Report on the California Initiative to Advance Precision Medicine
to the California Legislature
January 2018

California Initiative to Advance Precision Medicine Report
to the State of California Legislature
January 2018

Report prepared by The Governor's Office of Planning and Research in collaboration with University of California, San Francisco *pursuant* to Chapter 1.5 of Division 1 of Title 7 of the Government Code

Ken Alex, JD
Director, Governor's Office of Planning and Research; Senior Advisor, Office of Governor Edmund G. Brown Jr.

Lark Park
Senior Advisor, Office of Governor Edmund G. Brown Jr.

Elizabeth Baca, MD, MPA
Senior Health Advisor, Governor's Office of Planning and Research

Atul Butte, MD, PhD
Principal Investigator, California Initiative to Advance Precision Medicine; Director, Institute for Computational Health Sciences; Distinguished Professor of Pediatrics, University of California, San Francisco

India Hook-Barnard, PhD
Executive Director, California Initiative to Advance Precision Medicine
Director of Research Strategy; Associate Director, Precision Medicine, University of California, San Francisco

Uta Grieshammer, PhD
Scientific Officer, California Initiative to Advance Precision Medicine

Governor's Office of Planning and Research
1400 Tenth Street
Sacramento, California 95814
Phone: (916) 322-2318

Table of Contents

I. Executive Summary

In 2017, the California Initiative to Advance Precision Medicine (CIAPM) continued to stimulate statewide collaborations, discussions, and innovation to advance precision medicine. Initially launched by Governor Edmund G. Brown Jr. in 2015 with $3 million in state funding, CIAPM has grown into a $23 million state initiative – still the only one of its kind – representing unique partnerships between the state, the University of California system, private nonprofit and academic entities, and industry.

Since its inception, CIAPM has funded eight demonstration projects across the disease spectrum, an electronic catalog of precision medicine assets, starting with individuals and companies working in precision medicine (to be released in February 2018), an economic analysis of precision medicine, and is poised to release a $9 million precision medicine grant funding opportunity in a major disease area. To further examine the myriad policy issues in precision medicine, Governor Brown also established a 16-member Precision Medicine Advisory Committee in October 2017, with recommendations from the committee due in December 2018.

2017 Major Milestones:

- The first two demonstration projects (California Kids Cancer Comparison and Precision Diagnosis of Acute Infectious Diseases), originally awarded $1.2 million each in 2015, successfully completed the work related to their original grant terms in April. Both projects accomplished their goals to advance precision medicine in children's cancer and in infectious disease diagnostics, and both projects attracted significant third-party funding, as well as additional state funding through a supplemental competitive funding round.

- Early in 2017, the six additional demonstration projects that were selected in late 2016, initiated their work, broadening the CIAPM portfolio of demonstration projects to include remote monitoring using mobile technology, integration of diverse patient data, patient / physician support tools, advanced image analysis using artificial intelligence, and cutting edge sequencing technology to advance precision medicine. Two of these projects also received additional state funding through the 2017 supplemental competitive funding round, expanding the scope of their original projects.

- CIAPM hosted a supplemental competitive funding round in late summer, and in October awarded $1.46 million to four existing demonstration projects (out of a total of 7 projects that applied), based on the strength of their proposals.

- In August, CIAPM commissioned an economic analysis of precision medicine's impacts on the state's economy. CIAPM conducted a limited solicitation and awarded a $127,750 contract to the Bay Area Council Economic Institute and its collaborating institute, the San Diego Regional Economic Development Corporation. The full report will be available in early 2018.

- CIAPM continued its work to create an electronic catalog of precision medicine assets, starting with individuals, organizations, and businesses involved in some aspect of precision medicine work in California. The first draft of the directory will be released in February 2018 for public comment. More than 700 entries will be available through this catalog.

- In October 2017, CIAPM held its annual convening at University of California, San Diego. More than 150 people representing academia, nonprofit organizations, industry and government attended this two-day meeting, which highlighted progress within the eight demonstration projects and provided several panel discussions on data issues and opportunities in precision medicine.

- Early in 2017, CIAPM convened an expert academic advisory committee, consisting of seven members across the UC system, Stanford University and the University of Southern California. In October 2017, the Governor broadened this group with industry, patient advocacy and public health representatives, renamed it the Governor's Precision Medicine Advisory Committee, and assigned the committee specific tasks to be accomplished by December 2018.

- Since July 2017, OPR has conducted research related to the release of the next RFP, estimated at $9 million among all component parts, with an anticipated release date in early 2018.

II. Background

II.A. What is "Precision Medicine"?

Precision medicine, as articulated in the 2011 National Academy of Sciences report, "Toward Precision Medicine: Building a Knowledge Network for Biomedical Research and a New Taxonomy of Disease," aims to use advanced computing tools to integrate and analyze the vast amount of molecular, clinical, environmental and epidemiological data worldwide ("big data") to develop new diagnostics, therapeutics and mechanistic insights into diseases both rare and common, and understand why individuals respond differently to disease and certain therapies.[i]

Like Google Maps, which layers complex data (e.g., road maps, construction, traffic delays, bridges, ferries, transit delays, and building maps) in a seamless way, the goal of precision medicine is to develop similar integrated data/data-enhanced technology tools that link diverse data types relevant to health – from genetics and other molecular characteristics, to environmental exposures, and behavioral and social factors – to better navigate health outcomes.

II.B. Brief History of CIAPM: 2015-2016

Initially launched by Governor Edmund G. Brown Jr. in April 2015, the California Initiative to Advance Precision Medicine (CIAPM) administered by the Governor's Office of Planning and Research, in collaboration with the University of California, and hosted by the University of California, San Francisco, was created to maximize the use of the state's enormous resources in healthcare delivery, scientific and medical research, and data and technology development to improve human health through precision medicine.

In mid-2015 and late 2016, CIAPM hosted two peer-reviewed, competitive grant rounds, leading to the funding of eight patient-focused demonstration projects, totaling $9.6 million. A total of 17 internationally and nationally renowned precision medicine leaders were selected to join the peer-review selection committees that evaluated project applications in these two funding rounds.[ii]

- In 2014-15, OPR received a $3 million General Fund appropriation, which was used to establish CIAPM. In 2015, CIAPM released a limited submission request for proposals within the UC system, recruited a small expert panel to evaluate 11 submissions, and ultimately awarded two demonstration project grants of $1.2 million each to the California Kids Cancer Comparison (UC Santa Cruz) and the Precision Diagnosis of Acute Infectious Diseases (UCSF). The awards went to patient-focused demonstration projects intended to have positive health outcomes in the near-term, and required robust participation from partners outside the UC system.

- In 2016-17, OPR received an additional $10 million General Fund appropriation, which was primarily used to offer another competitive grant round, open to all public and private nonprofit or academic research centers. A 13-member expert review committee scored 29 applications, of which six demonstration projects were

awarded $1.2 million each in late 2016.[iii] Selection criteria were codified through 2016-17 trailer bill language, which included 1) Application of precision medicine to specific disease; 2) Challenges of system interoperability; 3) Approaches to economic analysis; 4) Standards for sharing data or protocols across institutions; 5) Navigation of Federal and State regulatory environment; 6) Acceleration of research discoveries to clinical environment; 7) Challenges relating to data, tools, and infrastructure; 8) Protection of privacy and personal health information; 9) Potential for reducing health disparities; and 10) Methods and protocols for participant/patient engagement.[iv]

- Additional funding beyond the demonstration projects included:
  - initiating an inventory of California's precision medicine assets;
  - conducting an analysis of the impact of precision medicine on California's economy; and
  - hosting conferences to bring together academics, researchers, industry, entrepreneurs, practitioners, patient groups and beyond to highlight challenges and discuss opportunities in precision medicine.

The remainder of this report presents an update on CIAPM activities in 2017, describing the process for allocating supplemental funding to existing demonstration projects, and providing an overview of the programmatic highlights, including an update of project activities for all funded projects.

