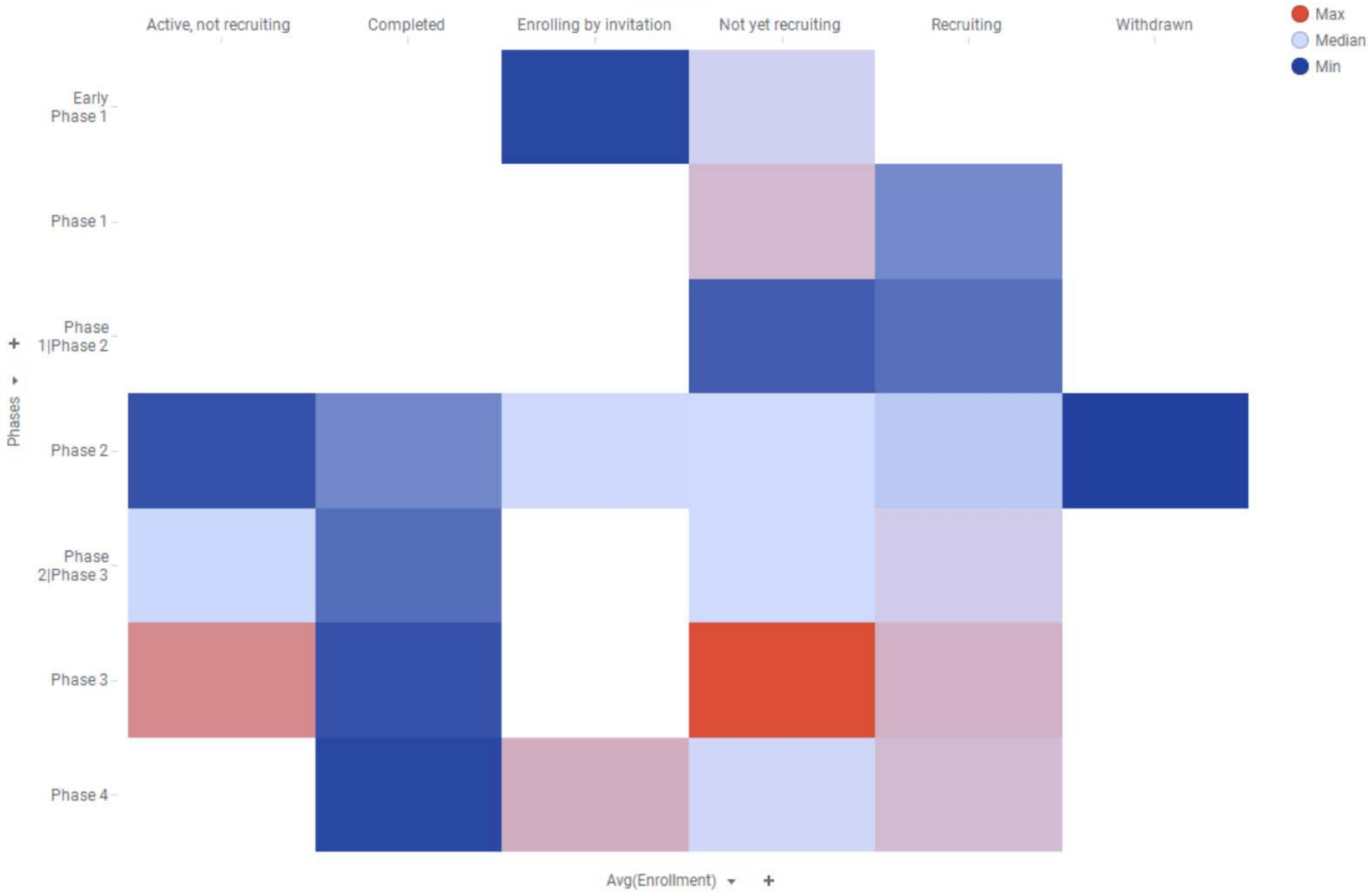
# REPOSITIONING CLINICAL TRIALS: ENROLLMENT




- COVID-19 only
- Filtered out:

Observational studies; "not repurposed" (e.g., experimental); withdrawn; "Phase" N/A, or not applicable).

- Median: 275 patients

https://clinicaltrials.gov/ct2/results?cond=COVID-19

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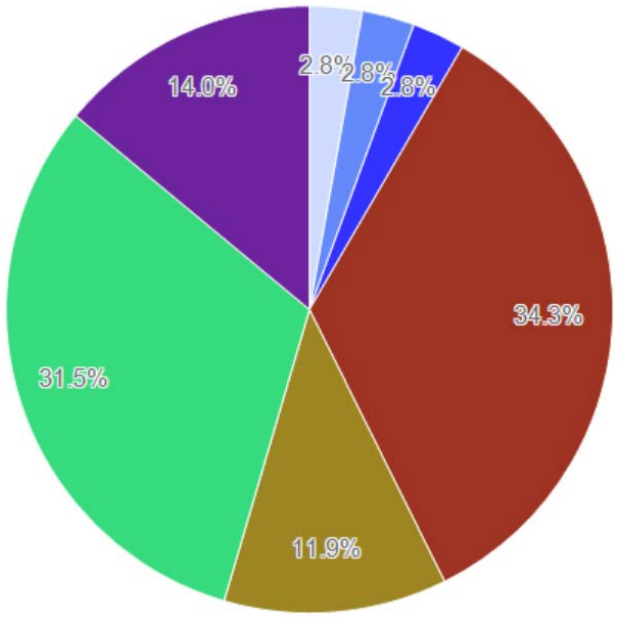
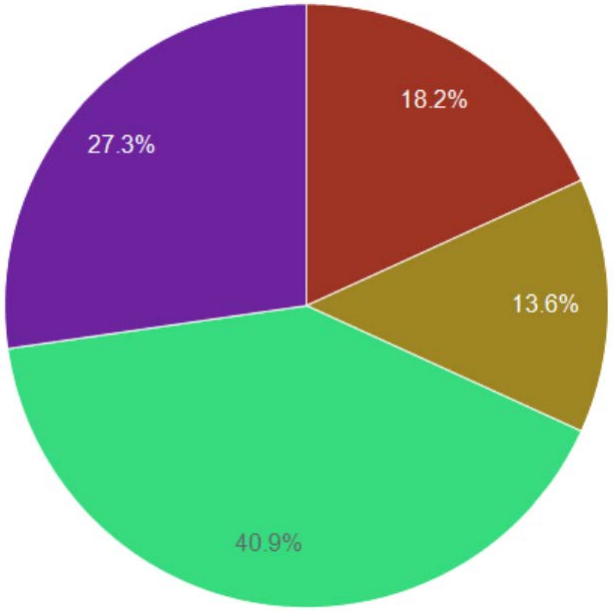
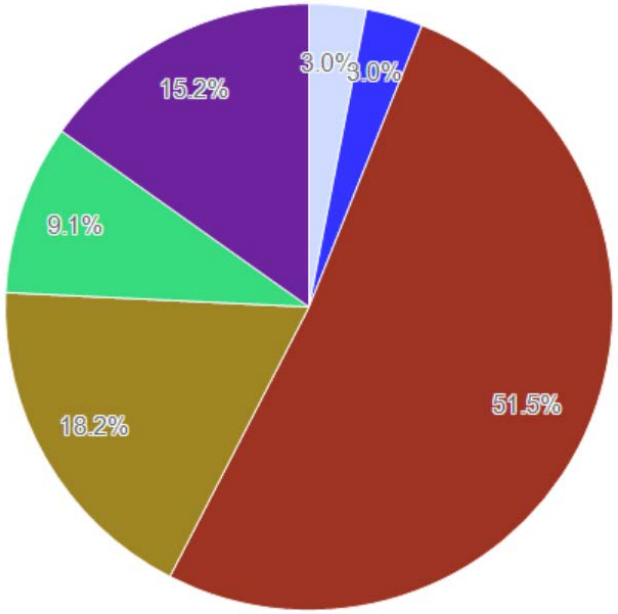
# REPOSITIONING CLINICAL TRIALS: SUMMARY


