UCSF Quantitative Biosciences Institute

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A SARS-CoV-2 Protein Interaction Map Reveals Targets for Drug-Repurposing

QBI Coronavirus Research Group

QCRG

http://qbi.ucsf.edu/COVID-19

Overview

- Created the first-ever blueprint of how SARS-2 hijacks human cells using all 30 viral proteins
- Using this map, uncovered key drug classes with high potential to fight COVID-19
- Identified an over-the-counter medicine that appears to promote infection
- Spurring the initiation of several clinical trials

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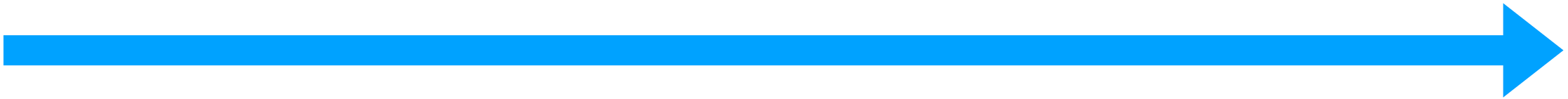
Emergence of Highly Pathogenic Human Coronaviruses: Enveloped, positive-sense single-stranded RNA genome



SARS-CoV	MERS-CoV	SARS-CoV-2
8000 Cases Worldwide	2500 Cases Worldwide	3,190,743 Cases Worldwide
10% Death Rate	36% Death Rate	227,368 Deaths

4/29/20

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***QCRG**:*
A non-profit research group

QCRG Members Across UCSF/MSSM/Institut Pasteur

A SARS-CoV-2 Protein Interaction Map Reveals Targets for Drug-Repurposing

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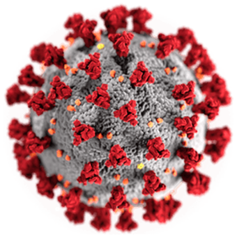
Breakthrough Approach Enables Rapid and Focused Identification of Agents Directed at Proteins Critical for Disease Progression

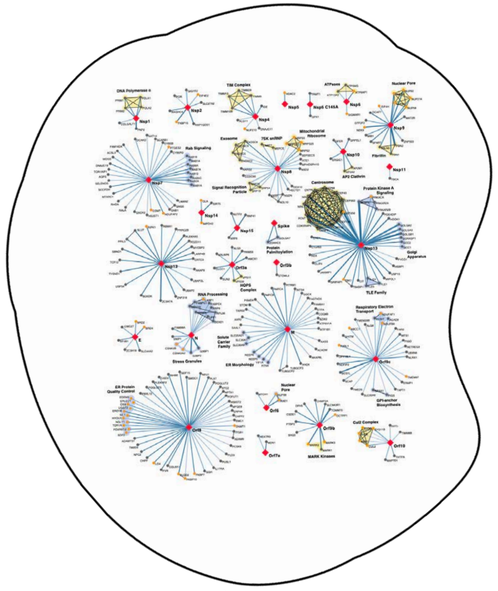
Homes in on most relevant therapeutics; enables prediction of other related but seemingly different types of drugs

SARS-CoV-2



Protein-protein interaction analysis

Virus-host interaction network



Biochemistry & structural analysis

Chemical biology

Bioinformatics

Infection experiments

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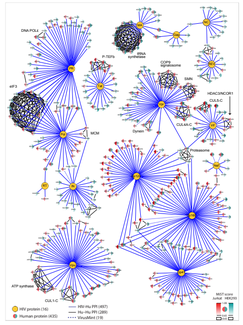
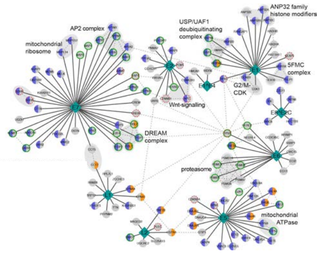
Previous Host-Pathogen Protein-Protein Interaction Networks

Time to completion: 2-3 years/map

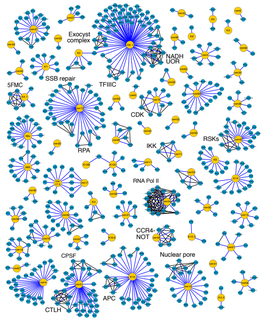
HIV-1
Jäger et al, Nature, 2012



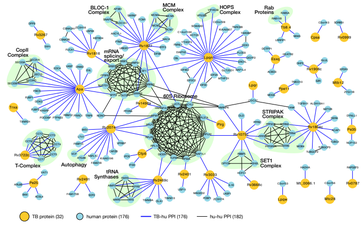
HPV
Eckhardt et al., Cancer Discovery, 2018



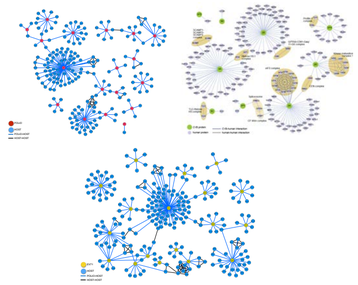
Kaposi Sarcoma's Herpes
Davis et al., Molecular Cell, 2015



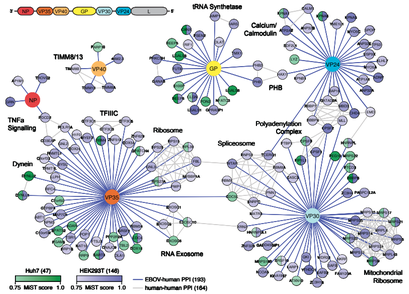
Tuberculosis
Penn et al., Molecular Cell, 2018



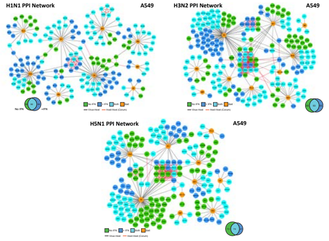
Enteroviruses: Polio vs Cox-B vs EV-71
CVB: Diep et al., Nature Microbiology, 2019



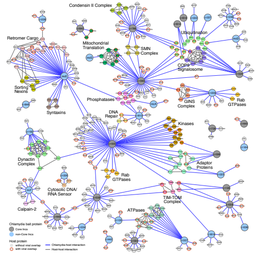
Ebola
Batra et al., Cell, 2018



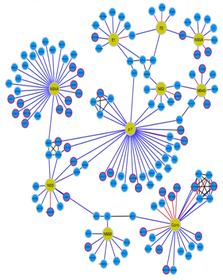
Influenza-A: H1N1 vs H5N1 vs H3N2



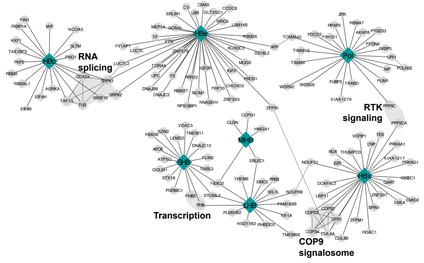
Chlamydia
Mirrashidi et al., Cell Host and Microbe, 2015



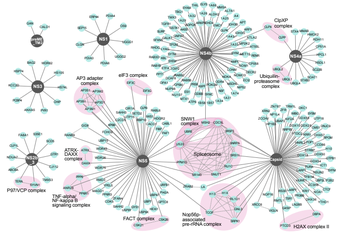
Hepatitis-C
Ramage et al., Molecular Cell, 2015



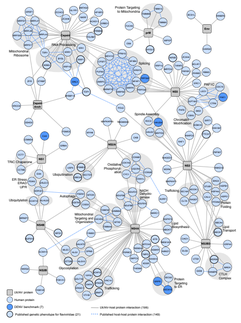
Hepatitis-B



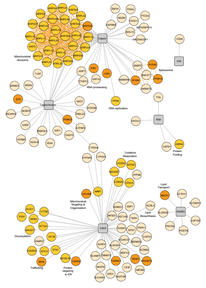
West Nile Virus
Li et al., Nature Microbiology, 2019



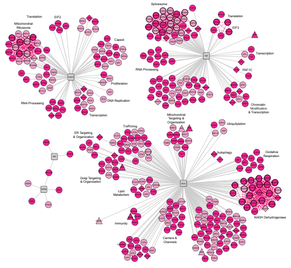
Dengue (human)
Shah et al., Cell, 2018



Dengue (mosquito)
Shah et al., Cell, 2018



Zika
Shah et al., Cell, 2018



SARS-CoV-2 Pandemic Project Timeline

12/31/19 Cluster of 41 Patients Reported to WHO

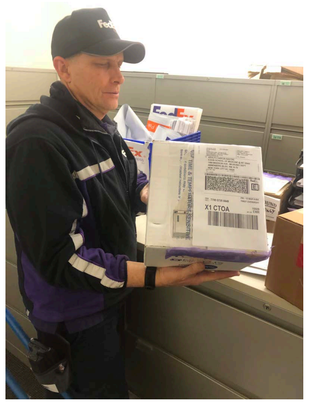
1/7/20 Virus Identified

1/24/20 Cloning of 26/29 ORFs and start of

2/6/20 First Death in US

3/6/20 Draft Host Map

3/12/20 First Drug Candidates Sent to NY/ Paris

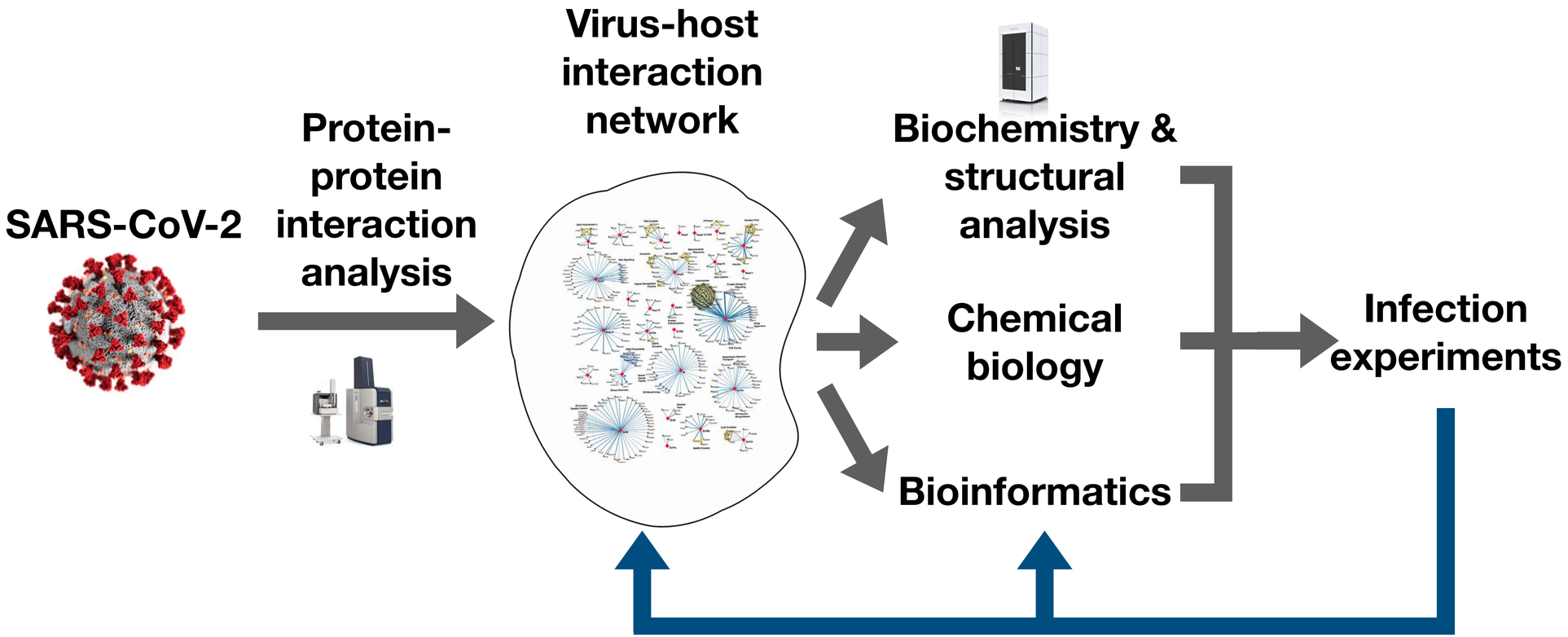


3/17/20 SF Shelter in Place Order—Lab shutdown except SARS-CoV-2 Related Research Projects

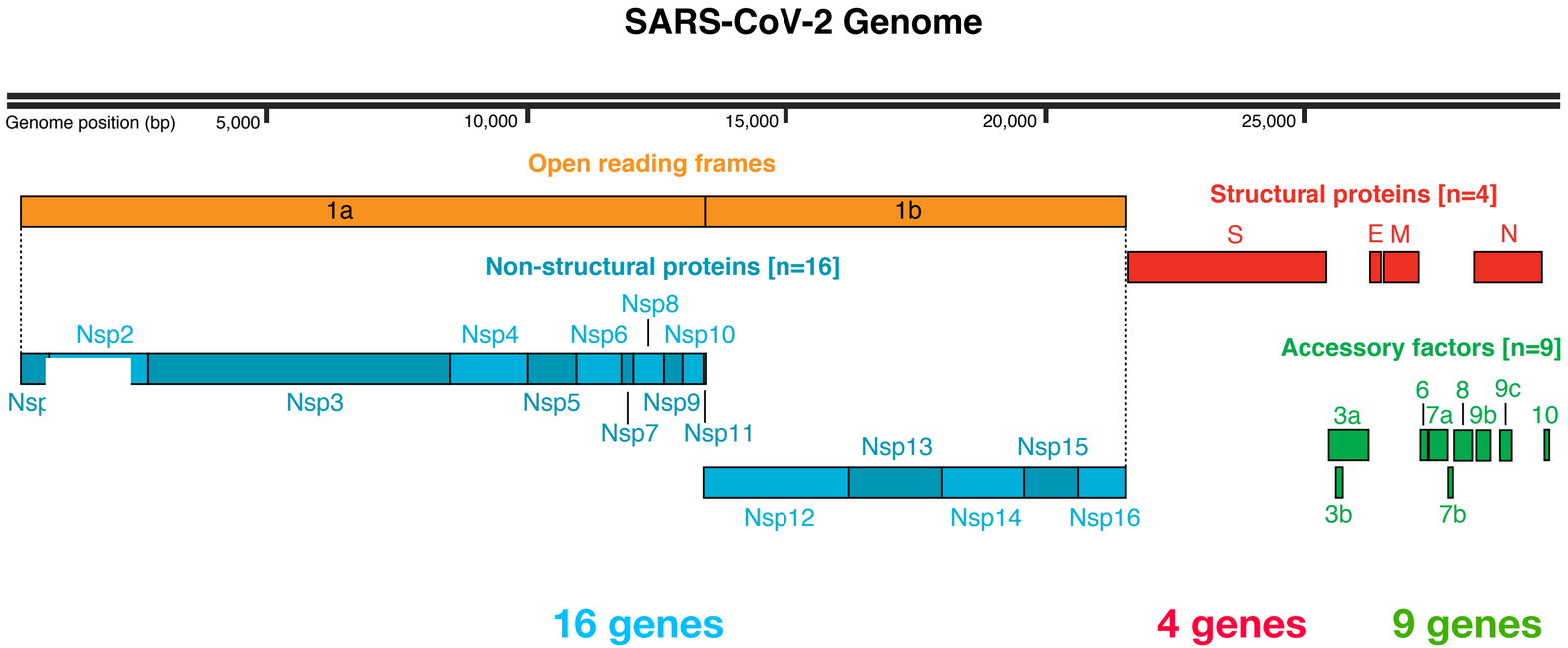
3/22/20 bioRxiv

Expression constructs sent to 300 laboratories in 35 countries.

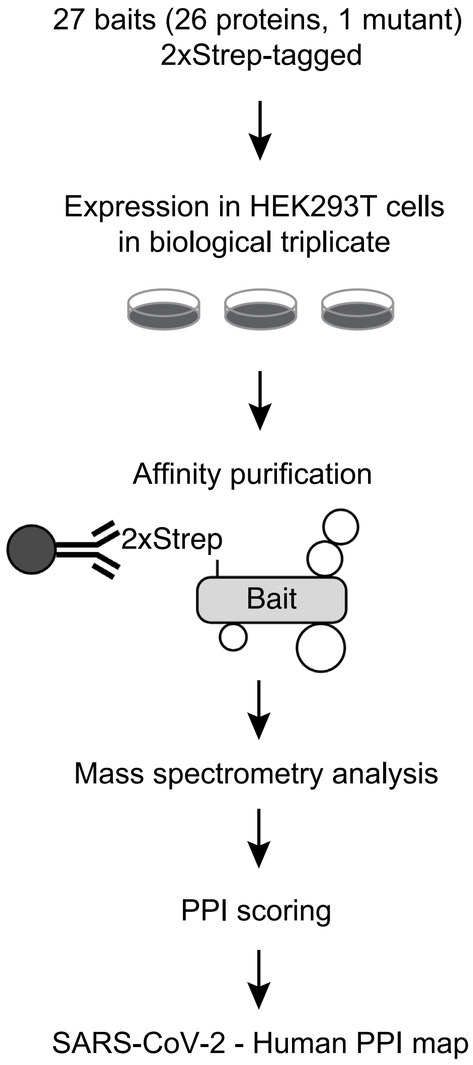
Targeting host factors a therapeutic strategy



Cloning and expression of SARS-CoV-2 proteins

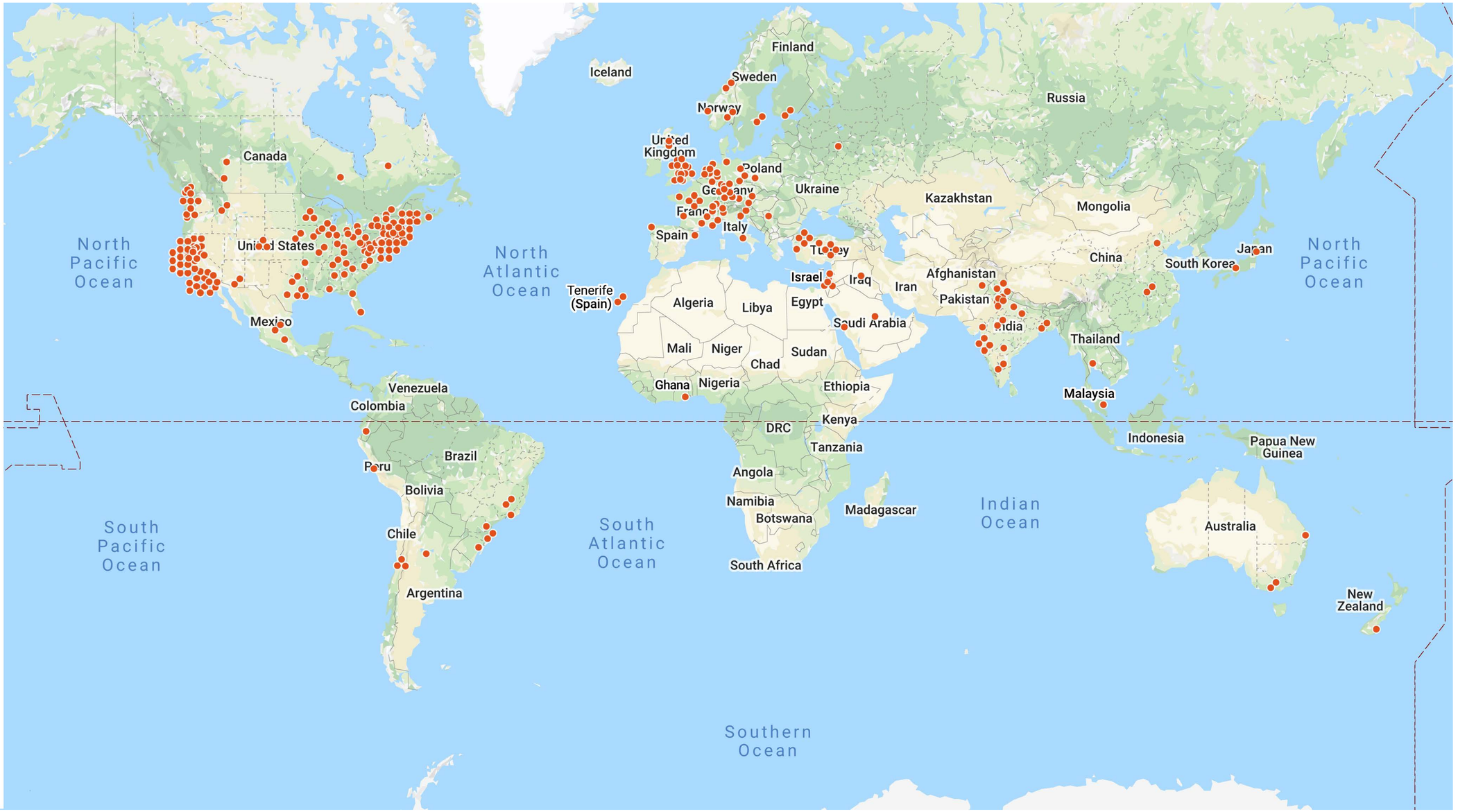


Total: 29 genes

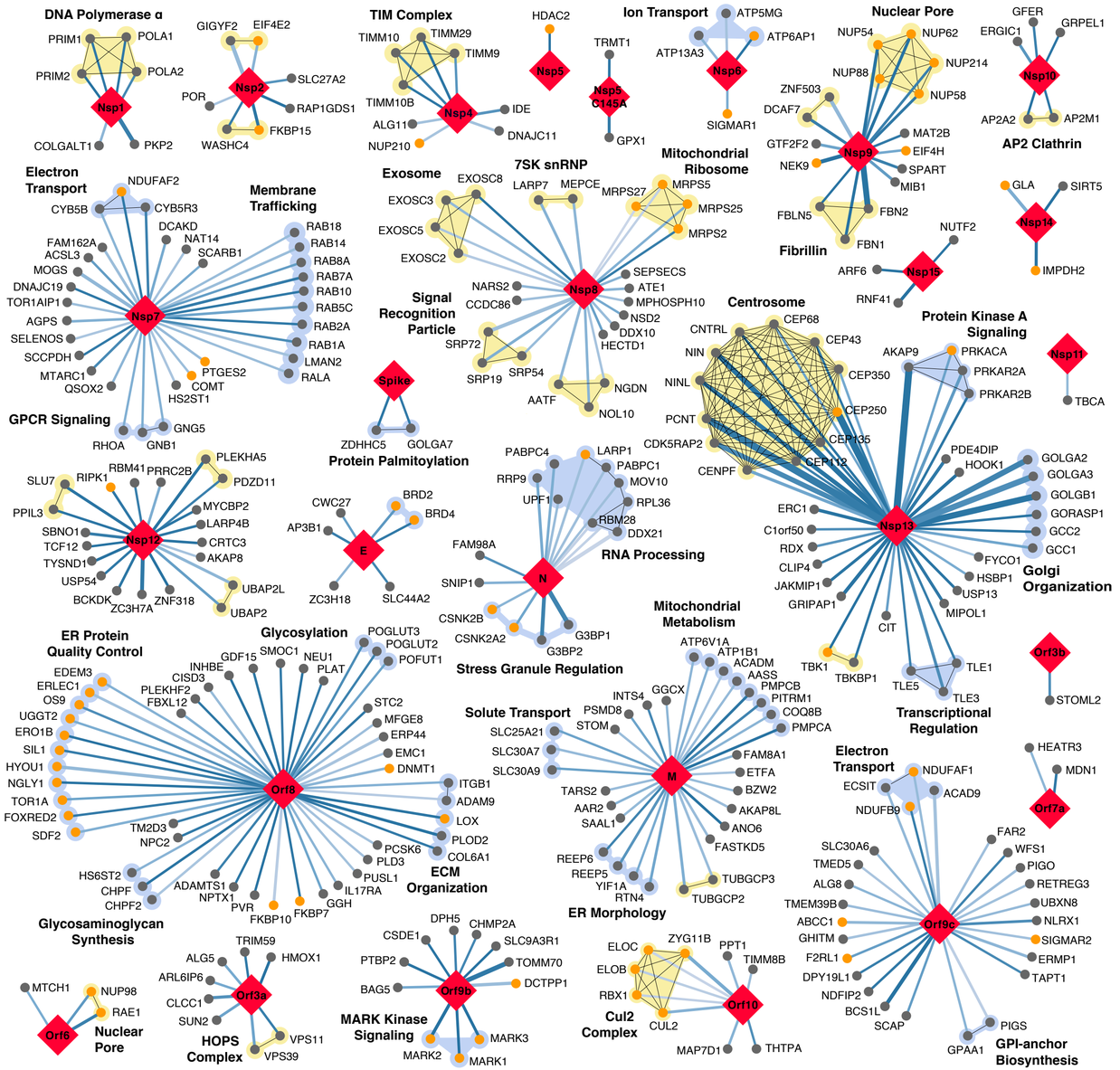


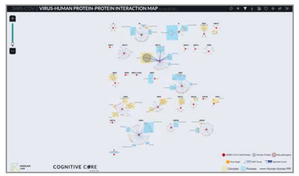
Plasmids to 314 Labs in 38 Countries

Nation	Shipments
Argentina	1
Australia	4
Austria	3
Brazil	7
Canada	12
Chile	3
China	3
Ecuador	1
Finland	2
France	11
Germany	18
Ghana	1
India	22
Iraq	1
Israel	4
Italy	2
Japan	2
Lebanon	1
Malaysia	1
Mexico	3
New Zealand	1
Norway	5
Pakistan	1
Palestine	1
Peru	1
Poland	1
Russia	1
Saudi Arabia	2
Serbia	1
Slovenia	2
Spain	4
Sweden	2
Switzerland	4
Thailand	1
The Netherlands	5
Turkey	10
UK	19
US	155
total	**318**



