

QBI 2016 - 2020

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HISTORICAL OVERVIEW

UC San Francisco announced the establishment of the Quantitative Biosciences Institute (QBI) in March of 2016 as a new ORU (Organized Research Unit) within the <u>School of Pharmacy</u>. The mission of QBI is to drive forward the application of computation, mathematics, and statistics toward a deeper understanding of complex problems in biology, with the ultimate goal of developing new treatments for disease in a disease agnostic environment.

The origins of QBI as an organized research unit (ORU) lie in a previously formed School of Pharmacy ORU, the <u>Molecular Design Institute (MDI)</u>, created in 1993 by Irwin "Tack" Kuntz, PhD, today a professor emeritus in the School of Pharmacy's Department of Pharmaceutical Chemistry. The initial goal of MDI was to promote the discovery, design and delivery of novel pharmaceutical agents. When attempts were made to create the MDI, many of the experimental and computational tools for drug design based on quantitative approaches were simply not available. Thanks to recent revolutions in quantitative and computational biology over the last 20 years, QBI was in a unique position to exploit quantitative approaches to uncover the underlying biology behind virtually any disease area and ultimately identify compounds and treatments that could have therapeutic value. The current Dean of the School of Pharmacy, B. Joseph Guglielmo, with strong support from the UCSF campus and the UC Office of the President, transformed MDI into QBI.

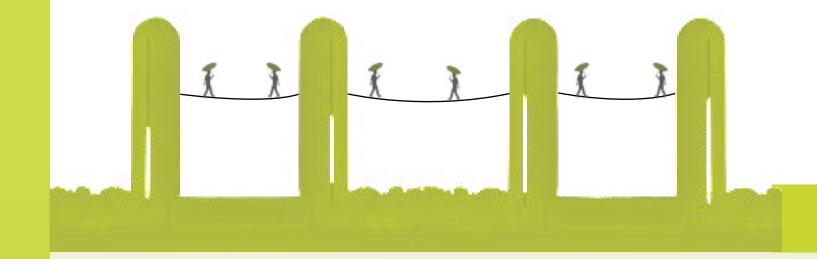
The founding director, Nevan Krogan, PhD, a professor in the Department of Cellular and Molecular Pharmacology and a senior investigator at the Gladstone Institutes, is known for his research on developing and using systems biology approaches to help clarify complex biological phenomena at a mechanistic level, often leading to therapeutic insights.

The goal at QBI is to help make precision medicine a reality by using quantitative research tools to understand the underlying biology behind different disease states, and then to use that knowledge to develop novel therapies and put them into the hands of clinicians.

In its first four years, QBI initially focused on oncology, psychiatric disorders, including autism, bipolar disorder, and schizophrenia, as well as infectious diseases, including those caused by HIV, Dengue and now SARS-CoV-2 viruses. With this early focus, QBI established several Cell Mapping Initiatives, including the <u>Cancer Cell Map Initiative</u> (CCMI), the <u>Host-Pathogen Map Initiative</u> (HPMI) and the <u>Psychiatric Cell Map Initiative</u> (PCMI), to study these diseases and disorders in a collaborative framework using unbiased, multi-disciplinary and quantitative approaches.

As an official University of California ORU, QBI is able to compete for large collaborative cross-disciplinary grants from the National Institutes of Health, which ultimately benefited the work of QBI faculty affiliates and established unique and highly collaborative relationships with entities around the world. The following report highlights the role QBI has played in increasing UCSF community participation by fostering scientific collaborations in a novel, modern and cutting-edge way.

As is the case with any ORU, the multi-School nature of QBI results in a direct QBI report to the Chancellor's Office. The University of California mandates that a Director of an ORU reports to the Chancellor or the Chancellor's designee. The Chancellor has appointed the Dean of SOP (currently B. Joseph Guglielmo) to be his designee and, therefore, the Director of QBI (currently Nevan Krogan) reports to him.



MISSION

The <u>Quantitative Biosciences Institute</u> (QBI) fosters collaborations across the biomedical and the physical sciences, seeking quantitative methods to address pressing problems in biology and biomedicine. Motivated by problems of human disease, QBI is committed to investigating fundamental biological mechanisms, because ultimately solutions to many diseases have been revealed by unexpected discoveries in the basic sciences.

Our initial motivation behind the formation of the Quantitative Biosciences Institute (QBI) at the University of California-San Francisco (UCSF) was simple: collaboration. We did not set out with a specific agenda in mind, but rather a discovery to determine who was of the same explorative and collaborative mindset. One major goal of QBI was focused on breaking down the walls in academia and creating teams between different sets of scientists working in diverse disciplines to tackle problems that can only be solved by many groups working together. Academic research is often focused on the individual scientist.

For example, grants are often awarded to a single investigator, tenure is assessed based on individual achievements, and most awards are given to a single scientist. In fact, if there is significant collaborative work, the contributions of individual investigators, especially more junior ones, are often questioned. This structure incentivizes research that is often unnecessarily competitive and siloed. We would argue that our current academic system can actually impede discovery. Increasingly, many big breakthroughs in biomedical research require teams to work together, where each group brings something unique but highly complementary to the problem.

QBI is leading by example with teams of scientists solving each individual problem – together. Technology, and the data derived from it, is at the heart of collaborative efforts, as QBI scientists are the experts developing experimental and computational tools that can be applied to many biological or biomedical problems. These tools allow for effective connection between the discovery research and clinical worlds, enabling novel therapies for disease.

VISION

STRATEGIC PLANNING

QBI is facilitating multidisciplinary, highly collaborative, ground-breaking research and outreach not only at UCSF butaround the world. To this end, we have implemented an aggressive and successful strategy in obtaining large center grants from both NIH and DARPA. Since 2016, QBI visited NIH and DARPA program officers over 20 times, each time updating our current program officers with progress but also reaching out to new ones. QBI also presented to Congress at the <u>Coalition for the Life Sciences</u> (CLS), on **September 14**, **2017**, a briefing entitled <u>Breaking Down Scientific Silos:</u> <u>Identifying Commonalities across Diseases</u>. These efforts ultimately helped to secure four collaborative NIH grants around the different cell mapping initiatives as well as significant funds from DARPA.

This strategy has accomplished two things:

- Brought together scientists from different disciplines, including the discovery and clinical worlds
- Provided funding to the scientific community which has led to additional funding through the evolution of collaborations

We have also partnered with a number of different entities on campus offering RFAs to bring together scientists in different disciplines. In total, we have provided \$2M in collaborative funding with the Cancer Center, the Departments of Psychiatry and Radiology. In total, 40 scientists have been funded through this mechanism.

This strategy has extended to other institutions in different countries. As described in more detail elsewhere, we have partnered with top institutions in different countries for joint symposia, with subsequent joint, cross-country RFAs. This strategy, which has been used in collaboration with the Curie Institute, Tel Aviv University and Freie Universität Berlin, has linked scientists at QBI with those around the world. Pending RFAs for 2021 include the Weizmann Institute, the Institut Pasteur and University College Dublin.

The COVID-19 pandemic worldwide caused us to quickly pivot to form the <u>QBI</u> <u>Coronavirus Research Group</u> (QCRG), a collaborative group of over 40 QBI labs, as well as many more around the world, that was focused on finding solutions for COVID-19. Simply put, this is a testament to the disease-agnostic infrastructure that we built and the world-wide connections we developed. Under the QCRG umbrella, we independently raised over \$6M through philanthropic efforts, approximately \$2M of which has already been distributed to QCRG investigators. These funds have facilitated additional grants from federal agencies and foundations. Based on this experience, we are encouraged to raise additional philanthropic funds for other disease areas building upon the connections we have made during this pandemic.

LEADERSHIP TEAM

QBI has a strong leadership team that facilitates decisions and guides the institute towards its goals. The members of the QBI Executive Committee, David Agard, Tanja Kortemme, Brian Shoichet and Andrej Sali, are experienced scientists and have been dedicated to supporting QBI and the greater UCSF community for years. Their exceptional achievements are a sound but optimistic lense through which they see and guide the future aspirations of the Institute.



David Agard



Brian Shoichet



Tanja Kortemme



Andrej Sali

QBI EXECUTIVE COMMITTEE



The QBI Associate Directors, Sourav Bandyopadhyay, Natalia Jura, James Fraser and Danica Fujimori, are the face of the future of science. These young scientists are focused on new approaches and bring a fresh perspective to the Institute and its direction.



Sourav Bandyopadhyay



James Fraser

QBI ASSOCIATE DIRECTORS

Natalia Jura



Danica Fujimori

QBI ADMINISTRATION TEAM

QBI has also built a productive administrative team led by Jacqueline Fabius, the Chief Operating Officer, who oversees all activities related to QBI. Jeff Beck, the Chief Financial Officer, and Prosper Godonoo, a post-award analyst, provide the expertise to coordinate QBI finances. Gina Nguyen, Director of Communications and Events, and Alexa Rocourt comprise the QBI media team responsible for events, media and outreach activities, communicating to the scientific community and general public. Finally, Vincenzo Pierotti, an administrative analyst, oversees HR, including recruiting and internships, as well as service contracts between the QBI and consultants and vendors.



Jacqueline Fabius



Jeffrey Beck



Prosper Godonoo



Gina Nguyen

SCIENTIFIC PROJECT MANAGERS

Key to QBI are also senior scientific project managers including Melanie Brewer and Kirsten Obernier, who manage and support the different center grants affiliated with QBI. Another science project manager, Lorena Zuliani-Alvarez, has recently been hired to manage the QCRG and will begin in December 2020. Finally, Peggy Ackerberg serves as Nevan Krogan's executive assistant, and helps him navigate, schedule and organize his meetings and events for QBI.