III. CIAPM Allocation of Funds – 2017

III.A. Allocation of Supplemental Funds from FY 2016-17 Budget

The 2016-17 budget allocated $10 million in funding to OPR for administering CIAPM, subject to a 10 percent limit on administrative expenditures. As indicated above, $7.2 million went to six new demonstration projects at $1.2 million each (reflecting the original award amounts for the initial two demonstration projects funded in 2015), leaving $1.8 million to fund other non-administrative activities, such as the asset inventory (statutorily required), economic analysis, and a competitive supplemental funding round.

As stated in the CIAPM Request for Proposals (RFP) 2016 "Depending on the availability of funds, CIAPM may offer an opportunity for a competitive renewal to all awarded CIAPM demonstration projects." For this purpose, CIAPM allocated $1.46 million from the FY 2016-17 funds, and invited all currently and previously funded CIAPM demonstration project principal investigators to compete for supplemental funding in 2017. The following provides an update on the RFP and review process in 2017.

Request for Proposals

To maximize the use of remaining funds, CIAPM developed a competitive solicitation process open to all current grantees. The CIAPM Limited Competition for Supplemental Funds: Request for Proposals (Appendix A) was posted on the CIAPM website and included an explanation of the process, eligibility criteria, proposal instructions, and review criteria based on statute.

Review Process

For this smaller solicitation, CIAPM recruited six of the thirteen selection committee members that participated in the second grant round, representing the expertise needed for these projects. One additional consultant was added to ensure adequate expertise, which is common practice for review committees such as with the National Institutes of Health (NIH). The participating selection committee members are listed, and their brief bios are provided (Appendix B).

Similar to prior grant rounds, CIAPM 's peer review process (Appendix C), posted on its website, was modeled on the NIH peer review process, and was designed to ensure that applications to the limited RFP were evaluated in a manner that was fair, equitable, timely and free of bias. Everyone who had access to proposals or who attended the review meetings was required to maintain confidentiality, and NIH conflict screening rules applied. The selection committee evaluated a total of seven submitted proposals according to statutory criteria, and recommended four demonstration projects for supplemental funding. The Governor's Office of Planning and Research then reviewed and approved the recommended projects for funding, including the recommended amounts, based on the scope of work represented in the submissions.

III.B. Allocation of Funds from FY 2017-18 Budget

The initial eight demonstration projects have represented diverse disease areas to show how precision medicine approaches can be applied in different disease areas ranging from multiple sclerosis to traumatic brain injury. In contrast, the $9 million from the 2017-18 budget allocation will be awarded to a set of projects addressing a specific disease entity. For the past six months, OPR has solicited input from experts in precision medicine to select a disease area that has high potential to advance health outcomes in California. OPR, through CIAPM, will release a competitive RFP in early 2018.

IV. Program Highlights

Key programs that CIAPM supports include: A) patient-focused demonstration projects intended to have positive health outcomes in the near-term; B) developing an electronic catalog of precision medicine assets to identify strengths and growth opportunities in California; C) conducting an economic analysis to understand the impact precision medicine has on California's economy; and D) bringing together precision medicine thought leaders across sectors to catalyze opportunities and overcome barriers. Progress in these four areas is highlighted in this section.

IV.A. Demonstration Projects

CIAPM's portfolio of eight demonstration projects covers a breadth of disease areas and institutions across California (Appendix D). Together, the eight projects have established more than sixty partnerships, with universities and research hospitals, companies, patient advocacy groups and institutions. Overall, 53 unique public and private entities are involved in the CIAPM demonstration projects. Furthermore, state funds have been leveraged in various ways: teams have been able to attract matching funds in the form

of capital and in-kind services; indirect costs have been waived; and some services and products have been procured at reduced costs.

Collectively, these projects aim to enable more precise, individually targeted prevention, diagnosis, and treatment of disease, and to illustrate that precision medicine can make a difference.

Brief description and accomplishments of the eight demonstration projects:

*Note: Demonstration projects are listed in alphabetic order by title. Partner institutions are listed in alphabetical order. New partners added after initial launch are noted with *.*

Projects started in 2015

1. **California Kids Cancer Comparison (CKCC)**
   Principal Investigator: David Haussler, UC Santa Cruz

   > "The goal of CKCC is to use our expertise in big data to help kids with cancer who are out of treatment options. We are committed to realizing the promise of precision medicine for kids with hard to treat cancers through genomic analysis." – David Haussler

   Partner institutions

   Research hospitals for which UC Santa Cruz provided analysis in real time for kids in treatment:
   British Columbia Cancer Agency*
   Children's Hospital Orange County
   Pacific Pediatric Neuro-Oncology Consortium (UCSF)
   Stanford University

   Research hospitals with which CKCC shared analysis and pipeline information:
   Children's Mercy Hospital in Kansas City*
   Sanford University of South Dakota Medical Center*
   University of Michigan, University of Pittsburg*

   Advocacy organizations with which CKCC works to monitor family and patient needs, and assist advocacy aims:
   Alex's Lemonade Stand Foundation
   Amazon Services
   Azure
   Jacob's Heart
   Key for a Cure*
   Kids v Cancer
   Live For Others Foundation*
   St. Baldrick's Foundation*

Team Finn
Team G Foundation
Unravel Pediatric Cancer

Commercial and industry companies with which CKCC has partnered on sequencing platforms, gene analysis, and cloud services:
DNAnexus
Microsoft*
NuMedii
Seven Bridges

Funding
Launched in October 2015, with $1.2 million in state funds. Completed original grant work in April 2017. Awarded supplemental funding of $490,533 under "CIAPM Limited Competition for Supplemental Funds: Request for Proposals" in October 2017. Supplemental project launched in December 2017 and is scheduled to conclude August 31, 2018.

The UCSC team has leveraged CKCC support to gain additional funding from other funding agencies, including St. Baldrick's Foundation for a 5 year grant of $2.5 million, Team G Foundation at $30,000, and Unravel Foundation at $90,000. They have obtained matching funding commitments from Live for Others Foundation at $50,000, Key for a Cure Foundation at $150,000, and local philanthropists, including George and Rafe Kraw at $50,000, creators of the Kraw Lecture Series on Science and Technology. The CKCC team is currently in discussion for other funds to establish a fellowship in big data computing at the Genomics Institute that will be dedicated to pediatric cancer analysis.

Project Background
Each year 500 California children with cancer either lack or do not respond to standard therapies and succumb to their disease. Precision medicine holds great promise to help patients with such incurable cancers by better matching treatments to the likely vulnerabilities of a patient's tumor. Before, cancers were treated largely based on location - for example, lung cancer or breast cancer. However, each tumor is not just located in a specific area, but has a molecular fingerprint. Some tumors, although from very different anatomical locations, have similar molecular fingerprints and therefore provide novel approaches to treatment. This allows each tumor's molecular defects to be analyzed to understand what is driving its uncontrolled growth and then a drug is chosen that specifically targets those molecular defects. Most precision medicine approaches to cancer focus on mutations found in the DNA of well-studied cancer genes. This approach has had limited success for children with cancer. On average, using this approach in children yields new leads in fewer than 10% of patients who are out of standard treatment options.

CKCC project seeks to find new effective treatments by using innovative computational approaches that rely on the comparison of a patient's tumor information to that of thousands of other tumors. In this comparison, CKCC examines not DNA but gene expression. Using this data-driven comparative approach, new treatment options may be revealed that are not found when analyzing one tumor on its own. This gene expression analysis compares each tumor to more than eleven thousand others.

As a first step toward assessing if this innovative concept has merit, the CKCC project was designed to test if comparative data analyses yield more treatment options than testing each tumor on its own, and to develop interest in the use of this novel computational approach amongst oncologists who treat children with cancer.