332 SARS-CoV-2-human PPIs include 69 druggable host factors





ZOIC LABS

https://ppi.zoiclabs.io/#/

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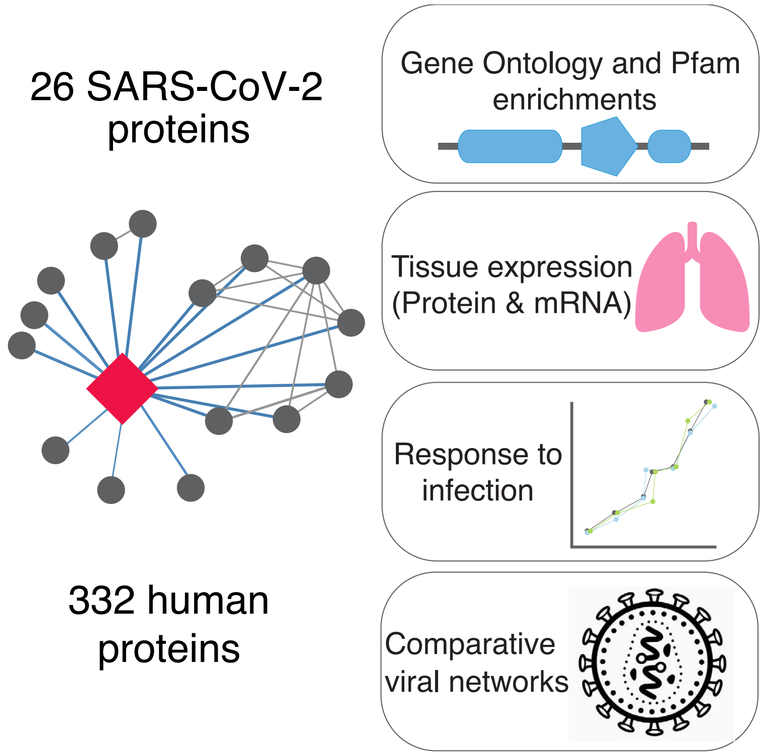
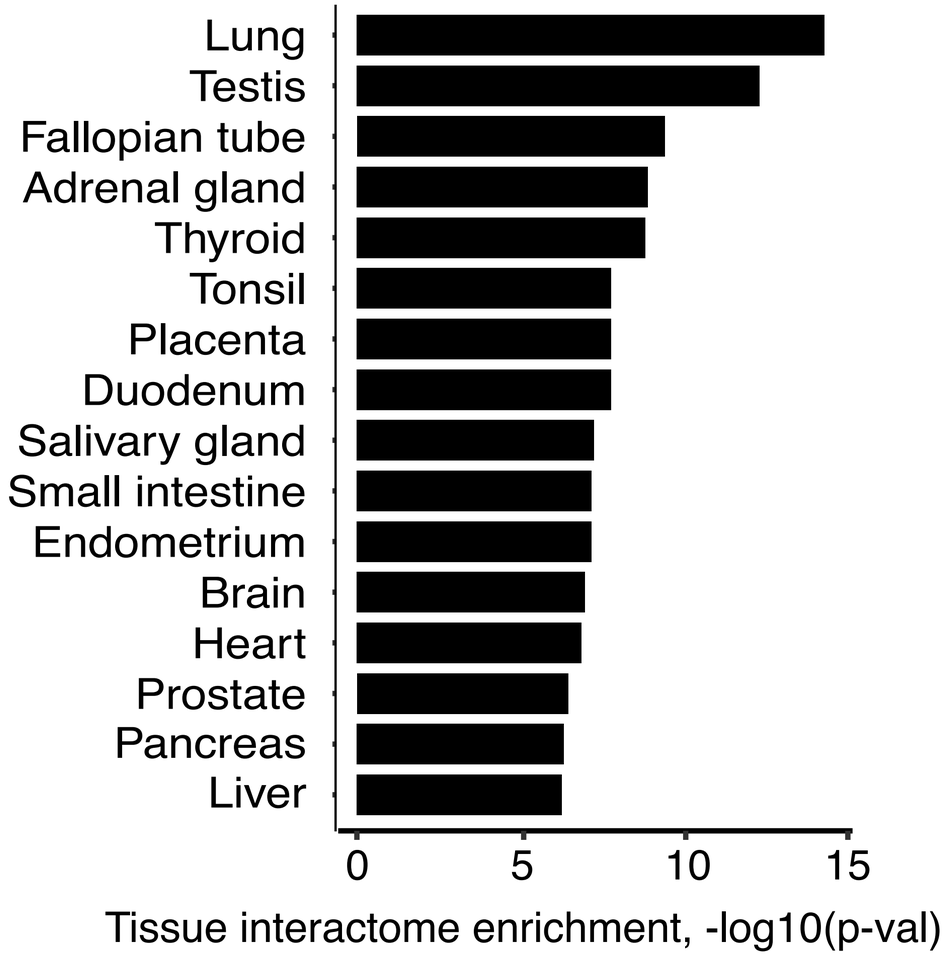
The Host Factor List From HEK293T Cells Show Bias for Lung Expression

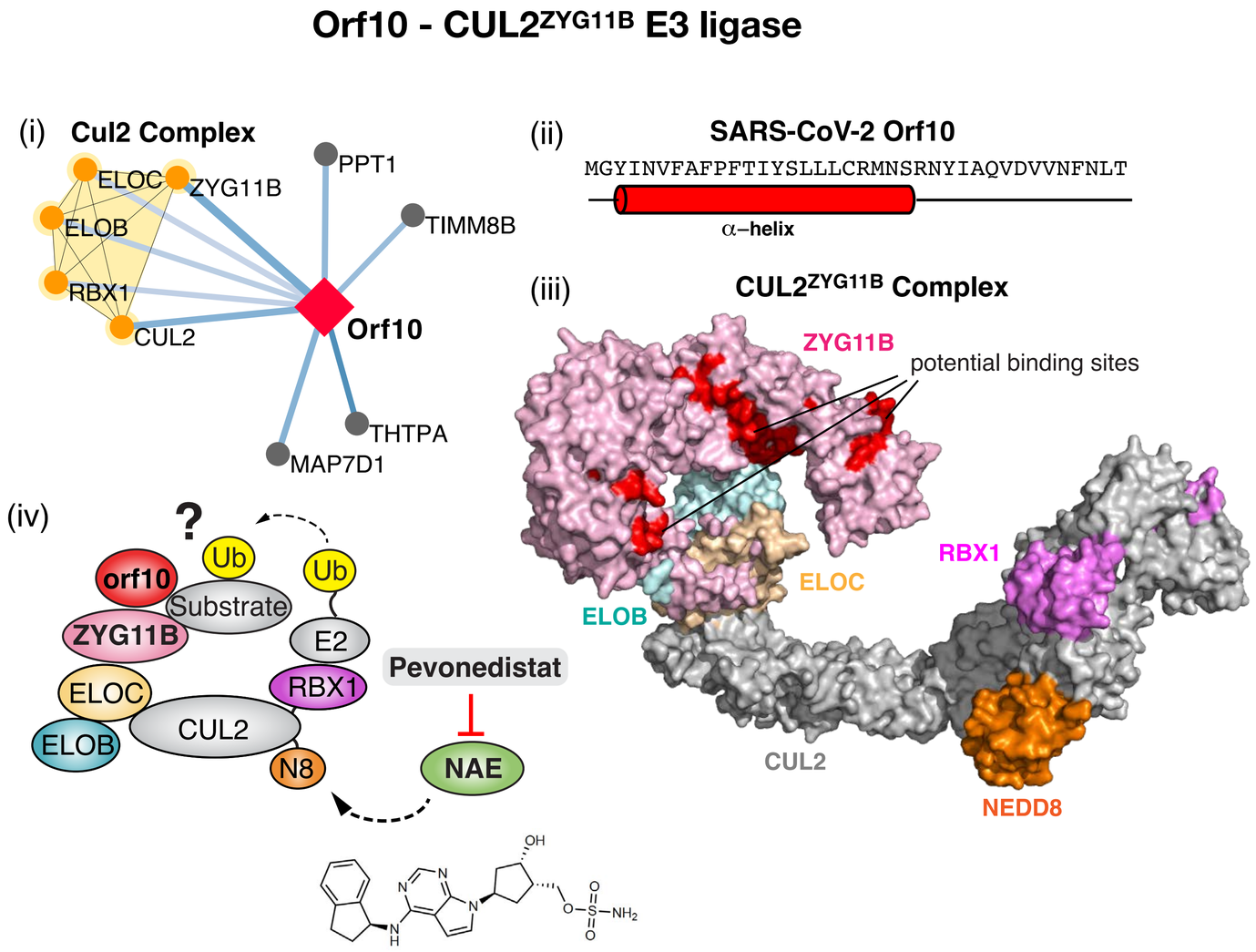
a



c



Novel aspects of SARS-CoV-2 biology

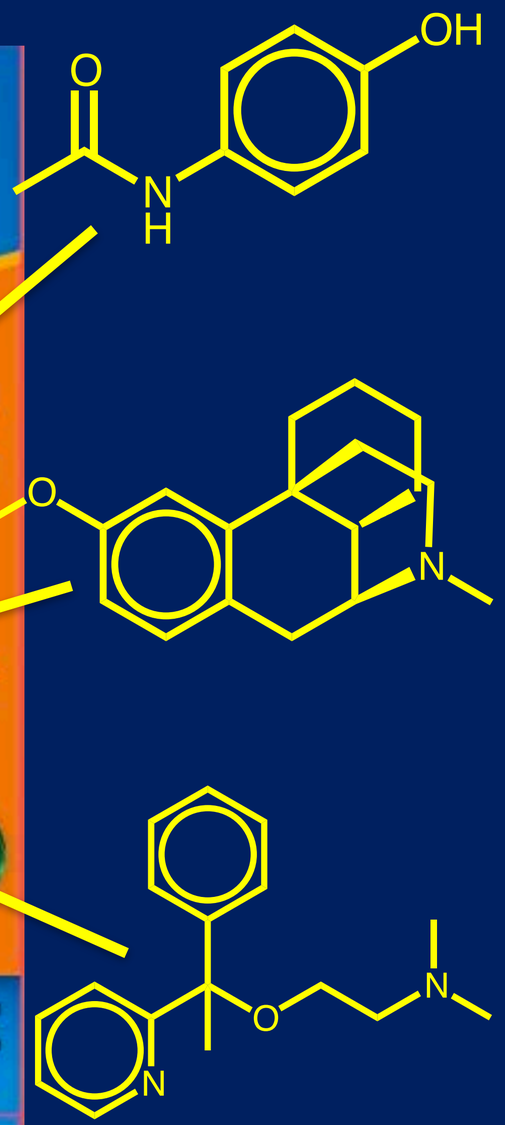


Davide Ruggero, Stephen Floor, John Gross, Tanja Kortemme, Andrej Sali, James Fraser

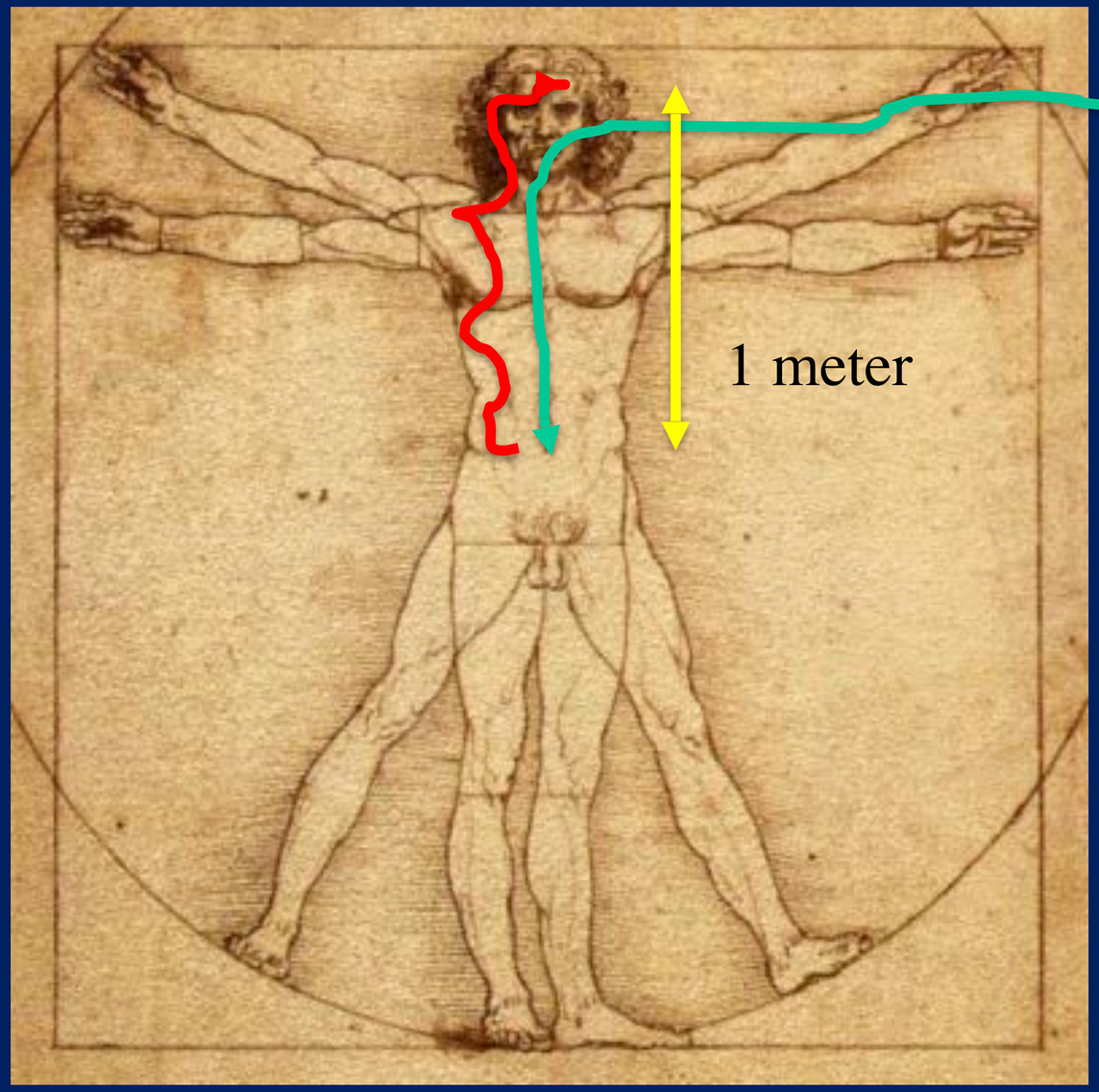
Drug discovery

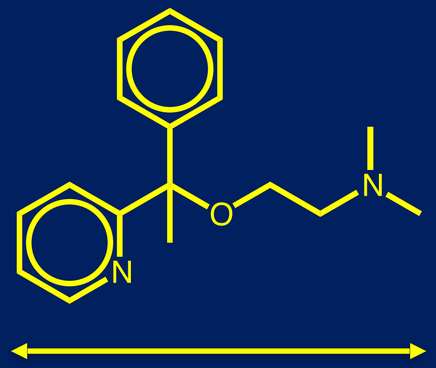
- Nature and mechanism of drugs
- Costs and success-rate of drug development
- Drug side effects
- Classic drug discovery for antiviral declatasvir
- Turning the tables on SARS-Cov-2
  - Repurposing drugs for the human proteins that the virus subverts

A drug is a chemical or protein that changes the function of a cell (human or infectious)



Drugs modulate “receptors” in tissues

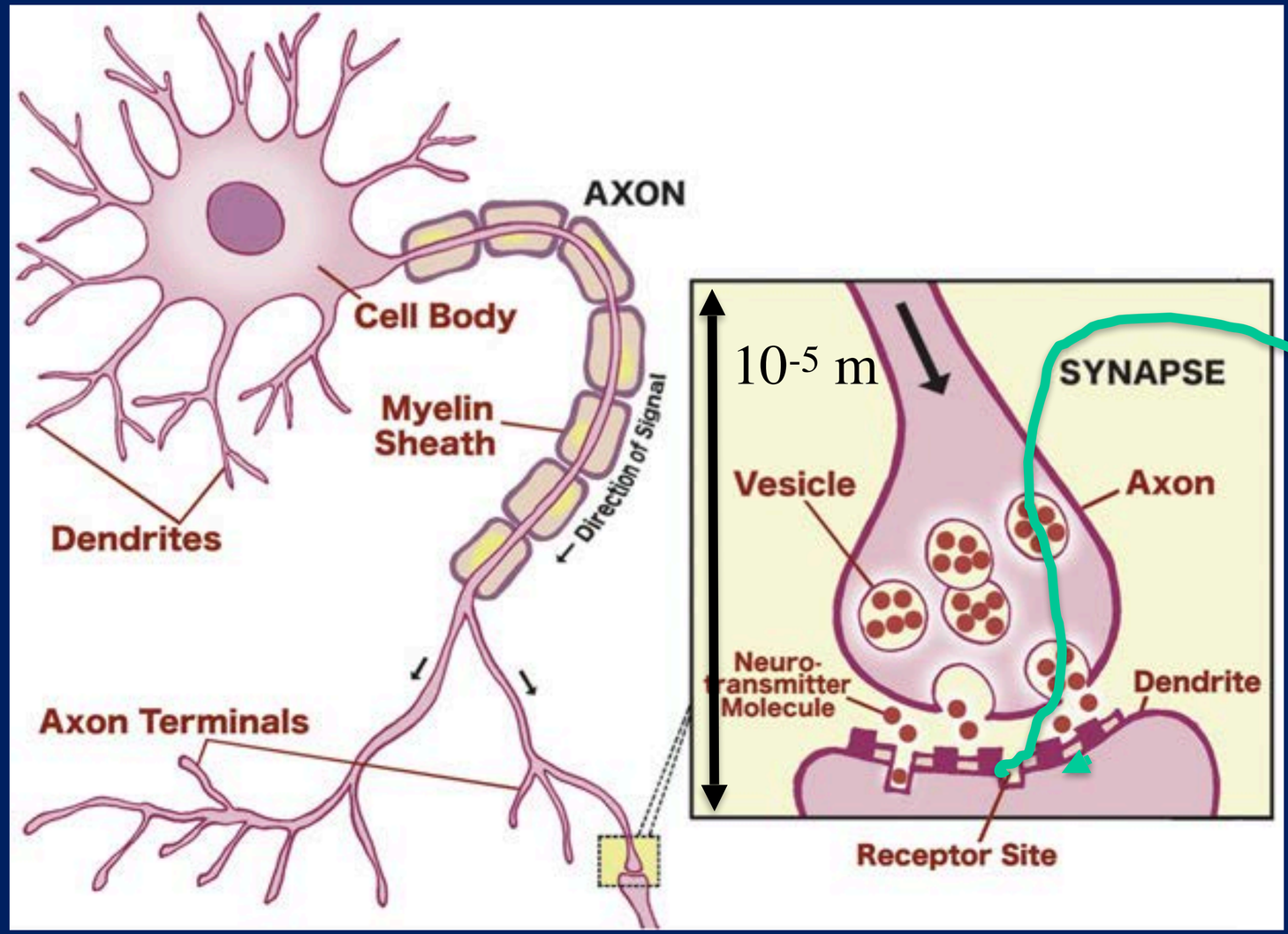


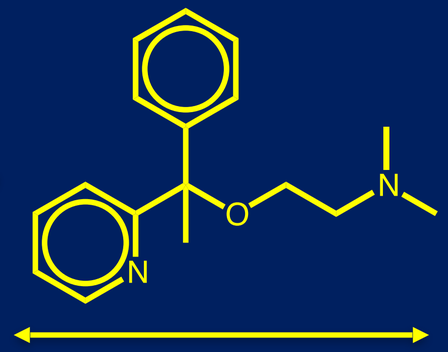


10^{-9} meter

10^{19} drug molecules/pill

The rheostats are receptors on cells, in doxylamines case, neurons





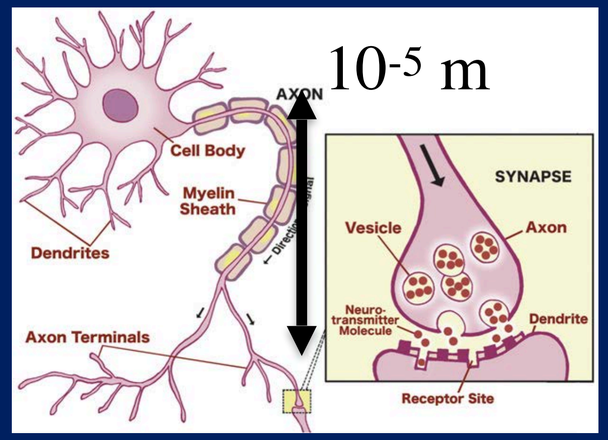
10^{-9} meter

10^{19} molecules/pill

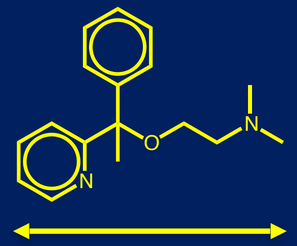
10^{11} neurons/brain

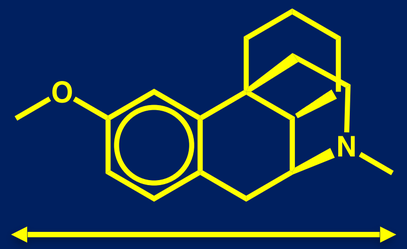
doxylamine blocks the histamine H_1 receptor