All repurposed; N = 201




Antiviral; N = 30




Biologics; N = 42

https://clinicaltrials.gov/ct2/results?cond=COVID-19

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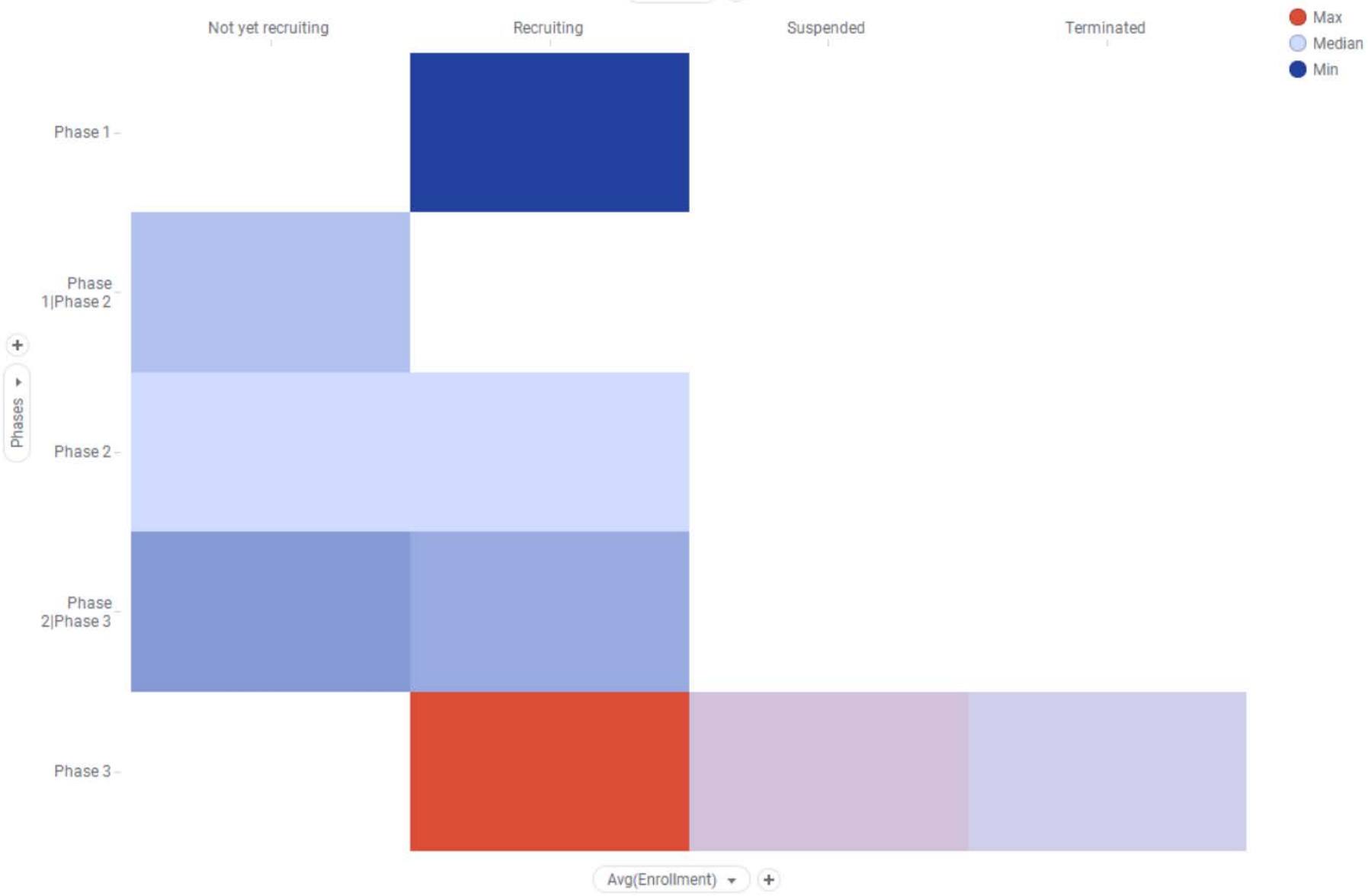
# EXPERIMENTAL CLINICAL TRIALS: ENROLLMENT




- COVID-19 only
- Filtered out: Observational studies; "not repurposed" (e.g., experimental); withdrawn; "Phase" N/A, or not applicable).
- Experimental drugs shown.
- Median: 160 patients

https://clinicaltrials.gov/ct2/results?cond=COVID-19

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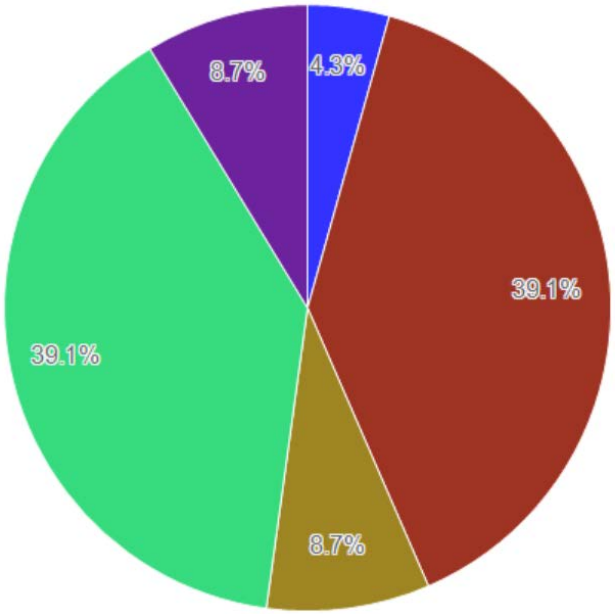
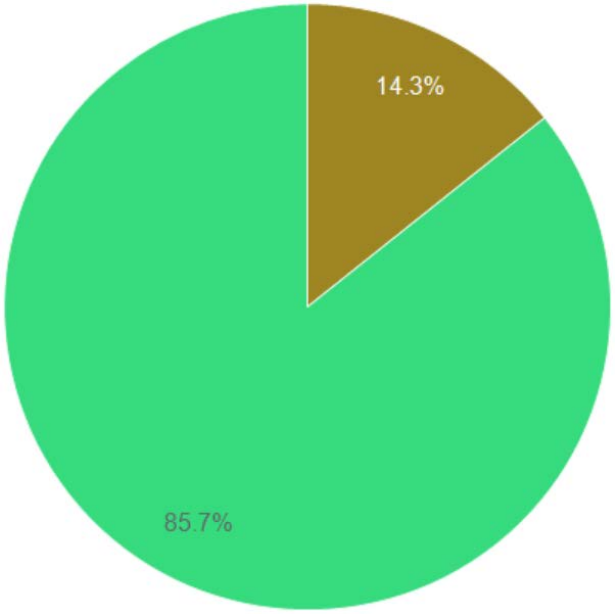
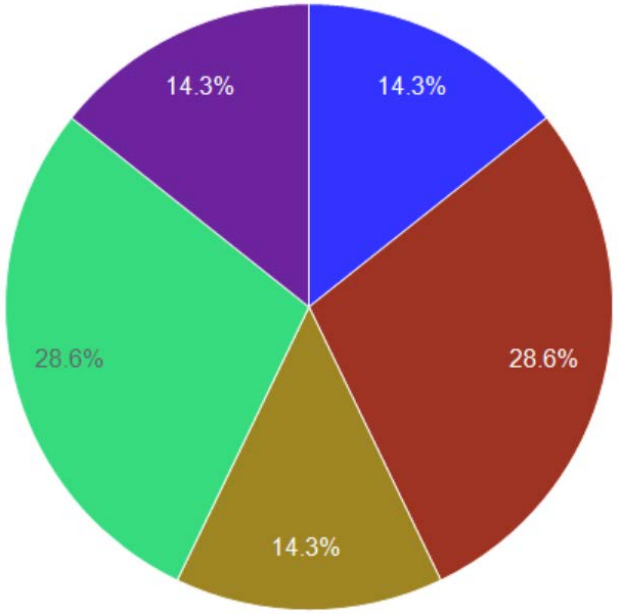
# EXPERIMENTAL CLINICAL TRIALS: SUMMARY




Experimental; N = 22




Remdesivir; N = 7
Strong animal results
2nd CT suspended in China
Most see no benefit




Biologics; N = 6


https://clinicaltrials.gov/ct2/results?cond=COVID-19

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# TAKE HOME MESSAGE

# MOST COVID-19 INTERVENTIONAL CLINICAL TRIALS ARE FOCUSED ON DRUG REPOSITIONING

The majority study HCQ (76 out of 201)



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# HOW MANY DRUGS FOR REPOSITIONING?

| | Drug Product Forms (Patents)* | Drug Products | Type N Drug Products | Drugs (Patents)* | RX Drugs ** |
|---|---|---|---|---|---|
| On-Patent | 12236 (4585) | 1057 | 1057 | **785** (738) | 762 |
| Off- Patent | 22131 | 11874 | 1906 | **1454** | 1404 |
| Discontinued | 16963 | 11388 | 2801 | **680**^ | n.a. |
| All Drugs | 51330 | 22362 | 5042 | 2557 | 1828 (1258) |

- Analysis based on the archived OrangeBook (2016 – 2019) and the latest **Orange Book Data Files** (*OBDFs*; EOBZIP_2019_10.zip content current as of: 10/18/2019) combined with the lists of **Newly Added Patents and Delisted Patents**
  - * Number of Patents; ** Number of RX drugs as single ingredient; ^ **1833** total, only **680** discontinued
    - Drug Product Forms = # of PIDs (all drug forms, routes, strengths etc)
    - Drug Products = # of Application Numbers
    - Type "N" Drug Products = # of Application Numbers of type "N". i.e., NDA (new drug application). The rest of the Drug products are "ANDA", i.e., abbreviated new drug applications.
    - Drugs = # of (active) ingredients, i.e., actual drug (includes combinations)
    - RX Drugs = # of drugs on prescription. The rest of the drugs are OTCs.
- Up to **1772 active ingredients** may be eligible for "off patent" repurposing