Project achievements

The CKCC team established a strong collaboration amongst their world-renowned genomics research center at UCSC and active precision medicine clinical trials that treat children with incurable cancers. The team created an effective, fast and secure method of obtaining large amounts of tumor data, analyzed tumor data from close to 100 patients enrolled in clinical trials and reported their findings to the treating clinicians. After rigorous review, the team identified molecular abnormalities for 100% of children. These data relate to samples that passed quality control thresholds (~100). The percentage of children for whom the CKCC approach identified novel molecular abnormalities significantly exceeded the initial goal of 20%. In 79% of cases these molecular abnormalities were identified by an automated analysis approach developed by the CKCC team, and in 21% of cases, the molecular abnormalities were determined manually by a CKCC data analyst. The CKCC team found that their comparative analyses outperformed the standard molecular analyses of the clinical trials, which focuses on DNA analysis of individual genomic information. By contrast, the CKCC team analyzes RNA data and compares individual RNA information against a compendium of shared RNA data. The CKCC team identified new possible treatment options in almost all cases, while the standard DNA (non-comparative) analyses yielded new options in only about a third of cases.

Other notable outcomes from this project include (i) integration of existing data from multiple public data sources and data contributed by clinical partners to create a large reference compendium with molecular information from thousands of tumors that the team made freely available for others to use in research, (ii) the development of an automated computational analysis process to help enable rapid turnaround times, (iii) the development of packaged ("dockerized") pipelines to allow data processing on partner sites, to minimize regulatory concerns regarding data transfer, (iv) new collaborations with researchers at University of Pittsburg and Nantomics to perform functional validation work in pre-clinical cancer models, and (v) based on clinician feedback, the development of effective communication strategies about their cutting edge analyses and findings to enable informed clinical decision making by oncologists. Team members also participated in multiple pediatric cancer advocacy events to

educate the patient community about precision medicine approaches to cancer therapy.

Importantly, the Reference Compendium developed by the CKCC team during the CKCC project is made up of adult and pediatric cancer data against which individual tumors from children currently in clinical trials are analyzed as part of the pan-cancer approach. Increasing the size of the Reference Compendium allows for more accurate comparative pan-cancer analysis; increasing the proportion of pediatric data allows the CKCC team to increase the comparative value of the analysis for these rare cancers; increasing the diversity of cancer types means a broader spectrum of cancers to compare new samples against. The CKCC team achieved this by adding cases that it analyzed as part of the CKCC partnerships and by mining public datasets. The CKCC team made this Reference Compendium of data available to all researchers and any interested family and patients at https://treehousegenomics.soe.ucsc.edu/explore-our-data/. These analyses methods are also available for other researchers to use on the website.

CKCC raised awareness regarding the value of data sharing, identified the existing barrier to effective, efficient data access, and has been part of an international effort to establish standards for responsible and effective sharing of cancer data, in an effort to directly impact implementation of precision medicine initiatives. (See two recent articles co-authored by David Haussler on the topic: *Sharing Clinical and Genomic Data on Cancer — The Need for Global Solutions,* The Clinical Cancer Genome Task Team of the Global Alliance for Genomics and Health, N Engl J Med 2017; 376, http://www.nejm.org/doi/full/10.1056/NEJMp1612254#t=article and *Facilitating a culture of responsible and effective sharing of cancer genome data*, Lillian L Siu, et al., *Nature Medicine*, 2016; 22 (5): 464 DOI: 10.1038/nm.4089, https://www.ncbi.nlm.nih.gov/pubmed/27149219.)

Supplemental project

With additional CIAPM and other financial support, the team will now take steps to advance their data-driven tumor analysis toward clinical testing by evaluating the effectiveness of comparative RNA-sequencing analysis within the clinical process, including assessing the impact on clinical decision-making, the patient and family understanding and engagement with genomic analysis, and tracking patient outcomes.

They will determine how their findings for each tumor influence decision making in pediatric cancer care by investigating how patients and families understand precision medicine testing and how to best educate oncologists about it. In a longer-term effort, started with CIAPM supplemental funding and funded by others once CIAPM funding ends, they will determine whether treatment decisions made based on their approach improve outcomes for children with currently incurable cancers. Information regarding acceptance of the genomic analysis will be useful in improving education and training during widespread use of genomic-based precision medicine.

The CKCC team will work closely with Stanford clinical research staff using rigorous data-handling processes and institutionally approved protocols and consent forms.

In line with UCSC's commitment to providing open access to data, all software developed by UCSC genomic researchers for CKCC is open source. This means that all RNA-sequencing processed data and accompanying analysis will be made publicly available to benefit researchers. The hope is that by maintaining open access, CKCC can help advance the state of pediatric cancer research.

2. Precision Diagnosis of Acute Infectious Diseases (PDAID)
Principal Investigator: Charles Chiu, University of California, San Francisco

> "We hope to leverage a single test that can simultaneously detect all pathogens – viruses, bacteria, fungi, and parasites – to make an immediate difference in the lives of patients and their families." – Charles Chiu

Partner Institutions
Abbott Laboratories, Inc.*
American Tissue Culture Collection (ATCC)*
Children's Hospital Colorado / University of Colorado in Denver, CO*
Children's Hospital Los Angeles*
Children's National Medical Center at Washington D.C.
DNAnexus, Inc.
Oxford Nanopore Technologies, Inc.*
Quest Diagnostics, Inc.
St. Jude Children's Research Hospital in Vanderbilt, TN*
Syapse, Inc.
University of California, Berkeley
University of California, Davis
University of California, Los Angeles
University of Maryland*
US Food and Drug Administration (FDA)*
Zuckerberg San Francisco General Hospital and Trauma Center*

Funding
California Initiative to Advance Precision Medicine (CIAPM)
10/1/2015 – 8/31/2018

- $1.2 million in state funds (completed in April 2017)
- $500,000 supplemental funding under "CIAPM Limited Competition for Supplemental Funds: Request for Proposals"
  "*Precision Diagnosis of Acute Infectious Diseases"*

Cohen Foundation Award (Chiu, PI)
2/1/2017 – 2/1/2020
- $1.3 million total

"Validation of sequencing-based clinical diagnostics for Lyme disease and other tickborne infections from blood"

DoD Tickborne Disease Research Program (Chiu, PI)
10/17/2017 -10/17/2020
- $265,097 total

"Development of a combined pathogen-host genomic assay for diagnosis of Lyme disease and other tickborne infections"

Sandler and Bowes Foundations (DeRisi and Chiu, PI)
9/1/2015 – 9/1/2018
- $2.4 million total

In-kind funding for establishment of a Center for Next-Gen Precision Diagnostics (https://nextgendiagnostics.ucsf.edu) and clinical assay development

Charles and Helen Schwab Foundation Award (Chiu, PI)
6/1/2016 - 6/1/2019
- $1.2 million total

"Clinical validation of host transcriptome assays for infectious disease diagnosis"

NIH/NIAID 4R33AI120977-03 (Chiu, PI)
1/1/2018 – 1/1/2021
- $900,000 total

"Real-time unbiased pathogen detection in febrile illnesses by nanopore sequencing"

George and Judy Marcus Foundation Award (Chiu and Miller, PI)
9/1/2017 – 9/1/2018
- $400,000 total

"Implementing precision diagnostics of infectious diseases in the clinical setting"

UCSF Medical Center (Miller and Chiu, PI)
5/1/2015 - present
- $500,000 total

In-kind funding for clinical validation of metagenomic next-generation sequencing testing in the CLIA-licensed UCSF Clinical Microbiology Laboratory

Project Background

Current tests fail to diagnose many life-threatening infections in a timely fashion. Different infectious agents require different diagnostic testing, and when initial tests do not reveal the cause of illness, critically ill patients undergo further testing that is often costly and time-consuming, frequently with vague or contradictory results. Healthcare decisions for those patients must therefore often be made on the basis

of limited and imperfect information, leading to increased health care costs and likelihood of death as many drugs may be tried without success.