Melanie Brewer



Vincenzo Pierotti

Kirsten Obernier

Lorena Zuliani-**Alvarez**





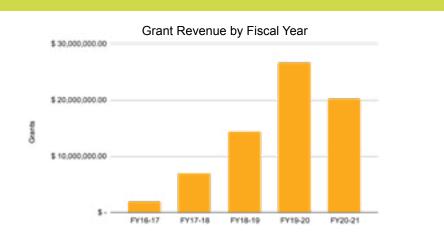
Peggy Ackerberg

FINANCE

QBI FINANCIAL SUMMARY

The Quantitative Biosciences Institute has a diverse portfolio of funding sources including federal and industry grants, gifts and sponsorships, chancellor's startup funding and campus funding sources. Refer to the table at the end of this section for a detailed financial report.

Grants – Since obtaining our first grant, the Cancer Cell Mapping Initiative (CCMI) in FY16-17, grant revenue has steadily increased. We have grown from \$1.9M in grant funding in that year to \$26.7M in FY19-20. Our current portfolio includes grants for CCMI, the HIV Accessory & Regulatory Complexes (HARC), Psychiatric Cell Mapping Initiative (PCMI), Host-Pathogen Mapping Initiative (HPMI) from the NIH and multiple projects with DARPA and Roche. Thus far in FY20-21, we have been awarded \$20.2M in funding and have two new center grant proposals under review.



General Gifts (non-COVID) – QBI has received periodic general donations from benefactors whose health benefited from discoveries made through our research. These donations began in FY17-18 and have totaled \$60K to date.

OPERATIONAL FUNDING

School of Pharmacy Administrative Startup – QBI received administrative startup support from the School of Pharmacy to establish a strong administrative and financial team for the ORU. This began with 10% FTE support from the SOP's Assistant CFO in FY16-17 and FY17-18. During fall FY17-18, 25% FTE was provided for a part-time financial analyst. This led to the hiring of a full time CFO in September 2018, who was supported 100% in the first year and 75% in the second year. Additional support was provided at 25% for an Administrative Officer in FY18-19 and 25% of a Post-Award Analyst from October 2019 to August 2020.

Operation Startup – We received \$1M in operational startup from the Chancellor in FY16-17 which we have used for our Women's Empowerment Fellowship, website development, media and events and general infrastructure costs.

Non-Sponsored Programmatic Funds – QBI has received funding from the Chancellor's Office and other units to support specific initiatives. For the Cancer Cell Mapping Initiative, we have received funding from the Chancellor at \$50K per year for five years of CSBC Pilot Projects and \$350K for five years of CSBT Fellowships. For the Psychiatric Cell Mapping Initiative, we received \$200K from the Department of Psychiatry in startup funding in FY17-18 which led to the funding of a U01.

EVENT SPONSORSHIPS

QBI has obtained significant sponsorships from organizations in support of our many symposiums and events. Sponsorships have grown from \$500 in FY17-18 to \$28K in FY18-19 and \$73.5K in FY19-20. As of October 2020, we have already obtained commitments for \$45K in sponsorships for FY20-21.



14

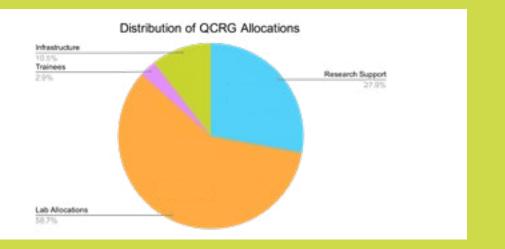
FUNDING DISTRIBUTIONS TO OTHER LABS

As an Organized Research Unit, QBI functions as a collaborative hub. Therefore a significant portion of our funding is shared with a variety of PIs and labs at UCSF and beyond.

Grants – Funding on our four NIH center grants and three DARPA projects are split amongst PIs within UCSF as well as UC San Diego, UC Berkeley, The Gladstone Institute, Fred Hutchinson Cancer Research Center, University of Washington, University of North Carolina, Chemspace, Mt. Sinai and University of Michigan.

We also have active collaborative pilot projects both within UCSF and with collaborators at UC San Diego, Northwestern University, Howard University, University of Rochester and UC Merced.

QCRG-Specific Gifts – With the establishment of the QBI Coronavirus Research Group (QCRG), we have been able to raise significant funding to support the COVID-19 research across 31 labs at UCSF and beyond. From March to October 2020, we have raised over \$6M, which is now being allocated or spent through direct lab expenditure, direct infusions of funds to participating labs, media consulting and the hiring of a QCRG Science Project Manager.



QCRG Funding – Since the inception of QCRG in March 2020, allocations from philanthropic support have been provided for trainee support, individual budgets for participating labs, research support funding and infrastructure.

Requests for Application (RFAs) – QBI has generated several Requests for Applications (RFAs) that have benefited the greater UCSF community. Our Bold & Basic program funded four two-year \$225K grants and three one-year \$50K fellowship beginning in the fall of FY17-18. Our second Bold & Basic RFA in the fall of 2019 again supported five two-year grants at \$160K and two one-year fellowships at \$50K. In total, we have given out \$2M in Bold & Basic RFAs.

We have established a series of partnerships with foreign institutions, including Freie Universät Berlin (FUB), the Curie Institute and Tel Aviv University, in which we have provided funding for QBI scientists through joint RFAs. The FUB RFA committed \$50K to five investigative groups in spring of 2020. The Curie RFA committed \$75K each to four groups and our Tel Aviv University RFA will provide a similar commitment in January 2021. In total, we have supported \$850K in collaborative RFAs.



RESEARCH PROGRAM LEADERSHIP

Academic research has the potential to be highly siloed, resulting in a reluctance to exchange ideas even if the respective investigators' research is closely related. These tendencies result in an overly competitive and less creative environment, which slows the speed of discovery. Existing reward structures including the way scientific research is funded and published have so far precluded a paradigm shift. However, times of crisis potentially catalyze change. We would argue the COVID-19 pandemic created the opportunity to work together more effectively, by breaking down silos and changing the way we do research.

One major way in which QBI has attacked these scientific silos has been the facilitation of a more organized approach for obtaining larger collaborative grants from federal agencies such as NIH and DARPA. QBI and its investigators have leveraged relationships at Mission Bay and Parnassus campuses, involving several ORUs/Institutes, including the Cancer Center, Clinical Translational Science Institute (CTSI), Gladstone Institutes and Cardiovascular Research Institute (CVRI), the Department of Psychiatry and the Weill Institute for Neurosciences. The creation of QBI has strengthened these connections and developed new ones. These efforts have resulted in long-term stability for QBI due to the acquisition of larger center grants, previously difficult, if not impossible, to accomplish in the past.

The QBI vision has initially centered upon team science through network mapping of the cell. Since much work has been done on identifying sets of genes linked to a variety of diseases, one obvious next step is to study how the corresponding proteins physically and functionally interact with each other in healthy and diseased states. These maps could help inform more mechanistic and structural studies as well as link to patient cohorts, so they could ultimately connect scientists across a wide array of disciplines, including genetics, bioinformatics, biochemistry, systems and structural biology and clinical science. Importantly, this vision is disease agnostic, making it applicable to virtually all disease areas. For example, specific initiatives that have already been born out of QBI and its investigators include:

- UCSD
- Berkeley, led by Jeff Cox, PhD
- Matthew W. State, MD, PhD
- cover a five-year span of funding

These three initiatives, the HARC center and the DARPA collaborative grants have brought in \$10.5M, \$8M, \$18M, \$24.1M, \$18.8M, and \$27.8M, respectively.

\$ 30,000,000 0

20,000,000,0

\$ 90,000,000-0



The Cancer Cell Map Initiative (CCMI), a collaborative project between QBI and the UC San Diego Department of Medicine, involving the cancer centers at both institutions as well as Trey Ideker, PhD, the chief of medical genetics at

The Host-Pathogen Mapping Initiative (<u>HPMI</u>), a joint program between QBI and the Henry Wheeler Center for Emerging and Neglected Disease (CEND) at UC

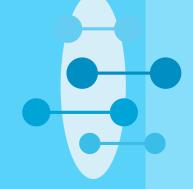
The Psychiatric Cell Map Initiative, (PCMI), an initiative started with Jeremy Willsey, PhD, focused on understanding the underlying biology behind various psychiatric disorders, including autism and schizophrenia, in collaboration with the UCSF Department of Psychiatry under the direction of department chair

A pre-existing center, HIV Accessory and Regulatory Complexes Center (HARC) was brought under the administration of QBI as well, creating a well-rounded and hefty portfolio bringing in significant funding to UCSF in a short amount of time to



CANCER CELL MAP INITIATIVE (CCMI)

NIH/NCI: U54 CA209891 **CCMI Period:** 05/11/2017 to 04/30/2022 **CCMI Funding:** \$2.1M/year Total Cost = \$10.5M overall **CCMI Publications:** 45 to date



Considering the large amount of sequence data associated with many different cancers, efforts are ongoing to extract mechanistic insight from this information. An integrated computational and experimental strategy is needed that will place these alterations into context of the higher order biological mechanisms in cancer cells. The goal of the Cancer Cell Map Initiative (CCMI) is to create a resource that can be used for cancer genome interpretation. This resource will allow us to identify key complexes and pathways in greater mechanistic detail to get a deeper understanding about the biology underlying different cancer states. Genomic data derived from tumor sequencing studies identifies key genes implicated in different cancer cells. Integrated physical and genetic networks based on these factors will help put the mutations into biological context, enabling the discovery of new disease genes as interacting partners become apparent. Ultimately, all of this knowledge will translate into improved ability to stratify and treat patients based on the particular networks that are altered.



CCMI CENTER GRANT FACULTY:

David Agard, Alan Ashworth, Laura Esserman, Jennifer Grandis, Silvio Gutkind (UCSD), Trey Ideker (UCSD), Nevan Krogan, Prashant Mali (UCSD), Jill Mesirov (UCSD), Laura van't Veer

ADDITIONAL FUNDING RECIPIENTS: Michael Boutros, Hani Goodarzi, Alon Goren (UCSD), Olivier Harismendy (UCSD), Natalia Jura, Minkyu Kim, Christian Metallo (UCSD), David Rideout (UCSD), Danielle Swaney, Pablo Tamayo (UCSD), Susan Taylor (UCSD), Keith Yamamoto



HIGHLIGHTS:

- Mol Cell. 2015 May 21; 58(4): 690-8.
- Foundation.
- Consortium.
- Center).