S. Avram & T. Oprea, *unpublished.*

12/04/19 revision

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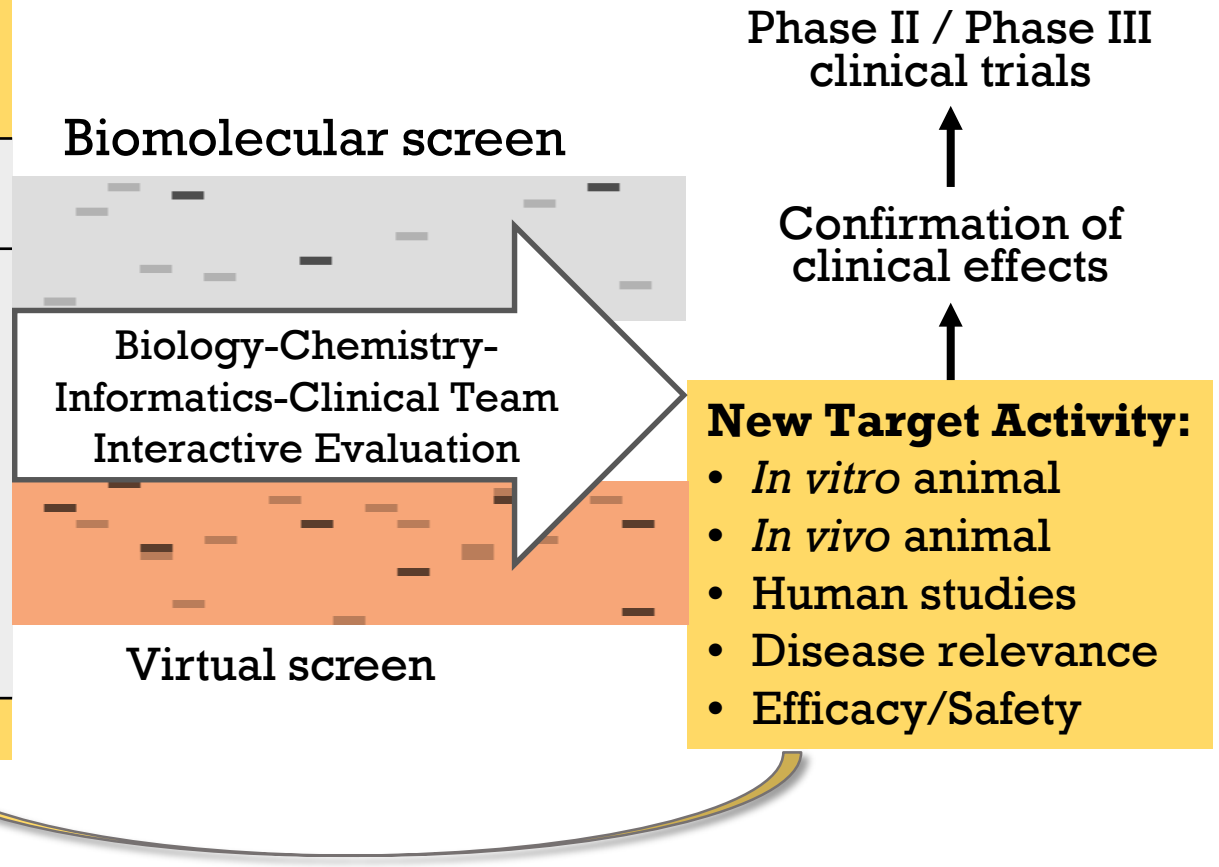
# DRUG REPOSITIONING INTELLIGENCE

## Algorithmic Evaluation of Drug Repositioning Opportunities

| Physico-Chemical Characteristics | Target & Ligand Based Virtual Screening | Disease-Target-Drug Associations |
|---|---|---|
| Chemical fingerprints, chemotypes, derivative chemical descriptors | Shape & electrostatics derived similarity or complementarity | Disease & Drug target GO Annotations from STRING, GO, KEGG, other sources |
| Solubility, Permeability, Distribution, relevant PK properties | 3D models for intended targets, followed by molecular docking | Contigency Tables, e.g., Fisher test for associations *augmented via AI/ML* |
| Metabolism, efflux transporters, toxicity end-points | Multiple tautomers / protomers / conformers / binding modes per protein | *Prioritize novel disease-target associations for off-patent drugs* |

**Iteratively** Compare, Integrate, Cross-check, Prioritize, Evaluate




*Implement exact annotations for drug indications and off label uses.*
*Mandate rigorous validation for computational models.*
*Support community-based therapy-area specific research.*

Turn DR into an international effort, preferably focused on diseases that lack cure

Oprea TI & Overington JP, *Assay Drug Dev Technol*. **2015** 13:299-306 link

12/04/19 revision

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# DATA SOURCES AND METHODS

- Krogan et al., preprint (cleaned-up by Lars Jensen, PhD)
- P-HIPSTER predictions
- Metapath/XGBoost AIML predictions
- STRING analysis (StringApp, Cytoscape)
- SmartGraph



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# SARS-COV-2 INTERACTOME: TCLIN/TCHEM

- **Tclin**
- There are 169 significant (Fold change above 10) between 23 viral and 56 human proteins. Some occur multiple times, and are likely to be crucial in the way the virus subverts intracellular machinery.
- These are currently evaluated for potential repurposing.
- **Tchem**
- The Spike protein only had one significant (Fold change above 10) Tclin target, so we added 8 Tchem proteins for Spike and 6 for E-protein.
- Looking for drugs hitting these targets as well.

- *Note:* Giovanni Bocci is virtually screening viral targets for drug repositioning, and Cristian Bologa is virtually screening human targets for repositioning

# TCLIN AND ASSOCIATED DRUGS

| PreyGene | Drug | Test |
|---|---|---|
| **XPO1** | **selinexor** | ++++ |
| IDH2 | enasidenib | +++ |
| GLA | migalastat | ++ |
| IMPDH2 | mycophenolate mofetil | +++ |
| UMPS | oteracil | ++++ |
| FDPS | zoledronic acid | ++++ |
| PSMB2 | bortezomib | ++++ |
| **NDUFA10** | **metformin** | +++++ |
| **NDUFB10** | metformin | |
| **MT-ND1** | metformin | |
| **MT-ND3** | metformin | |
| **MT-ND5** | metformin | |
| DNMT1 | **azacitidine** | +++++ |
| ITGB1 | Natalizumab | ++++ |
| SLC29A1 | Dipyridamole | +++ |
| **CRBN** | **lenalidomide** | +++++ |

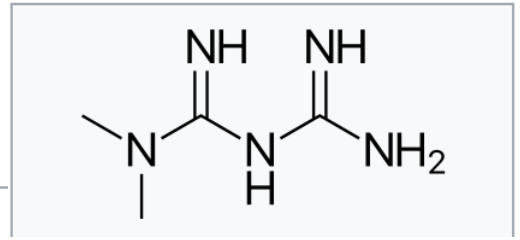
## Moroxydine

From Wikipedia, the free encyclopedia

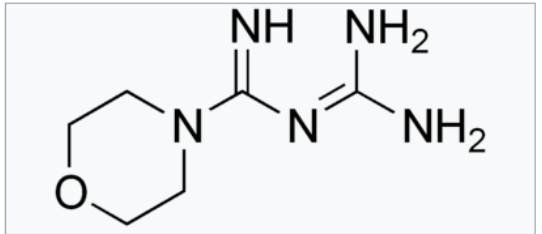
**Moroxydine** is an antiviral drug that was originally developed in the 1950s as an influenza treatment. It has potential applications against a number of RNA and DNA viruses.[1] Structurally moroxydine is a heterocyclic biguanidine.

It was reported in March 2014 that three kindergartens in two provinces of China had been found to be secretly dosing their students with moroxydine hydrochloride to try to prevent them from becoming ill. The kindergartens are paid only for the days that pupils attend and wanted to ensure that they maximised their earnings.[2]