dextromethorphan activates the $Sigma_1$ receptor



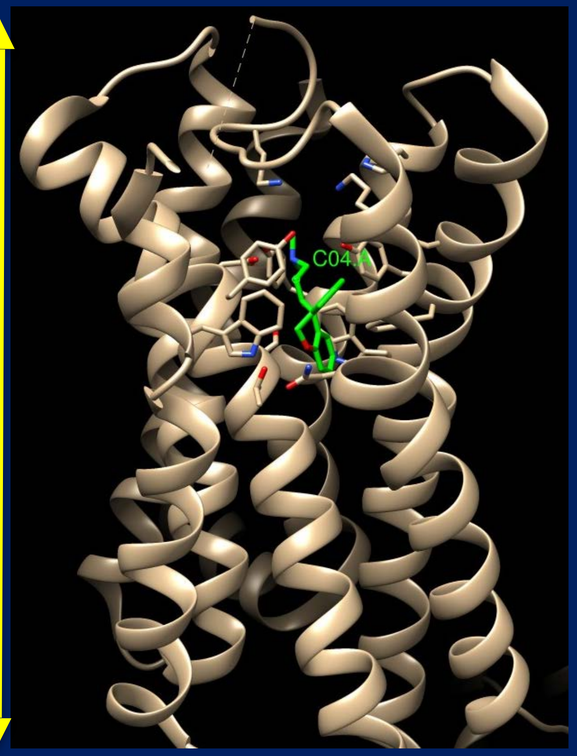
10^{-5} m

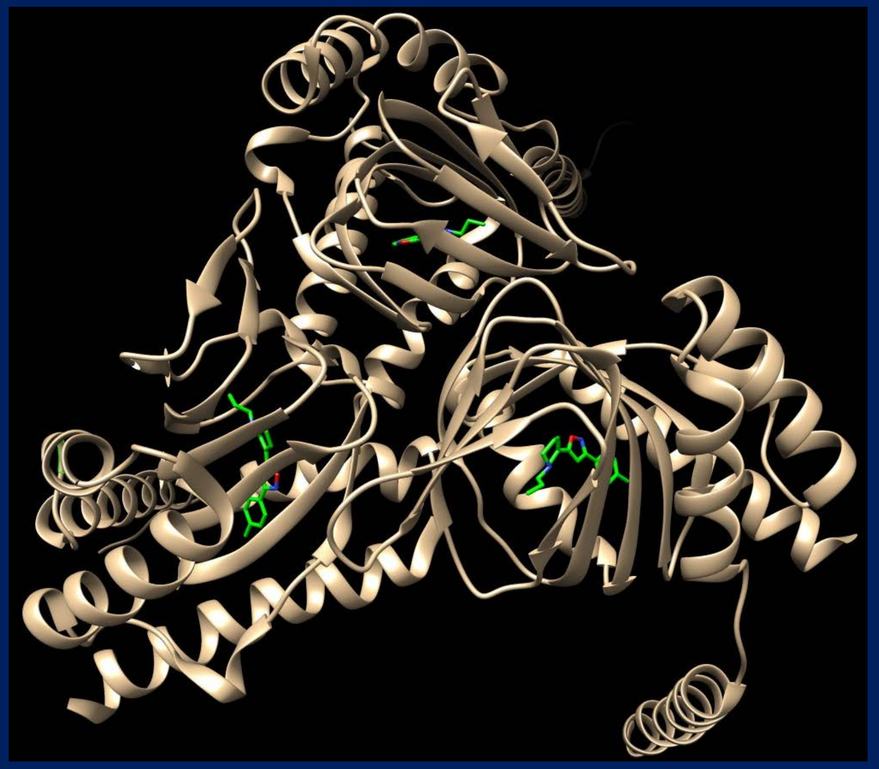




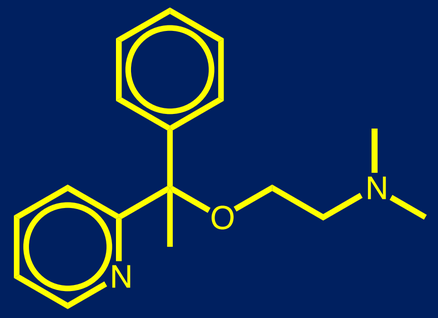
10^{-9} meter

$6x10^{-9}$ m



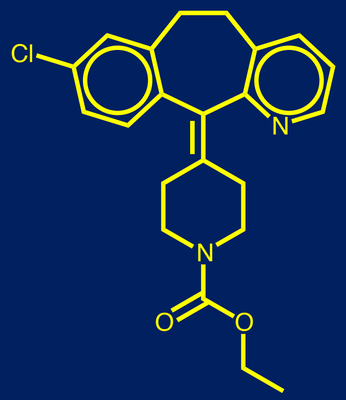


Side effects & alternative targets



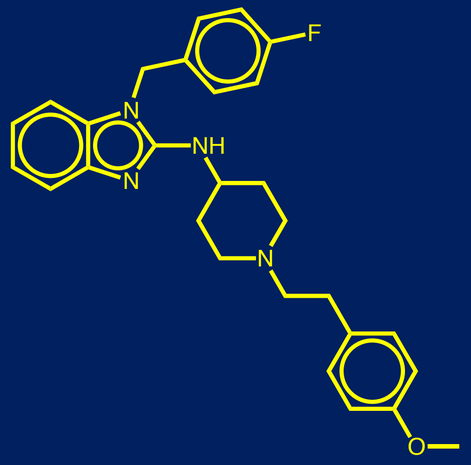
H1: strong
M1/2: decent
Sigma: decent
HERG: weak

sedation, lurid dreams, tachycardia, dry mouth



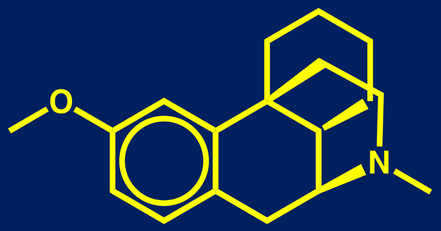
H1: very strong
M1/2: decent
HERG: weak

Dry mouth, low sedation



H1: strong
M1/2: modest
Sigma: decent
HERG: strong (!)

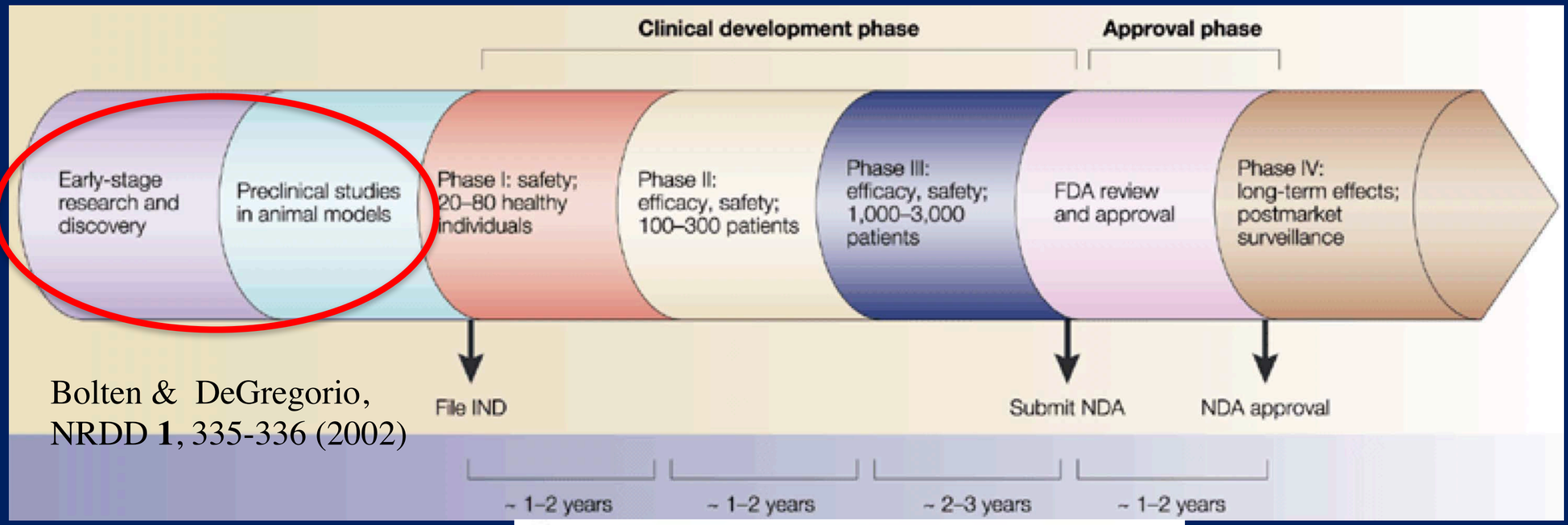
Heart attack



Sigma: decent
SERT: decent
NMDA: decent

Dependence, sleep disturbance

The drug discovery pipeline

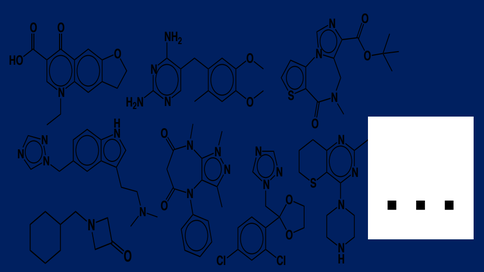


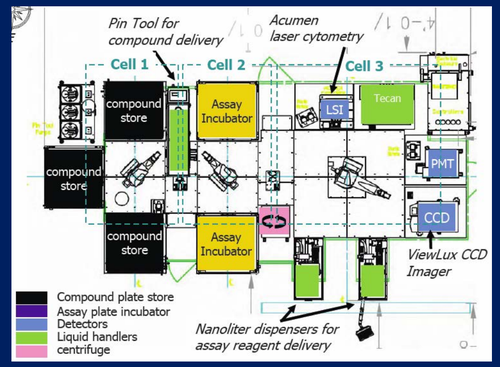
Bolten & DeGregorio, NRDD **1**, 335-336 (2002)

phase 1 to new drug, 5% success rate

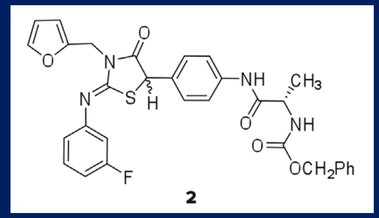
Anti HCV Daclatasvir: 2003 to 2015

> 10^6 molecules

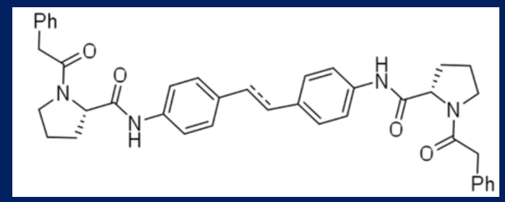




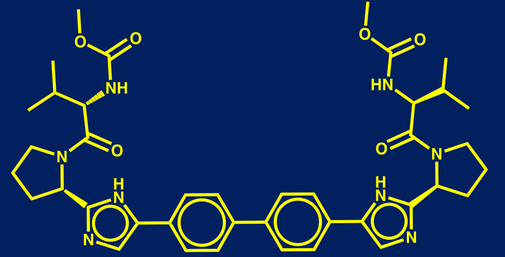
1 (!) confirmed hit



chemistry
in vitro biology



chemistry
pharm tox
Animal efficacy



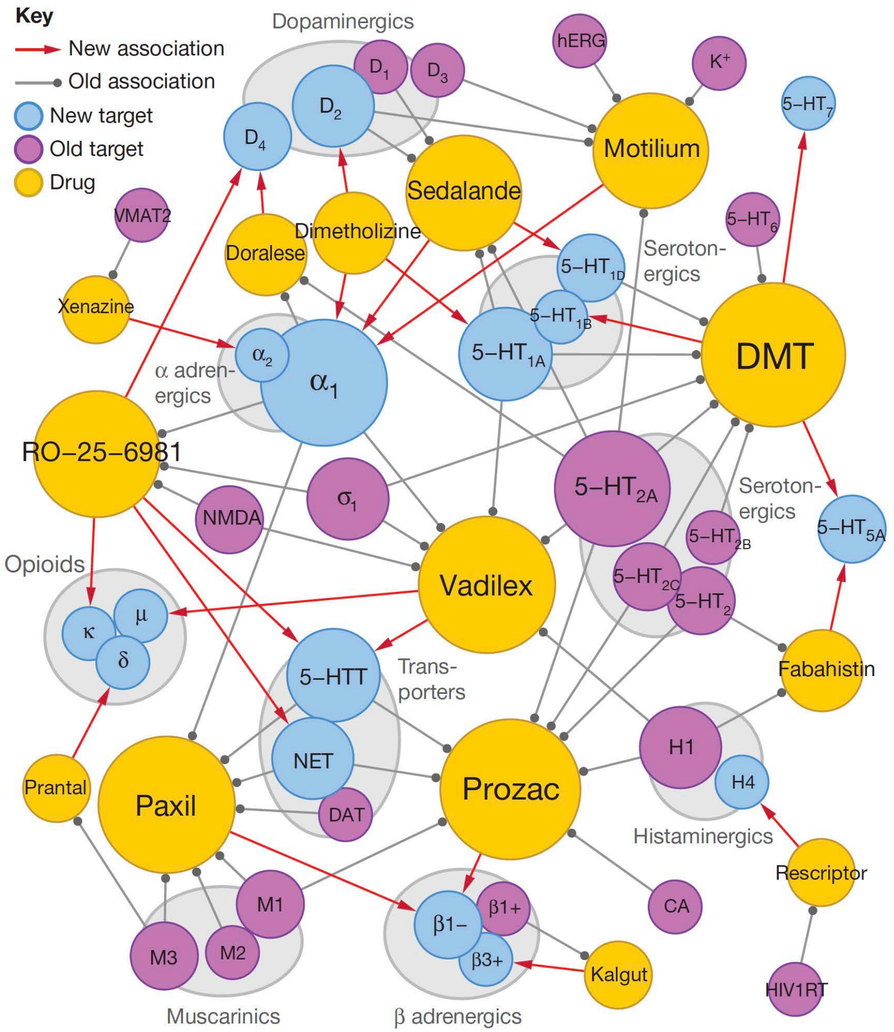
IND application
Phase 1 (2007/8)
Phase 2
Phase 3

Declatasvir
12 years

Statistics Based Chemoinformatics
Ligand Similarity Ensemble Approach (SEA)

Predicting new molecular targets for known drugs

Michael J. Keiser[1,2]*, Vincent Setola[3]*, John J. Irwin[1], Christian Laggner[1], Atheir I. Abbas[4], Sandra J. Hufeisen[5], Niels H. Jensen[5], Michael B. Kuijer[3], Roberto C. Matos[3], Thuy B. Tran[3], Ryan Whaley[3], Richard A. Glennon[6], Jérôme Hert[1], Kelan L. H. Thomas[1,7], Douglas D. Edwards[1], Brian K. Shoichet[1] & Bryan L. Roth[3,5]



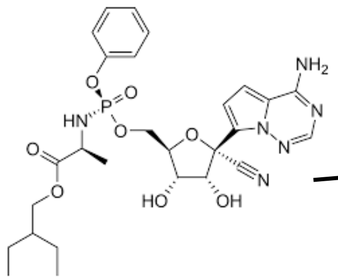
≈ 2,000 FDA Approved Drugs
≈ 10,000 Clinical Stage Drugs
>>>> Pre-clinical Drug Candidates

Keiser, M. J., et al. (2009)

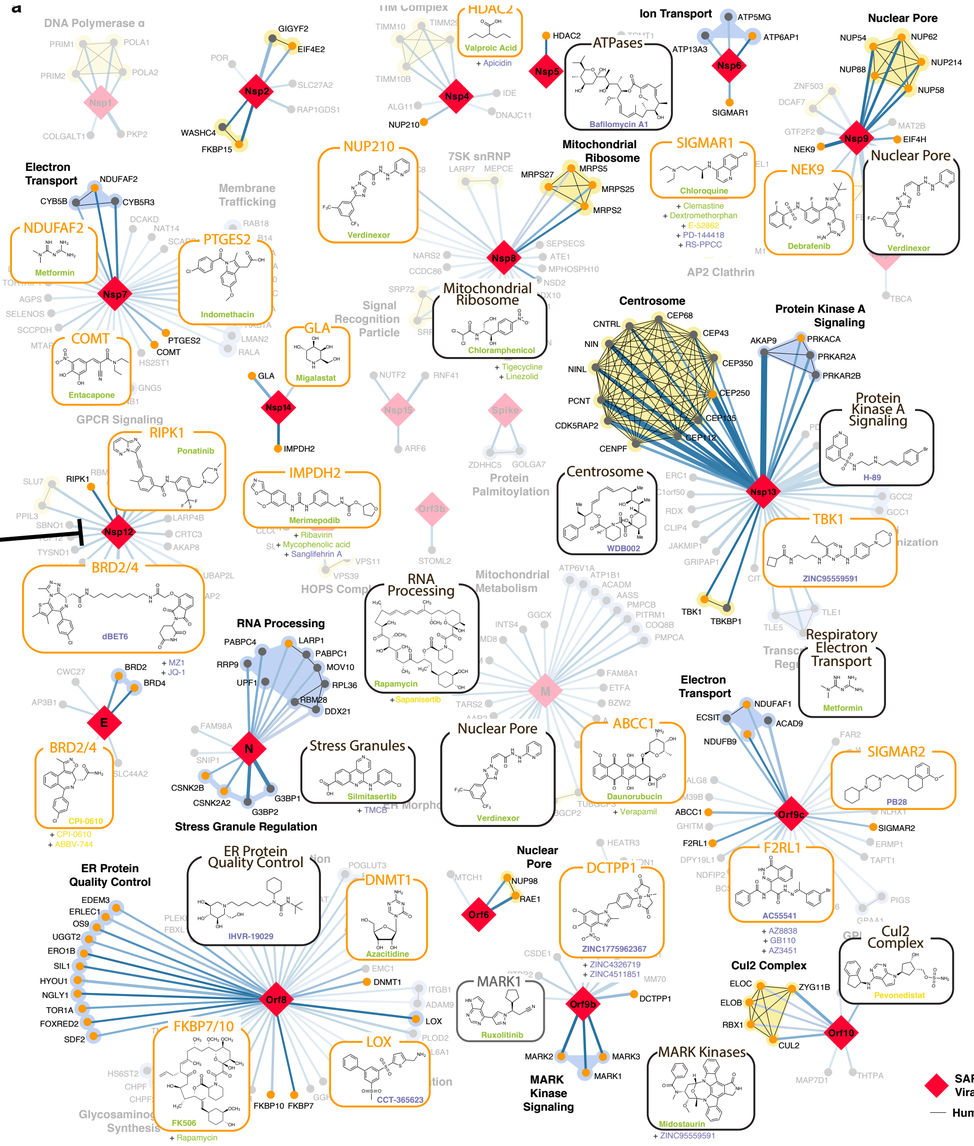
69 Candidates Identified

Approved Drugs + Drugs in Clinical Trials + Preclinical Compounds

Remdesivir
Direct Acting
Antiviral inhibitor of
Nsp12:
RNA-dependent
RNA Polymerase



Will become standard of care based on NIAID sponsored COVID trial results released yesterday



69 Existing drugs targeting SARS-CoV-2 human host factors

Camostat1	Linezolid1	Ruxolitinib	Pevonedistat	Apicidin	JQ1	ZINC4326719
Captopril	Lisinopril	S-verapamil	RVX-208	AZ3451	MZ1	ZINC4511851
Chloramphenicol	Metformin	Silmitasertib	Sapanisertib	AZ8838	PB28	ZINC95559591
Chloroquine	Midostaurin	Tigecycline	Tomivosertib	Bafilomycin A1	PD-144418	
Dabrafenib	Migalastat	Valproic Acid	Verdinexor	CCT 365623	PS3061	
Daunorubicin	Mycophenolic acid	ABBV-744	WDB002	Compound 10	RS-PPCC	
Entacapone	Nafamostat1	CPI-0610	XL413	Compound 2	Sanglifehrin A	
FK-506	Ponatinib	E-52862	Zotatifin	dBET6	Ternatin 4	
Haloperidol	Rapamycin	IHVR-19029	4E2RCat	GB110	TMCB	
Indomethacin	Ribavirin	Merimepodib	AC-55541	H-89	ZINC1775962367	

Approved Clinical Trial Pre-Clinical

Brian Shoichet, Kevan Shokat

Paper and authors

The authors have not filed for patent protection on the SARS-CoV-2 host interactions or the use of predicted drugs for treating COVID-19 to ensure all the information is freely available to accelerate the discovery of a treatment.

Cold Spring Harbor Laboratory

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bioRxiv is receiving many new papers on coronavirus SARS-CoV-2. A reminder: these are preliminary reports that have not been peer-reviewed. They should not be regarded as conclusive, guide clinical practice/health-related behavior, or be reported in news media as established information.

New Results

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3 comments

Posted March 22, 2020.

A SARS-CoV-2-Human Protein-Protein Interaction Map Reveals Drug Targets and Potential Drug-Repurposing

David E. Gordon, Gwendolyn M. Jang, Mehdi Bouhaddou, Jiewei Xu, Kirsten Obernier, Matthew J O'Meara, Jeffrey Z. Guo, Danielle L. Swaney, Tia A. Tummino, Ruth Huttenhain, Robyn Kaake, Alicia L. Richards, Beril Tutuncuoglu, Helene Foussard, Jyoti Batra, Kelsey Haas, Maya Modak, Minkyu Kim, Paige Haas, Benjamin J. Polacco, Hannes Braberg, Jacqueline M. Fabius, Manon Eckhardt, Margaret Soucheray, Melanie Brewer, Merve Cakir, Michael J. McGregor, Qiongyu Li, Zun Zar Chi Naing, Yuan Zhou, Shiming Peng, Ilsa T. Kirby, James E. Melnyk, John S Chorba, Kevin Lou, Shizhong A. Dai, Wenqi Shen, Ying Shi, Ziyang Zhang, Inigo Barrio-Hernandez, Danish Memon, Claudia Hernandez-Armenta, Christopher J.P. Mathy, Tina Perica, Kala B. Pilla, Sai J. Ganesan, Daniel J. Saltzberg, Rakesh Ramachandran, Xi Liu, Sara B. Rosenthal, Lorenzo Calviello, Srivats Venkataramanan, Yizhu Lin, Stephanie A. Wankowicz, Markus Bohn, Raphael Trenker, Janet M. Young, Devin Cavero, Joe Hiatt, Theo Roth, Ujjwal Rathore, Advait Subramanian, Julia Noack, Mathieu Hubert, Ferdinand Roesch, Thomas Vallet, Björn Meyer, Kris M. White, Lisa Miorin, David Agard, Michael Emerman, Davide Ruggero, Adolfo Garc&iacute-Sastre, Natalia Jura, Mark von Zastrow, Jack Taunton, Olivier Schwartz, Marco Vignuzzi, Christophe d'Enfert, Shaeri Mukherjee, Matt Jacobson, Harmit S. Malik, Danica G Fujimori, Trey Ideker, Charles S Craik, Stephen Floor, James S. Fraser, John Gross, Andrej Sali, Tanja Kortemme, Pedro Beltrao, Kevan Shokat, Brian K. Shoichet, Nevan J. Krogan

doi: https://doi.org/10.1101/2020.03.22.002386

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Subject Areas

All Articles

Animal Behavior and Cognition

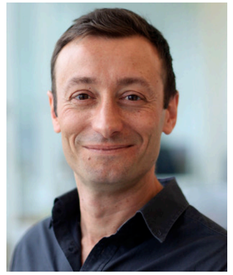
Biochemistry

Bioengineering

Bioinformatics

Biophysics

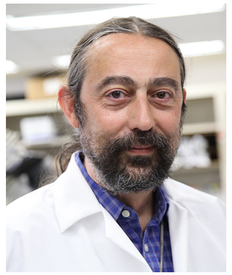
Collaborators



Marco Vignuzzi

Olivier Schwartz

Institut Pasteur, Paris

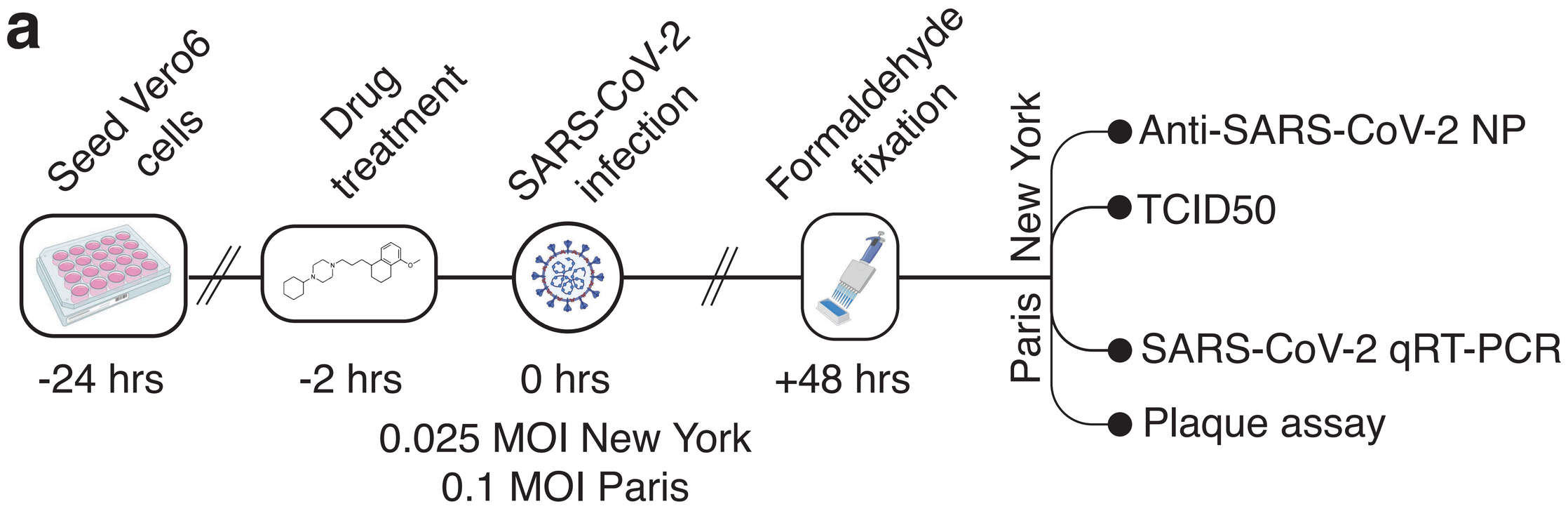


Adolfo Garcia-Sastre

Kris White

Mount Sinai, New York

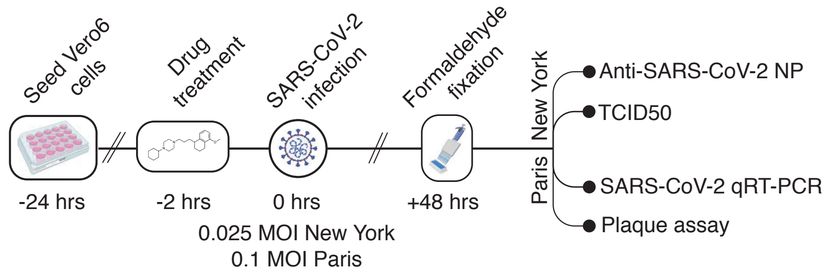
SARS-CoV-2 Replication Assays



The SARS-CoV-2 Infectible Vero E6 Cell line characteristics

- Cell line model of choice for culture of emerging pathogens.
- Female African Green Monkey Bladder Cells primary culture started 1962 (Chiba Japan)
- Found to be highly susceptible to various viruses (SV-40, measles, rubella, arbo-, adenoviruses)
- Express Receptor for SARS-CoV-2 Ace2
- Pseudo-diploid.—immortalized but not transformed if kept at low passage
- Contains a homozygous deletion in Chromosome 12: loss of alpha- and beta-1 Interferon genes, and CDKN2A/CDKN2B (tumor suppressor locus for inhibitor of CDK4 and activator of p53)