Cancer Cel Map Initiative

Krogan NJ et al. The cancer cell map initiative: defining the hallmark networks of cancer.

CCMI Launched with Support from UC San Diego, UCSF and the Fred B. Luddy

CCMI Awarded \$150,000 Innovation Award from the Roddenberry Foundation.

CCMI Awarded a \$10 million Grant as a New Member of the NCI's Cancer Systems Biology

Cell Mapping Initiatives Aim to Uncover Hidden Pathways of Disease: Projects Are Exploring Common Biology of Cancer, Infection and Psychiatric Disease (UCSF News

HOST PATHOGEN MAP INITIATIVE (HPMI)

NIH/NIAID: U19 AI135990 HPMI Period: 8/17/18 to 7/31/22 **HPMI Funding:** \$2M/year Total costs = \$8M overall HPMI Publications: 25 to date

The mission of the Host Pathogen Map Initiative (<u>HPMI</u>) is to comprehensively map the gene and protein networks underlying infectious disease, and to develop technologies by which these maps will enable basic and clinical investigations to lead to novel and targeted therapies. Biomedical research is increasingly dependent on knowledge of molecular networks of multiple types; such networks define a hierarchy of structures and processes in a cell, giving rise to all of its normal and diseased behaviors. HPMI will leverage advanced interaction mapping, computational facilities and infectious disease platforms which have been established at the University of California San Francisco (UCSF), San Diego (UCSD) and Berkeley (UCB) campuses to generate and analyze host-pathogen networks, focusing initially on *Mycobacterium* tuberculosis (Mtb) and Staphylococcus aureus (SA) but includes many viruses as well, including SARS-CoV-2.

HPMI COLLABORATIVE FACULTY:

David Agard, Greg Barton (UCB), Jeff Cox (UCB), Jennifer Doudna, Thomas Hawn (University of Washington), Trey Ideker (UCSD), Nevan Krogan, Alex Marson, Oren Rosenberg, Andrej Sali, Sarah Stanley (UCB)

\$8 MILLION

HIGHLIGHTS:

- Jun;21(6):339-354.
- autoimmunity. Nature. 2019 Nov;575(7782):371-374.
- pathogenesis and beyond. Elife. 2019 Jun 17:8:e45957.





Host Pathoger

Budzik JM et al. Dynamic post-translational modification profiling of Mycobacterium tuberculosis-infected primary macrophages. Elife. 2020 Jan 17;9. doi: 10.7554/eLife.51461.

Eckhardt M et al. A systems approach to infectious disease. Nat Rev Genet. 2020

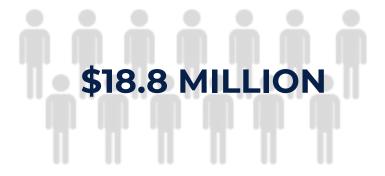
Majer O et al. UNC93B1 recruits syntenin-1 to dampen TLR7 signalling and prevent

Penn BH et al. An Mtb-Human Protein-Protein Interaction Map Identifies a Switch between Host Antiviral and Antibacterial Responses. Mol Cell. 2018 Aug 16;71(4):637-648.

Roberts AW et al. Cas9 conditionally-immortalized macrophages as a tool for bacterial

PSYCHIATRIC CELL MAP INITIATIVE (PCMI)

PCMI Period: 9/5/18 to 6/30/23 NIH/NIGMS: 1U01MH115747 **PCMI Funding:** \$3.76M/year Total costs = \$18.8M overall PCMI Publications: 13 to date



The Psychiatric Cell Map Initiative (PCMI) is aimed at a comprehensive understanding of the complex interactions among psychiatric-disorder- associated genes and proteins, and how they differ in atypical and healthy states in relevant cell types. To develop this integrative, multidisciplinary platform, we focus on ASD (Autism Spectrum Disorder), as recent success in gene discovery perform high-throughput experiments in models derived from human induced pluripotent stem cells (iPSCs), including NGN2-induced cortical excitatory neurons and *ASCL1/DLX2*-induced inhibitory neurons, in primary human midfetal excitatory and inhibitory cortical cells, and in a powerful vertebrate model system, Xenopus tropicalis. Characterization of high-resolution interaction networks, involving detailed structural analyses, in a developmentally oriented, cell type specific manner, will build on genetic findings to advance ASD neurobiology and set the stage to translate this platform to other neuropsychiatric disorders such as intellectual disability, epilepsy, Tourette disorder, schizophrenia and bipolar disorder.

PCMI COLLABORATIVE FACULTY:

Jennifer Doudna, Steven Finkbeiner, Ruth Huttenhain, Trey Ideker (UCSD), Martin Kampmann, Michael Keiser, Nevan Krogan, Tomasz Nowakowski, Brian Shoichet, Matt State, Mark von Zastrow, Jeremy Willsey

ADDITIONAL FUNDING RECIPIENTS: Eugene Yeo (UCSD)



HIGHLIGHTS:

- Neurol. 2020 Sep;16(9):465-480.
- 22;147(21).
- Jul 26;174(3):505-520.



Psychiatric Ce

Kampmann M. CRISPR-based functional genomics for neurological disease. Nat Rev

Sestan N et al. Lost in Translation: Traversing the Complex Path from Genomics to Therapeutics in Autism Spectrum Disorder. Neuron. 2018 Oct 24;100(2):406-423.

Willsey HR et al. The neurodevelopmental disorder risk gene DYRK1A is required for ciliogenesis and control of brain size in Xenopus embryos. Development. 2020 Jun

Willsey AJ et al. The Psychiatric Cell Map Initiative: A Convergent Systems Biological Approach to Illuminating Key Molecular Pathways in Neuropsychiatric Disorders. Cell. 2018

HIV ACCESSORY AND REGULATORY COMPLEXES (HARC)

NIH/NIAID: P50 AI150476 HARC Period: 9/1/17 to 8/31/2022 **HARC Funding:** \$4.82M/year Total Cost = \$24.1M overall HARC Publications: 71 to date (HARC is currently on its 3rd renewal)

The mission of the HIV Accessory and Regulatory Complexes Center (HARC) is to elucidate the molecular basis of virus and host systems that are essential for, or contribute to, the pathogenesis of HIV/AIDS, including the physical/functional interactions that occur between viral and human proteins, membranes, lipids and nucleic acids (both DNA and RNA). A molecular understanding of viral-host interactions, functions and mechanisms may reveal new therapeutic strategies for intervention, including host-directed strategies that may escape the limitations of current drug regimens where mutations in the targeted HIV enzymes can diminish drug efficacy.

HARC COLLABORATIVE FACULTY:

Nevan Krogan, Yifan Cheng, Charles Craik, Jennifer Doudna (UCB), Michael Emmerman (Fred Hutchinson Cancer Research Institute), Alan Frankel, John Gross, James Hurley (UCB), Harmit Malik (Fred Hutchinson Cancer Research Institute), Alex Marson (Gladstone Institutes), Matija Peterlin, Andrej Sali, Robert Stroud

ADDITIONAL FUNDING RECIPIENTS:

Jamie Cate (UCB), Lilian Cohn, David Drubin (UC Berkeley), Oliver Fregoso (UCLA), Judd Hultquist (Northwestern University), Natalia Jura, Namita Kumari (Howard University), Geeta Narlikar, Alessandra Sacco (Sanford Burnham), Ruth Serra-Moreno (University of Rochester), Nate Sherer (University of Wisconsin), Michael Thompson (UC Merced)

\$24.1 MILLION

HIGHLIGHTS:

- Apr 16;78(2):197-209.
- interrogation of HIV-host factor interactions. Nat Protoc. 2019 Jan;14(1):1-27.
- Degradation in HIV Infection. Cell Host Microbe. 2019 Jul 10;26(1):86-99.
- Downregulation. Cell. 2018 Jul 26;174(3):659-671.
- targeting. Nature. 2018 Jul;559(7714):405-409.





Gordon DE et al. A Quantitative Genetic Interaction Map of HIV Infection. Mol Cell. 2020

Hultquist JF et al. CRISPR-Cas9 genome engineering of primary CD4+ T cells for the

Hüttenhain R et al. ARIH2 Is a Vif-Dependent Regulator of CUL5-Mediated APOBEC3G

Morris KL et al. HIV-1 Nefs Are Cargo-Sensitive AP-1 Trimerization Switches in Tetherin

Roth et al. <u>Reprogramming human T cell function and specificity with non-viral genome</u>

DARPA PANACEA



DARPA 1.0 Period: 09/01/19 to 08/31/2024 **DARPA:** HR00111920020 DARPA 1.0 Funding: \$4.9M/year Total Cost = \$24.7M overall

The Panacea project will discover and develop chemically novel analgesics by targeting multiple pain modulating receptors, particularly new targets identified using an unbiased approach in a nerve injury mouse model. Such guided-polypharmacology will confer unprecedented efficacy and selectivity against adverse effects common among current analgesics. Current pain therapeutics act on single targets. When polypharmacology occurs, it is unintended and often detrimental. Examples are opioid analgesics like morphine, fentanyl, and oxycodone. Whereas opioids have brought life-saving analgesia to millions, their core pharmacology confers grave dangers. Panacea will bring an innovative approach by integrating three new technologies and approaches:

- The unbiased discovery of new targets in pain neurons and related cells, using genomic and proteomic techniques
- Ultra-large library docking against sets of the new targets, and established targets with which they network, for drug discovery
- Guided polypharmacology of the new molecules for selectivity and efficacy

This guided polypharmacology approach to pain has never been attempted.Successful prosecution of this ambitious project will change the field.