To help address this problem, the Chiu team has pioneered the use of state-of-the-art genome sequencing to detect almost all known infectious agents in a single test, quickly revealing the cause of bacterial, viral, fungal or parasitic infections that routinely elude physicians. During the research phase of developing this data-intensive precision diagnostic test, the team already showed that it can save lives.

The goal of the Precision Diagnosis of Acute Infectious Diseases (PDAID) project was to translate the use of their fast and comprehensive diagnostic test – named the "metagenomic next-generation sequencing (mNGS) test" – from the research laboratory to a routine clinical setting and to collect systematic evidence for its clinical and economic utility. Ultimately, the goal is to make this data-intensive test widely accessible to patients in California and beyond.

Project achievements

In accordance with federal regulatory standards (Clinical Laboratory Improvement Amendments, CLIA), the PDAID team confirmed in a licensed clinical laboratory that their precision diagnostic test has the appropriate sensitivity and accuracy for diagnosing brain infections, enabling them to start offering the test to physicians worldwide. The team initiated a clinical study in nine hospitals in California and nationwide, enrolling 215 patients critically ill with brain inflammation for whom standard diagnostic testing had not revealed the cause of their illness. They created and used a multidisciplinary consult team to help treating physicians interpret findings from this novel type of test and guide treatment.

The results from this study are highly promising. Notably, mNGS alone identified an infectious cause of a patient's mysterious illness in approximately 11% of cases, and confirmed results of concurrent testing in another 11%. Notably, all of these cases were undiagnosed at the time of enrollment despite extensive conventional testing, and in many of them mNGS was performed as a test of last resort. In addition, surveys of participating clinical partners indicated that a negative result from this comprehensive test helped provide confidence in ruling out infection and thus encouraging pursuit of non-infectious causes for brain inflammation, such as autoimmune disease. This helps clinicians make further testing and treatment decisions for critically ill patients, especially since without information from the precision diagnostic test, doctors have to make decisions with even less information on hand. In one instance, identification of the cause of an infection in a patient with brain inflammation and hepatitis – hepatitis E virus (rare in the United States) – and appropriate antiviral treatment likely spared the patient from having to undergo a liver transplant.

The PDAID project included additional efforts toward enabling the wider use of the precision diagnostic test. The team (i) made progress toward confirming CLIA standard sensitivity and accuracy of the test for diagnosing blood infections, (ii) migrated the software that is needed for the state-of-the-art analysis to a secure cloud (internet-accessible) platform that maintains patient confidentiality, so that infectious disease teams in other locations will be able to use this test in the future, and (iii) initiated an economic analysis to understand under what circumstances, considering costs and outcomes, it makes most sense to use the test.

A key deliverable from the PDAID project is the global availability of a clinical reference test from UCSF for diagnosis of brain infections from spinal fluid (more information available at https://nextgendiagnostics.ucsf.edu). To date, clinical reference testing outside of the PDAID project has been performed for >50 patients, mostly from California (80%), but also from other parts of the United States and internationally in countries such as Portugal. In the next few months, the team will also make available a precision diagnostic test for blood infections in patients with life-threatening sepsis. Finally, as part of the PDAID project, the team has engaged in discussions with the FDA for regulatory approval of the test so that it can ultimately be commercialized and licensed to other laboratories in the United States and worldwide.

The PDAID project effectively leveraged CIAPM funding. The team obtained multiple resources in-kind, such as materials and expert time at UCSF, and human tissue samples needed for clinical confirmation work from commercial partners such as Quest Diagnostics, one of the largest clinical diagnostic companies in the world. The PDAID project attracted substantial additional funding from various philanthropic sources, for a combined total exceeding $7 million (see above).

Supplemental project

To continue driving the data-intensive precision diagnostic test for infectious diseases into clinical practice and broaden and optimize its use, the team will complete the CLIA standard confirmation of the test for diagnosing blood infections and initiate a clinical study with patients with blood infections, which will be completed after CIAPM funding ends. They will also complete the economic analysis. The team will work toward automation of sample processing for the test and they will further develop the use of a portable miniature device that produces sequencing results even faster (3 hours) than is currently achievable (2-3 days) with this test. The team will also leverage their already generated large volume sequencing data for research into determinants of antibiotic resistance, an increasingly serious threat to global public health and into developing and harnessing machine learning (deep learning) approaches to diagnosing infectious or non-infectious (e.g. autoimmune) causes of illness on the basis of the human host response.

Projects started in 2017

3. **Artificial Intelligence for Imaging of Brain Emergencies**
   Principal Investigator: Pratik Mukherjee, UC San Francisco

> "The idea is to accelerate the detection of emergency features on CT scans of the head, so that critical decisions about patient care can be made more rapidly. These are life and death decisions where minutes count. Anything that accelerates this is crucial and can save lives and reduce long-term disability from these disorders." — Pratik Mukherjee

Partner institutions

Brain Trauma Foundation (BTF)

Community Regional Medical Center in Fresno

Stanford University

TBI Endpoints Development (TED) Project*

Transforming Research and Clinical Knowledge in Traumatic Brain Injury (TRACK-TBI) Consortium*

UC Berkeley

Zuckerberg San Francisco General Hospital and Trauma Center

Funding

Launched in January 2017, with $1.2 million in state funds. Expected end date is August 31, 2018. In kind support from BTF, TRACK-TBI, and TED.

Project Background

Every 28 seconds, an American suffers a catastrophic neurologic emergency, which affects 15 million adults and children annually. Very rapid diagnosis is essential for the successful treatment of catastrophic neurologic emergencies, such as stroke or traumatic brain injury. Radiologists interpret complex X-ray images (computed tomography (CT) scans) of the head to assess and diagnose brain damage. The goal of this project is to assist radiologists by applying state-of-the-art artificial intelligence (AI) technology to automate image analysis and speed up diagnosis in order to prevent damage to fragile brain tissue and avoid irreversible brain injury. Importantly, this AI system will be implemented in the "cloud", i.e. will be made accessible through the internet, so that CT scans can be uploaded for analysis from anywhere in the world. This technology will also enable cataloging of clinically significant "digital markers" in brain images, which will facilitate future data-driven precision medicine research by enabling integration of image data, via digital markers, with other types of data relevant to human health.

Project Status

AI methods depend on large amounts of data for "learning" to recognize patterns, i.e., in this case, to recognize and interpret regions of the brain affected in a neurologic emergency. The team has obtained access to more than 100,000 head CT images and has imported more than 50,000 images so far and used them to "train" their AI method. The team are on track to exceed their goal of ingesting more than 100,000 images by the end of the project. In particular, the addition of images from the national multi-center TRACK-TBI and TED studies should significantly increase our expected data intake from the originally targeted goal of 100,000 images.

The team also adopts the latest method improvements as they occur in the fast advancing field of AI, and pursues its own novel method development. A manuscript jointly authored by team members from UCSF and UC Berkeley reporting an innovation in deep learning for analysis of head CT images, and applicable to medical imaging more broadly, has been submitted for publication and presentation in early 2018 at the Computer Vision and Pattern Recognition (CVPR) conference, which is one of the premier international forums for AI research. A second manuscript is in preparation for reporting interim results for a clinical audience.

By comparing the AI method's current ability to detect brain emergencies in CT scans to the ability of radiologists, the team has shown that its accuracy has been increasing as the number of images used to "train" it has been growing; the AI method has almost reached radiologists' level of performance for both detection and measurement of the abnormalities. Since meticulous delineation of complex 3D shapes is impractical for large numbers of medical images, given limitations on radiologists' time, this new AI technology will be the first method available for generating these quantitative biomarkers for use in large-scale Precision Medicine studies of massive imaging datasets.

Further improvements are expected over the next few months as more images are included to train the AI method. Since the goal is to enable upload and analysis of CT images from anywhere in the world, the team also trains the AI method on images obtained from different types of CT scanners. Under those circumstances, the accuracy of the AI method is currently a little lower than when using images from a single scanner, but is approaching similar levels. The team is also making progress on a different AI method that will not only detect and localize but also classify the type of brain emergency to further assist rapid diagnosis.