**Metformin**



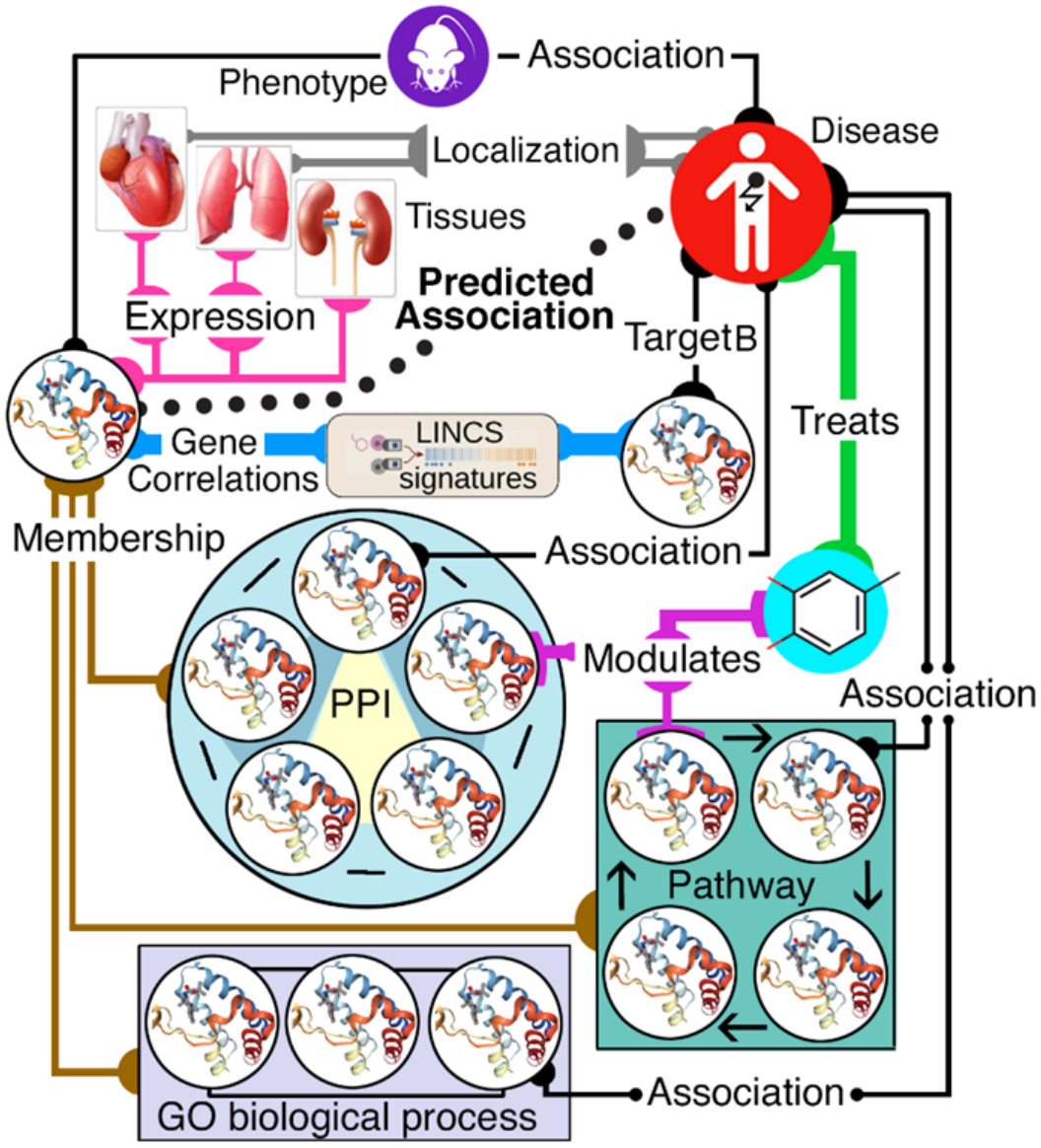

**Moroxydine**




| Names |
|---|
| IUPAC name<br>*N*-(Diaminomethylidene)morpholine-4-carboximidamide |
| Other names<br>Moroxidine |
| **Identifiers** |

Metformin is remarkably similar to moroxydine.
From Krogan et al data, metformin targets ~20 proteins. Other potential mechanisms of action to be explored (based on the summary Table).

# PROTEIN KNOWLEDGE GRAPHS






- IDG KMC2 seeks knowledge gaps across the five branches of the "knowledge tree":
- Genotype; Phenotype; Interactions & Pathways; Structure & Function; and Expression, respectively.
- We can use biological systems network modeling to infer novel relationships based on available evidence, and infer new "function" and "role in disease" data based on other layers of evidence
- Primary focus on **Tdark** & **Tbio**

O. Ursu, T Oprea et al., IDG2 KMC

2/1/18 revision

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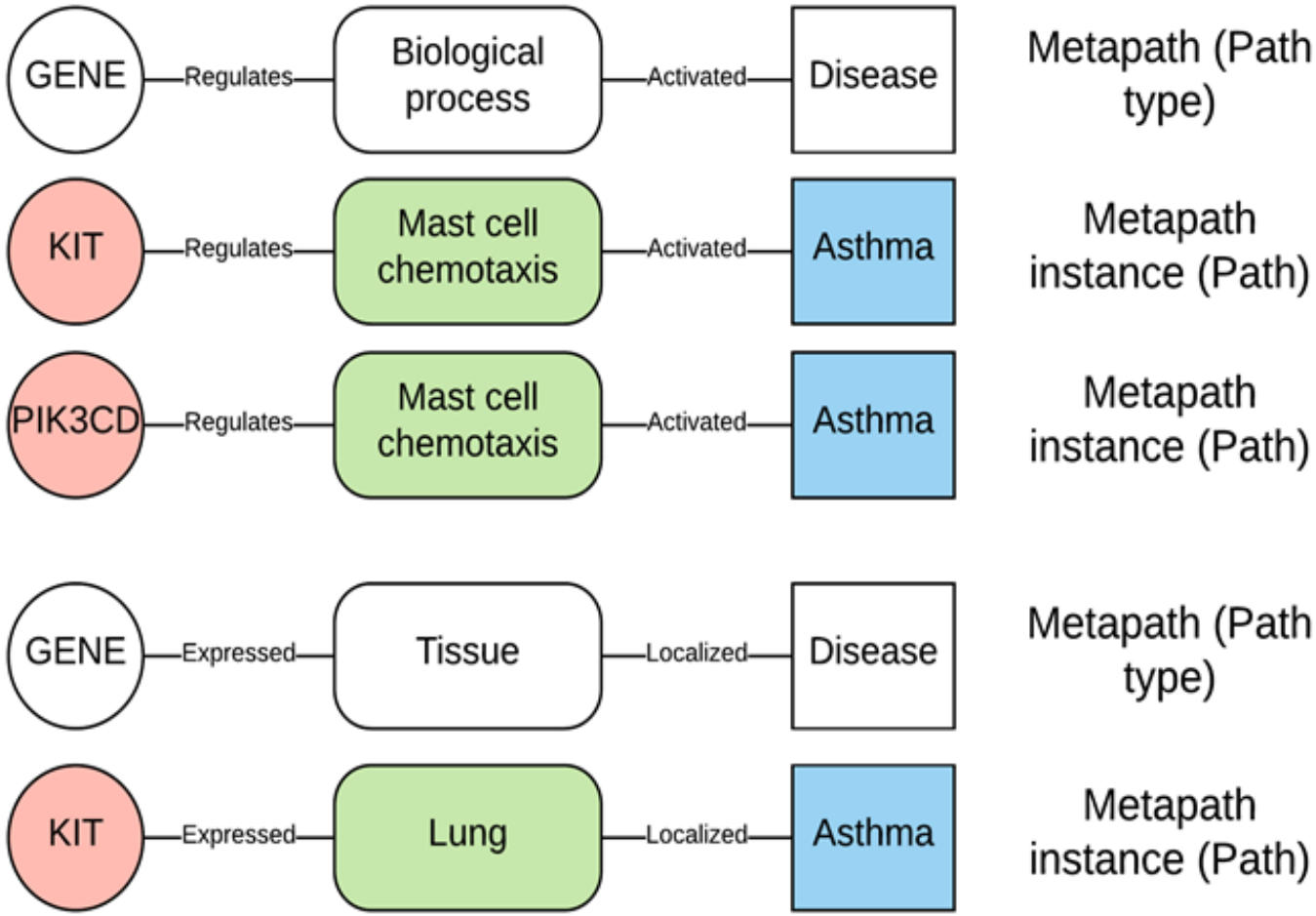
# THE METAPATH APPROACH




- a *meta-path* is a path consisting of a sequence of relations defined between different object types (*i.e.*, structural paths at the meta level)
- Our metapaths encode type-specific network topology between the source node (e.g., Protein) and the destination node (e.g., Disease).
- This approach enables the trans-formation of assertions/evidence chains of heterogeneous biological data types into a ML ready format.

Similar assertions or evidence form metapaths (white).
Instances of metapath (paths) are used to determine the strength of the evidence linking a gene to disease/phenotype/function.