PANACEA COLLABORATIVE FACULTY AND PARTNERS:

Allan Basbaum, Nevan Krogan, Matt Jacobson, John Irwin, Aashish Manglik, Yurii Moroz (ChemSpace), Bryan Roth (UNC), Brian Shoichet, Mark Von Zastrow



DARPA FOCUSED PHARMA

DARPA 2.0 Period: 06/01/2020 to 05/31/2024 **DARPA:** HR001119S0092 **DARPA 2.0 Funding:** \$1.42M/year Total Cost = \$5.7M overall

This project will discover and develop novel neuropsychiatric drugs with antidepressant, anxiolytic and anti-addictive activities that selectively engage the 5-HT2A serotonin receptor (HTR2A) in a pathway-specific manner. Exemplar compounds will confer rapid-acting therapeutic actions devoid of hallucinogenic and rewarding actions. The ultimate goal of this project is to develop rapidly acting novel chemical entities with antidepressant, anxiolytic and anti-addictive-drug like actions and devoid of reinforcing and hallucinogen-like actions in vivo.

DARPA 2.0 COLLABORATIVE FACULTY AND PARTNERS:

Bryan Roth (UNC), Ruth Huttenhain, John Irwin, Nevan Krogan, Brian Shoichet







\$5.7 MIL



EDUCATION PROGRAM LEADERSHIP

QBI WORKSHOPS & LECTURES

Under the tutelage of the Cancer Cell Map Initiative (CCMI), QBI offered 24 tutorials and workshops between 2016 and 2020 to the community both in San Francisco and in San Diego. These workshops welcomed participants ranging from elementary schoolchildren who took part in CRISPR lessons with fruit to trainees who learned Integrative Genomic Analysis with GenePattern. The workshops were widely popular creating a regular demand for repeat workshops both in San Francisco and San Diego.



September 27, 2016 July 11, 2017 **September 13, 2017 September 30, 2017** October 14, 2017 November 7, 2017 **December 6, 2017** December 13, 2017 December 15, 2017 January 11, 2018 February 8, 2018 March 7, 2018 March 14, 2018 June 5, 2018 June 5, 2018 June 5, 2018 June 7, 2018 June 26, 2018 **September 20, 2018**

Cancer Cell Map Workshop, UCSF CSBC and PS-ON junior Investigators Meeting, NIH 2017 Cell Mapping Symposium, UCSF Mass Spectrometry Mini Symposium, UCSD Taste for the Cure 2017: A Taste of Science, JCC, San Francisco Integrative Genomic Analysis with GenePattern, UCSD **CRISPR Screening Workshop**, UCSD Elsevier in the Classroom-Pathway Studio, UCSD Integrative Genomic Analysis with GenePattern, UCSD UC San Diego – Ensembl Tutorial, UCSD Mass Spectrometry Symposium, UCSF San Francisco STEM Career Day, UCSF Integrative Genomic Analysis with GenePattern, UCSF Career Development Seminar Series, UCSD Introduction to Cytoscape and Network Biology for Beginners, UCSF Cytoscape Workshop 2018, UCSD Integrative Genomic Analysis with GenePattern, UCSF Cytoscape Automation in R and Python for Bioinformaticians, UCSF Integrative Genomic Analysis with GenePattern, UCSD



QBI SABBATICALS

QBI has started a sabbatical program where PIs from different institutions come to UCSF and work with investigators from QBI. From 2017 to 2020, QBI welcomed three PIs from different institutions to build collaborative research bridges through sabbatical visits. These include: Aseem Ansari from St. Jude Children's Research Hospital, Christian Freund from Freie Universität Berlin and Christian Ottmann from Technology University in Eindhoven. In particular, the relationship with Freie Universität blossomed following the sabbatical by Dr. Freund which led to a joint symposium, a formal MOU and a joint RFA for collaborative projects.



October 20, 2018 October 29, 2018 November 1, 2018 January 18, 2019 January 22, 2019 February 14, 2019 February 19, 2019 February 21, 2019 March 5, 2019 March 6, 2019 July-August 2019 October 12, 2019 October 28, 2019 November 2019 January 16, 2020 January 17, 2020 January 23, 2020 January 24, 2020 October 21, 2020 Upcoming 2021

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QBI WORKSHOPS & LECTURES

Taste for the Cure 2018: A Taste of Science, JCC, San Francisco Cell Mapping Symposium, UCSD Bay Area Science Festival Explorer Tour, UCSF Ensembl Tutorial, UCSD Ensembl Tutorial. UCSF Introduction to Cytoscape and Network Biology, UCSF **QBI Mass Spectrometry Symposium**, UCSF Integrative Genomic Analysis with GenePattern, UCSD San Francisco STEM Career Day, UCSF Integrative Genomic Analysis with GenePattern, UCSF Grant Writing and Science Presentation Workshop, Makerere University, Uganda Taste for the Cure 2019: A Taste for Science, JCC, San Francisco Bay Area Science Festival: Cancer Cell Map Initiative- Lab Explorer Tour, UCSF Grant Writing and Science Presentation Workshop, Jagiellonian University, Poland Ensembl Tutorial. UCSD **Ensembl Tutorial**. UCSD

Analyze Your Data using Networks with NDEx and Cytoscape, UCSF Single-cell Analysis with GenePattern Notebook Environment, UCSD Bay Area Science Festival: Cancer Cell Map Initiative, UCSF virtual Collaborative Basic Research Mini-Course for Inquiry Immersion, UCSF virtual



FACULTY RETENTION

QBI strongly embraces the UCSF PRIDE values. Retention efforts are an important mechanism to diversify our faculty. Why has it been difficult to retain recruited faculty members, specifically women and underrepresented minorities? If we see patterns, what can be done to address those issues?

Obtaining sufficient funds and attracting/retaining high caliber faculty remains imperative. In particular, we are endeavoring to develop ways to mitigate implicit bias in the recruitment and retention of faculty. At QBI, we have an objective to assist with recruitment and retention of faculty who share our commitments to diversity and service to underserved or vulnerable populations while conducting quantitative basic research. On an annual basis the ORU has committed to contributing to the financial security of faculty from whom we anticipate scholarly contributions, an ability to make a unique contribution to the ORU and/or the school, and the nominee's potential to have a positive impact on the department's and/or school's culture of diversity. QBI has contributed to the retention of the following faculty since 2016.



Michelle Arkin



Ryan Hernandez



Natalia Jura

Dr. Michelle Arkin is a Professor and incoming Department Chair of Pharmaceutical Chemistry at the University of California, San Francisco. She is a faculty member of QBI and the Helen Diller Family Comprehensive Cancer Center, and an Adjunct Professor at the Buck Institute of Research on Aging. Her lab focuses on chemical biology of protein-protein interaction networks and other challenging targets in diseases such as Alzheimer's Disease and cancer. She recently co-founded two startup companies based on these programs. Dr. Arkin also co-directs the UCSF Small Molecule Discovery Center (SMDC), which works with investigators in academics, biotech, and pharma to develop first-in-class probes and drug leads for novel targets across therapeutic areas. Dr. Arkin is the President of the Academic Drug Discovery Consortium, a Director of the Society for Laboratory Automation and Screening (SLAS), and a member of the Editorial board of the Assay Guidance Manual, RSC Chemical Biology and several chemical biology journals. Dr. Arkin represents UCSF in the National Cancer Institute's Chemical Biology Consortium and the Accelerating Therapeutics for Opportunities in Medicine (ATOM) consortium. Before UCSF, Dr. Arkin was the Associate Director of Cell Biology at Sunesis Pharmaceuticals, where she helped discover inhibitors of protein-protein interactions, including IL-2/IL-2R and LFA1/ICAM (liftigrast).

Dr. Ryan Hernandez is an Associate Professor in the Department of Bioengineering and Therapeutic Sciences, Director of the Biological and Medical Informatics (BMI) graduate program, and an Associate Director of the Quantitative Biosciences Institute from 2016 to 2018. His work specializes in computational and statistical genomics, with a focus on using evolutionary thinking to understand complex biological patterns. His world-renowned work in population genetics has been published in a broad range of scientific journals, and cited over 32,000 times. Dr. Hernandez is one of only a few Latino PIs across all of the basic sciences at UCSF, and is deeply committed to increasing diversity, equity, and inclusion in the sciences at all levels of academia. As Director of the BMI graduate program, he helped guide the program from a male-dominated student body toward equal representation of male and female students. He was the co-PI on a UCSF Initiative for Maximizing Student Development (IMSD) training grant designed to support the academic and research competitiveness of historically underrepresented and marginalized students and to facilitate their progress toward careers in biomedical research. Dr. Hernandez is now co-leading an effort to build the Post-baccalaureate Research Opportunity to Promote Equity in Learning (PROPEL) program, which has an explicit focus on empowering students from historically underrepresented and marginalized backgrounds that have just completed their undergraduate degrees with the research experience that they will need to be competitive for admission to graduate programs and to be selected for national fellowships.

Dr. Natalia Jura is an Associate Professor at the Department of Cellular and Molecular Pharmacology and an Investigator at the Cardiovascular Research Institute at the School of Medicine, University of California, San Francisco (UCSF). She is also an Associate Director of the Quantitative Biosciences Institute at UCSF. Dr. Jura's group at UCSF focuses on understanding how soluble protein kinases and membrane-associated receptor kinases assemble into functional complexes and regulate their signaling through molecular interactions with regulatory proteins. Her group also investigates alternative non-catalytic roles of protein kinases as scaffolds in cellular signaling pathways and applies this knowledge for design of small molecule inhibitors that target these poorly understood kinase functions in human diseases. Dr. Jura's scientific contributions have been recognized by a number of prestigious grants, including NIH, NCI R01 awards, career award from the Susan Komen Breast Cancer Foundation, and from the Lung Cancer Research Foundation. In her position of an Associate Director at QBI, Dr. Jura oversees promotion of interdisciplinary collaborative research at UCSF and beyond. Her leadership skills have recently been recognized by the Women in Biochemistry and Molecular Biology Leadership Award from the American Society for Biochemistry and Molecular Biology (ASBMB).