Negotiations are nearing the final stages between UCSF and a commercial partner for technology transfer. Details are currently under a confidential disclosure agreement, but, if the partnership is successfully finalized, the plan is for a rapid roadmap to commercialization, with initial clinical applications of the technology potentially available to patients via cloud-based delivery to their healthcare providers by the end of 2018.

4. Early Prediction of Major Adverse Cardiovascular Events Using Remote Monitoring

Principal Investigators: Brennan Spiegel; Noel Bairey-Merz, Jennifer van Eyk; Cedars-Sinai Medical Center

> "People die of heart attacks and strokes, despite all of the medications, treatments and science we've evolved. And one of the reasons it happens is we are not able to monitor them closely enough to know when to really engage our patients." — Brennan Spiegel

Partner institutions

Agilent

AliveCor*

Beckman Coulter

DocuSign

Fitabase

Fitbit

HealthLoop

Neoteryx

SCIEX

Tasso*

Thermo Fisher Scientific

University of California, Los Angeles

Funding

The project launched in January 2017, with $1.2 million in state funds and a total of $639,090 in contributions (Cedars-Sinai $200,000, Neoteryx $12,000, Cambridge Isotope Labs $19,090, Thermo Fisher Scientific $100,000, Beckman Coulter $50,000, and SCIEX $258,000). The project was awarded supplemental funds of $223,261 under "CIAPM Limited Competition for Supplemental Funds: Request for Proposals" in October 2017 with an additional $131,775 in contributions (AliveCor $53,350, SCIEX $1,445, Tasso $10,000, and Cedars-Sinai $55,782). Both the original project and the supplemental project, launched in December 2017, are scheduled to conclude August 31, 2018.

Project Background

Cardiovascular disease is the leading cause of death for both men and women in California. Prevention and treatment of heart disease are most effective when disease is detected early, but early signs can be easily missed since people spend most of their life away from a doctor or hospital where it is challenging to monitor disease progression. If predictive markers are identified earlier, then impending major adverse cardiac events (MACE) may be prevented through treatment intensification and efforts to enhance compliance with life-saving therapy. Accurate assessment of

cardiovascular risk is essential for clinical decision making in that the benefits, risks, and costs of alternative strategies must be weighed ahead of choosing the best treatment for individuals. The outcome of interest for this study is MACE, which the team defines as a composite outcome of events including death (all cause), non-fatal MI, non-fatal stroke, or hospitalization for heart failure.

This project aims to establish whether remote monitoring of patients in their daily lives can be used to detect an impending heart attack or stroke, which would allow earlier, more effective treatment. Researchers will look for the earliest signs of impending disease by monitoring patients, who will wear a specialized watch that measures activity, sleep, heart rate, and stress levels. Patients will also report levels of anxiety and depression, and quality of life through a smartphone or computer, as well as periodically send finger prick blood samples by mail to measure more than 500 different blood chemicals. By combining these different types of data, the team will seek a "signal in the noise" that predicts who may be about to have a heart attack or stroke and will also evaluate the cost-effectiveness of this approach for managing Californians at risk for heart disease. Additionally, this project will also look to estimate the cost-effectiveness and budget impact of remote monitoring for MACE – a potentially expensive outcome. Using summary results from this study, the team will create hypothesis-generating cost-effectiveness, cost-utility, and budget impact models to estimate the projected return on investment of remote monitoring.

Project Status

The team finalized their study protocol and standardized procedures, obtained approval from the Institutional Review Board (IRB, an institution's IRB approves, monitors, and reviews biomedical and behavioral research involving humans.), held planning meetings with various collaborators, trained research coordinators for patient recruitment and enrollment, and initiated the clinical study. The team completed recruitment and enrollment of 200 patients, the full cohort for this study, in eight months with extensive involvement of a multi-disciplinary team of scientists, clinicians, nurses, academic, and community physicians, and diverse data (Fitbit, electrical activity of the heart, questionnaires, blood drops) are being collected on patients; the result is one of the most extensive, longitudinal remote monitoring studies in history in terms of the breadth and depth of patient data. Approximately 500 Patients of the Barbara Streisand Women's Heart Center, the Preventive Rehabilitation Cardiac Center, and Cedars-Sinai Medical Group were identified for screening and contacted for enrollment. Of total subjects enrolled, 147 were White, 19 Black or African-American, 18 Hispanic, and 16 Asian. Approximately 90 patients have completed the 3-month study and approximately 60 patients have extended into the 24-week cohort.

To optimize the mechanics of blood drop collection at home, the team enhanced instructions provided to patients and they implemented technical solutions to ensure adequate blood chemical analysis when blood drop collection devices are not

completely filled. The team is optimizing data flow and processing and has started analyzing blood chemicals.

One of the challenges with remote monitoring projects is continued use of devices and submission of self-reports by participants. The team is using the online service HealthLoop to remind participants of tasks, and has observed unexpectedly high compliance so far, an early sign that effective data collection will support a rigorous analysis at the end of the project. There has been a 71% average response rate for Healthloop and about 92% of the patients are extremely likely to recommend this system. In communicating with HealthLoop, the company has indicated that our study has achieved the highest patient engagement of any they have seen in their portfolio to date.

For the Fitbit monitoring, there have been continued interim analyses of Fitbit activity, sleep and heart-rate data which revealed wear-time exceeding 90% across a full 24-hour day on at least 30 days in the study. The level of adherence remains unprecedented compared to ambulatory assessment of fitness data in prior studies.

For the AliveCor Kardia addition, a total of 168 patients have been setup, over 3,000 EKGs received, and currently 97% of patients are connected to this system. The team has observed a high direct patient involvement. Patient feedback has shown that most patients see this project as an opportunity to make meaningful contributions to heart disease, improve the quality of patient care, and make a difference in the lives of others. Patients have enjoyed the remote monitoring aspect of this project because it allows them to have more ownership over managing their health and being more aware of their symptoms. Remote patient monitoring has also provided patients with a sense of security by allowing them to stay connected.

Supplemental project

To potentially enhance their ability to predict an impending heart attack or stroke and work toward implementation of the remote monitoring approach in clinical practice, the team will add several analyses and measurements for each participating patient. They will include (i) an assessment of genomic risk for heart disease, (ii) artificial intelligence (AI)-based modeling of the electrical activity of each patient's heart throughout the study, (iii) testing a different home blood collection device to determine if it offers easier and higher quality samples than the current device, (iv) more sophisticated computational analyses on remotely collected data to determine if prediction scores can be updated more frequently, i.e., on a day-by-day basis, (v) new analyses comparing biosensor and questionnaire data, and (vi) analyses to explore why there has been such a high adherence with remote data collection, with an aim to disseminate the research and root cause.

5. **Full Genome Analysis to Guide Precision Medicine**

Principal Investigator: David Martin, Children's Hospital Oakland Research Institute (CHORI)

> "This project will directly benefit patients and families by solving medical mysteries that have required lengthy diagnostic odysseys with uncertain outcomes. The answers produced by this new analysis will give patients and their doctors insights that will permit appropriate management of the condition and thereby reduce the costs of care. The project will also, through collaboration with other centers, expand the number of conditions in which we will be able to deliver a definite diagnosis." — David Martin

Partner institutions

GenomeOne*

Human Longevity*

Illumina

University of California, San Francisco (UCSF)

UCSF Benioff Children's Hospital Oakland

University of California, Berkeley

Funding

Launched in January 2017, with $1.2 million in state funds. Expected end date is August 31, 2018. All personnel, except Hazel Perry and Dario Boffelli, provide their time in kind. Computational resources in excess of the supported level are provided in kind at CHORI, UCSF, and UC Berkeley.