G. Fu et al., *BMC Bioinformatics* **2016**, 17:160 is an early example for drug discovery



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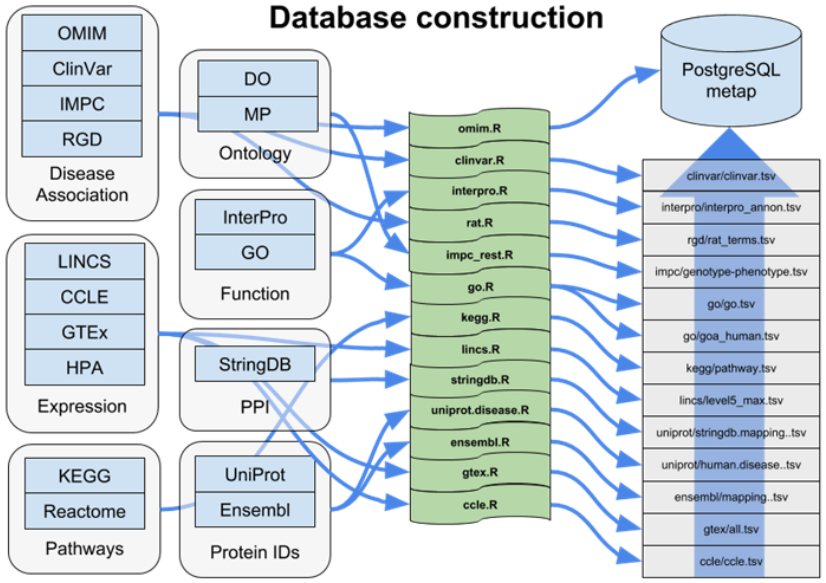
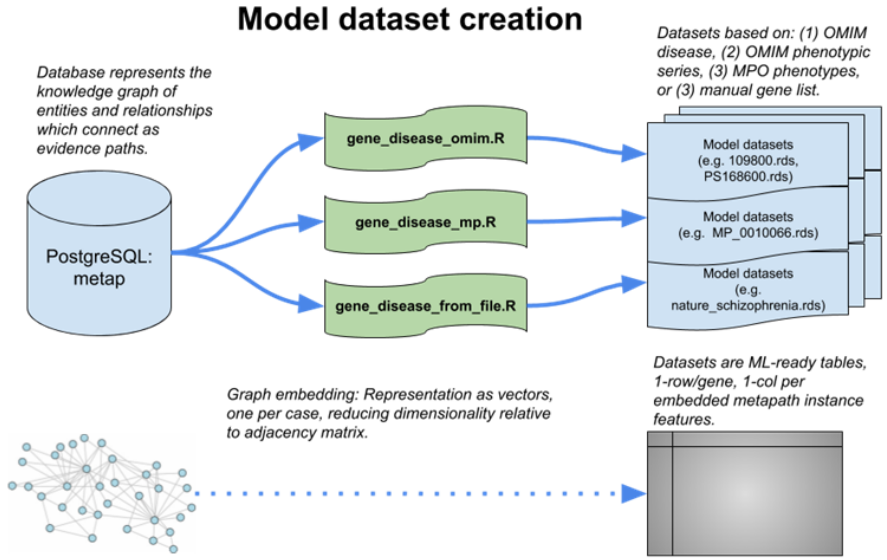
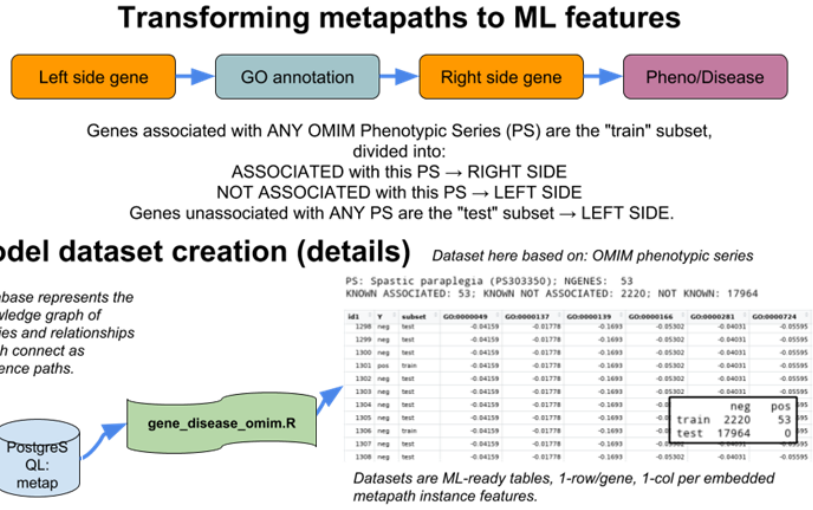
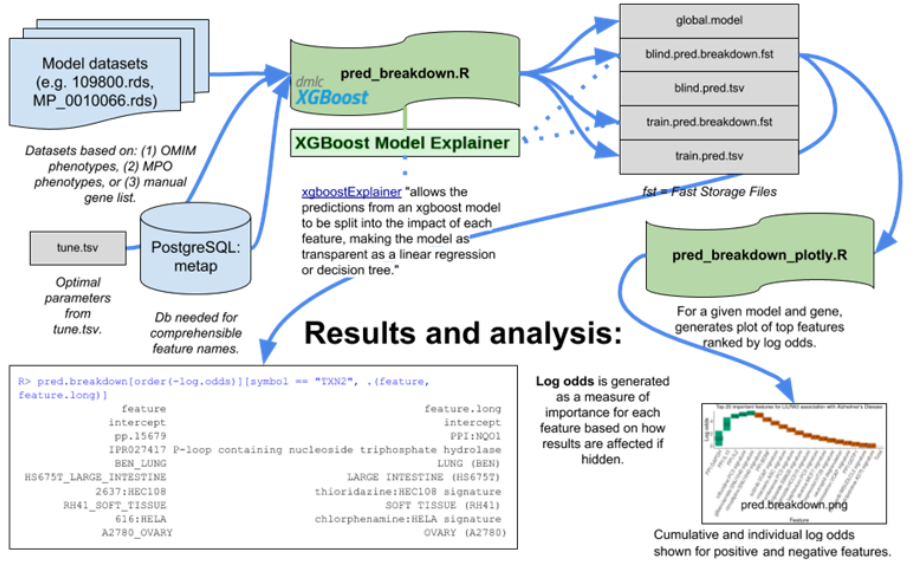
# METAPATH/XGBOOST ML WORKFLOW




All datasets are merged, via R scripts, into a PostgreSQL. Python under development.

Graph embedding transforms evidence paths into vectors, converting data into matrices.

Input genes are positive labels. OMIM (not input) are negative labels (we prefer *true negatives* where possible).

XGBoost runs 100 models. The "median model" (AUC, F1) is then selected for analysis and prediction to avoid overfitting.

J.J. Yang, P. Kumar, D. Byrd et al., IDG2 KMC

10/15/19 revision

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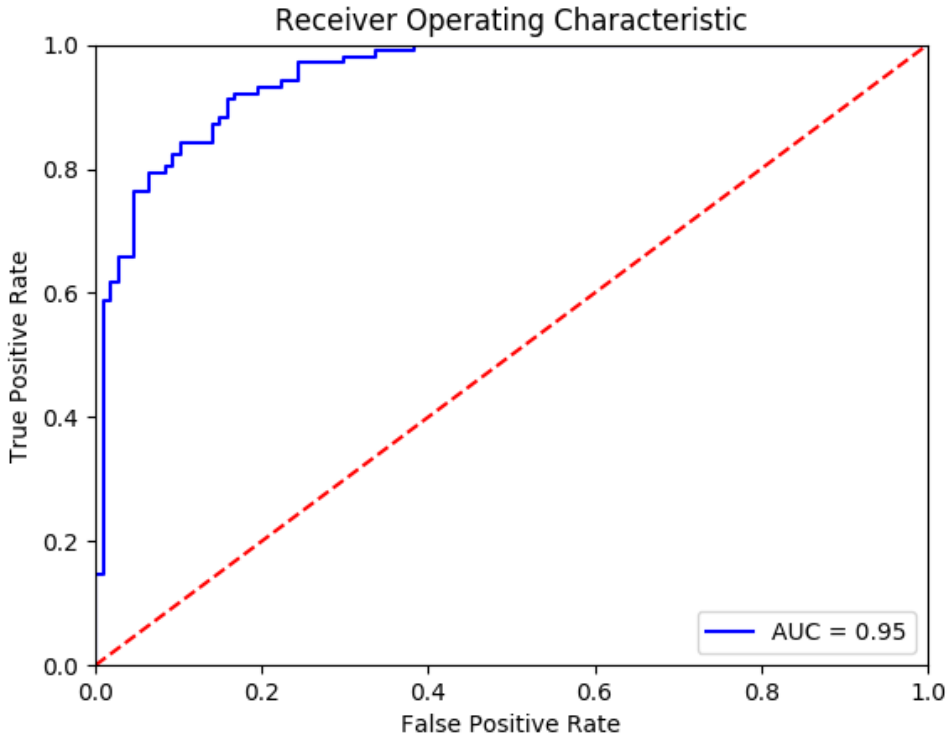
# METAPATH / XGBOOST MODEL INPUT

- P-HIPSTER: ACE2 (experimental) plus 25 other predicted proteins
- CD147 (experimental)
- 71 proteins (mass proteomic pull-down, Krogan et al paper)
- Total 98 positives
- Another 120 negatives from the Krogan paper
- 6 models built, based on variations of this input

# METAPATH / XGBOOST MODEL OUTPUT

- 986 proteins were predicted with "high confidence" by the 6 models
- 136 are predicted by 3 or more models.
- 99 of the 3x predicted proteins were Tbio/Tchem/Tclin
- These were used in combination with the input proteins plus the viral proteins from Krogan et al to examine the network models.