FELLOWSHIP

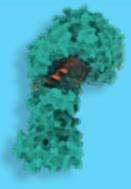
The QBI Fellows Program brings exceptionally promising young scientists to the institute where they can establish independent research programs with the aid of supportive senior scientists. Fellows are small group leaders with Principal Investigator status at the University, which enables them to obtain extramural grants to support the growth of their programs. This program seeks recently graduated PhD's focused on quantitative biology whose potential as investigators indicates they would benefit from a supported and mentored transition to independence. QBI support is granted for two years, extendable and is sufficient to maintain a small laboratory of two to four members.

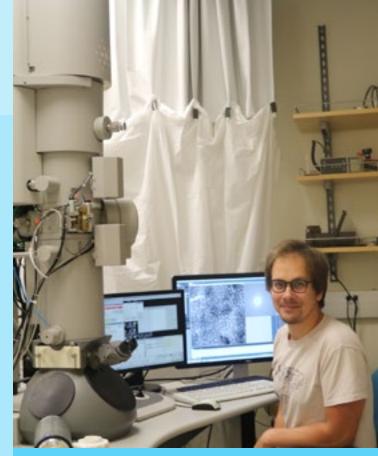
QBI Fellows enrich our interactive intellectual community with their enthusiasm and sole focus on research, and are at the same time mentored by our community. The combination of independence, singular focus, and effective mentoring facilitates the development of remarkable young scientists, who are becoming the next generation of scientific leaders, both at UCSF and in the larger biomedical research community.

Our first QBI fellow was **Klim Verba**, an expert in structural biology, especially in the area of cryo-EM. Since his undergraduate studies Klim has been fascinated by how protein structure enables function. He delved deeper into the world of biophysics and structural biology during his PhD training in David Agard's lab, where he was able to visualize the interactions between molecular chaperone Hsp90 and its kinase substrate by cryoEM, the first structure of Hsp90 with any substrate at high resolution. This raised the question in his mind of how general these unfolded states are for protein kinases and to what end, and how they are being used functionally.

With this question in mind, he started as a QBI fellow in 2018. Having his own lab and independent funding gave him the opportunity to join the vibrant investigator community at UCSF which resulted in many collaborations, with Drs. Fraser, Jura and Gordan, just to name a few. Importantly, being a QBI fellow enabled him to grow as a mentor with two full time students and two post-doctoral fellows in his lab. Being in the "transitional" position of a QBI fellow means that he receives a great deal of support from other investigators at the QBI, which is invaluable. His position as a fellow also exposed him to opportunities in leadership that wouldn't have otherwise been available. Together with Oren Rosenberg, he leads the QCRG Structural Biology Consortium consisting of over 40 trainee volunteers from different labs at UCSF. The goal is to apply structural biology expertise to better understand at a molecular level the host-pathogen interface of SARS-CoV-2. They have made tremendous progress in this area, resulting in three publications in a short period of five months with a number of other manuscripts still in preparation.

Lastly, he organized two novel hackathons bringing together non scientists from the Bay Area and biomedical scientists at UCSF and other local institutions. Over 50 people attended these events, exposing non scientists with interest in science to the cutting edge biomedical research and exposing many biomedical scientists to the latest developments in machine learning and other computational methods.







QBISCHOLARSHIP

FOR WOMEN FROM DEVELOPING NATIONS IN BIOSCIENCES

The Quantitative Biosciences Institute, launched a new scholarship for women from developing nations with the aim of empowering women by providing support and capacity building in biosciences research. Strengthening communication, collaboration and capacity building across institutions and borders, and empowering women in bioscience in developing countries to further advance research and eventual treatments or cures to diseases is one of the major goals of the QBI Scholarship. Under this QBI aim, and led by Jaqueline Fabius, QBI COO, we offer a one-year, non-accredited transdisciplinary scholarship focused on bioscience and disease research.

In the academic year of 2017-2018 this scholarship gave our inaugural scholar, Jacqueline Kyosimiire-Lugemwa from Uganda, the opportunity to come and work with UCSF world class scientists at QBI. In coordination with UN WOMEN, in the first year the call for applications was open to candidates who are citizens of Kenya and Uganda. Importantly QBI wanted to offer a scholarship that took into account challenges that women in the workforce face, and what often in the past has led to women not applying for opportunities. Family life and needs were taken into account to allow for a customized experience. The segments of time allotment at QBI and the home institute were planned with some flexibility, working together with the applicant to find the most feasible and sustainable solution.



In order to assure a sustainable continuation of acquired knowledge, QBI supported collaborative work visits from UCSF to the home institute along with the applicant, to assist in the implementation of newly learned methods/techniques at the home institute during and at the end of the fellowship.

Our inaugural scholar thrived and returned to Uganda with great success acquiring two grants rather quickly and advancing in her career. She is now a key collaborator in Uganda.

"You guys are making me popular, thanks for all the great work you are doing. That exposure has changed me for good, I have now submitted 2 grant proposals one to L'Oréal UNESCO for women from developing countries and another to Organisation for Women from developing countries, both are small but ok for me now. I also submitted my paper to the Journal of Infectious diseases this week. It feels so good to be able to do these." - May 16, 2019

Another cohort of scholars has been selected and were to come to QBI in 2020-2021, however the pandemic has put those plans on hold for one woman from Nigeria, one woman from Ghana and two women from Poland. We look forward to receiving them once the pandemic is no longer an issue.









DIVERSITY

QBI aims to decrease social inequalities and increase diversity within the community by initiating opportunities for women and other underrepresented minorities on campus and across the globe.

The QBI staff itself is diverse; in addition to a strong representation of women, five of the twelve are people of color and/or Asian, and four of the twelve are first generation Americans.

QBI offers activities in support of diversity and inclusion and In 2020, the media team launched a series of panels highlighting LGBTQ and transgender communities as well as women.

HIV 2020: Where Are We Now?; The Intersection of HIV Research and

• Community Service

HIV 2020: Where Are We Now?; Beliefs and Barriers to PrEP Among Trans Men

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Science in the Time of Corona: Has COVID-19 Changed How Women and

• Mothers Do Research, and What Can We Learn From This?

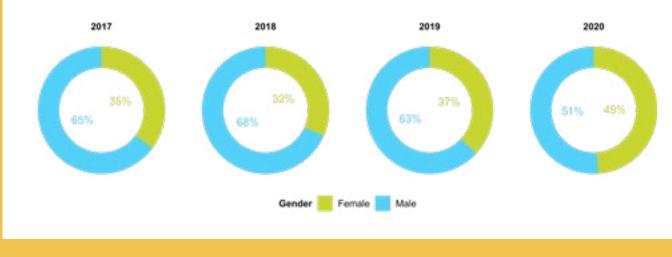




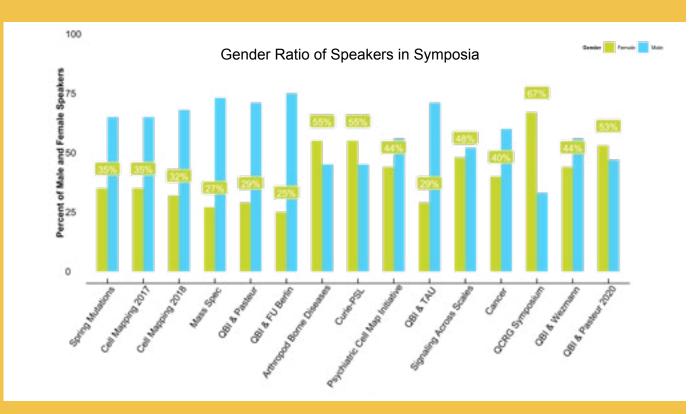
How do you balance bringing up child care duties / challenges with keeping coworkers from seeing you mainly through the lens of being a mother?



Increase in Gender Balance in Symposia Speakers



There has been a steady increase in the participation of women scientists in our symposia from 2016 onwards; the share of women speakers increased by 14 percentage points. Not only was there a 40% increase in the share of women speakers between 2017 and 2020, but seven out 15 symposia have been organized or co-organized with women scientists. QBI has also set a goal of having 50% of its speakers at symposia be women.



In October of 2019, Jacqueline Fabius, the QBI COO, was awarded the Chancellor's Award for the Advancement of Women. She spearheaded QBI's efforts to elevate women scientists, selecting early-career women scientists to organize QBI's various symposia and ensuring that these events feature at least 50 percent women speakers. She also single-handedly established the QBI Scholarship for Women From Developing Nations in Biosciences, which granted its first scholarship, to HIV researcher Jacqueline Kyosimiire-Lugemwa, PhD, of Uganda, in 2017-2018.

COMMUNICATION & EVENTS



UQ,

QBI ONLINE SEMINAR

JULY 1, 10:00 AM



SEMINARS

QBI launched the seminar series in 2017 featuring world-renowned speakers invited and hosted by faculty members. This robust series was immediately pivoted to an online format with the coronavirus pandemic and continues to be quite popular. To date we have had 30 in-person seminars and seven online, for a total of 37.











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JULY 28. 1.00 PM



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EMBER 21. 6-00 PM PD









SALONS

To reach potential influencers in various fields, QBI teamed up with the company POSTHOC to create curated gatherings with QBI experts in cancer, psychiatry and infectious diseases research. These events, which took place in San Francisco and Washington D.C., allowed people to meet and interact with scientists in person. POSTHOC Salons are designed for organizations that need to reach the people that could have an impact: the engaged, the curious, and those committed to changing the world for the better, and who are ready and keen to collaborate.







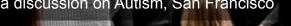
The Elusive Cure – an Evening with Alan Ashworth, a discussion on cancer research, San Francisco





Silicon Valley to DC – The Elusive Cure, featuring Trey Ideker, Nevan Krogan, Laura van't Veer, Washington, D.C.