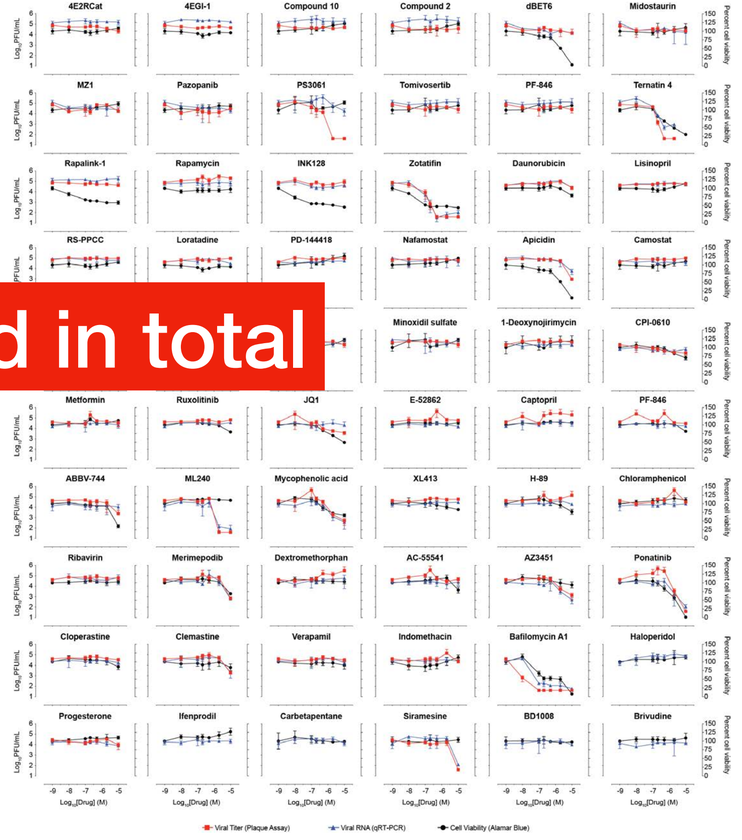
Antiviral activity of host-directed drugs and compounds



Mt Sinai: 37 drugs/compounds

47 tested in total

Institut Pasteur: 44 drugs/compounds



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Ten Agents Showed Efficacy in Killing Virus

Results Consistent in Different Assays Across Two Labs and Continents

Protein Translation/Biogenesis Inhibitors:

- Zotatifin
- Ternatin-4/plitidepsin

SigmaR1 and SigmaR2 Modulators:

- *Antihistamines*
  - Cloperastine
  - Clemastine
- *Antipsychotics*
  - Haloperidol
  - **Melperone**
- *Antimalarials*
  - Hydroxychloroquine
- *Hormone*
  - Progesterone
- *Antianxiety*
  - Siramesine
- *Preclinical*
  - PB28 and PD-144418

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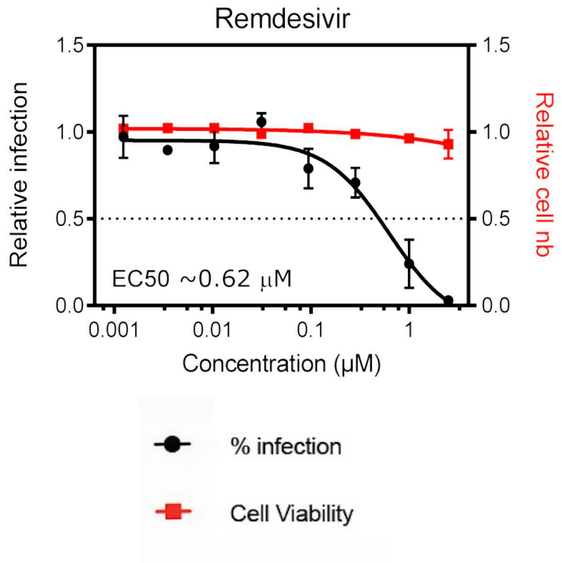
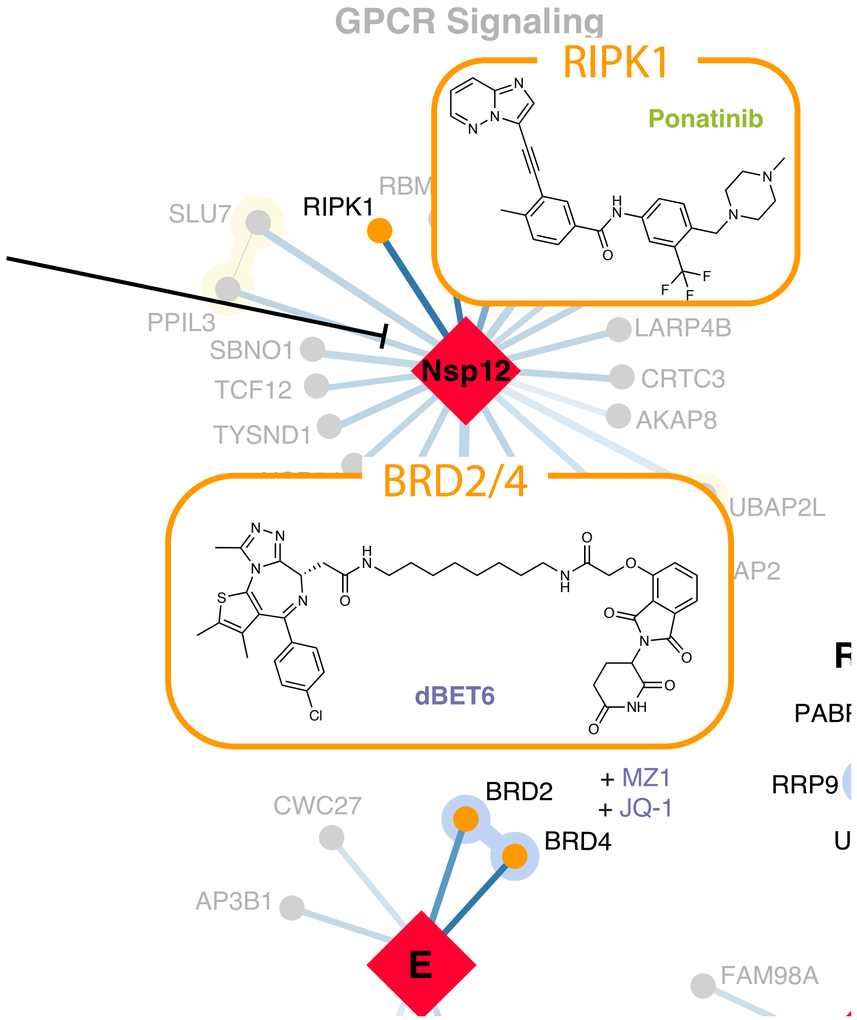
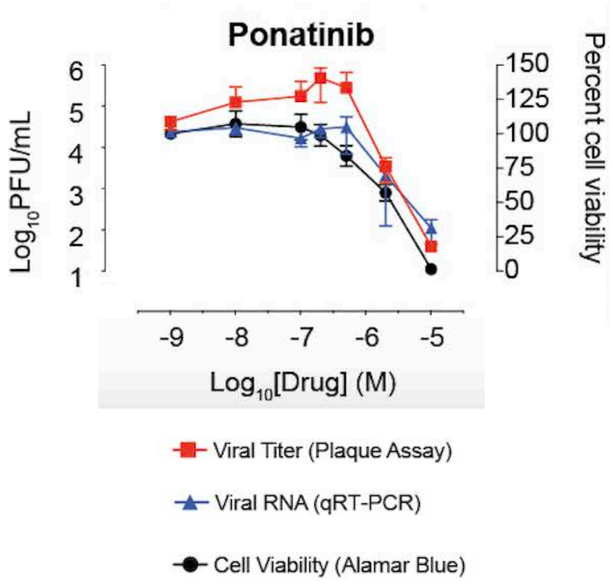
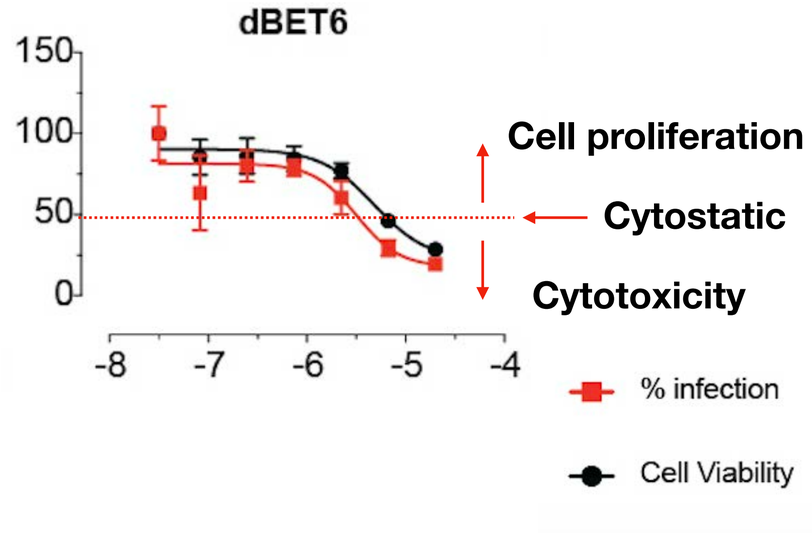
Direct Acting and Host Factor Targeting Agents



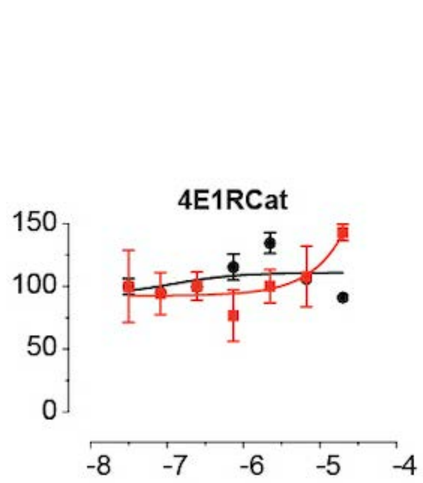
Riva et. al.
bioRxiv preprint doi: https://doi.org/10.1101/2020.04.16.044016.

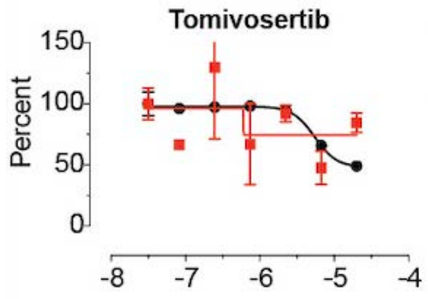


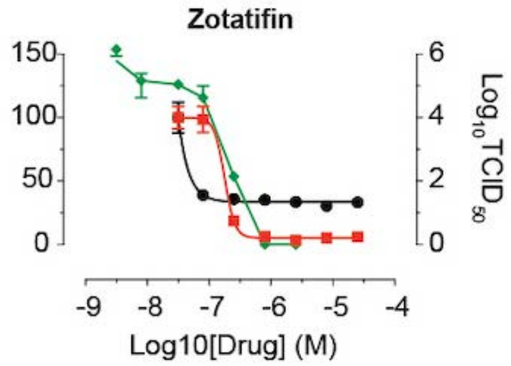




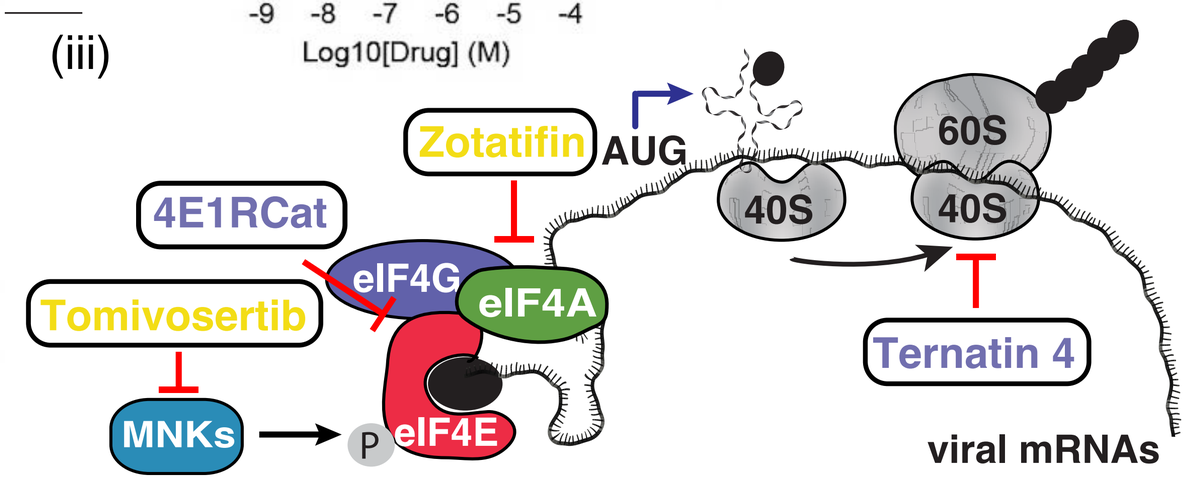
Protein Biogenesis as a Selectively Targetable Vulnerability

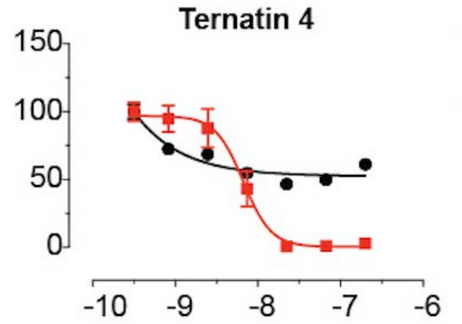


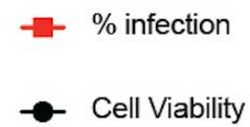




(iii)







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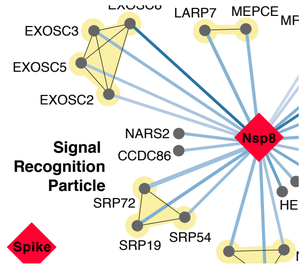
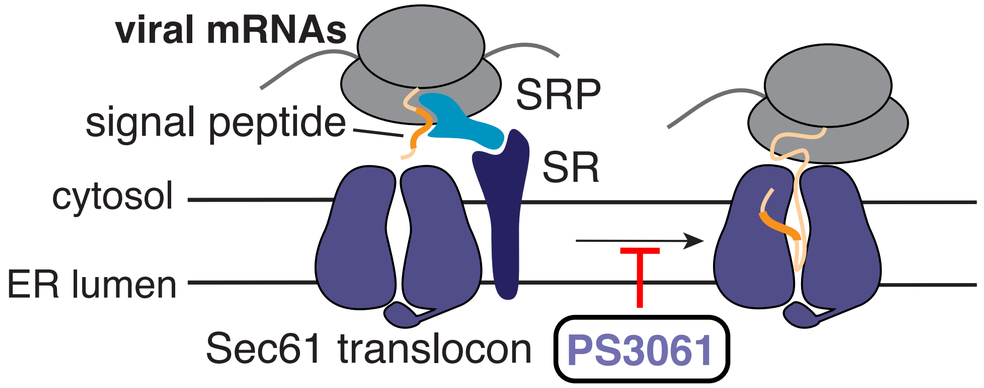
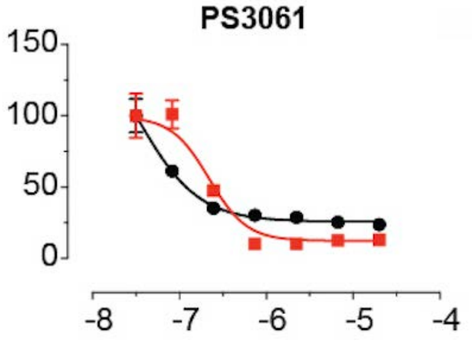
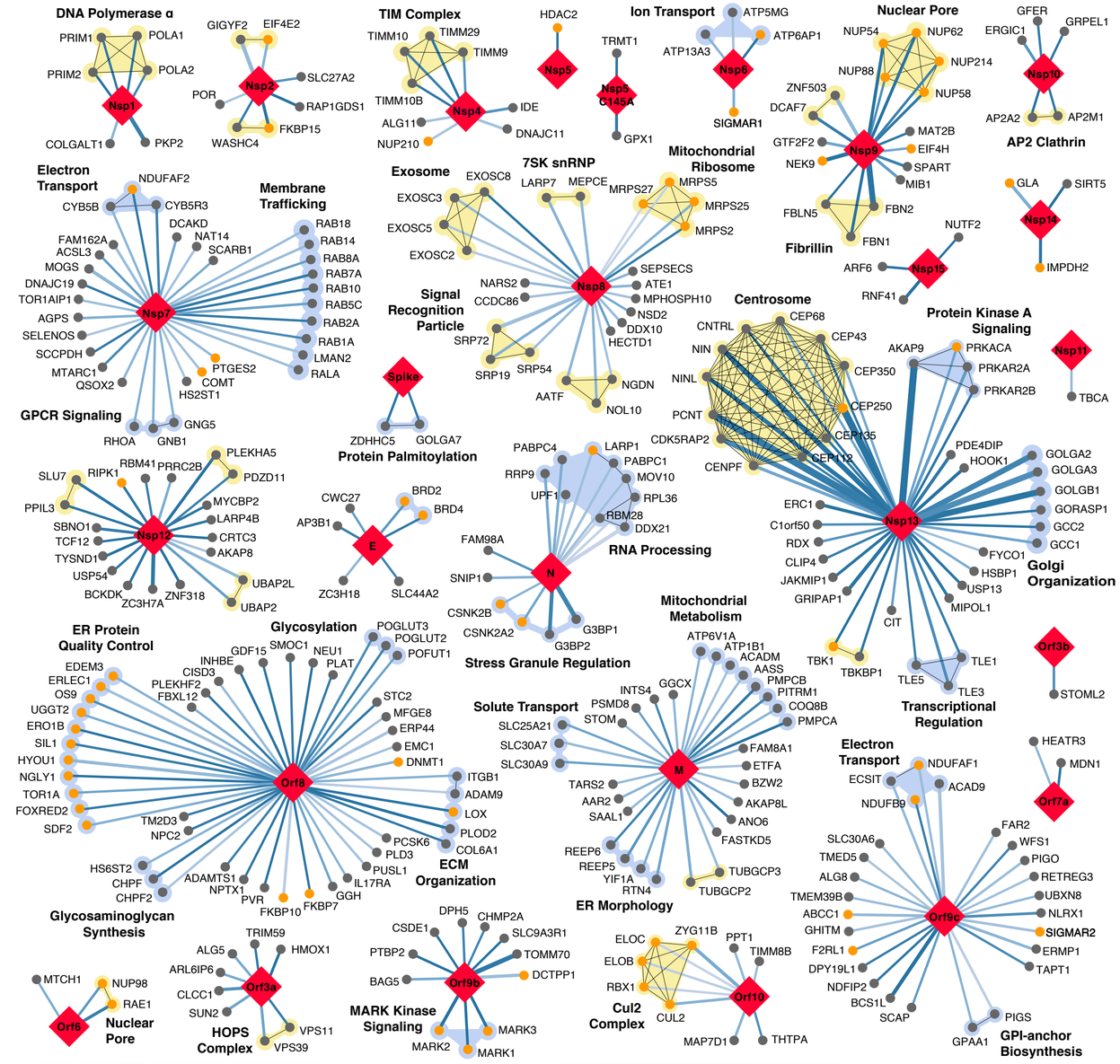






332 SARS-CoV-2-human PPIs include 69 druggable host factors



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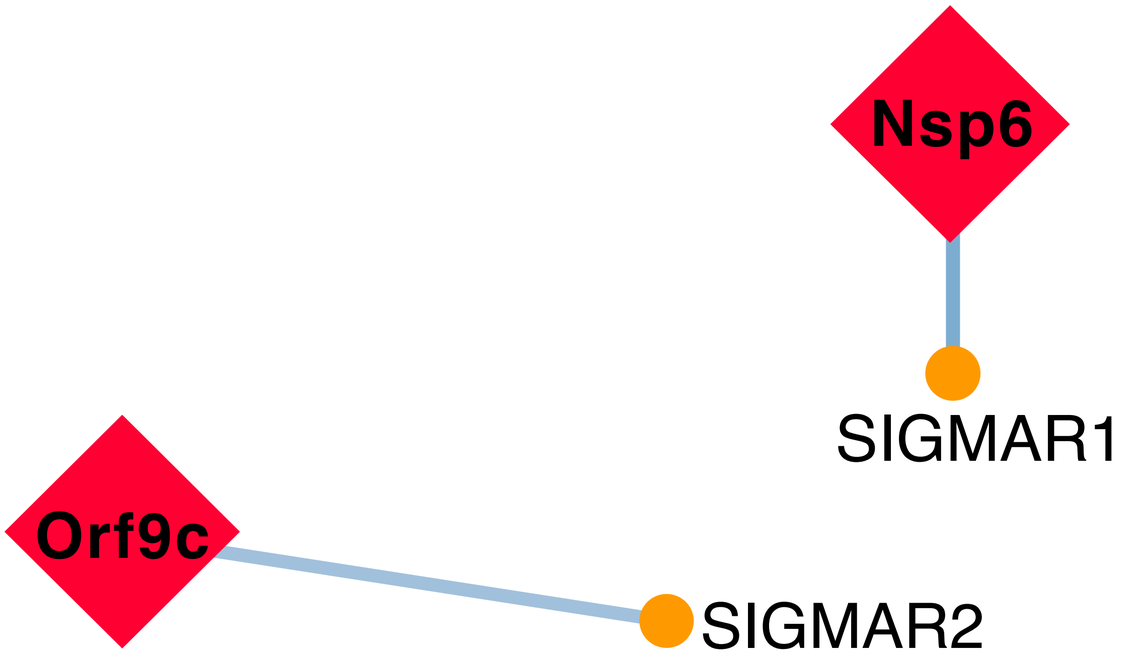
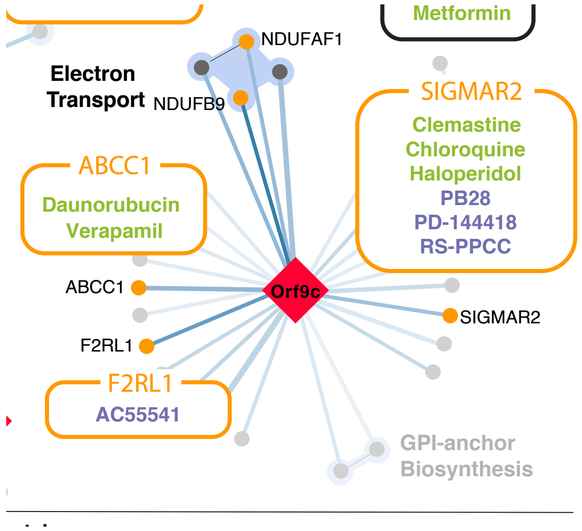
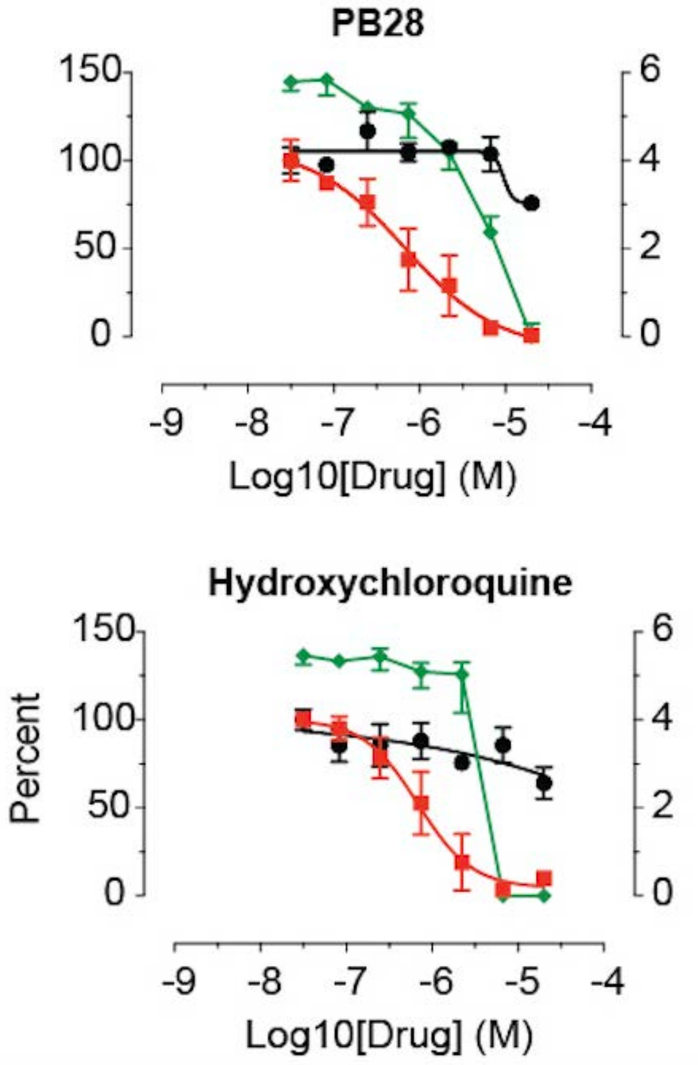
332 SARS-CoV-2-human PPIs include 69 druggable host factors