Project Background

Parents of children born with genetic diseases often spend years trying to find out the causes of their children's illnesses, and sometimes they never do. Currently, only 2,000 of the 20,000 genes in a person's genome are useful in making a diagnosis. This project will advance precision medicine by developing methods that improve researchers' ability to identify mutations that cause inherited disease and to find the cause of previously difficult to diagnose genetic conditions. This will be accomplished by a comprehensive genome analysis, called "full genome analysis" (FGA), that provides a more complete picture of abnormalities in an individual's DNA than is currently achieved. FGA may identify mutations in known genes that are invisible using standard methods of genome sequencing (although some mutations will be difficult to identify if they have not previously been described), and will facilitate the analysis of the 95% of the genome that does not encode proteins. One of the goals of the project is to demonstrate the utility of FGA as a diagnostic tool, compared with other targeted genetic tests, and streamline the execution of genetic testing in a single test. The project also plans to develop a standardized pipeline for acquisition and delivery of FGA.

The team will partner with other international teams with the long-term goal of creating a catalog of all DNA variants that can cause human disease. The team have established collaborations with the teams of Debbie Nickerson, Professor of Genome Sciences, University of Washington at Seattle, Marcel Dinger, Chief Executive Officer of Genome.One (Australia), and David Rowitch, Professor and Head of Paediatrics at University of Cambridge (United Kingdom). The project will include racially and ethnically diverse patient groups, which have traditionally been under-recruited for genomic analysis, thus adding novel and important information to improve diagnosis and care for the population at large.

Project Status

The project team obtained IRB approval at both participating hospitals, UCSF and UCSF Benioff Children's Hospital Oakland, and established regular meetings for participating investigators, including physicians who treat children with inherited diseases, to identify possible study participants. The team is focusing on diseases that are extremely severe and extremely rare, with the goal of identifying genetic variants associated with or resolving the genetic basis of these diseases. The team also hired staff to coordinate case recruitment, and formed a subgroup on the analysis of a portion of the genome that does not encode for proteins; this part of the genome controls the activity of genes and harbors many disease-causing variants, but is normally overlooked in the analysis of genome data.

As of the end of the reporting period (Dec. 2017), 59 potential cases were discussed, 39 cases were identified as being appropriate for this study, and the families of 17 cases were recruited (affected child and parents) out of a planned 50 cases for the overall project. The team collected samples and carried out whole genome sequencing and mapping in the samples. First-pass analysis was performed on eight cases, and four diagnoses were made: three are due to *de novo* gene mutations and one due to a translocation. Detection of the latter type of variant is a strength of FGA; the translocation would have been missed by a standard analysis limited to gene mutations. Diagnoses are made after consulting with the referring clinician, who will then use this information to determine further options for treatment of the disease in the affected child.

During this time period, the team also carried out test sequencing runs with various sequencing companies, in order to identify the best provider for both cost and quality, and will continue to explore sequencing partnerships for the remaining samples of the study. Partnerships with sequencing companies who also develop their own infrastructure for analysis and diagnosis offers promise of further interactions and development of tools and resources for the diagnosis of genetic disorders. For example, California-based Human Longevity carried out sequencing of a set of cases and collaborated in the analysis of the resulting data; this interaction facilitated the identification of the disease-causing variant in one of the cases. The team plans to explore further the potential of these partnerships.

6. Personal Mobile and Contextual Precision Health (PERCEPT)

Principal Investigator: Nicholas Anderson, UC Davis

> "We want to focus on the actual lived experience of the patients in the world and provide them a new platform for sharing personal monitoring data and real health experiences with their care providers. We want to reach and support patients who are not now being reached by making personalized health planning available to them through their own mobile health devices and based on their unique and individual concerns." - Nick Anderson

Partner institutions

iHealthLabs*

Overlap Health

University California, Berkeley

University of California, San Francisco

Funding

Launched in January 2017, with $1.2 million in state funds. Expected end date is August 31, 2018. iHealth contributed in-kind support of $10,000 in services and device discounts.

Project Background

Patients exist in an increasingly diverse digital ecosystem where they generate abundant personal data through mobile technology they use in their daily lives. This data ranges from simple activity tracking and socially shared health status to rich biometric monitoring data, and if linked and coordinated with clinical health states has the potential to help both patients and their doctors improve the precise and personalized management of chronic diseases and wellness. Due to the complex and expanding landscape of commercial devices, social media and evolving concerns of privacy in the digital era, engaging patients to provide personalized and sustainable data that can be integrated to support interpretation in the context of their clinical care remains a major challenge.

The goal of this project is to provide a framework of tools and engagement approaches that allow for patients with chronic disease to participate in the management of their chronic disease. Hypertension and depression are both significant chronic conditions to the California population, and are the team's focus in acquiring blood pressure, mobility, mood, activity and medication compliance data from their mobile devices. These data are linked to patients' individual health care management plans and informed by access to their clinical data from their patient records in the electronic health records at the two pilot medical centers at UC Davis and UC San Francisco. In collaboration with UC Berkeley's focus on design and

usability of mobile technology, we have implemented a system based on open source technology with our partner company Overlap Health. The products of this project are: to (i) create cloud-based (internet accessible) and secure clinical and mobile data repositories for patient-linked mobile health data, (ii) create patient and physician-centered tools, to visualize the integrated data in an easily understandable fashion (dashboard), (iii) recruit patients from UC Davis and UCSF (100 with hypertension; 100 with depression) to collect this data, and (iv) engage patients in the design of both the applications, the analysis of the data, and the design of the engagement models for this study.

Project status

During 2017, the PERCEPT team accomplished all major milestones related to the development of agreements, protocols and plans; backend workflow and data integration; and front-end user interface through iOS and Android user apps. The team is currently conducting a rolling recruitment/enrollment of patients into this clinical study and continues to refine its recruitment model to include new social-media and targeted engagement approaches.

In the first quarter, the team established a Business Associates Agreement between UCSF, UC Davis and Overlap Health; recruited a project advisory committee with community and industry representatives; and developed a clinical trial patient recruitment plan that directly identifies eligible patients in the electronic health record (EHR) systems at UC Davis and UCSF. Patients on the advisory group are not enrolled as patients in the study, but have recommended that enrolled patients be given broader opportunities to both evaluate the engagement approaches of this study, the mobile applications, and the study data analysis work. Future advisory meetings will include enrolled patients who either complete or drop out of the study as collaborators on these areas.

After participatory design and usability testing, the team completed the app development phase for the Apple operating system (iOS), and completion of the feature-identical Android version of the tool launched December 16th. Both apps integrate with third-party blood pressure, mobility and activity applications and devices, and synchronize with the clinical data interface and the visualization tools for patient management.

All medical records for patients in the study are hosted within the electronic health records of the partner medical centers. This demonstration project is being managed as a formal clinical trial, and has received a clinical IRB approval at UCSF, UC Davis and UC Berkeley. Directly linking from each patient's medical records into a cloud-hosted mobile health monitoring environment managed by a private partner is novel, as it bridges both multiple technical as well as clinically governed environments. To ensure the highest level of security for this pilot research study, the team developed and obtained approval by both institutions' IRBs for the clinical study protocol and is

currently enrolling patients into the study through a variety of recruitment channels. The future deployment plans of this project are to have these technologies and engagement models part of the clinical care expectations, and not governed as a research trial, and we are actively developing clinical adoption paths with the internal medicine departments of UCSF and UC Berkeley, and seeking to evaluate a new partnership study of the system in practice in early 2018.