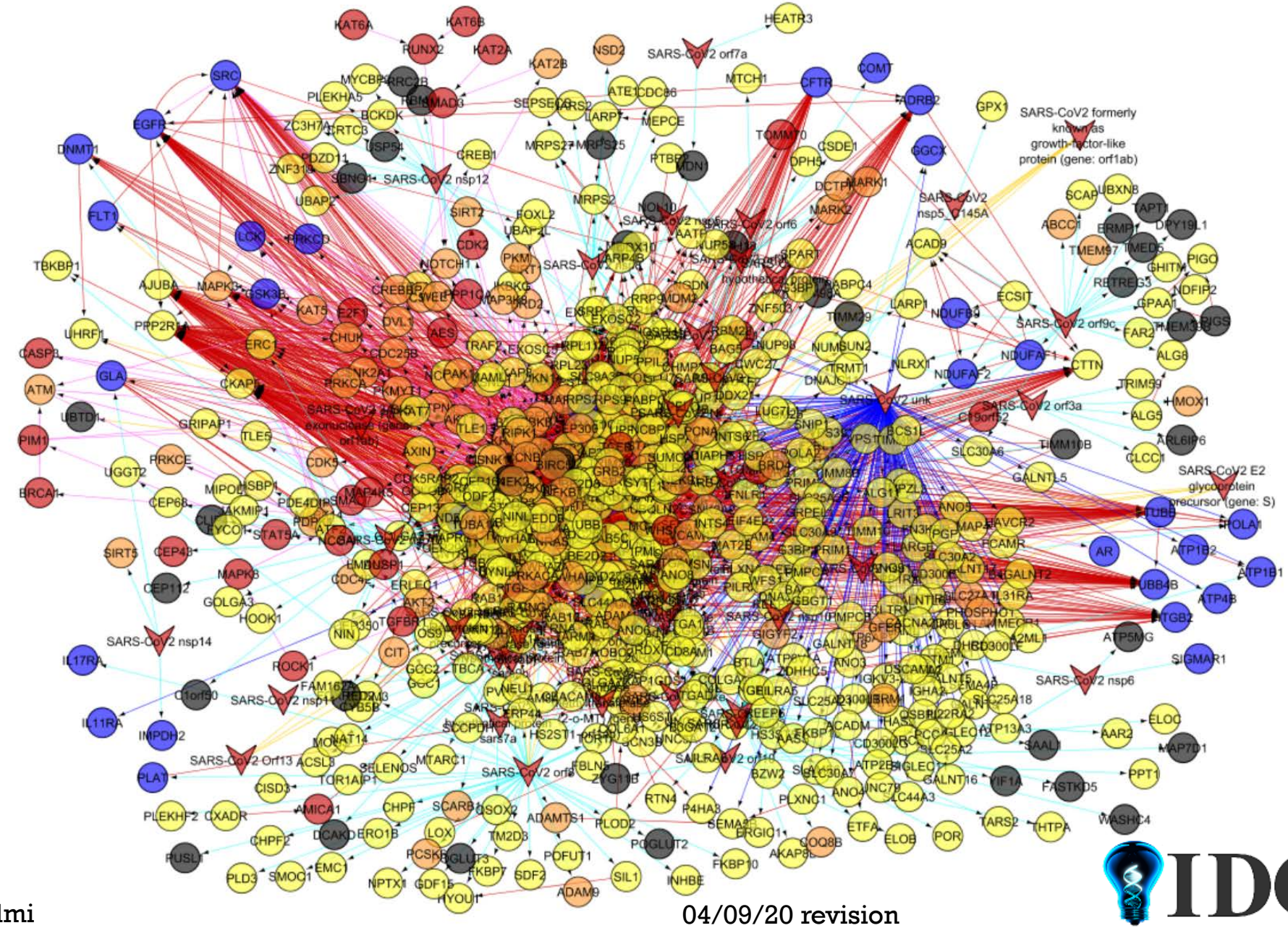

| | |
|---|---|
| Tbio | |
| Tchem | |
| Tclin | |

# SARS-COV-2 HUMAN PROTEIN INTERACTOME

SARS-CoV-2 proteins interact with multiple Tclin targets (blue).

*Less priority given to ATP- and tubulin- type related targets.*

*Exploration in progress…*




| | |
|---|---|
| Tbio | |
| Tchem | |
| Tclin | |
| human | ○ |
| virus | ⩛ |

Analysis by Gergely Zahoranszky-Kohalmi

04/09/20 revision

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# EARLY RESULTS

- **HDAC2**
- Interacts with SARS-CoV2 nsp5 and with SARS-CoV2-Spike.
- HDAC inhibitors: *"HDIs have a long history of use in psychiatry and neurology as mood stabilizers and anti-epileptics. More recently they are being investigated as possible treatments for cancers, parasitic and inflammatory diseases."*

- HDACs or HDAC inhibitors can be used to treat viral infections including coronavirus infections:
- https://www.ncbi.nlm.nih.gov/pubmed/?term=28780424
- https://www.ncbi.nlm.nih.gov/pubmed/?term=23807710

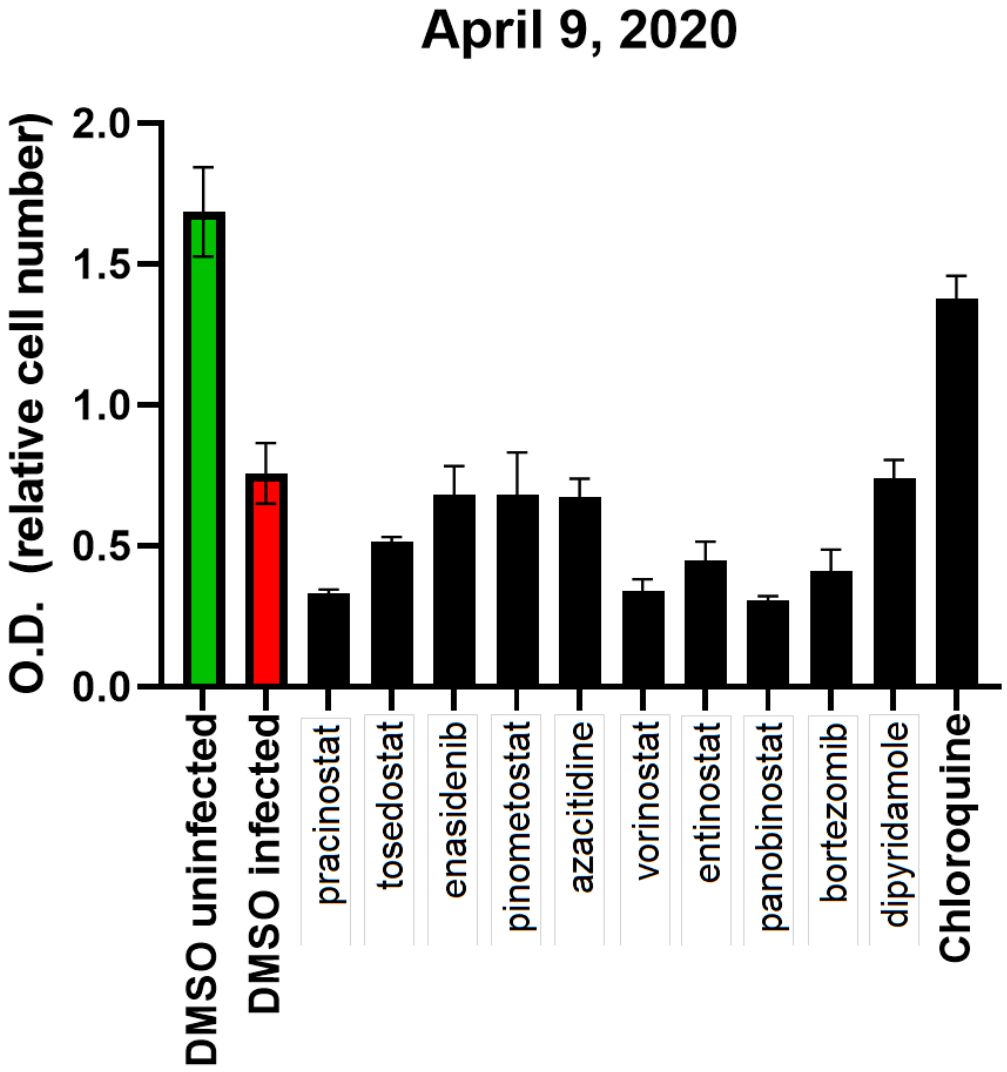
# WAKE UP CALL ON HDAC2

- **From:** Willson, Tim [mailto:tim.willson[at]unc.edu]
  **Sent:** Thursday, March 26, 2020 4:38 PM
  Reference 1 says in its abstract "Surprisingly, the antiviral activity of U18666A was suppressed by the histone deacetylase inhibitor (HDACi), Vorinostat"
- Reference 2 says in the abstract "Not surprisingly, viruses have evolved a wide array of mechanisms to subvert HDAC functions."
- I have not read the papers, but sounds like an HDAC inhibitor is likely to promote replication of the virus

- Viruses appear to HDAC activity so they can initiate their own replication. So the association is real, it just favors viruses. Tim suggested the reverse effect by blocking HATs, histone acetyl transferases.

# INDIRECT(?) CONFIRMATION

- Pracinostat, vorinostat and panobinostat appear to *accelerate* the virus-induced killing process
- Alternatively, these drugs directly kill VEROE6 cells.
- This preliminary finding encourages us to further pursue the histone deacetylase hypothesis

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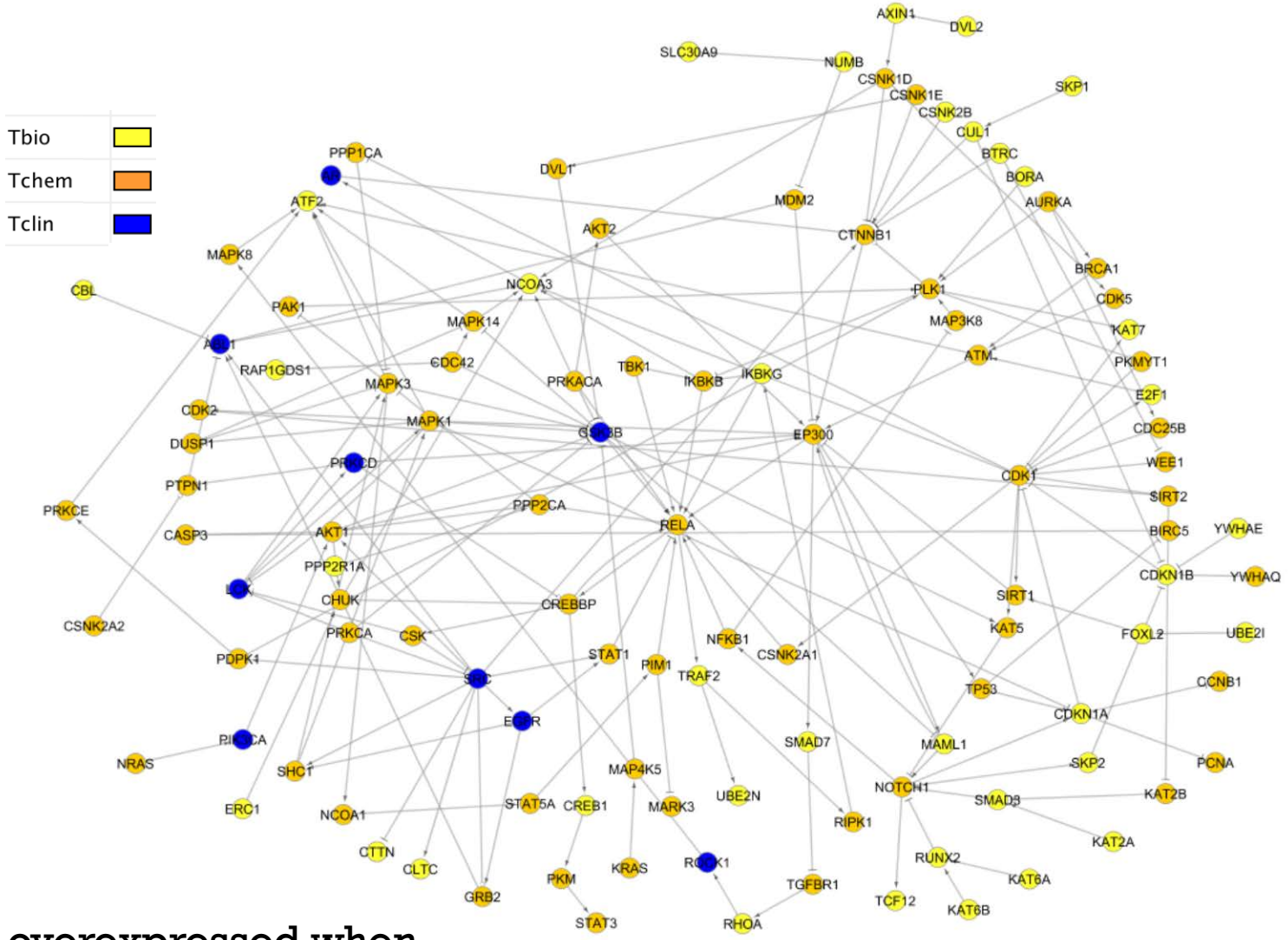
# HATS