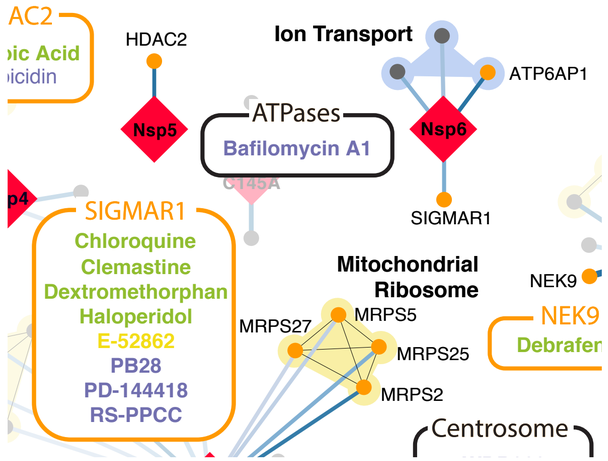


Hydroxychloroquine and Sigma R1 & Sigma R2 Receptors Are Very Attractive Host Factor Targets



Mitochondria + ER





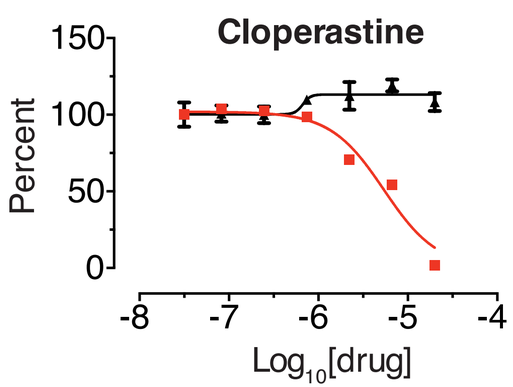
Vesicle Trafficking

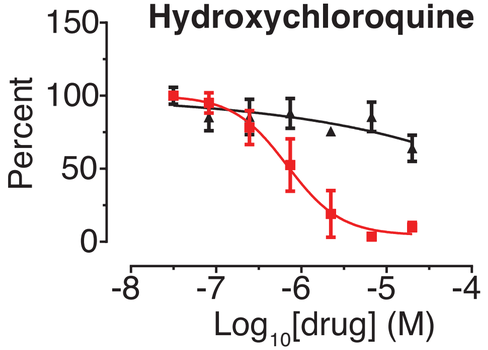
% infection

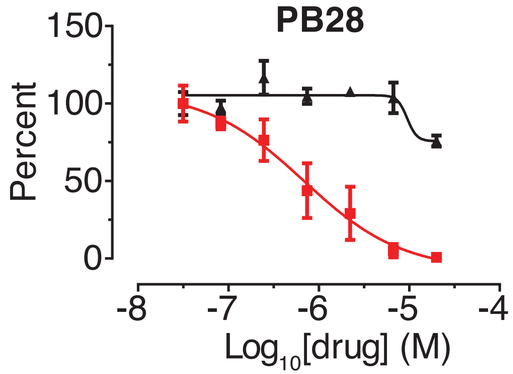
Cell Viability

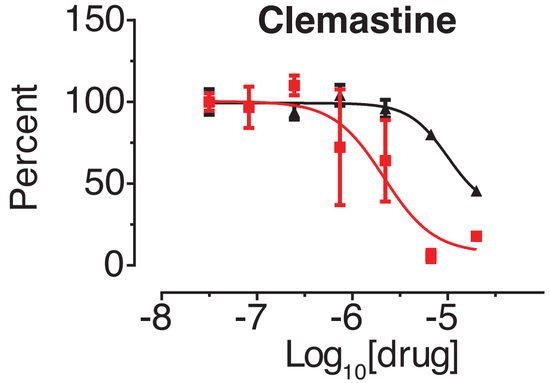
$TCID_{50}$

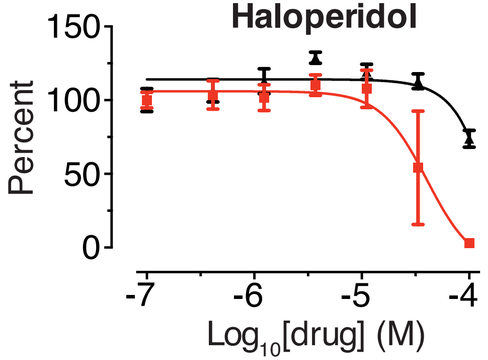
Drugs/Compounds that Bind SigmaR1/R2

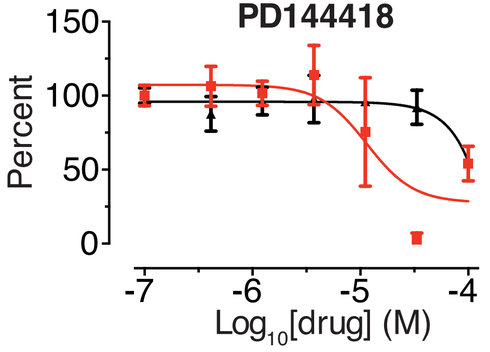












SARS-CoV-2 (Anti-NP)

Cell viability

Antihistamines

Cloperastine

Clemastine

Antipsychotics

Haloperidol

Melperone

Antimalarials

Hydroxychloroquine

Hormone

Progesterone

Antianxiety

Siramesine

Preclinical

PB28

PD144418

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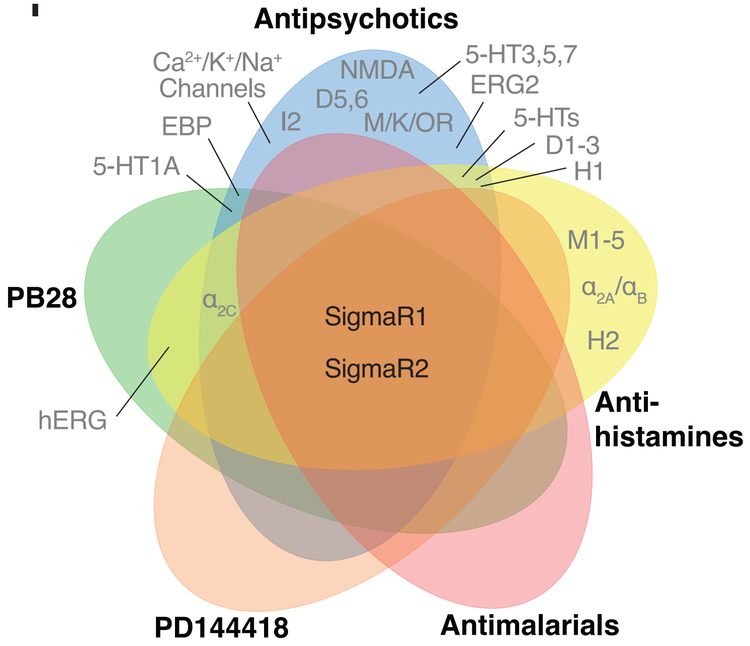
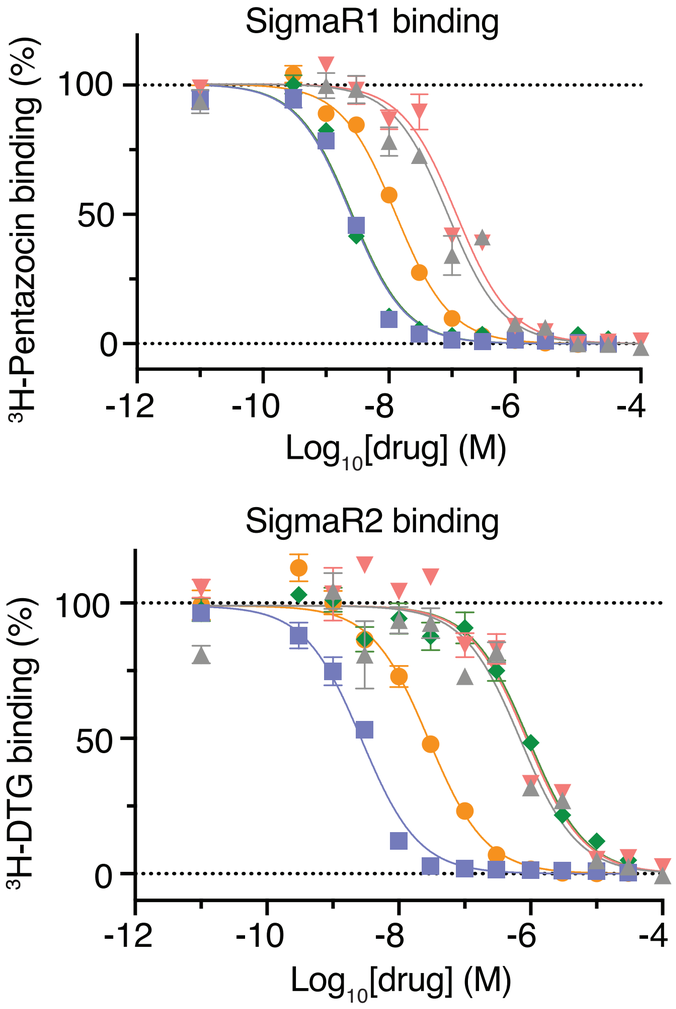
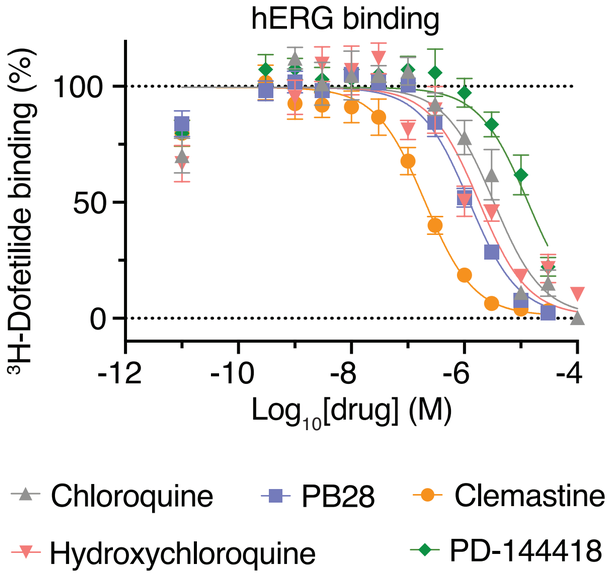
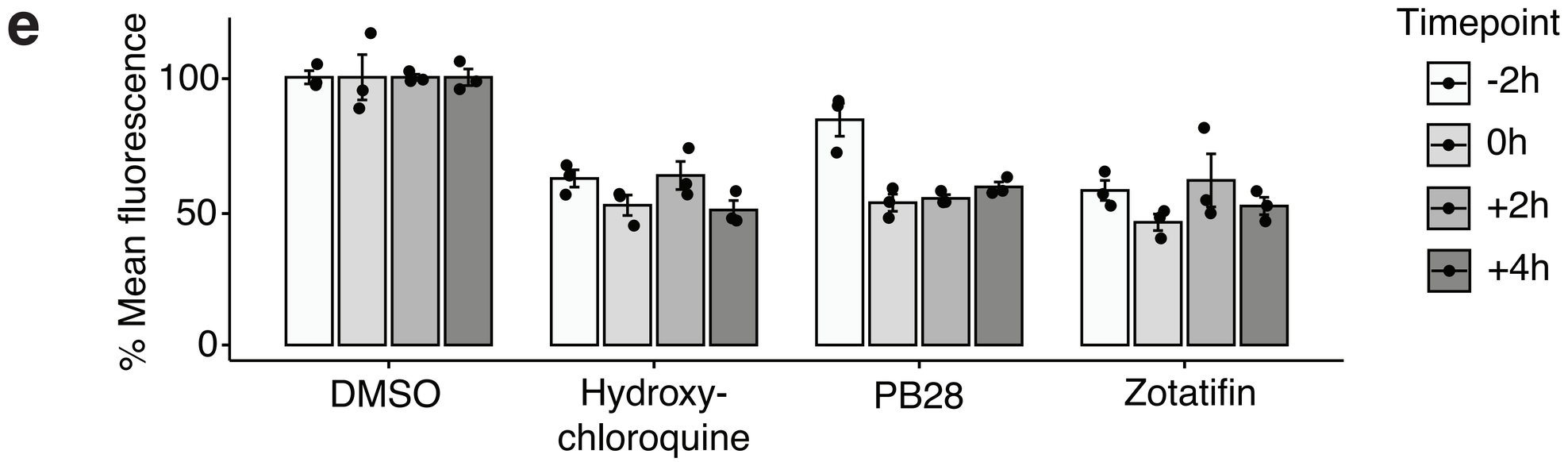
Homing in on Sigma R1/R2 and Avoiding the known Toxicity of the HERG Channel (Causes sudden cardiac death)







Time to treatment test of mechanism



MOI = 2, Agent added up to 4 hours after virus

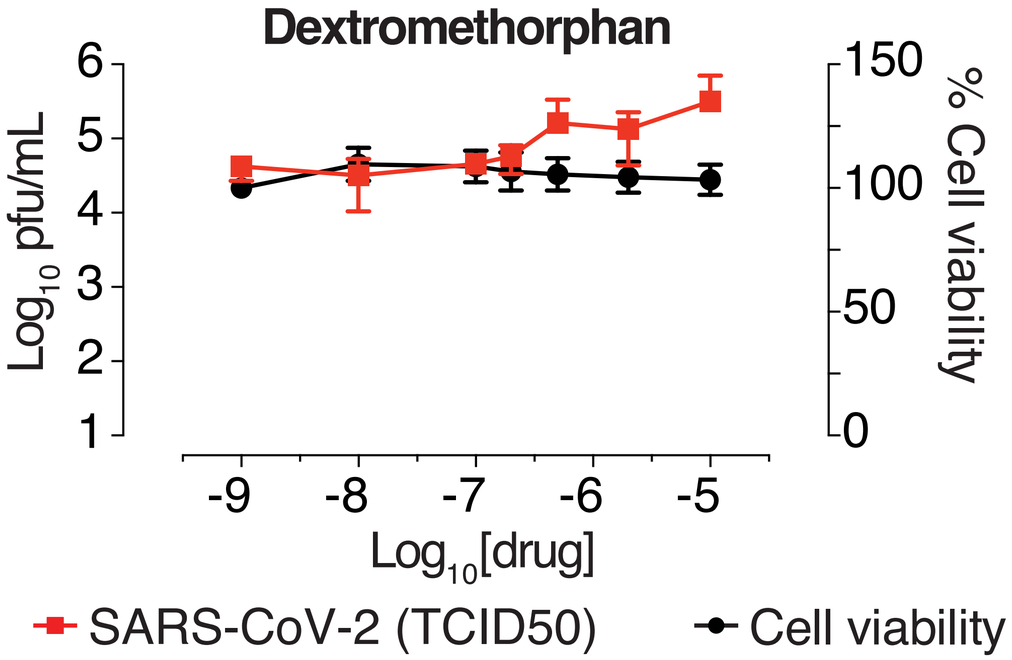
Additional Observations

- Molecules that target the Sigma1 and Sigma2 receptors perturb the virus through different mechanisms than the translation inhibitors, potentially including through cell stress response
- It may be that a combination approach is warranted, including combination with antivirals (remdesivir)

.

Dextromethorphan Appears to be Pro-Viral

- Used in many over-the-counter cough syrups
- During the pandemic, should caution against its use until further study



What's Next?

- Data shared with drug makers, government authorities and public health officials
- Several companies are taking agents into clinical trials to evaluate their anti-viral effectiveness and therapeutic index
- Continuing our research on COVID-19
- Unique and groundbreaking approach has pan-pathogenic applications
- Following COVID-19 response, research will resume in a number of disease areas
- Independent from institutional/corporate affiliations or barriers; breaking scientific silos and accelerating data results

Scientific Silos

Different Laboratories

Different Institutions

Academia and Pharma

Scientific Silos

Different Laboratories

Different Institutions

Academia and Pharma

QCRG Collaborators, Partners

UCSF Quantitative Biosciences Institute

Icahn School of Medicine at Mount Sinai

Institut Pasteur

UCSF University of California San Francisco

GLADSTONE INSTITUTES

hhmi Howard Hughes Medical Institute

EMBL

UC San Diego

UNC SCHOOL OF MEDICINE

Buck Live better longer.

FRED HUTCH CURES START HERE®

UNIVERSITY OF MICHIGAN

Benchling

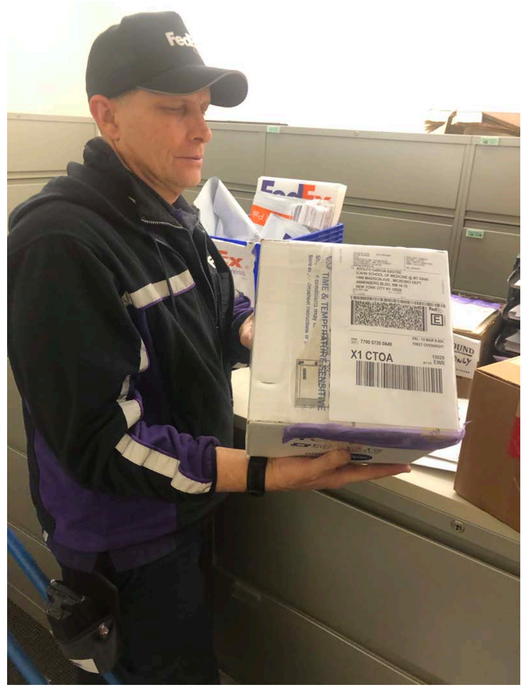
ZOIC LABS

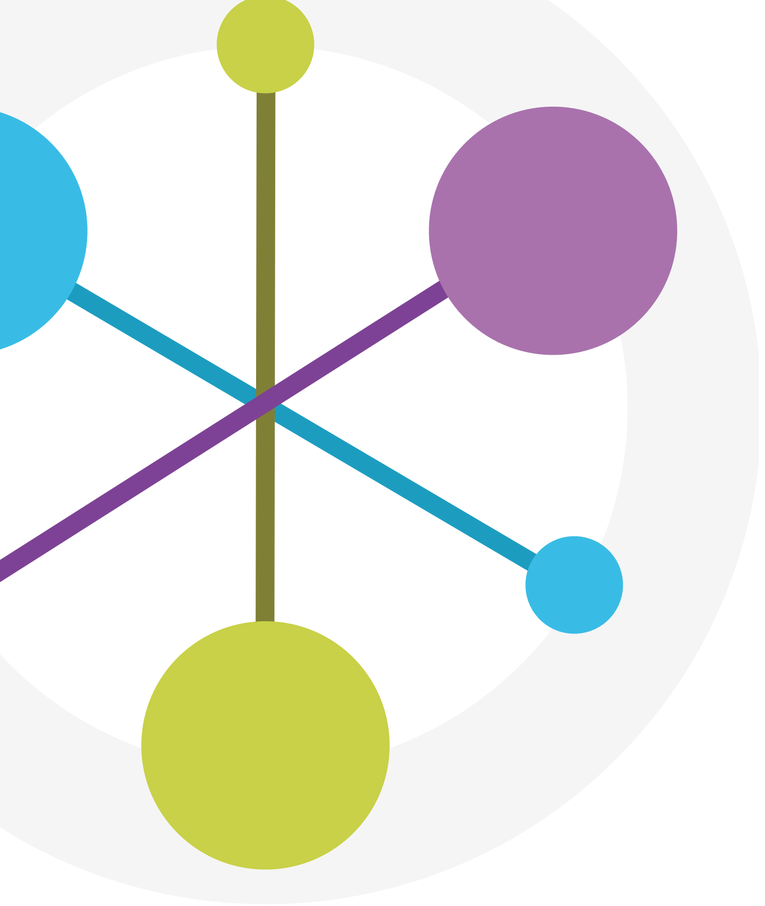
addgene The nonprofit plasmid repository

ACKNOWLEDGEMENTS

The authors would like to thank Todd from FedEx for his heroic effort helping us to ship out drugs and SARS-CoV-2 expression constructs across the globe. We thank Randy Albrecht for support with BSL3 procedures. **The authors acknowledge their partners and families for support in child care** and other matters
during this time.