ART EXHIBITS

QBI has collaborated with other institutes within UCSF, including the Institute of Global Health Sciences and the Global Brain Health Institute at UCSF, for ancillary events to complement scientific presentations. Art exhibitions and live panel discussions have sometimes been part of the agenda to create more social atmospheres that enable different conversations.

QBI HAPPY HOUR

Inspired by the faculty's demand for more social interaction among scientists, the QBI Happy Hour Series started as a unique concept, in which three nominated postdocs gave 5-minute flash presentations highlighting the research from three different labs at a local bar with built-in presentation screens. Warm food and beverages kept the attendees nourished, while the presenting researcher served their knowledge behind the bar. In light of the pandemic, QBI pivoted to producing experiential events such as virtual retreats and town halls on novel platforms including Discord.









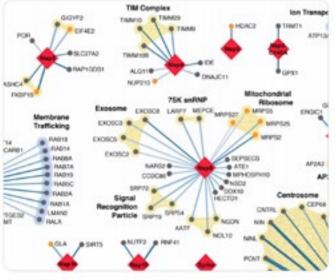






Twee

The @QBI_UCSF Coronavirus Research Group (QCRG) is happy to present our Virus-Human #SARSCoV2 Protein Interaction Map published in @nature. We tested clinically-approved drugs/compounds derived from our map and found many with potential to treat #COVID19. nature.com/articles/s4158...



6:37 AM - Apr 30, 2020 - Twitter Web App

311 Retweets 44 Quote Tweets 688 Likes







the linet on user 13 in the Denominal Hall, Ryens suttimum at 2.25. Q What do uses do it your work? A We denote now imaging fandmiques and here ways for factor at imaging data in order to be able improve the characterization of human disease. In many function



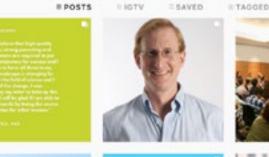
WHAT IS BASIC RESEARCH?

SOCIAL MEDIA

The QBI communications team engages with audiences through spreading messages to the community by staying abreast of significant social media landscape shifts. Consequently, our social media strategy has kept us relevant in times of uncertainty. In an increasingly immediate world of communication, QBI manages multiple social media efforts to establish its presence.







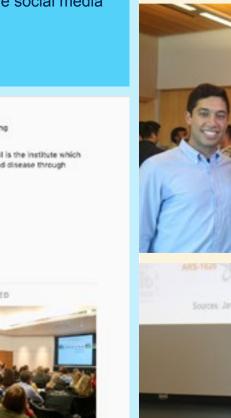






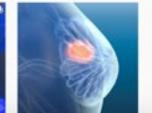






















QBI INTERNS SYMPOSIUM

QBI launched a paid summer internship program for young scientists interested in biomedical research. Each year, the interns work with a mentor and gain hands-on laboratory experience while increasing their understanding of different science career paths. The program ends with a talk presentation, where the interns present their work at a symposium.

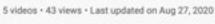
QBI TV

Although QBI TV existed prior to the pandemic, it took on another level of importance at the pandemic's rise in 2020. All QBI events shifted online, with the first one in March, followed by a calendar of seminars, symposia, and unique programming.

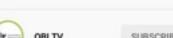


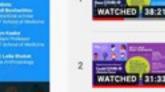


Science in the Time of Corona

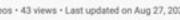














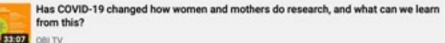




OBLITY







Developing Therapies for COVID-19: Understanding the Mechanisms of Attack to

Scientists across the globe are working to find a treatment for COVID-19 | GMA

Does COVID-19 Have the Potential to Restructure Scientific Research?



1 9 6 O Inform Treatment

Could COVID-19 change the role of conferences in science?

COVID-19 Campus-wide Research at UCSF May 5, 2020

QBI Coronavirus Research Group (QCRG)

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WATCHED



QBI Coronavirus Research Group

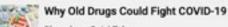
18 videos + 123 views + Last updated on Oct 15, 2020







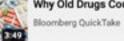
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od Morning America

1:27:07 University of California Television (UCTV)

UC San Francisco (UCSF)



QBI Media

1.0 4 SECONDS 60

HIV 2020

WHERE ARE WE NOW



PLAY ALL

HIV 2020: Where Are We Now?

3 videos - 33 views - Updated yesterday



60 Seconds: A QCRG Minute 7 videos • 114 views • Last updated on Oct 9, 2020 =+ X / ··· While dealing with COVID-19 data influx, we want to help you make sense of relevant research in 60 seconds. Tune in to hear from our QCRG scientists!

When COVID-19 started spreading rapidly around the world, QBI joined forces with researchers at UCSF, Gladstone Institute, Icahn School of Medicine at Mount Sinai, Institut Pasteur, Howard Hughes Medical Institute and more, to apply their expertise to aid in finding a treatment for the growing pandemic. Together, this group of researchers now known as QBI Coronavirus Research Group (QCRG), were the first to extensively map out the genome of COVID-19 and discover that the virus interacts with 332 human host proteins and the research continues to progress.



ATCHED 311

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SUBSCRIBED



50

	HIV 2020: Where Are We Now? QBI TV
	HIV 2020: Where Are We Now? The Intersection of HIV Research and Community Service Q8I TV
	HIV 2020: Where Are We Now?; Beliefs and Barriers to PrEP Among Trans Men Q8I TV
	60 Seconds: A QCRG Minute QBITV
/	60 Seconds: A QCRG Minute, featuring Aashisk Manglik QBI TV
	60 Seconds: A QCRG Minute, featuring Sarah Rockwood
92	60 Seconds: A QCRG Minute, featuring Jim Wells QBITV
1	60 Seconds: A QCRG Minute, featuring Klim Verba and Oren Rosenberg QBI TV
12	60 Seconds: A QCRG Minute, featuring the QCRG SBC "Purification" Subgroup
	60 Seconds: A QCRG Minute, featuring the QCRG SBC "Crystallography" Subarrow



SYMPOSIA

The QBI Symposia Series aims to strengthen partnerships, improve new developmental processes, and share insights on the latest state of the art approaches for developing new technologies, therapeutic targets, and strategies addressing unique biological challenges. Our joint international symposia focus on fostering collaborations across oceans and borders. Outcomes from the highly successful series include joint research grants, student and faculty exchange programs, and skill-sharing opportunities. In late March 2020, due to the pandemic, all symposia moved online. The first online symposium we held had over 800 attendees.

There has been a steady increase in the participation of women scientists in our symposia from 2016 onwards. Not only has there been a 40% increase in the share of women speakers between 2017 and 2020, but seven out fifteen symposia have been organized or coorganized with women scientists.



March 14, 2017: San Francisco September 13, 2017: San Francisco . October 29, 2018: San Diego February 19, 2019: San Francisco March 18, 2019: San Francisco May 27, 2019: Berlin, Germany

June 18, 2019: San Francisco September 5, 2019: Paris, France

November 13, 2019: San Francisco December 4, 2019: Tel Aviv, Israel

January 28, 2020: San Francisco February 24, 2020: San Francisco

- - Spring Mutations Symposium, James Fraser & Nevan Krogan. <u>View</u> **Cell Mapping Symposium**, Nevan Krogan & Trey Ideker. View Cell Mapping Symposium, Trey Ideker, Nevan Krogan & Jeremy Willsey. View Mass Spectrometry Symposium, Danielle Swaney & Ruth Huttenhain. <u>View</u> **QBI/Pasteur Symposium**, Christophe D'Enfert & Nevan Krogan. <u>View</u> Wahl. View
 - View
 - Ron Shamir. View
 - Bandyopadhyay. <u>View</u>





QBI/Freie Universitat Symposium, Christian Freund, Nevan Krogan, Tanja Kortemme & Markus

Arthropod-Borne Disease Symposium, Seemay Chou & Andrea Swei. View QBI/Institut Curie|PSL-Q-Life Institut Symposium, Aura Carreira, Bruno Goud & Nevan Krogan.

Psychiatric Cell Map Initiative Symposium, Jeremy Willsey, Hao Li, & Nevan Krogan. <u>View</u> QBI/UCSF-TAU Symposium in Computational Biology and Drug Discovery, Nevan Krogan &

QBI Signaling Across Scales Symposium, Natalia Jura, Pedro Beltrao & Nevan Krogan. View Quantitative Biology of the Cancer Cell Symposium, Davide Ruggero & Sourav







ONLINE SYMPOSIA

June 19, 2020: online July 22, 2020: online

October 13-14, 2020: online

October 29-30, 2020: online

November 9-13, 2020: online December 1-2, 2020: online

POSTPONED SYMPOSIA

Given the directive to restrict large gathering in light of the coronavirus pandemic, the following events have been postponed. We plan to reschedule for a later date once we have confirmation we can return to normal business operations.

QCRG COVID-19 Research Symposium, QCRG. View Kortemme, Noam Stern-Ginossar, Dan Tawfik & Yitzhak Pilpel. View Nevan Krogan. View

Marie-Hélène Verlhac, Bruno Goud & Nevan Krogan. View

London

- **QBI/Allen Institute Mini-symposium,** Nevan Krogan & Rick Horwitz, Seattle, Washington QBI World Molecular Engineering Network Conference, San Jose Del Cabo, Mexico **QBI/NYU Nano-Symposium,** Jeff Boeke & Nevan Krogan, New York West Africa Symposium, Jacqueline Fabius & Nevan Krogan, Sierra Leone, Africa PKU/QBI Symposium on Chemical Biology, Jim Wells, San Francisco QBI/ PKU Symposium on Computational Biology, Nevan Krogan, China **QBI/Leloir Institute Foundation Symposium,** Nevan Krogan & Andrea Gamarnik, Buenos

- Aires, Argentina

- QBI/Weizmann Institute Symposium on Molecular Systems Biology, Nevan Krogan, Tanja
- 2nd Annual QBI/Institut Pasteur Symposium on Infectious Disease, Nevan Krogan, Shaeri Mukherjee, Gerald Spaeth, Carmen Buchreiser, & Julia Chamot-Rooke. View
- QBI/SBI Symposium on Molecular Networks of Cancer and Other Diseases, Walter Kolch &
- QBI/French Consulate Scienctific Conference on Big Data and Health. View QBI & Insitut Curie/Q-Life Complex Biological Phenomenon and Quantitative Approaches,

QBI/Crick Symposium on Quantitative Mapping of the Cell, Nevan Krogan & Simon Boulton,



INTERNATIONAL MOUs

Since 2017, QBI has actively pursued both domestic and international relationships to foster meaningful collaborations among scientists worldwide. Typically international introductory visits were followed by joint symposia, which then reinforced the science leading the relationships' bottom-up approach. Once interest was clear and established on both sides, QBI and the partner institution signed formal agreements to start collaborative projects and raise funds together.