7. Precision Medicine for Early Prostate Cancer: Integrating Biological and Patient Complexity Variables to Predict Treatment Response

Principal Investigator: Sheldon Greenfield, MD (University of California, Irvine and UCI Medical Center)

> "Right now the evidence supports treatment decisions for the average patient. This study will give doctors much better data on which to base recommendations for individual patients." — Sheldon Greenfield

Partner institutions

Cedars-Sinai Medical Center

University of California, Los Angeles Medical Center

Veterans Affairs Long Beach Healthcare

Veterans Affairs Los Angeles

GenomeDx Biosciences

Ambry Genetics Corporation*

Funding

This study was launched in January 2017, with $1.2 million in state funds and received a supplemental award of $246,205 under "CIAPM Limited Competition for Supplemental Funds: Request for Proposals" in October 2017. Both the original project and the supplemental project, launched in December 2017, are scheduled to conclude by August 31, 2018. In-kind contributions from Health Policy Research Institute and the Donald Bren Foundation adds $480,000 in support from UCI. The team have also leveraged in-kind support from two California corporations. GenomeDX Biosciences who will perform the Decipher genomic tests and Ambry Genetics Corporation who will conduct the genetic tests on prostate tissue. Both companies have agreed to absorb the costs of these tests should they not be covered by Medicare or insurance.

Project Background

Prostate cancer is the most common cancer in men and is the second leading cause of cancer death in men, affecting roughly one in seven men over their lifetime. Patients diagnosed with prostate cancer can face difficult choices about treatments that may involve significant side effects. Often doctors must counsel them without adequate data to explain the likelihood that a given therapy will succeed. The goal of

this project is to develop ways to predict, prior to treatment, which therapy will work best for each patient, given how far his disease has progressed and his tolerance for side effects. The project aims to employ a computational approach that takes into account socioeconomic, health status and other types of data, including traditional severity indicators, and a genomic test that measures the probability of a patient's cancer spreading after surgery. The final combined prediction model will aid doctors and patients in personalizing prostate cancer treatment decisions to maximize effectiveness and minimize side effects, and choose the treatment optimal for individual patients.

Project status

The project team initiated several tasks, including forming and recruiting a Patient Stakeholder Advisory Committee and a National Steering Committee; hiring several staff, including a research coordinator for each study site, a project statistician, and a study wide Project Manager. Key components, such as implementation of genetic testing procedures, data collection and management, and data quality assurance were also addressed through team meetings. Early on, the team was able to develop an extensive patient questionnaire, finalize study materials and data collection instruments, and conduct focus groups to review study measures and overall study design. Additionally, the team developed a recruitment plan, including scripts and tracking; instituted enrollment tracking; and established several modes of survey collection (e.g., phone, in-person, mail, electronic). The team was able to receive IRB approval and began recruitment early in the year.

In the middle of the year, the team sought additional partnerships and funding to enable longer study of this cohort and introduce germline panel testing (see Supplemental Project section below). Urologists and geneticists believe that the combination of tissue and germline will improve the predictions of both the patient reported and the cancer outcomes, specifically progression of the tumor. Ambry Genetics Corporation has agreed to perform the germline tests at no cost to the project and is under negotiations with UCI to provide further funding. By extending the enrollment period, although slightly reducing observation time for some of the patients, we will recruit about 500 patients and, should other funding become available, we will be able to recruit 600 enrollments for the entire study. All enrolled patients will have the six-month questionnaire and most will have the one year outcomes. The team has started to organize and consolidate patient data, collected from the five different hospital sites, in preparation for creating the baseline database. One of our initial baseline analyses will be on the comparison of Decipher genetic data across ethnic groups. It is known that there are differences in genetic markers in prostate cancer between ethnic groups but most of the prior research has not been prospectively collected, does not examine the interaction between tumor genetics and germline, and does not include the patients' characteristics that are useful in predicting the various outcomes. This could lead to different clinical practice guidelines for different ethnic groups.

The team is continuing to pursue its goals of validating the national Comparative Effectiveness Analysis of Surgery and Radiation (CEASAR) study (a 3-year longitudinal cohort study measuring the outcomes of 3,691 men with early stage prostate cancer) in a diverse patient population and evaluating the impact of adding genetic biomarker information to the prediction models for outcomes. The team is well along in developing the five-institution combined registry in Southern California.

Supplemental project

To potentially improve the predictive power of the combined prediction model, the team will collect two additional data points from each participating patient. The team will add a six-month time point for collecting detailed patient characteristics to the current twelve-month data collection point and they will include a second genomic test (germline), offered by the company Ambry Genetics, to assess each patient's inherited predisposition to prostate cancer.

8. **Precision Medicine for Multiple Sclerosis: Making It Work**

Principal Investigator: Walter F. Stewart, Sutter Health

> "In the digital age, we are in a position to take research findings and more quickly apply them in the doctor's office—supporting patients and their health care teams *today.* Through the app, care teams will immediately see what's working or not working for patients based on the data and evidence. This empowers care teams and patients alike to make informed decisions together with the benefit of the timeliest, most applicable information."
> — Walter "Buzz" Stewart

Partner institutions

Genentech*

Jordan Research and Education Institute

National Multiple Sclerosis Society

University of California, San Francisco

Funding

Launched in January 2017, with $1.2 million in state funds. Early discovery work was supported by $100,000 from the Conrad N. Hilton Foundation, as well as funds from Sutter Health Philanthropy (i.e., $75,000). Efforts to implement a mobile application pilot will be supported by $250,000 from Genentech. Finally, the Genentech Foundation provided $400,000 in funding to explore the use of quantitative image analysis for developing cohorts of MS patients within health system that could serve to inform treatment guidance. Expected end date is August 31, 2018.

Project Background

Multiple sclerosis (MS) is a nervous system disease that can affect the brain, spinal cord, and other organs. Patients with MS may face decades of physical disability and uncertainty around how quickly the disease will progress. Effective care and therapies are now available to both slow disease progression and to mitigate secondary consequences of MS, but doctors who see MS patients may not be aware of all of the options or how to best use these options in improving patient outcomes.

This project is based on an interactive application developed at UCSF that allows doctors and patients to see how a patient's unique characteristics compare to other patients like them. This is expected to help predict treatment outcomes and assist with selecting treatments most likely to slow disease progression and meet patient needs.

In this project, Sutter Health and UCSF are partnering with patients and the National Multiple Sclerosis Society (NMSS) to design and develop a scalable application, called MS-SHARE, which will instantly compare disease progression data from a large well-managed MS patient cohort at UCSF with real time data from the patient's electronic health record, and with information that patients report about their symptoms between medical appointments. Once MS-SHARE is fully developed, the team will study its adoption in six Sutter general neurology practices, measuring physicians' use and patients' experience with the app as a first step toward implementing precision medicine technology that was developed at an academic medical center into everyday care at community hospitals.

Project Status

To date, the project team has established a stakeholder advisory board, recruited pilot site neurologists and developed several protocols focused on effective implementation of the app, including a patient post-encounter protocol, a patient communications protocol, and a training protocol. Sutter's access to patient cohort data at UCSF was established and development of the initial components of the MS-SHARE application have been developed and are ready for implementation.

To optimize the design of MS-SHARE, three Sutter neurologists participated in over 20 hours of design meetings, providing insight on how the application could streamline clinical workflows and reduce the amount of time clinicians spend in the electronic health record. To improve the patient experience, interviews with 10 patient advisors totaling 30 hours of feedback and covering 111 topics were conducted throughout the year. This combined feedback was then reviewed at a series of five stakeholder advisory group meetings in which investigators, Sutter neurologists, software designers, a representative from NMSS, and patient advisors made decisions about how best to design and implement various aspects of the

solution, including the patient questionnaire, the MS-SHARE web application, and integrating a mobile application into care.

Six Sutter neurologists, with several hundred patients, representing geographic, practice size and demographic diversity, have been recruited and prepared for the study. These general neurologists have been eager to participate in a project which not only has the potential to improve the level of care they deliver, but also to provide their patients access to the research and clinical decision support provided by UCSF.

The MS-SHARE application went live in the electronic health record before the end of 2017, and will continue to undergo user acceptance testing and refinements during the piloting phase. Recruitment of control site neurologists is ongoing. The IRB protocol has been submitted, and approval is expected before the end of January, when it will be required to collect impact data evaluating the study. The next project phase will consist of integrating the web-based app into clinical care, evaluating the patterns of use and early impact, as well as piloting the use of a mobile application developed by Roche/Genentech.