David E. Gordon*[1,2,3,4], Gwendolyn M. Jang*[1,2,3,4], Mehdi Bouhaddou*[1,2,3,4], Jiewei Xu*[1,2,3,4], Kirsten Obernier*[1,2,3,4], Kris M. White*[5,6], Matthew J. O'Meara*[7], Veronica V. Rezelj*[8], Jeffrey Z. Guo[1,2,3,4], Danielle L. Swaney[1,2,3,4], Tia A. Tummino[1,2,9], Ruth Huettenhain[1,2,3,4], Robyn M. Kaake[1,2,3,4], Alicia L. Richards[1,2,3,4], Beril Tutuncuoglu[1,2,3,4], Helene Foussard[1,2,3,4], Jyoti Batra[1,2,3,4], Kelsey Haas[1,2,3,4], Maya Modak[1,2,3,4], Minkyu Kim[1,2,3,4], Paige Haas[1,2,3,4], Benjamin J. Polacco[1,2,3,4], Hannes Braberg[1,2,3,4], Jacqueline M. Fabius[1,2,3,4], Manon Eckhardt[1,2,3,4], Margaret Soucheray[1,2,3,4], Melanie J. Bennett[1,2,3,4], Merve Cakir[1,2,3,4], Michael J. McGregor[1,2,3,4], Qiongyu Li[1,2,3,4], Bjoern Meyer[8], Ferdinand Roesch[8], Thomas Vallet[8], Alice Mac Kain[8], Lisa Miorin[5,6], Elena Moreno [5,6], Zun Zar Chi Naing[1,2,3,4], Yuan Zhou[1,2,3,4], Shiming Peng[1,2,9], Ying Shi[1,2,4,11], Ziyang Zhang[1,2,4,11], Wenqi Shen[1,2,4,11], Ilsa T. Kirby[1,2,4,11], James E. Melnyk[1,2,4,11], John S. Chorba[1,2,4,11], Kevin Lou[1,2,4,11], Shizhong A. Dai[1,2,4,11], Inigo Barrio-Hernandez[12], Danish Memon[12], Claudia Hernandez-Armenta[12], Jiankun Lyu[1,2,9], Christopher J.P. Mathy[1,2,13,14], Tina Perica[1,2,13], Kala B. Pilla[1,2,13], Sai J. Ganesan[1,2,13], Daniel J. Saltzberg[1,2,13], Ramachandran Rakesh[1,2,13], Xi Liu[1,2,9], Sara B. Rosenthal[15], Lorenzo Calviello[1,16], Srivats Venkataramanan[1,16], Jose Liboy-Lugo[1,16], Yizhu Lin[1,16], Xi-Ping Huang[17], YongFeng Liu[17], Stephanie A. Wankowicz[1,2,11,18], Markus Bohn[1,2,9], Maliheh Safari[1,2,19], Fatima S. Ugur[1,2,4,9], Cassandra Koh[8], Nastaran Sadat Savar[8], Quang Dinh Tran[8], Djoshkun Shengjuler[8], Sabrina J Fletcher[8], Michael C. O'Neal[20], Yiming Cai[20], Jason C.J.Chang[20], David J. Broadhurst[20], Saker Klippsten[20], Phillip P. Sharp[4], Nicole A. Wenzell[1,2,4], Duygu Kuzuoglu[1,2,4,21,22], Hao-Yuan Wang[1,2,4], Raphael Trenker[1,2,23], Janet M. Young[24], Devin A. Cavero[3,26], Joseph Hiatt[3,25,26], Theodore L. Roth[3,25,26], Ujjwal Rathore[3,26], Advait Subramanian[1,2,26], Julia Noack[1,2,26], Mathieu Hubert[10], Robert M. Stroud[1,2,19], Alan D. Frankel[1,2,19], Oren S. Rosenberg[1,2,19,27], Kliment A Verba[1,2,9], David A. Agard[1,2,19], Melanie Ott[1,2,3,27], Michael Emerman[28], Natalia Jura[1,2,4,23], Mark von Zastrow[1,2,4,29], Eric Verdin[1,27,30], Alan Ashworth[1,2,21], Olivier Schwartz[10], Christophe d'Enfert[31], Shaeri Mukherjee[1,2,26], Matt Jacobson[1,2,9], Harmit S. Malik[24], Danica G. Fujimori[1,2,4,9], Trey Ideker[1,32], Charles S. Craik[1,2,9,21], Stephen N. Floor[1,16,21], James S. Fraser[1,2,13], John D. Gross[1,2,9], Andrej Sali[1,2,9,13], Bryan L. Roth[17], Davide Ruggero[1,2,4,21,22], Jack Taunton[1,2,4], Tanja Kortemme[1,2,13,14], Pedro Beltrao[1,12], Marco Vignuzzi†[8], Adolfo García-Sastre†[5,6,33,34], Kevan M. Shokat†[1,2,4,11], Brian K. Shoichet†[1,2,9], Nevan J. Krogan†[1,2,3,4,5]





UCSF Quantitative Biosciences Institute

Breaking down silos

103 Labs

Collaborative Research
Quantitative
Basic science
Disease agnostic
Experimental & Computational

Cell Mapping Initiatives

HPMI — Host Pathogen Map Initiative

CCMI — Cancer Cell Map Initiative

PCMI — Psychiatric Cell Map Initiative

Investing in the young

QBI Scholarship for
Women from Developing Nations

QBI Fellowship
2-year fellowships

Education Outreach

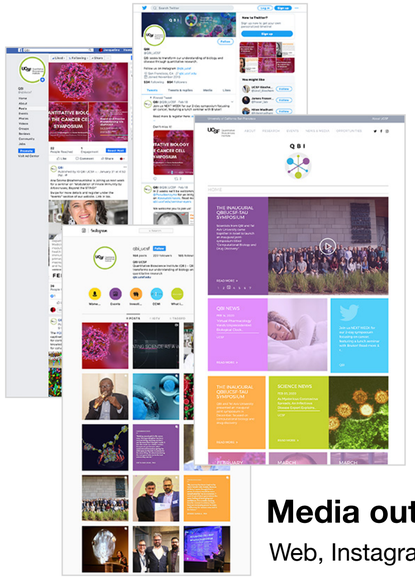
UCSF Quantitative Biosciences Institute

Symposia

13 scheduled for 2020

RFAs

2018 - $1.1M
2019 - $1.2M
2020 - $300K



Media outreach

Web, Instagram, Twitter, Facebook

Seminar series

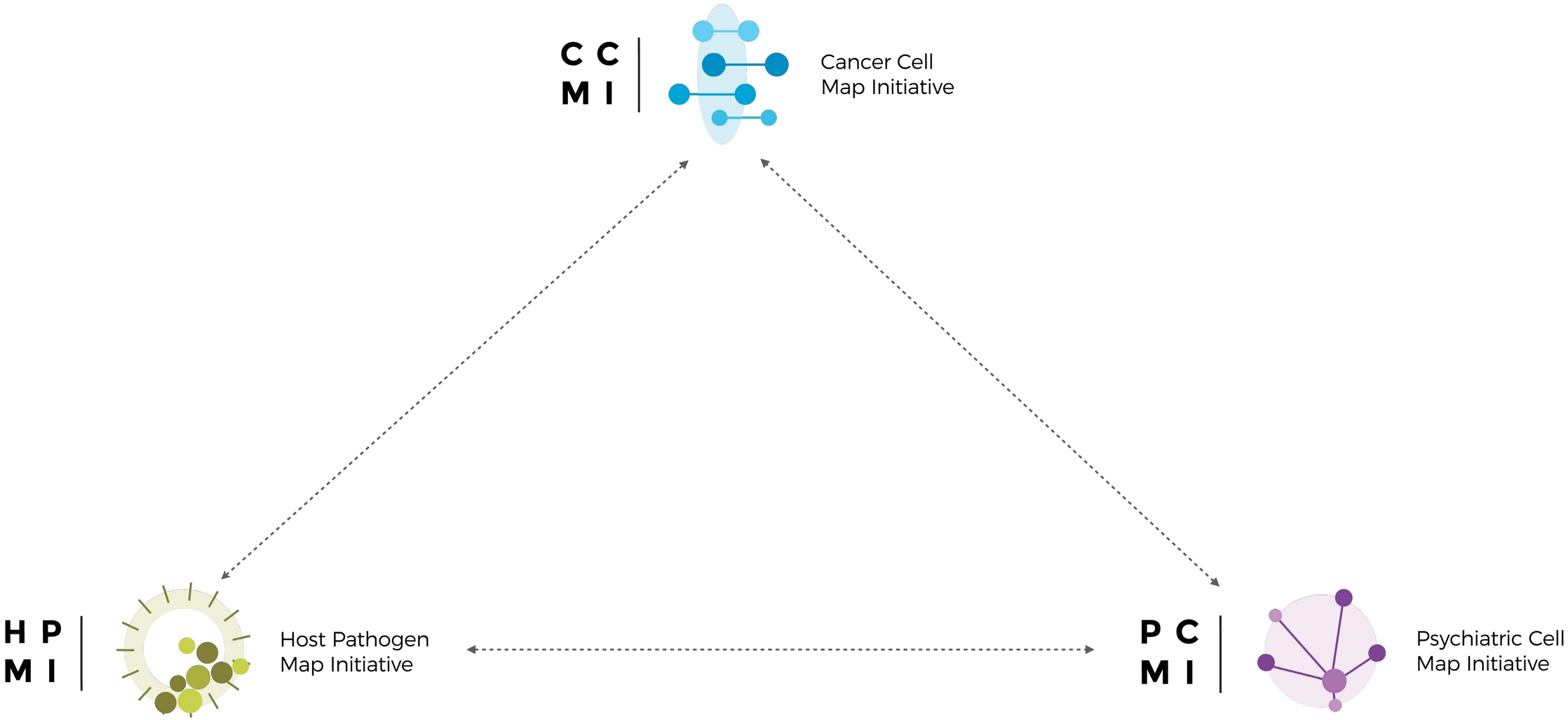
2018 - 8 seminars
2019 - 10 seminars

QBI is a University of California organized research unit reporting through the UCSF School of Pharmacy

QBI International Collaborations

Establishing a culture of collaboration

QBI Initiatives: Cell Mapping



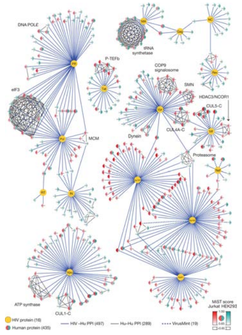
What if?

- What if in the same way we map the cells, we started mapping the world with collaborative interactions?
- Cell mapping = World mapping
- Protein Protein Interactions = People People Interactions

Host-Pathogen Protein-Protein Interaction Networks

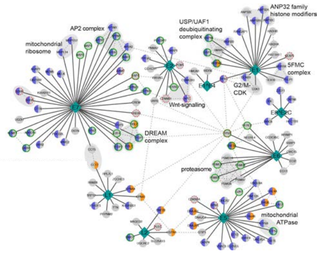
HIV-1

Jäger et al, Nature, 2012



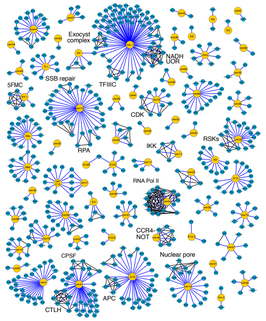
HPV

Eckhardt et al., Cancer Discovery, 2018



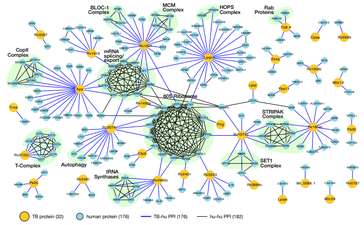
Kaposi Sarcoma's Herpes

Davis et al., Molecular Cell, 2015



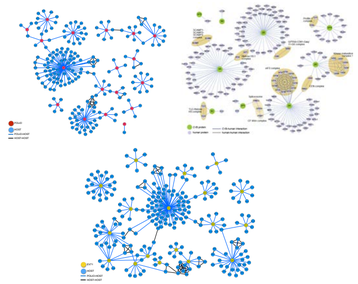
Tuberculosis

Penn et al., Molecular Cell, 2018



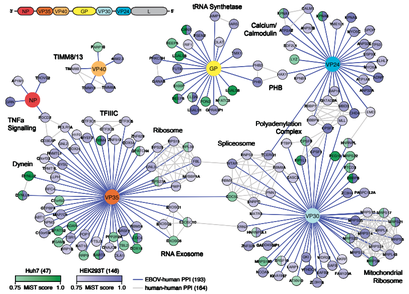
Enteroviruses: Polio vs Cox-B vs EV-71

CVB: Diep et al., Nature Microbiology, 2019

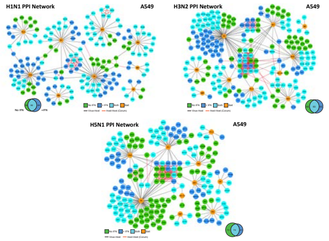


Ebola

Batra et al., Cell, 2018

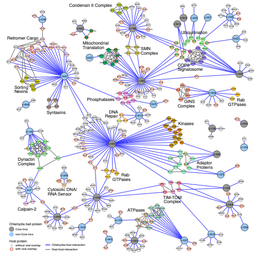


Influenza-A: H1N1 vs H5N1 vs H3N2



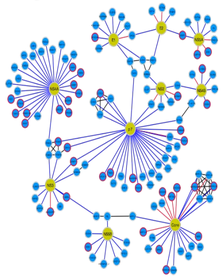
Chlamydia

Mirrashidi et al., Cell Host and Microbe, 2015

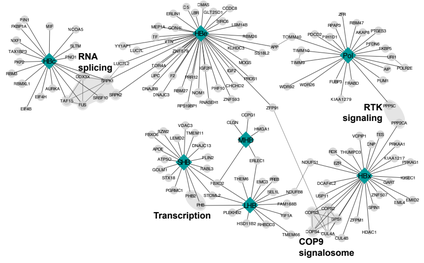


Hepatitis-C

Ramage et al., Molecular Cell, 2015

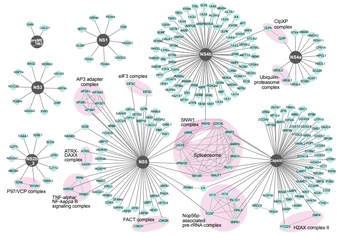


Hepatitis-B



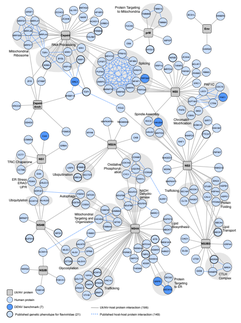
West Nile Virus

Li et al., Nature Microbiology, 2019



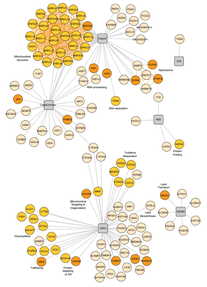
Dengue (human)

Shah et al., Cell, 2018



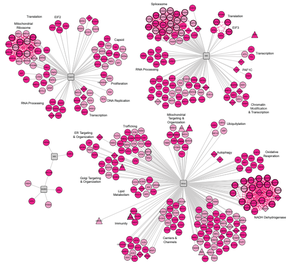
Dengue (mosquito)