The importance of these global relationships has never been more evident than in 2020 during the pandemic when scientists worldwide worked together through the QCRG mechanism to rapidly find solutions to the COVID-19 virus. Hence, we organized the QBI Coronavirus Research Group (QCRG) Symposium on COVID-19 in June 19, 2020, which featured collaborating scientists from the West Coast USA, East Coast USA, Midwest USA, Argentina, France, Israel, and Nigeria.

Current International MOUs:

- Curie Institute, Paris, France
- Freie Universität, Berlin, Germany
- Redeemer's University, Ede, Nigeria
- Tel Aviv University, Tel Aviv, Israel
- University College Dublin, Dublin, Ireland
- Institut Pasteur, Paris, France
- Jagiellonian University, Krakow, Poland

Redeemer's University



University College Dublin











INTERNATIONAL RELATIONSHIPS

In addition to building international relationships around the world, QBI has had a particular focus on Developing Nations, emerging economies in the Eastern Bloc nations, South America, and capacity building. In this vein, QBI has built relationships with Makerere University in Kampala, Uganda, Redeemer's University in Ede, Nigeria, Zanmi Lasanté clinic in Hinche, Haiti, and Jagiellonian University in Krakow, Poland. Relationships have been and are being formed through workshops, QBI introductory seminar series, and joint grant writing to foster collaborations through capacity building.

In addition to these efforts, joint symposia, the QBI Scholarship for Women from Developing Nations in Biosciences and postdoc exchanges welcome our new partners to QBI and create a foundation for solid collaborations in the future. Gilead and Roche donated \$80K towards the first Western African Symposium on Infectious Diseases in Sierra Leone.





DECISION MAKING

With any decision impacting others, the Director initiates a discussion with all those involved. One-on-one interactions often reveal important insights not as easily communicated in a group setting and allows all involved to voice their opinion. In those decisions requiring more input, the QBI Executive Committee and the Associate Directors are consulted. Regular meetings provide opportunities to discuss decisions, and a consensus is sought. Topics that have been discussed in the past include laboratory space issues, MOU formation, RFAs, faculty retention, sabbaticals, scholarship formation, support for faculty parents, and strategy to deal with issues related to grant indirects. The Director consults with his direct supervisor, B. Joseph Guglielmo, Dean of the School of Pharmacy, in those instances that are deemed more difficult.

From 2016 to October 2020 there have been 26 Executive Committee meetings and 13 Associate Directors meetings.

CONFLICT RESOLUTION

SPACING AT QBI

As is the case for much of UCSF, space allocation and management is complicated. As background, as an ORU, QBI is responsible for the oversight of all research space in Byers Hall. The space allocation at QBI is complicated for a number of reasons. The office space and laboratories are spacious and modern. Consequently, the supply of space is always short relative to faculty demand.

QBI's approach to space allotment is to initially let the neighborhood of scientists provide input on what science and scientist best fits in their environment. Suites that are aligned in this way have experienced great harmony. However, it has been taken into consideration that some offices were occupied prior to the rules and new tenants can only be addressed when these original tenants leave.

QBI's approach to disagreements has been for the neighborhood to develop a proposal and then present it to the QBI Executive Committee for final approval. In those instances in which the neighborhood cannot agree, the issue is reviewed by the QBI Director who consults with the Executive Committee for a decision. In those instances in which agreement between QBI and an individual faculty member or neighborhood cannot take place, it is forwarded to the Dean of the School of Pharmacy and the campus Space Committee for final resolution.

Quantitative Institute

Nevan Krogan, PhD Director and Professor

Quantitative Biosciences Institute

UCSF Byers Hall Box 2530 1700 4th St Rm 308D San Francisco CA 94158

tel: 415-476-2980 fax: 415-514-9736

gbi.ucsf.edu

nevan.krogan@ucsf.edu

pharmacy.ucsf.edu/nevan-krogan

Principles of QBI Space Allocation:

· The neighborhood will be considered advisory to the Director and Executive Committee of QBI.

The neighborhood recommendation will be forwarded to QBI for any decision regarding Byers space. The Director will make the decision upon recommendation from the Executive Committee. Any member of the Executive Committee involved in the space decision in their own neighborhood must recuse themselves from the Executive Committee recommendation.

- space system.

Sincerely

Near Krogen

Nevan Krogan Director QBI and Professor



· Initial recommendations will originate with consultation from the neighborhood. A neighborhood is defined as those PIs occupying one side of a floor. In the instance of dry lab space, all Pis on the floor will be consulted.

UCSF RASP utilization metrics will be considered in QBI space allocation decisions. The QBI Director must request input from all department chairs responsible for the respective faculty involved in the space allocation.

 If there is agreement with the space allocation, an MOU will be created, specifying the terms of the agreement. Such agreement will be forwarded to the Dean of the School of Pharmacy, who will notify campus Space and Planning and update the Archibus

 If there is disagreement, the QBI Director will forward the details of the disagreement. to the Dean of the School of Pharmacy for a final decision.

The Dean of the School of Pharmacy will consult with the QBI Director, relevant department chairs and deans for a final decision.

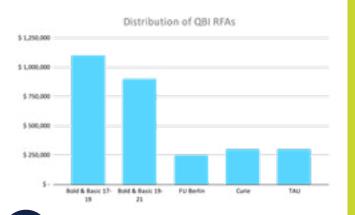
 In those instances in which disagreement continues, the Dean will present the case to the UCSF Space Management Subcommittee.

INFLUENCE ON MORALE

QBI HAPPY HOUR

A 2016 survey suggested a need for additional social gatherings for QBI scientists. QBI reflected upon this need and initiated QBI Happy Hours. Prior to the pandemic, once a month, three QBI labs were chosen to each nominate a Postdoctoral fellow to give a 5-minute, 3-slide presentation at a local bar where arrangements had been made to provide free warm food and beverages. The Postdocs would stand behind the bar in front of a large digital screen, speak through a microphone and talk about their latest research, followed by five minutes of questions. This unique environment was quite successful, with strong interest in a relaxed setting. There were a number of instances in which collaborations started between labs who had never previously been aware of each other's research. Prior to each event, the Postdocs were featured on QBI social media with 1-minute interviews to start a buzz. A Postdoc at one of the events once exclaimed exuberantly, "It's like Match.com for scientists!". To date there have been 15 QBI Happy Hours, which are currently suspended due to the pandemic.





RFAs

QBI wanted to make its mark on funding collaborative and bold science. The RFAs that are offered by QBI always focus on collaborative work, particularly for proposals that are unlikely to be funded through traditional funding mechanisms such as NIH. The first QBI RFA which requested proposals that combined cancer and psychiatric diseases, received over 80 applications. Additional RFAs over the four years have also focused on international collaborations with joint funding from overseas partner institutions. Since 2017 QBI has awarded **\$2.85M** to **31 scientists**.



ART EXHIBITS & OTHER EVENTS

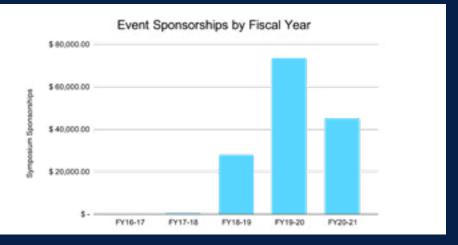
In an attempt to change the conversation, or rather add to it, QBI has had a few special events to accompany some of its symposia, namely two art exhibits and a special panel. These concomitant events brought a different atmosphere to the scientific experience which is often more of a templated affair of presentations, food, posters, more presentations.

Around the Arthropod Disease symposium in 2019, a panel called "What's next? Lunch Panel" focused on Lyme Disease with Patricia Rosa, Don Ganem and Wendy Adams, brought together experts from NIH, UCSF and industry to discuss this important disease and the latest discoveries. The panel attracted over 100 participants both from the lay audience and the UCSF community.

Connected to the same symposium, QBI partnered with USAID for a photography exhibit focused on communities affected by Zika in Central America. The exhibit was on display at Mission Hall for a month. Another art exhibit accompanied the Psychiatric Cell Map Initiative symposium and featured art focused on the brain as well as art produced by people living with Autism.

EVENT SPONSORSHIPS

For the past two years, all QBI events have been at capacity. Since we've transformed into digital platforms, a more than a 150% increase in attendance has been observed. Comprising 103 affiliate faculty members supervising full functioning laboratories, QBI offers excellent sponsors' opportunities to gain visibility with leading scientists and industry decision-makers across various life science disciplines. To date, QBI has raised **\$144,000** in event sponsorship funds.







»SYNTHEGO





Genentech







Amplify.





QCRG

Times of Crisis as a Catalyst for Positive Change

The current SARS-CoV-2 pandemic has highlighted the need for speedy discovery and fast development of therapeutic strategies. Since its emergence, the novel coronavirus has put extraordinary strain on global health and the economy. At the same time, many scientists and physicians have come together with astonishing speed, racing to find treatments and a vaccine in a truly unprecedented manner. Research usually taking years to complete is being completed in weeks. Because of the hard work and dedication of many in the scientific community, by Spring 2020, drug candidates were already being tested in labs and clinical trials across the world.