| | | |
|---|---|---|
| EP300 | Q09472 | Tchem |
| **HAT1** | O14929 | Tbio |
| KAT2A | Q92830 | Tbio |
| KAT2B | Q92831 | Tchem |
| KAT5 | Q92993 | Tchem |
| KAT6A | Q92794 | Tbio |
| KAT6B | Q8WYB5 | Tbio |
| KAT7 | O95251 | Tbio |
| KAT8 | Q9H7Z6 | Tchem |
| NAA60 | Q9H7X0 | Tbio |
| RBBP7 | Q16576 | Tbio |
| **CREBBP** | Q92793 | Tchem |
| ATF2 | P15336 | Tbio |
| TAF1 | P21675 | Tchem |
| **NAA40** | Q86UY6 | Tbio |
| NCOA1 | Q15788 | Tchem |
| **NCOA3** | Q9Y6Q9 | Tbio |

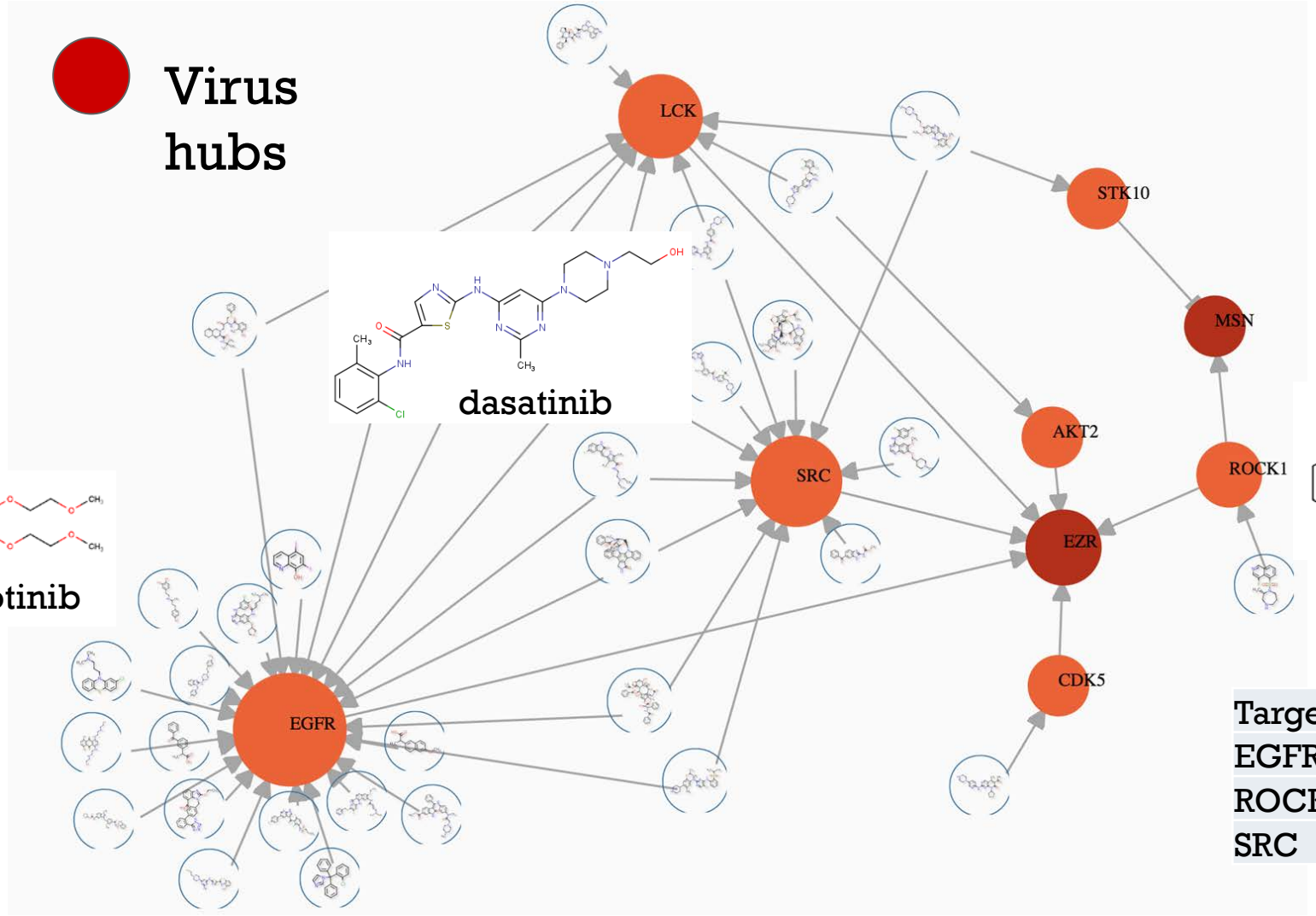



- One of the HATs, RBBP7, is consistently overexpressed when interacting w/ SARS-CoV2. Two others, HAT1 and NAA40, are relatively under-expressed (data from Krogan et al)
- No other HATs are on the list.
- Graph (right): "chemicalizing" the HATs network using SmartGraph

SmartGraph Analysis by Gergely Zahoranszky-Kohalmi

04/02/20 revision

# DRUG-TARGET INTERACTIOME MODULATING HATs




Tclin end-nodes that may modulate HAT function

*Exploration in progress…*

| Target | Drug | Test |
|---|---|---|
| EGFR | erlotinib | ++++ |
| ROCK1 | fasudil | +++ |
| SRC | dasatinib | ++++ |

SmartGraph Analysis by Gergely Zahoranszky-Kohalmi

04/09/20 revision

# VIRTUAL SCREENING AGAINST SARS-COV-2 VIRAL TARGETS

| No. | Name | Pocket | Type | Priority |
|---|---|---|---|---|
| 1 | chloroquine | | active ligand | 1 |
| 2 | remdesivir (pro-drug) | | active ligand | 1 |
| 3 | 2-O-MTase | 4A | binding site | 1 |
| 4 | 3CLpro | 1B | binding site | 1 |
| 5 | 3CLpro | 2AB | binding site | 1 |
| 6 | 3CLpro | 3AB | binding site | 1 |
| 7 | Helicase | 9B | binding site | 1 |
| 8 | Helicase | 10B | binding site | 1 |
| 9 | Helicase | 18B | binding site | 1 |
| 10 | N7-MTase | 13D | binding site | 1 |
| 11 | RdRp | 6A | binding site | 1 |
| 12 | RdRp | 17A | binding site | 1 |
| 13 | remdesivir triphosphate | 5A | active ligand | 2 |
| 14 | 2-O-MTase | 5A | binding site | 2 |
| 15 | Helicase | 11B,12B | binding site | 2 |
| 16 | N7-MTase | 14D | binding site | 2 |
| 17 | NendoU | 15A | binding site | 2 |
| 18 | RdRp | 7A | binding site | 2 |
| 19 | RdRp | 8A | binding site | 2 |

| Drug | CMax (uM) | PDB Template |
|---|---|---|
| tegaserod | 0.01 | 5E6J |
| triamterene | 0.33 | 6NUR |
| meloxicam | 5.41 | 5E6J\|6NUR |
| ibuprofen | 295.71 | 5E6J\|6NUR |
| naproxen | 408.24 | 5E6J\|6NUR |
| hydrochlorothiazide | 0.25 | 6NUR |
| baclofen | 0.75 | 5E6J |
| trimethoprim | 4.13 | 5E6J\|6NUR |
| ethambutol | 17.13 | 5E6J\|6NUR |
| cidofovir | 70.20 | 5E6J\|6NUR |
| ixazomib | 0.17 | 5E6J |
| safinamide | 3.31 | 5E6J\|6NUR |
| avibactam | 55.04 | 6NUR |