Shah et al., Cell, 2018

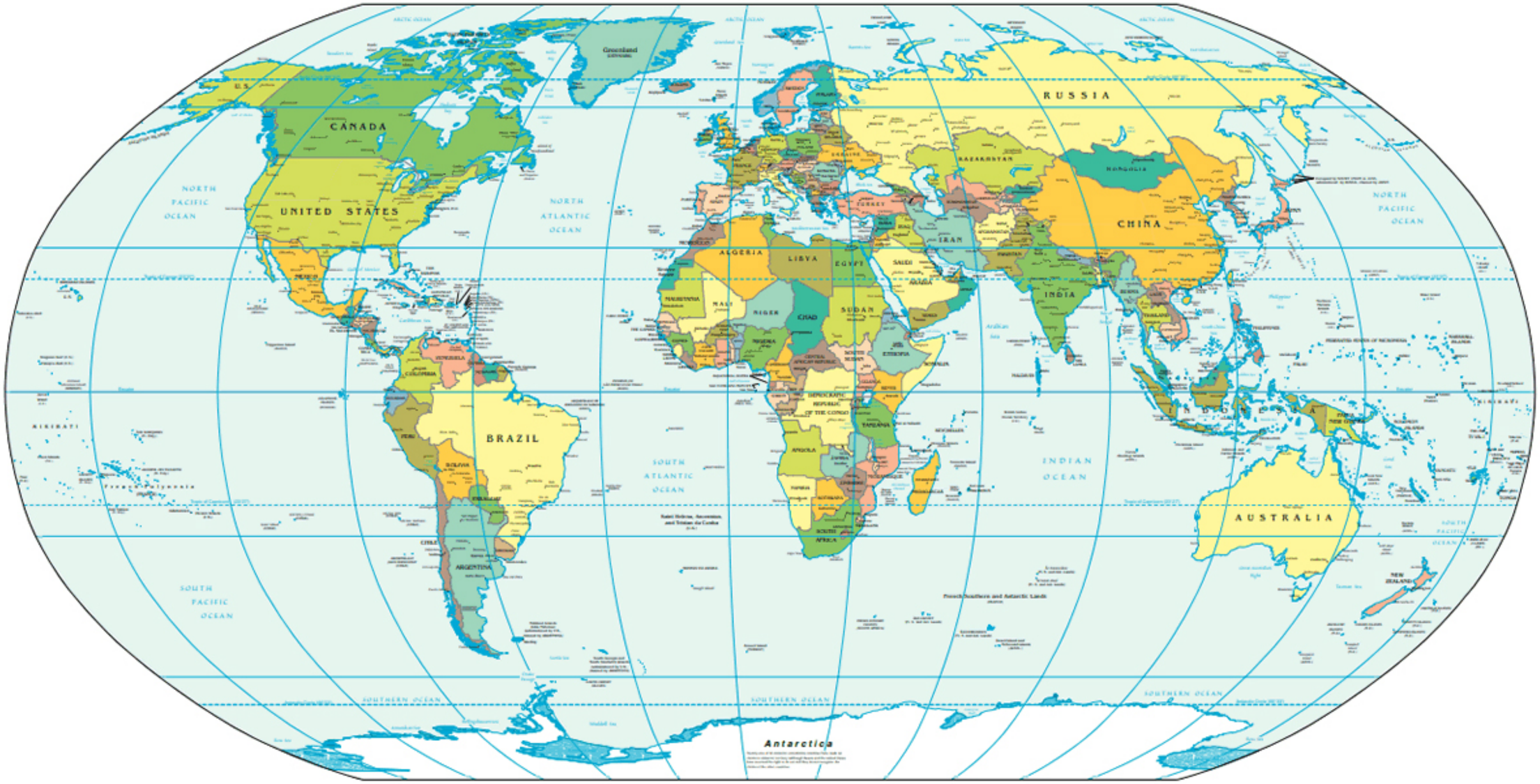


Zika

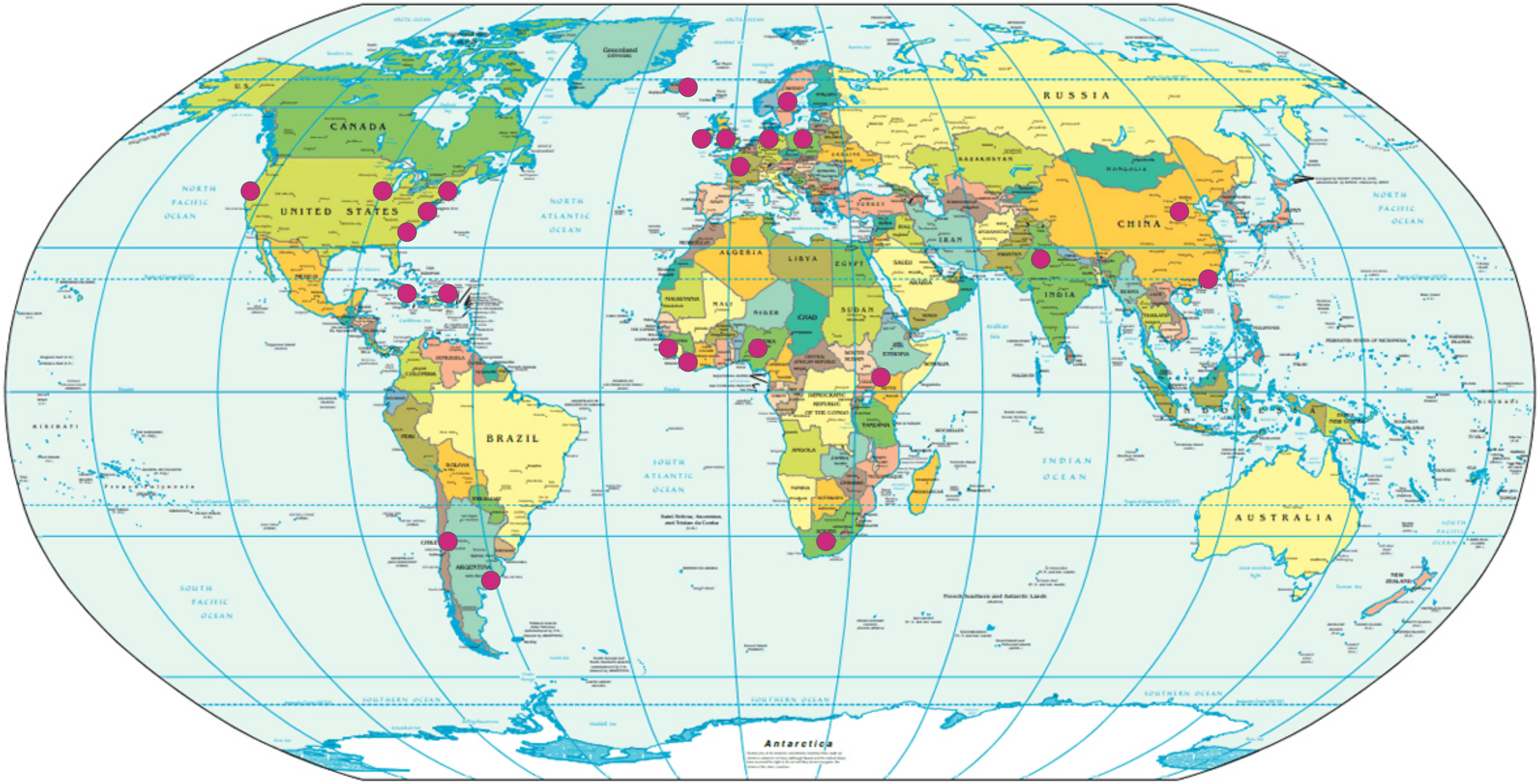
Shah et al., Cell, 2018



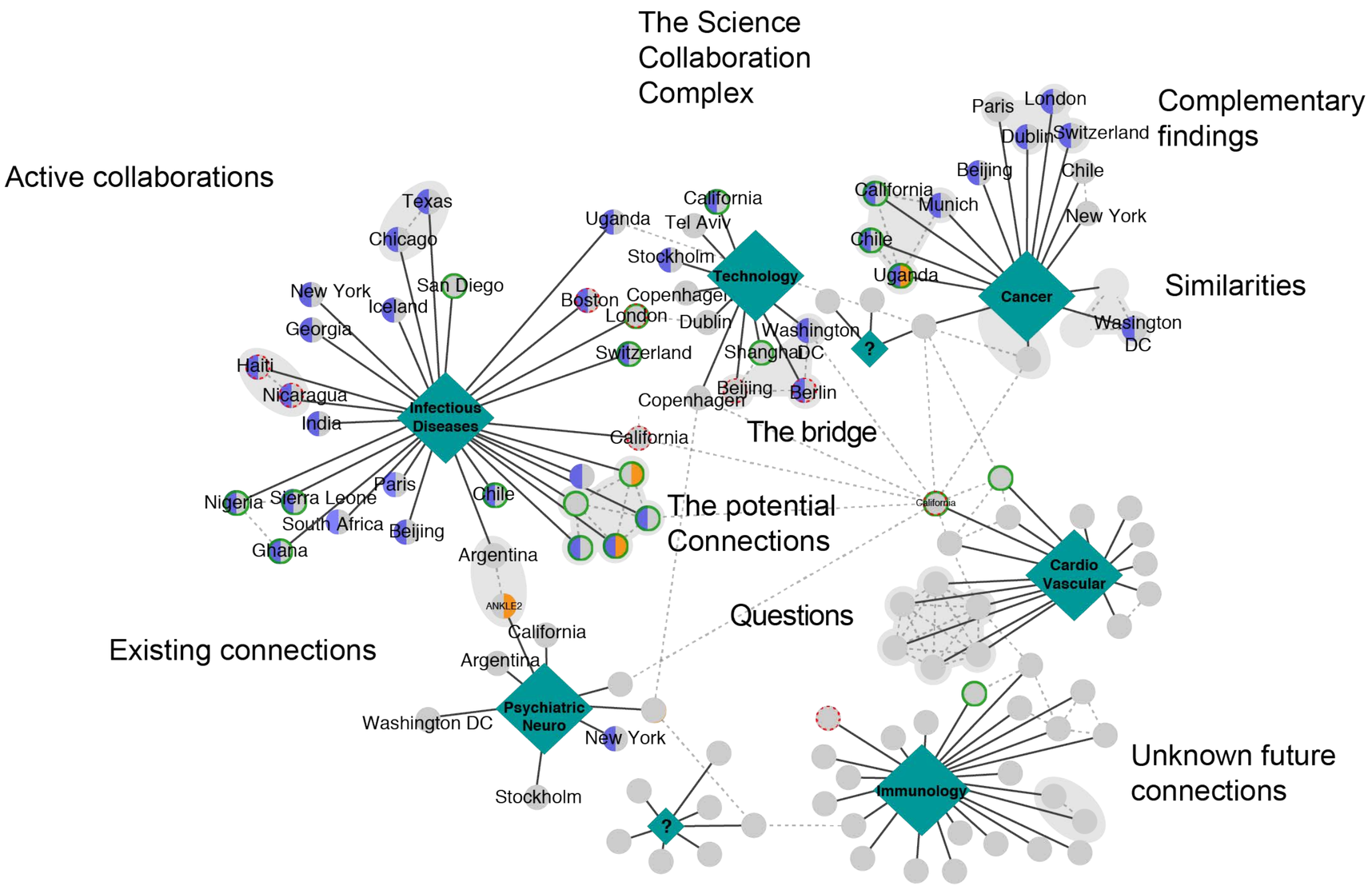
QBI International Collaborations



QBI International Collaborations



QBI Collaborative Network



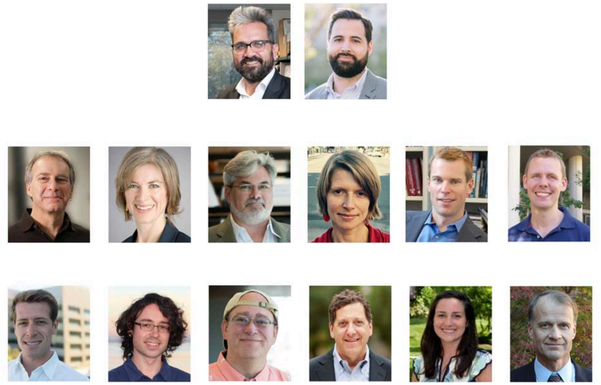
QBI Center Grants - $85M

Collaborative science at UCSF and beyond

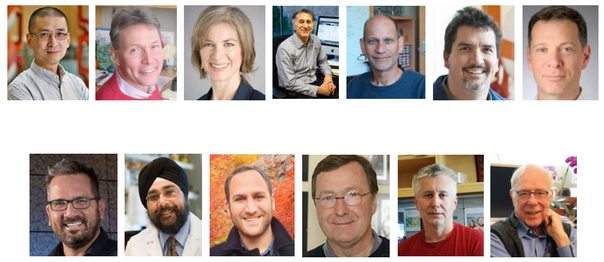
CCMI Cancer Cell Map Initiative

HPMI Host Pathogen Map Initiative

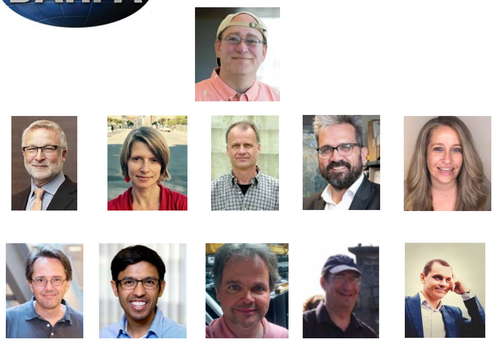
PCMI Psychiatric Cell Map Initiative



The HARC Center



DARPA

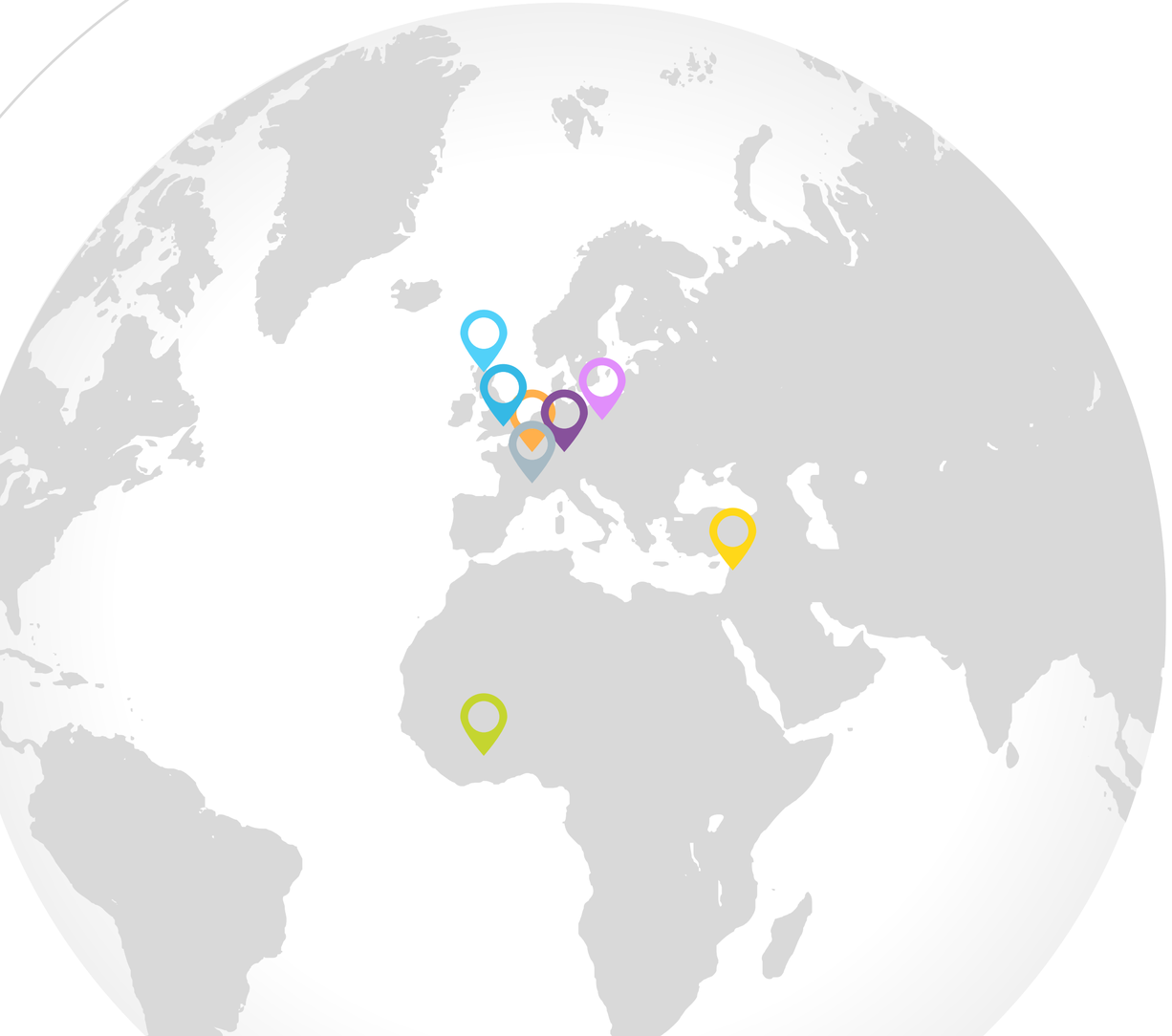


Collaborative Meetings and MOUs

- International Relationships built on science
- Fostered with collaborative symposia
- Formalized with MOUs & RFAs for collaborative research

QBI International Collaborations

Breaking down silos



Freie Universität Berlin, Germany
Integrative Structural Biology

University College Dublin, Ireland
Quantitative Biology and Cancer

Institut Curie / PSL, France
Quantitative Biosciences

Redeemer's University, Nigeria
Hemorrhagic Fevers and viruses

Jagiellonian University, Poland
Structural Biology and Exchanges

Tel Aviv University, Israel
Bioinformatics and Drug Discovery

Crick Institute, UK
Cell Mapping

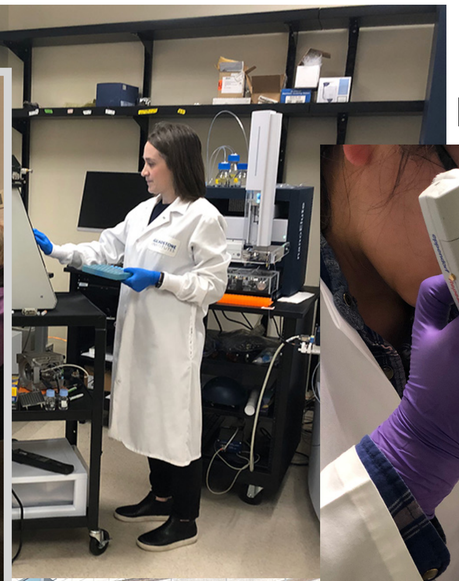
Institut Pasteur, France
Infectious Diseases

The formation of QCRG

Understanding the context of a coming pandemic and taking action

QCRG - The Beginning

Late Friday night, early March



Prepping MS

The team forms

Discussing immediate action

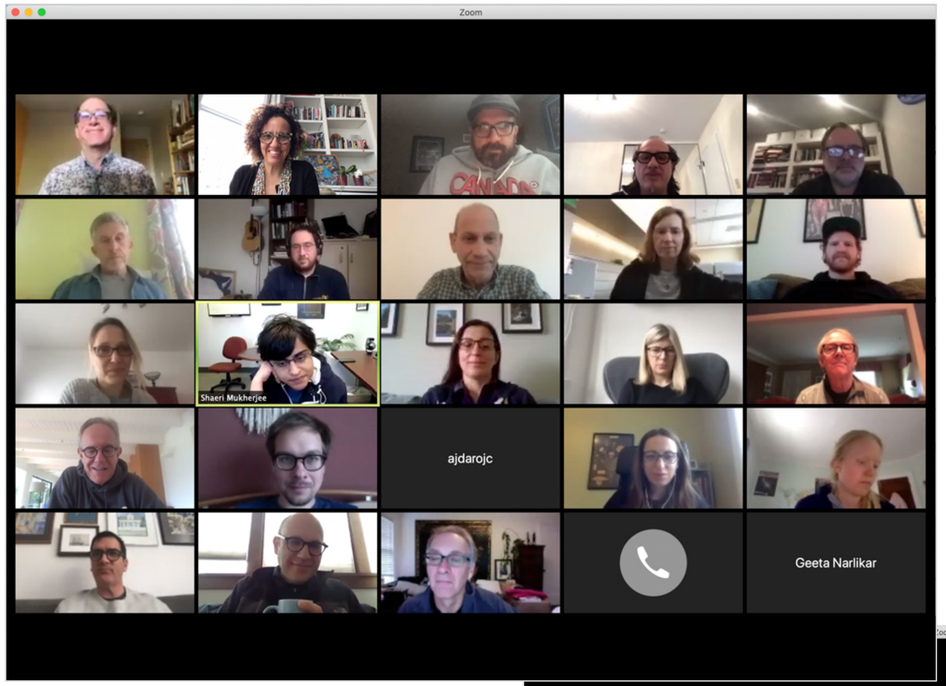
Mad rush to finish all mass spec experiments to create **the map** before the campus shutdown

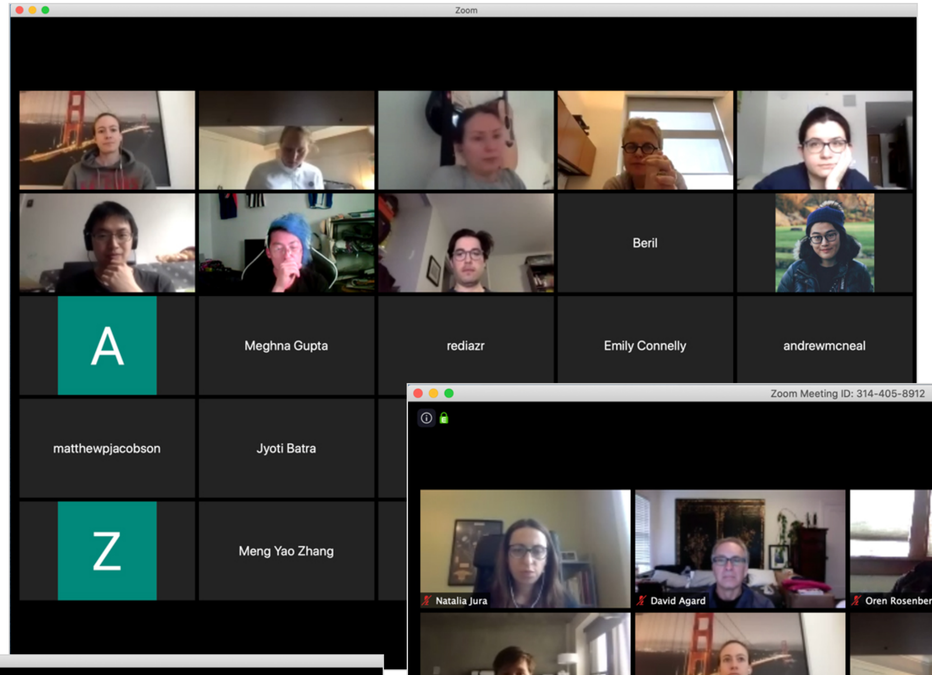
Running MS samples

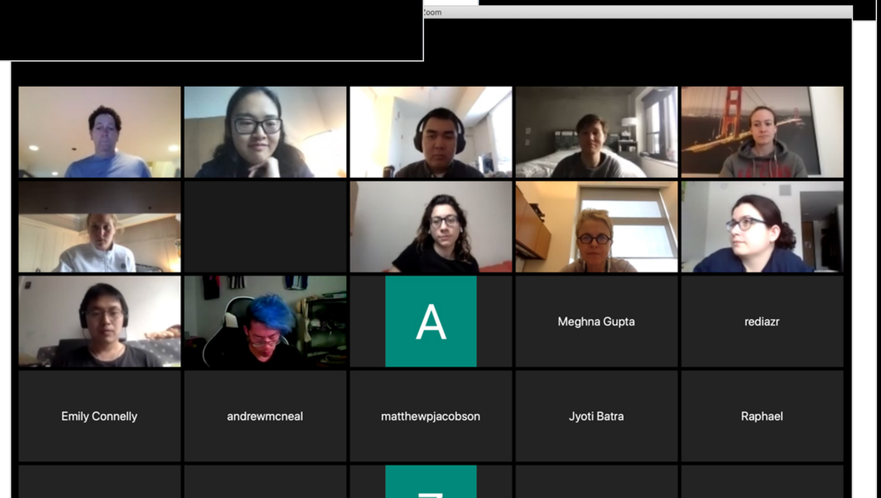
Suddenly everyone working from home

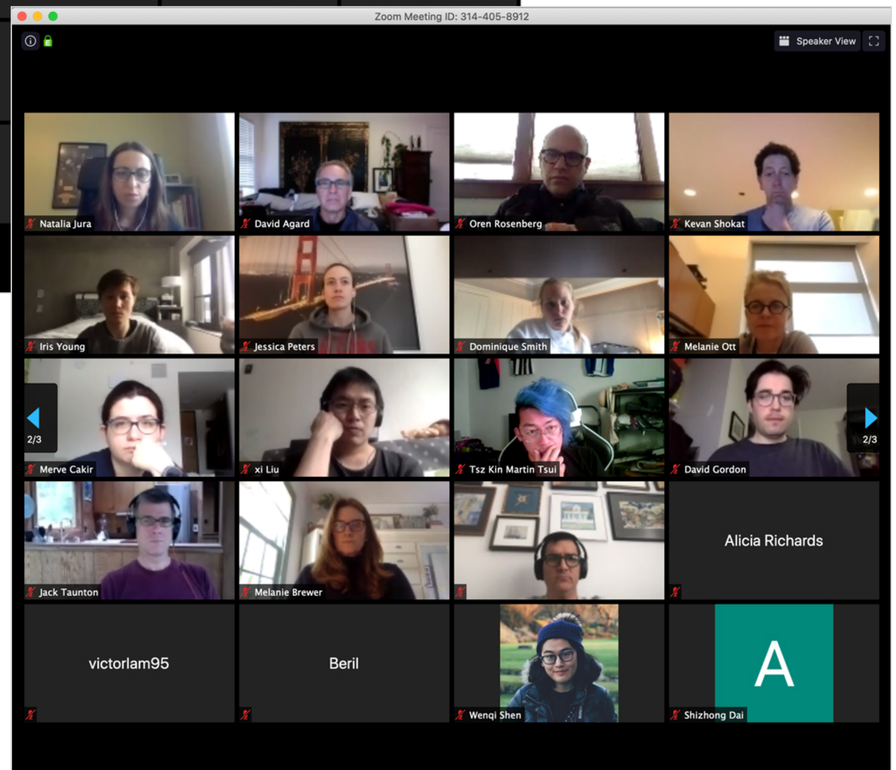
COVID-19, Quarantine 2020

Extensive Teamwork - Science on Zoom







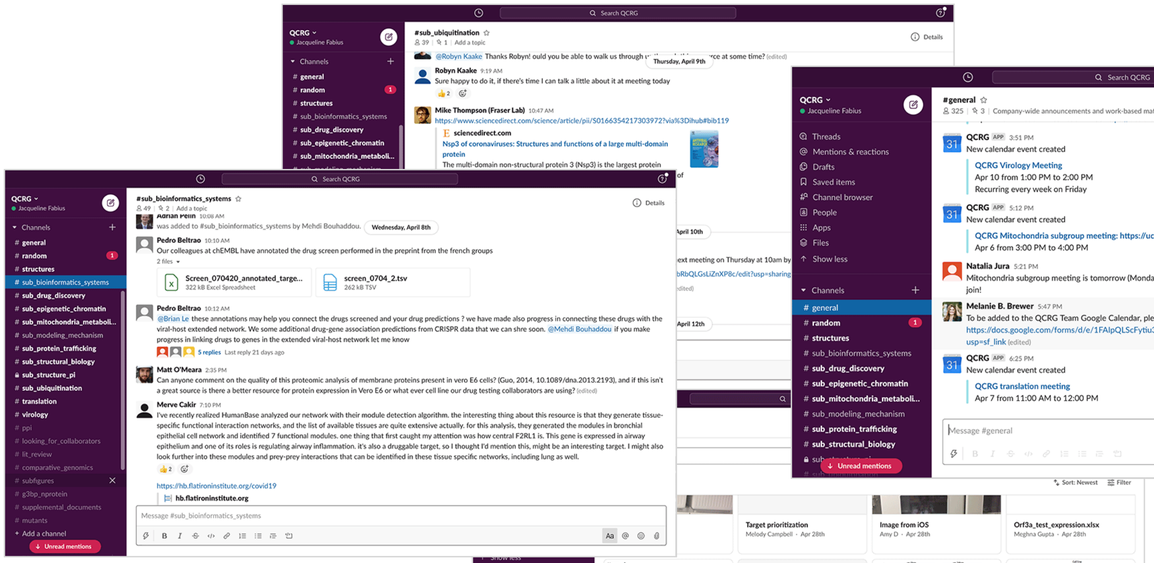


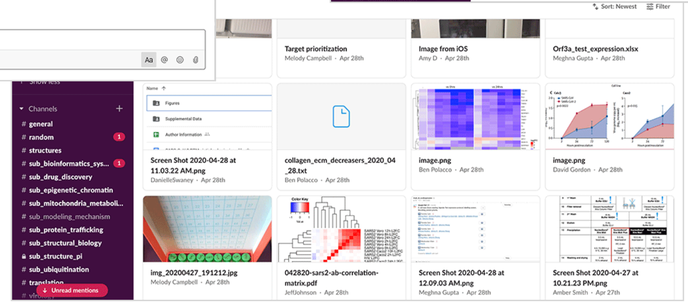
- 178 scientist on one call
- Multiple calls a week
- Subgroups formed

Science communication lends itself well to Zoom: people used to presentation and Q & A format.

Tools for the team

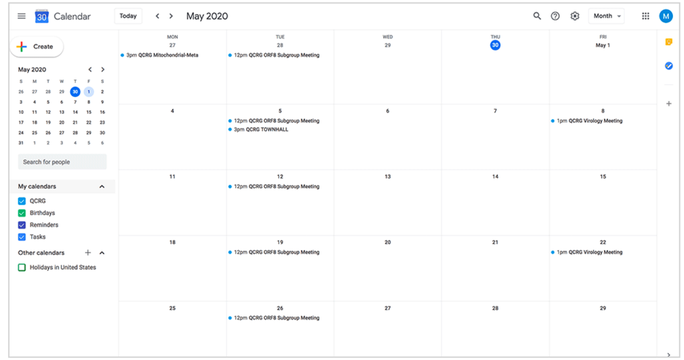
Slack



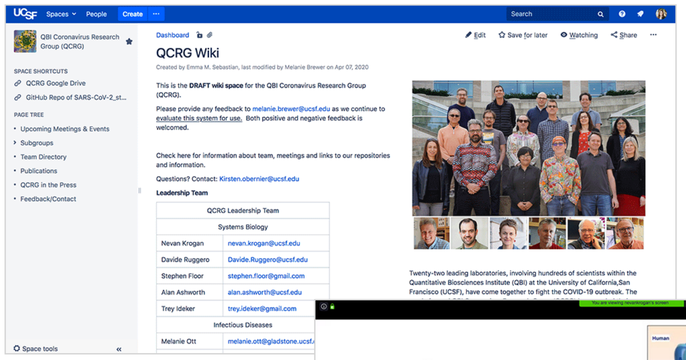


- Communication and exchange of findings in real time
- Connect calendars
- Upload files

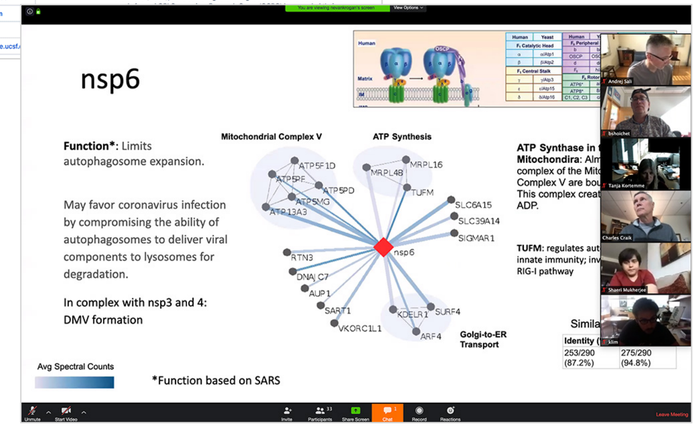
Google Calendar



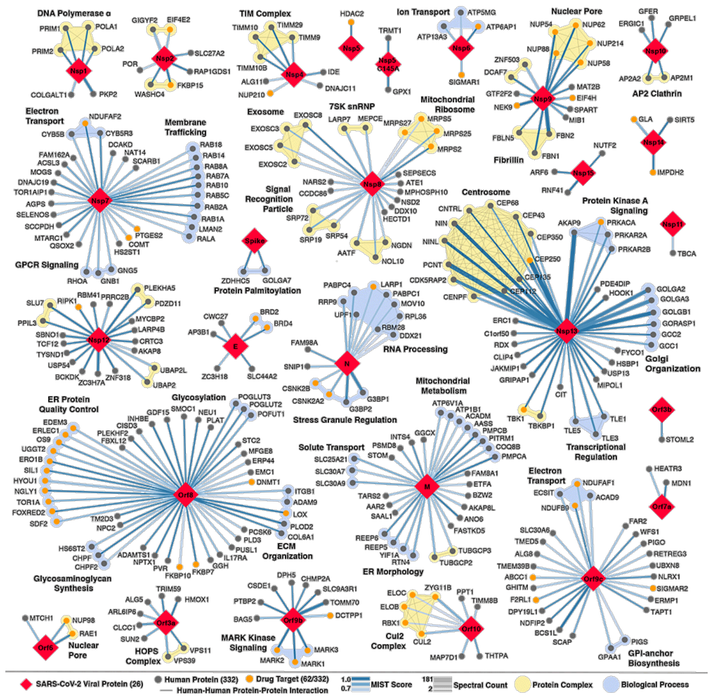
QCRG Wiki



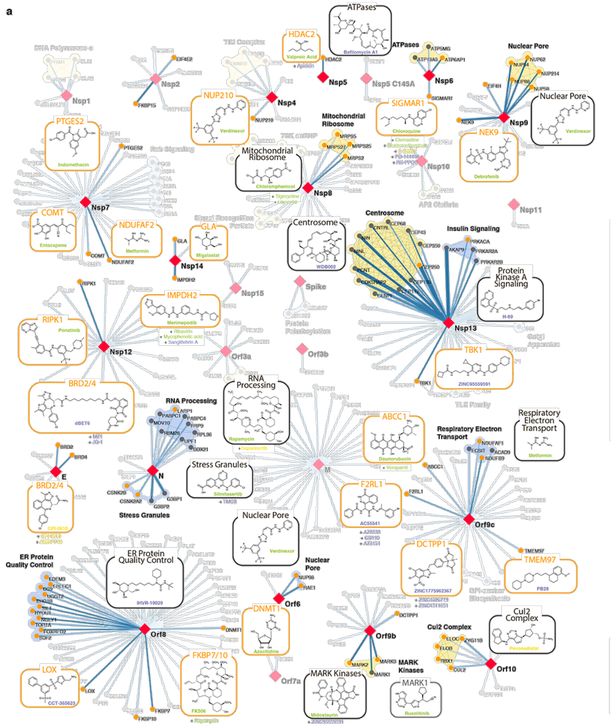
Zoom



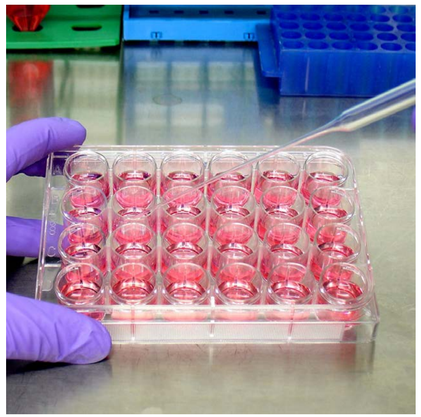
Map to Drug Identification to Virus Testing