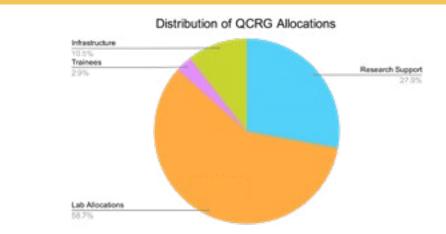
Faced with a problem that requires expertise across disciplines combined with unprecedented speed of discovery, we were able to form the QBI Coronavirus Research Group (QCRG) in a matter of days. By tapping into previously fostered connections at UCSF, across the Bay Area, the US, and around the world, we brought together scientists involved in many different disciplines, including virology and chemistry as well as computational, systems and structural biology, and many more. As a group of over 200 researchers, we mapped the proteinprotein interactions of SARS-CoV-2 in human cells, as well as the phosphorylation landscape of infected monkey cells, predicted known drug targets as potential treatment options, developed infectivity assays on two continents, and tested the drugs and compounds for antiviral activity within a matter of months (Gordon et al., 2020a; Bouhaddou et al., 2020).

We have also carried out a pan-coronavirus analysis focusing on not just SARS-CoV-2 but SARS-CoV-1 and MERS as well, to identify common molecular mechanisms across coronaviruses pointing to several new therapeutic directions (Gordon et al., 2020b). This recent work is a truly multidisciplinary effort, involving genetics, virology, biochemistry, proteomics, computational and structural biology from almost 200 authors from over 30 laboratories around the world. We have also contributed to other work including efforts to identify antibodies or nanobodies for the potential treatment of infected individuals (Schoof et al., 2020; Braken et al., 2020). A perspective piece is soon to be published in Cell describing these world-wide and collaborative efforts (Fabius and Krogan).

Finally, as a testament to open science, we have, as of October 2020, sent plasmids from these studies to 378 laboratories in 42 countries free of charge and without material transfer agreements (MTAs), which notoriously slow down research. Simply put, these reagents are helping to spur on hundreds of publications on SARS-CoV-2.

QCRG was established in March and by the end of July had raised over \$6M from 128 donors, which, to date, is being distributed to 31 labs at QBI.

Finally, QBI has shown it can pivot quickly to a new biomedical need and we feel we will be even more effective and productive when the next one arises.



QCRG Papers to date:

- Gordon et al. <u>A SARS-CoV-2 Protein Interaction Map Reveals Targets for Drug</u> Repurposing (Nature, 2020)
- (*Cell*, 2020)
- by Locking Spike into an Inactive Conformation (Science, 2020)
- neutralize SARS-CoV-2 (Nature Chemical Biology, 2020)
- Pan-Viral Disease Mechanisms (Science, 2020)
- COVID-19 (in review)

Bouhaddou et al. The Global Phosphorylation Landscape of SARS-CoV-2 Infection

• Schoof et al. <u>An Ultra-high Affinity Synthetic Nanobody Blocks SARS-CoV-2 Infection</u>

Braken et al. <u>Bi-paratopic and multivalent VH domains block ACE2 binding and</u>

Gordon et al. <u>Comparative Host-Coronavirus Protein Interaction Networks Reveal</u>

• White et al. Plitidepsin (aplidin) demonstrates potent in vitro and in vivo efficacy against SARS-CoV-2 infection and has significant potential as a therapeutic for the treatment of

COVID-19 GRANTS

DARPA

DARPA: HR00111920020 DARPA COVID Period: 04/01/20 to 08/31/2021 **DARPA COVID Funding:** \$6M Total Cost overall

The goal of this program is to repurpose drugs, investigational new drugs (INDs), and occasionally advanced clinical candidates for activity against SARS-CoV-2 (SARS-2), exploiting human targets the virus subverts in its life cycle. A secondary goal seeks novel leads for drug discovery targeting both viral and human proteins, taking a structure-based approach. More broadly, we hope to build a pipeline that will not only be useful for rapid drug development against COVID-19, but may be more widely used against future pandemics.

DARPA COVID-19 COLLABORATIVE FACULTY AND PARTNERS:

Brian Shoichet, Nevan Krogan, Adolfo Garcia-Sastre (Mount Sinai), David Agard, Kliment Verba, Kevan Shokat

\$6 MILLION



FASTGRANTS (https://fastgrants.org)

Philanthropists pooled resources together to offer FastGrants for rapid research on COVID-19. The process from application submission to award decision was under a week and the funds were available immediately.

QCRG- \$200K

QCRG is functionally assessing the role of the 332 human factors, which we have shown to physically interact with SARS-CoV-2 protein, in virus replication assays to evaluate antiviral activity of repurposed drugs for host-directed therapeutics against SARS-CoV-2.

QCRG Structural Biology Consortium - \$100K

A FastGrant COVID19 grant is used to carry out structural biology on hostviral protein complexes initially identified by the Krogan group. The established QCRG Structural Biology Consortium consists of over 50 volunteer trainees from over 15 different labs at UCSF to rapidly structurally characterize top 50 host-viral protein complexes. By bringing molecular details to these interactions, this work will lead to deeper understanding of how the virus hijacks the human cells.

QCRG PRESS

The QCRG started attracting the media from its inception and saw a steady flow of attention from the press towards UCSF as a result. The following are ten highlighted stories, and below are listed some of the media outlets that covered the stories around the world.

- SF Chronicle: <u>Chasing a Killer</u>
- SF Chronicle: <u>UCSF-led researchers dig deep into coronavirus structure</u>, identify drugs that could diminish COVID effects
- SF Chronicle: <u>UCSF team has discovered drugs that block coronavirus</u>, <u>paving way for 'a better drug sooner'</u>
- New York Times: <u>Hundreds of Scientists Scramble to Find a Coronavirus</u> <u>Treatment</u>
- New York Times: <u>Old Drugs May Find a New Purpose: Fighting the</u> <u>Coronavirus</u>
- New York Times: <u>Bad News Wrapped in Protein: Inside the Coronavirus</u> <u>Genome</u>
- New York Times: <u>Scientists Identify 69 Drugs to Test Against the Coronavirus</u>
- ABC: <u>'Race against the clock': Scientists testing if existing drugs can fight</u> <u>novel coronavirus right now</u>
- LA Times: Inside the body, the coronavirus is even more sinister than scientists had realized
- Al Jazeera: <u>What if a COVID-19 treatment could be ready within weeks?</u>
- USA Today: <u>Startling images reveal coronavirus forming tentacles in cells. It</u> <u>may help identify new treatments</u>



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LEADERSHIP SUMMARY

The Director tries to lead through inclusiveness, communication and via example.

The QBI philosophy encourages scientists from widely ranging scientific disciplines, backgrounds and styles to collaborate. There has been a consistent effort to include younger and female scientists in our events, both domestic and international.

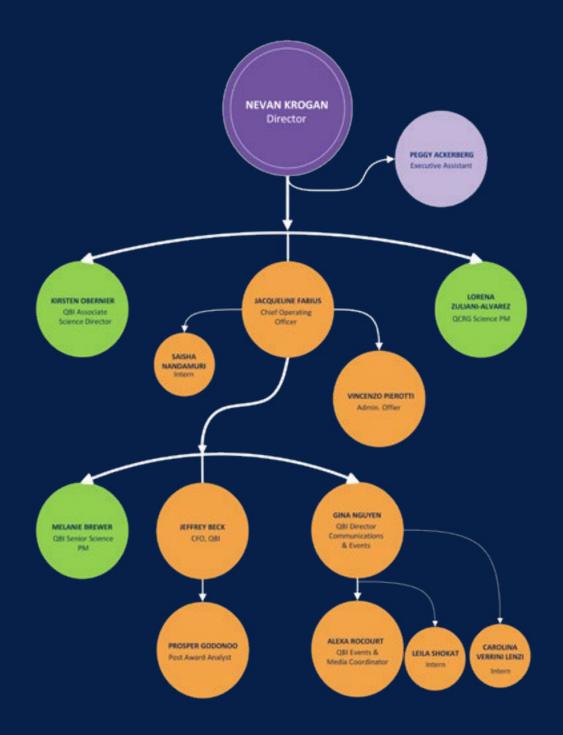
Second, communication of vision and ideas is key for success. While communicating with over a hundred scientists all at the same time is very difficult, a strong attempt is made to interact with different individuals or small groups. While this strategy can be more time constraining, it can also be more effective as scientists are often more comfortable discussing issues one-on-one or in smaller groups. This communication is again preferentially extended to younger scientists as they are most in need of mentorship as they build their careers.

Finally, one of the best ways to lead is through example. In order to succeed, there needs to be a strong work ethic, flexibility and innovation and the championing of diversity and inclusion of women. The Director tries to inspire and motivate others to do the same through the creation of innovative, highly collaborative, international and exciting scientific programs, like the QCRG, as well as fun and unorthodox events. Also, one important component of the future is to have more of an emphasis on inclusion of diversity and women, something QBI and the Director are working towards to set an example for the scientific community at UCSF.

FUTURE GOALS

While we have had success over the last four years, there are areas where we could improve. For example, QBI is striving to diversify its funding sources. We have had success in obtaining large center grants from federal agencies, which we will aim to continue to do, and efforts will be placed on partnering with industry through collaborative agreements. Although we have had recent success with philanthropy though QCRG, we aim to augment funding through donors around our various initiatives and programs. Furthermore, as housing is becoming a more pressing need in the bay area, we want to provide housing options for scientists associated with QBI, especially those that are coming from abroad on scholarships and sabbaticals. And as always, we endeavor to be more inclusive at every level with every group in the activities we generate. All of these efforts, past and future, are aimed at bringing together people, both at UCSF and abroad, to find solutions for the most serious biomedical problems.

QBI ORGANIZATIONAL CHARTS





74

Breaking down silos.