Start: 3,981 small molecules drugs from DrugCentral. Enumerated tautomeric and protomeric forms available at pH 7.4 with minimum abundance of 25% (total, 6057 structures).
These were *initially* docked into the main SARS-CoV targets (selected drugs on the right):

- 5E6J: SARS Coronavirus Papain-like Protease
- 6NUR: SARS-CoV nsp12 polymerase

*Work in progress*

Work by Giovanni Bocci

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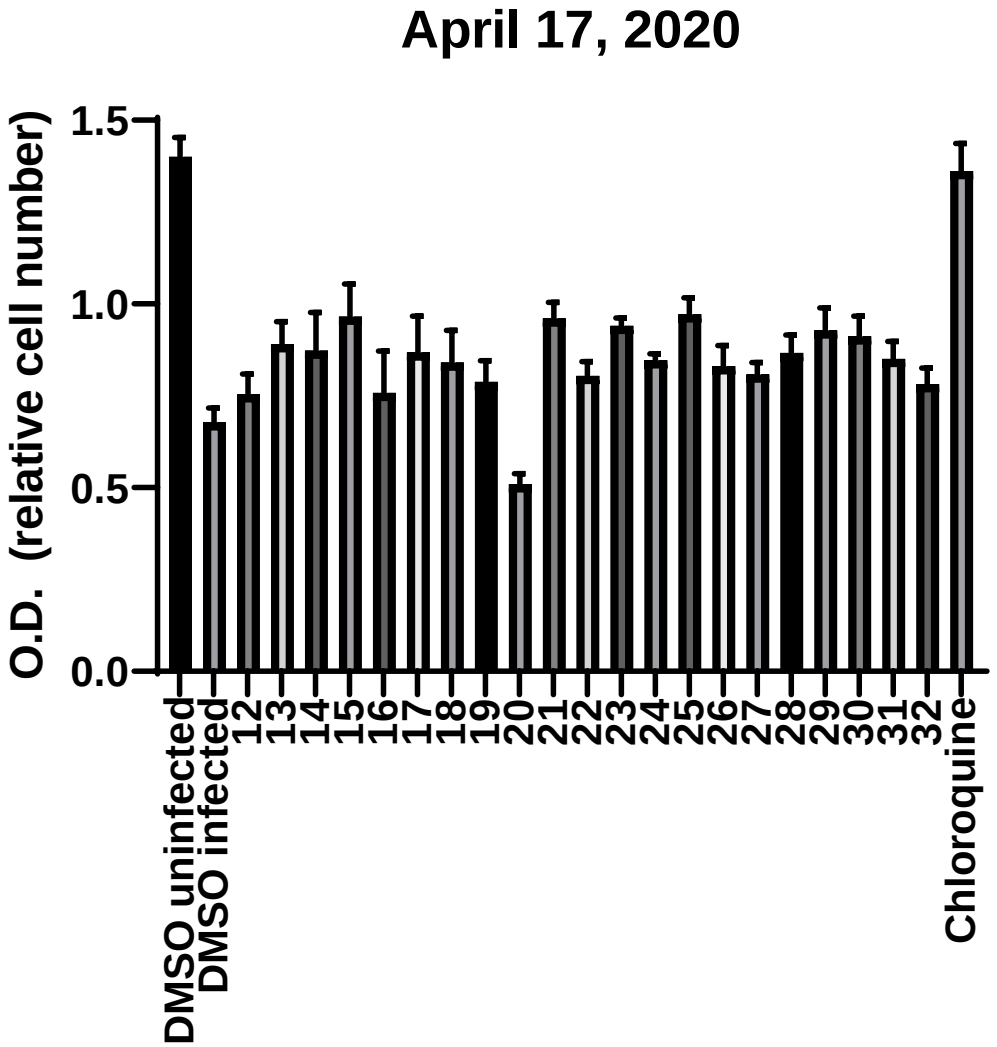
# FURTHER EXPERIMENTAL RESULTS

| Drug Name | Prediction Source | VeroE6 -CoV2 | BDDCS |
|---|---|---|---|
| *Lenalidomide* | MP/XGb | x | 4 |
| *Mycophenolate* | MP/XGb | x | 2 |
| Fasudil HCl | Network | xx | 1 |
| Safinamide Mesylate | SBVS-CoV2 | xx | 2 |
| Meloxicam | SBVS-CoV2 | x | 2 |
| Ibuprofen | SBVS-CoV2 | x | 2 |
| Ethambutol HCl | SBVS-CoV2 | x | 3 |
| Trimethoprim | SBVS-CoV2 | xx | 3 |
| Triamterene | SBVS-CoV2 | x | 2 |




- Currently pursuing further experiments on these drugs, plus experiments on *combinations.*

Experiments by Steven Bradfute

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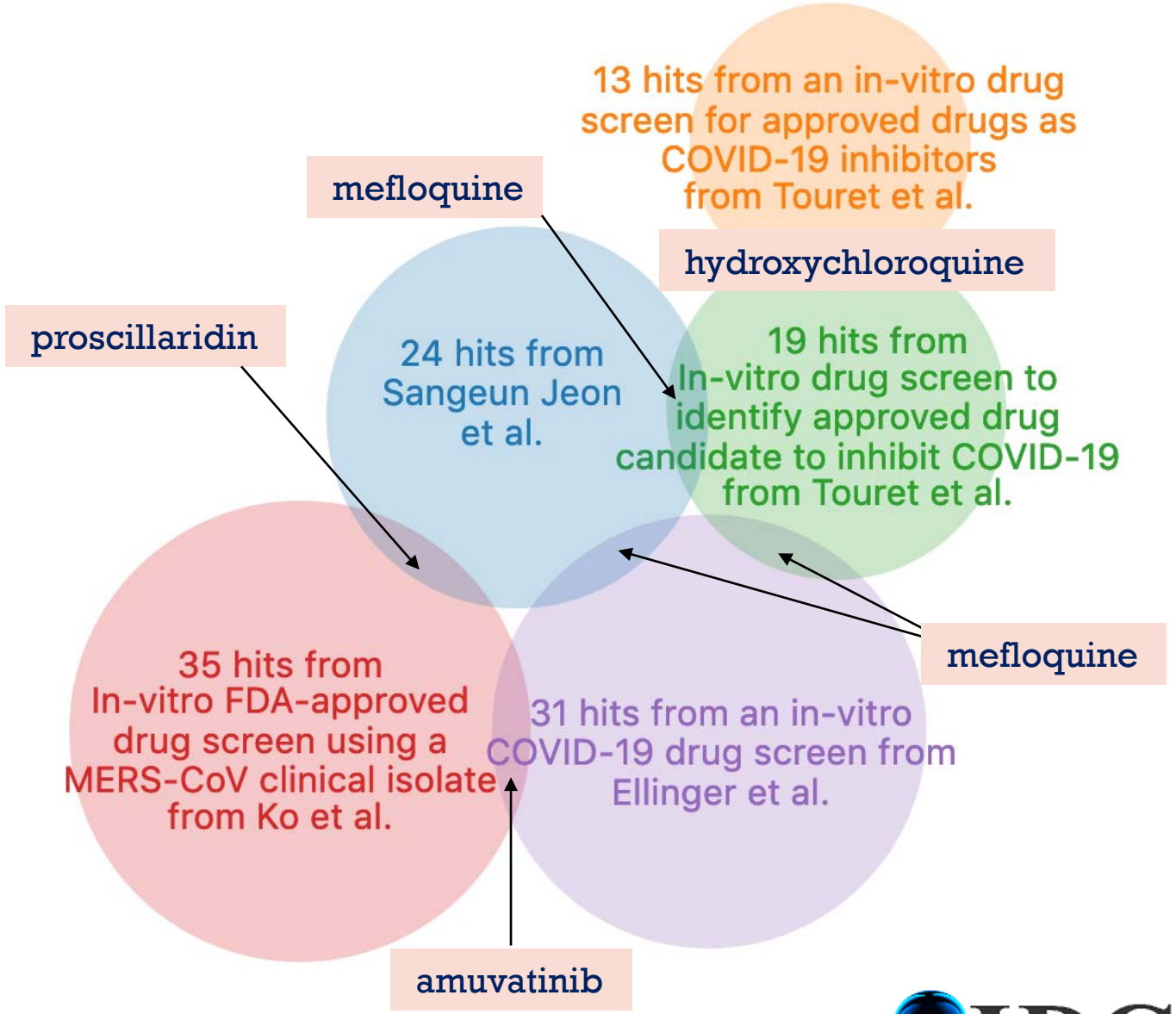
# EXPERIMENTAL CONFIRMATION

- "If you have one clock, you know what time it is. Having two clocks, you can no longer tell time precisely."
- Many experimental papers have been published. The overlap between them is not exactly encouraging.
- Comparing multiple experiments, we start to understand the need for confirmation, the essence of science.
- The combination of computational and experimental screening is more likely to lead to practical therapeutic solutions.




Experimental papers overlap by Avi Ma'ayan

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# TAKE HOME MESSAGE

# DRUG REPOSITIONING FOR COVID-19 IS AN ITERATIVE EXERCISE

Experiments need to inform future experiments
Multiple approaches lead to different drugs

4/23/20 revision

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