Map

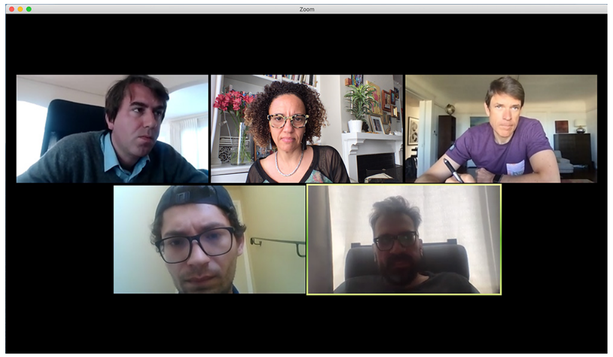


Map with drug & compounds overlaid



Experiments in NY & Paris
In virus

Support From All Sides



SF French Consulate

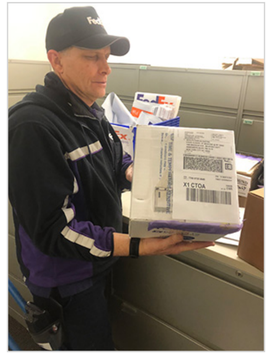
French Ambassador

FedEx

DOUANES & DROITS INDIRECTS

French Customs

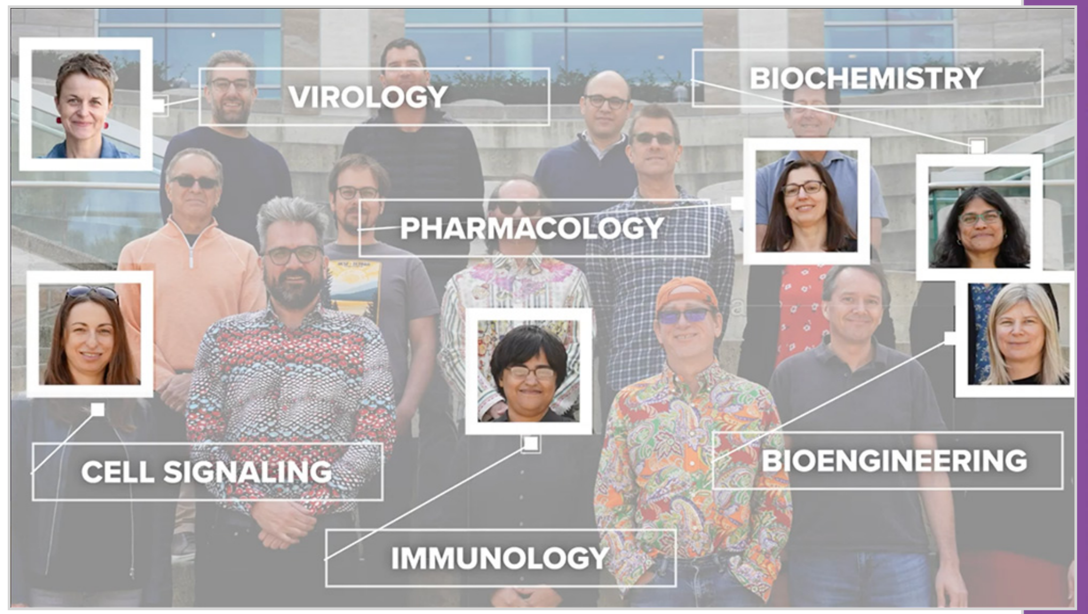
Compounds

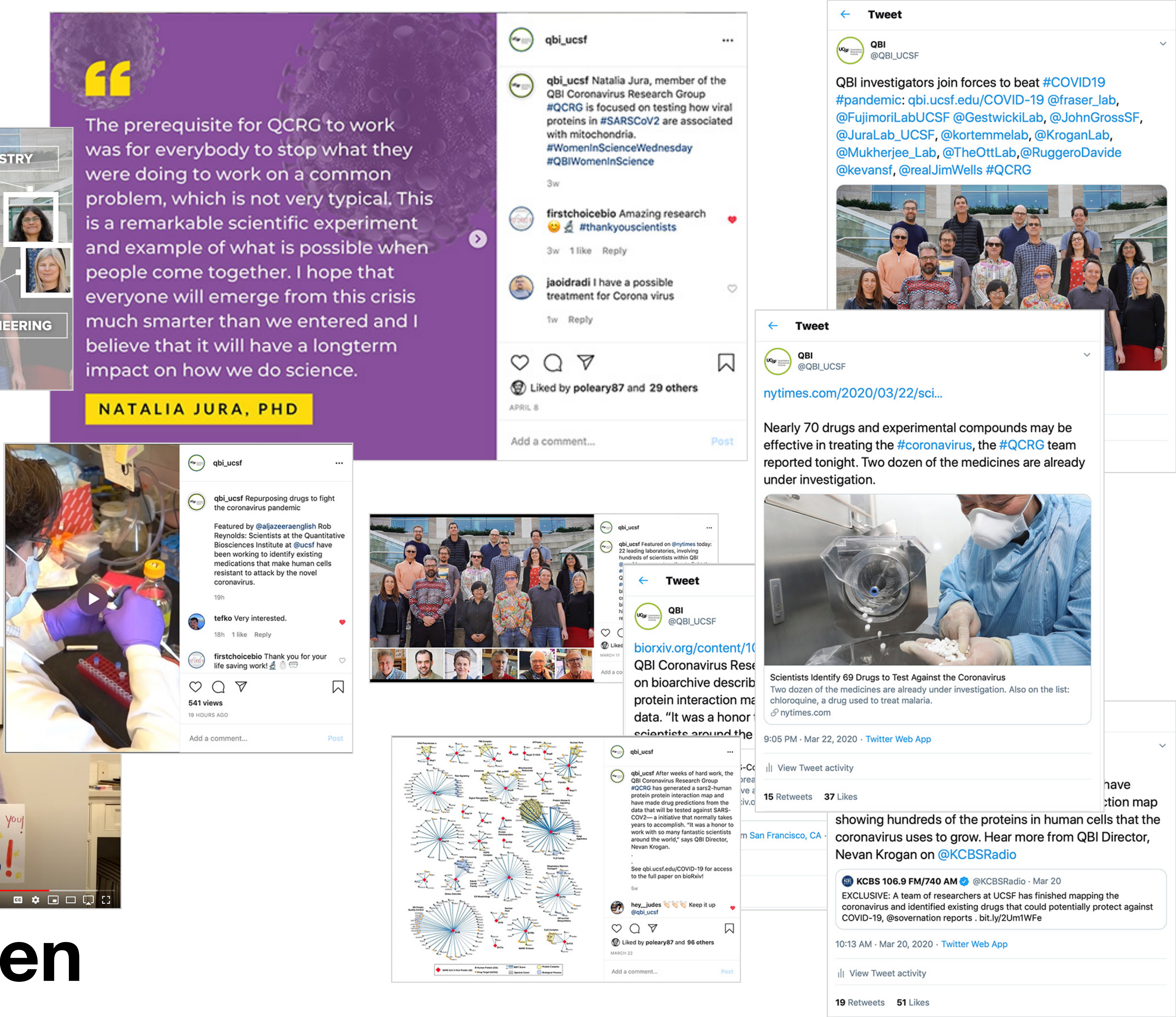


Todd @ FedEx

Institut Pasteur

Building Our Narrative - Engaging People

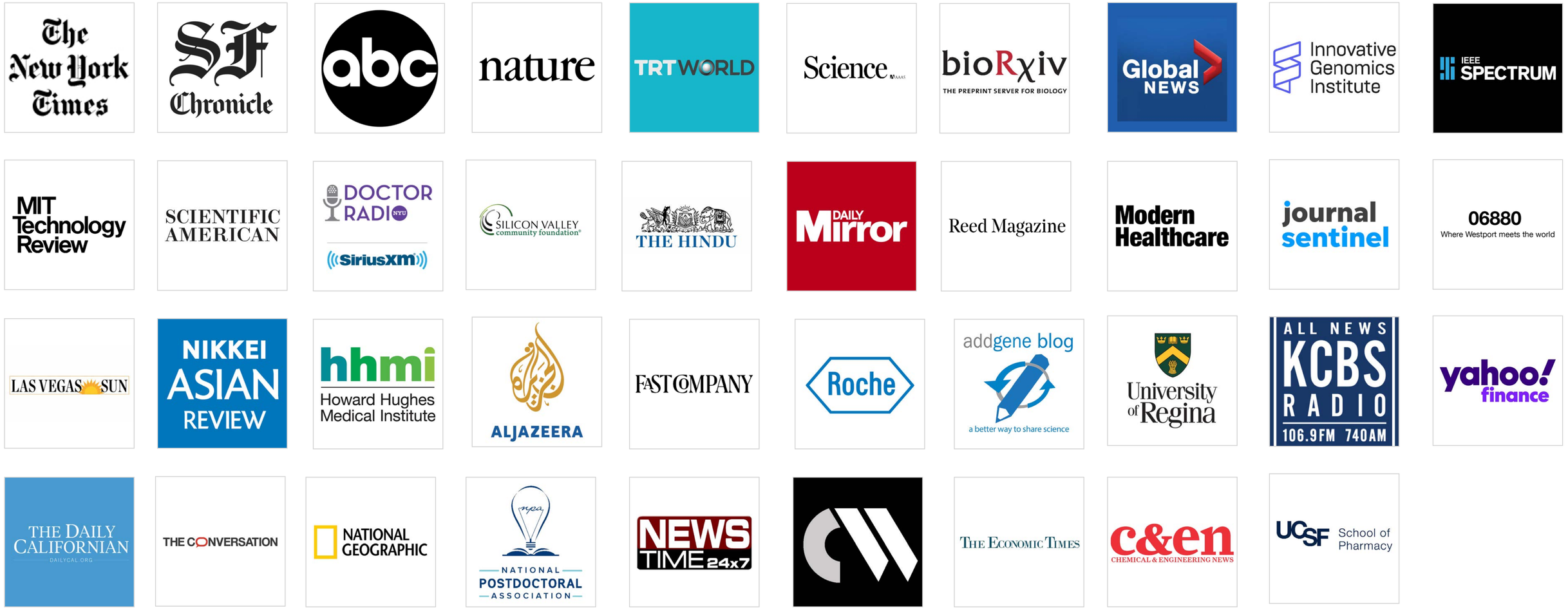




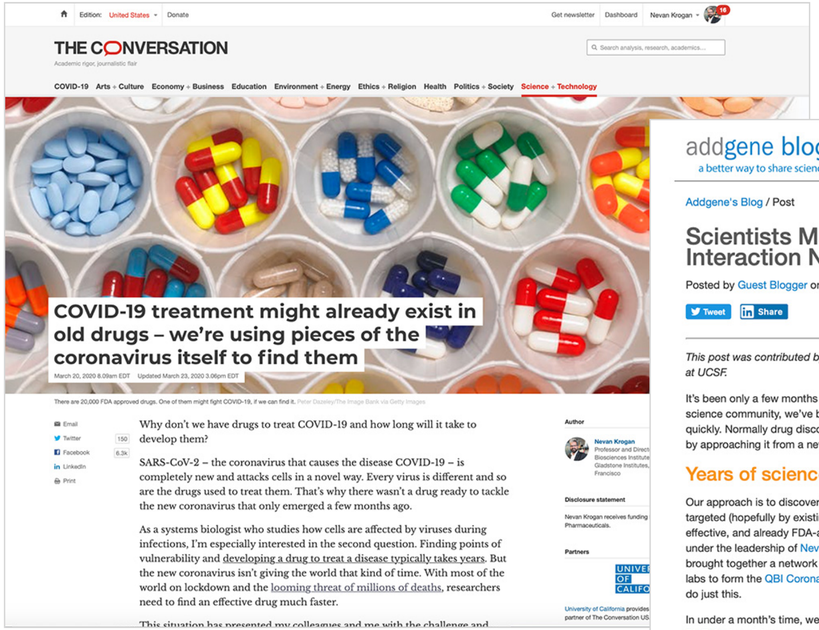
- Public
- Donors
- Staff
- Government agencies, NIH, DARPA, etc.
- Biotech / Pharma
- Media

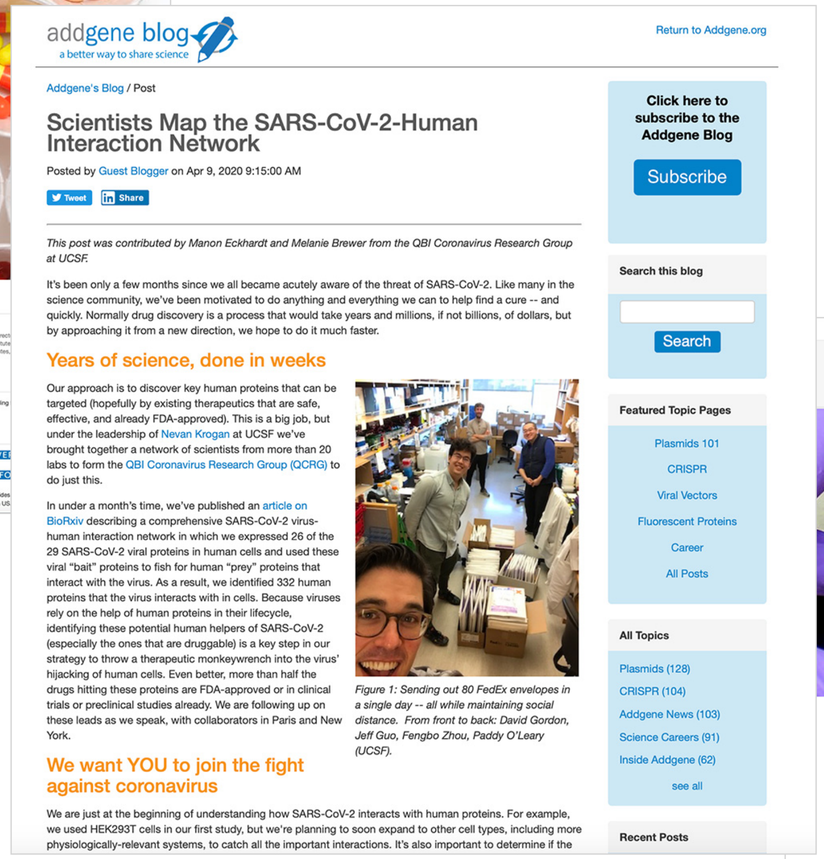
Keep people informed - often

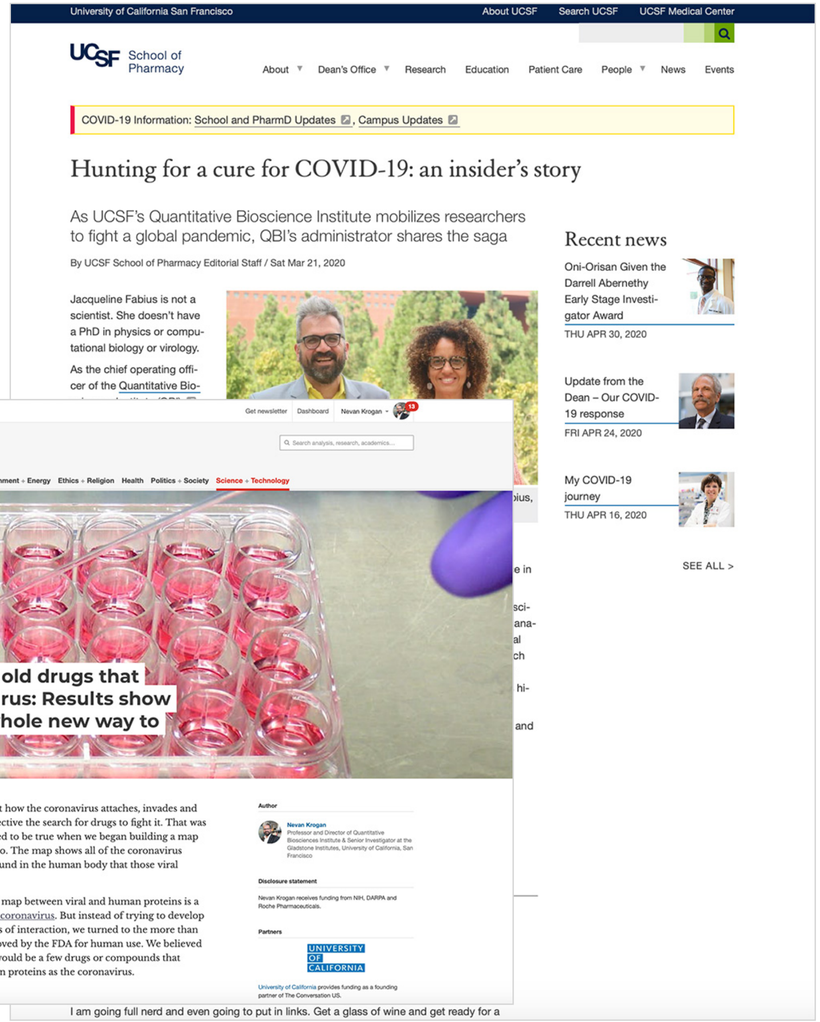
Sudden Media Explosion



Write Our Story







Strategize your message

Put stories out there in your own voice with emphasis on what is important to your vision

This stuff is complicated

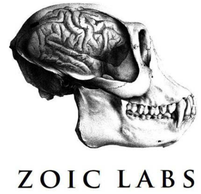
Have a real voice that speaks to a lay audience: write for your friends and family

An Army of Willingness

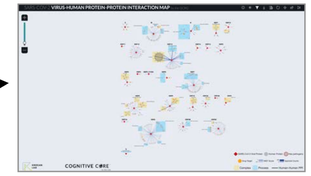
Co-founder Twitter

Y Combinator

Lumi Labs



ZOIC LABS



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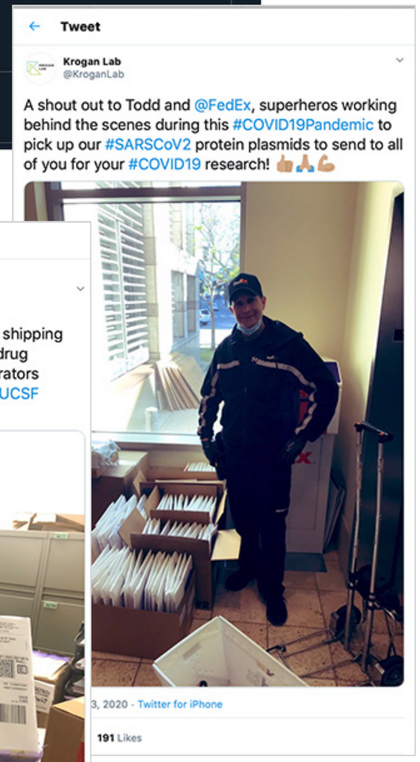
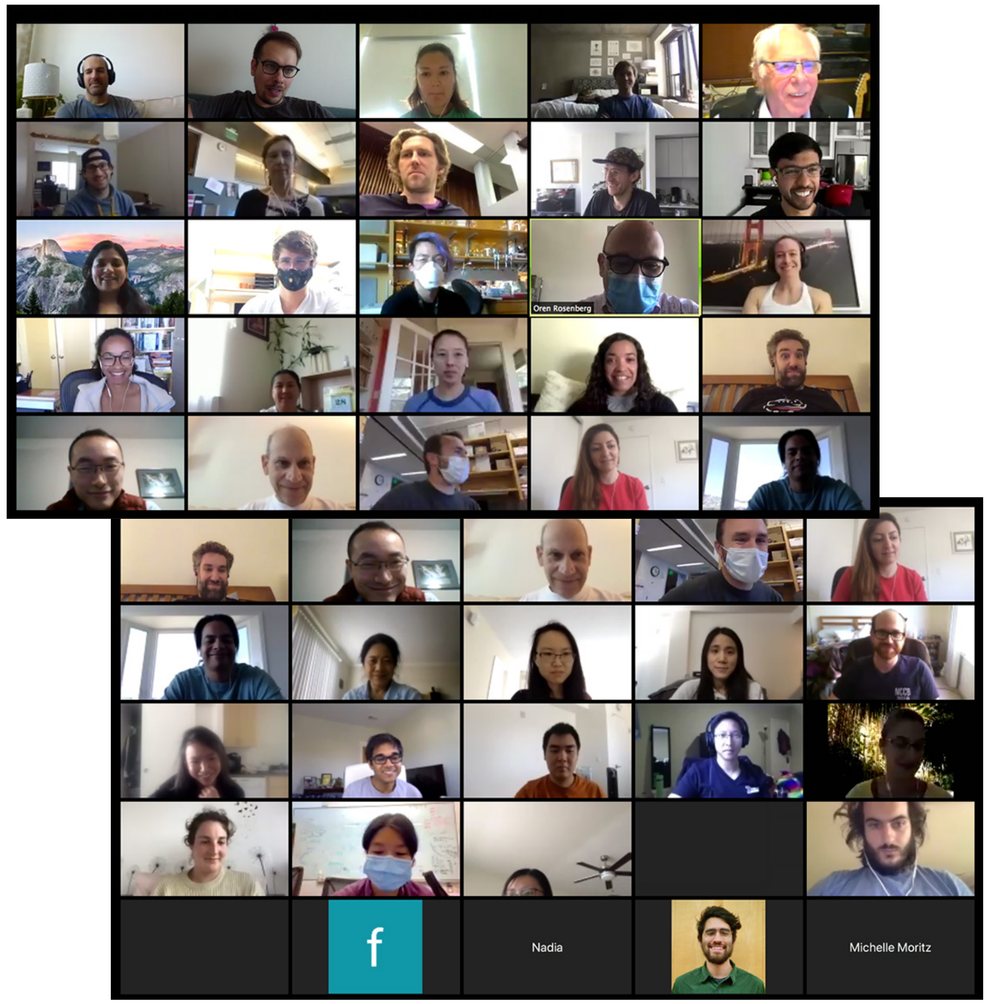


addgene
The nonprofit plasmid repository

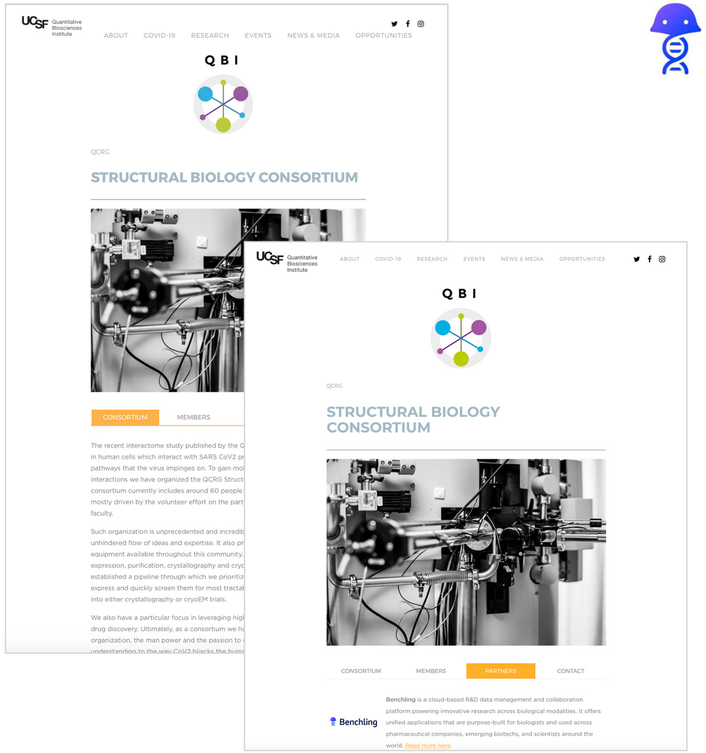
Benchling

SYNTHEGO

Being Open to Resulting Innovation: Structural Biology Consortium

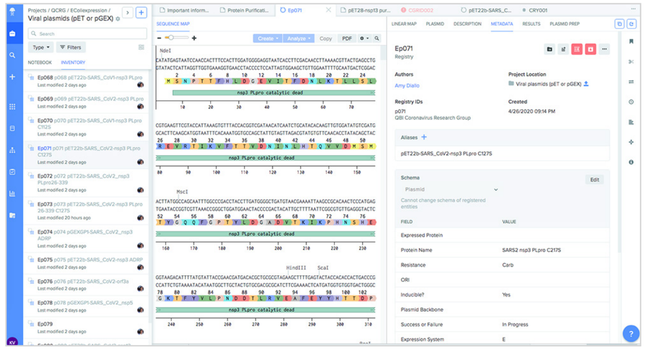


Ready to support innovation and partnerships born from it



React to growth and allow for it immediately with information infrastructure

Benchling



Be ready to accept engagement and generosity and have a platform for it

Stay Tuned…

Because things are changing all the time!

Find out more

UCSF Quantitative Biosciences Institute

www.qbi.ucsf.edu