IV.B. Precision Medicine Assets

Precision medicine requires multiple specialties, such as bioinformaticians, statisticians, clinicians, patient advocate groups, among others. It also requires specific infrastructure such as advanced computing facilities or the electronic health records shared between institutions such as the University of California medical centers. Additionally, companies and funders are an important component of financing and realizing the scalability of precision medicine.

An important goal of CIAPM has been to create an environment in the state that facilitates the sharing of resources and knowledge, and further advances strategic areas for future growth and investment. As a first step to creating a resource that can be utilized by researchers, entrepreneurs, funders, foundations, patient advocate groups, and the state, CIAPM is publishing an electronic directory that will 1) highlight which stakeholders are involved in precision medicine; 2) help identify potential collaborators at one's own institution; 3) help identify collaborators across disease areas and technological approaches. Additionally, CIAPM will highlight the geographic concentrations of precision medicine activities in California.

The directory is designed to be a publicly available catalog of companies, researchers, institutions, and initiatives that are engaged in efforts that support precision medicine in California, with the shared goal of driving discovery and innovation, improving health outcomes, decreasing the cost of medical care, and increasing the competitiveness of academic and commercial health-related projects.

Some of the diverse disciplines contributing to precision medicine include artificial intelligence, computation, data science, diagnostics, drug discovery, genomics, mobile

health technologies, microbiome, proteomics, and measurement of environmental and social factors.

CIAPM has developed an initial directory, which includes more than 700 researchers, institutions, companies and initiatives. This inventory/catalog was developed from 1) Awarded demonstration project investigators, collaborators, industry collaborators, and institutions; 2) RFP applicants, project investigators, collaborators, industry collaborators, institutions; 3) Attendees from 2015, 2016 and 2017 convenings; 4) Listing of additional researchers and organizations that have interacted with CIAPM since its inception; and 5) Additional research on the web. Assets are listed by name of the individual or organization, and tagged with relevant information, as appropriate, such as type of organization, location / zip code, title and degree of individuals, website link (Appendix E).

The initial directory is in a draft form that will be made available on the CIAPM website in February 2018 for additional public comment and review. This will allow stakeholders to be identified, provide feedback, and correct any outstanding information.

In the future, CIAPM will look at data sets available in California, as well as computational infrastructure, and the clinical context where precision medicine is growing most rapidly.

IV.C. Economic Impact Analysis

In summer of 2017, CIAPM commissioned an analysis to look at how this new approach to research, health and healthcare is impacting the people of California and the state's economy.

To identify an external partner to perform the economic impact analysis, CIAPM implemented a competitive bidding process in late summer, distributed an RFP to selected suppliers with appropriate expertise and, in October, awarded the contract to the Bay Area Council Economic Institute (BACEI), a think tank focused on economic and policy issues facing the Bay Area region, with its collaborating institution, the San Diego Regional Economic Development Corporation (EDC) providing additional regional expertise. The team is 1) defining the precision medicine industry for the purposes of an economic analysis; 2) determining labor market and industry characteristics, such as total industry employment (state and regional) over time; occupational distributions within the industry over time; wages, education levels, etc.; and past and projected output and growth rates; 3) conducting an economic impact analysis, and; 4) in collaboration with CIAPM, generating materials to disseminate the results.

Work on the project has been underway since September and CIAPM has been working closely with BACEI and the EDC, particularly on portions of the analysis concerned with defining the precision medicine industry.

BACEI and the EDC attended CIAPM's annual meeting and presented an overview of the project to hear perspectives and gather feedback on the project. The team has also

conducted a literature review of similar industry-defining and output-measuring efforts both inside and outside of the state. Additionally, separate from the CIAPM advisory committee, BACEI and EDC established an advisory group specific to the project consisting of experts in the field from industry and education, and convened its first meeting to examine perspectives within the field about how the industry should be defined. The team has also conducted a review, with CIAPM's assistance, of likely sub-industries for inclusion in the analysis. The directory of organizations assembled through the asset inventory has also informed this work. The team has completed sampling of organizations within each sub-industry to estimate the employment attributable to precision medicine.

The completion of the identification of related industries and the sampling of organizations from within these industries gives BACEI and the EDC the necessary components for determining the scale of precision medicine activities in the state. Preliminary estimates put total statewide employment for the precision medicine industry at almost 30,000. For comparison, employment in Chemical Manufacturing, excluding Pharmaceutical and Medicine Manufacturing was 30,900 in California in 2014. The full economic impact estimate is expected to be complete by January 15th, 2018, and release of the final report is expected in Spring 2018.

IV.D. Convenings

California is a large, diverse state with several robust sectors, including biotechnology, technology, and academia. Although many individual professional groups create opportunities for collaboration, cross-disciplinary opportunities to advance precision medicine are considerably less common. By convening diverse stakeholders to discuss challenges and opportunities in precision medicine, the State will be better prepared to implement precision medicine in a way that benefits all Californians.

To date, CIAPM has hosted five convenings with about 450 participants, covering a wide array of topics. Convenings in 2017 are detailed further in this section. Prior convenings are detailed in the 2016 CIAPM report to the Legislature.

All-teams workshop

In February 2017, CIAPM convened all eight CIAPM demonstration project teams to identify potential synergies, share knowledge, discuss sustainability of projects and coordinate communications about the projects and the initiative. The meeting included over 40 individuals, representing all eight teams, the Academic Committee (see section V) and CIAPM/GO/OPR staff.

In addition to updates about each project, participants engaged in moderated discussions such as, sustainability of projects beyond CIAPM funding and topics suggested and chosen by the participants, i.e., data sharing challenges and opportunities and how to measure clinical utility and value of precision medicine approaches.

CIAPM annual meeting

In October 2017, CIAPM hosted a two-day convening in partnership with University of California, San Diego, to bring diverse precision medicine stakeholders together. UC San Diego Health also provided financial and personnel support. The focus of this meeting was on data in the context of the changing health care landscape, including the shifting relationship between research and clinical practice. In addition, all eight demonstration projects were represented with presentations by team leads (Appendix F).

The meeting included over 150 individuals, representing academia, non-profit organizations, industry and governmental institutions.

The convening provided:

- Information on national initiatives such as the national precision medicine program (All of Us), the Million Veteran Program and the Accelerating Therapeutics for Opportunities in Medicine (ATOM) consortium. Representatives from these efforts participated in the panel discussions.
- Opportunities for demonstration projects team leads to provide updates on their projects, present ideas, network, and connect with new partners.
- Focused panel discussions on:
    - Data needs for precision medicine
    - Data needs for precision medicine – cohorts
    - Enabling safe and effective data sharing
    - In what direction will precision medicine bend the cost curve?
    - Ethical considerations in data generation and use
    - Mapping technology opportunities

V. Advisory Committee

CIAPM Academic Committee

With the expansion of the initiative through additional funding appropriated in the FY 2016-17 budget, CIAPM recruited an academic committee in 2017, to advise the core CIAPM team on operational and strategic matters. The Committee was comprised of seven members broadly representative of precision medicine expertise and perspectives from research institutions throughout California (Appendix G).

The Academic Committee met three times in 2017 (February 8, May 30 and August 31, 2017), first in an in-person meeting in San Francisco, and then via teleconference. The Committee provided valuable feedback on (i) demonstration projects, including their evaluations, (ii) objectives, scope and approaches for the California precision medicine asset inventory, (iii) the economic impact analysis and (iv) the CIAPM annual convening. The Academic Committee was not involved in funding decisions or selection of the demonstration projects.

Governor Precision Medicine Advisory Committee

On October 5, 2017, Governor Edmund G. Brown Jr. established the Governor's Advisory Committee on Precision Medicine (PMAC) (Appendix H). PMAC absorbed the Academic Committee, and the seven Academic Committee members became members of PMAC. This 16-member committee encompasses the range of expertise necessary in precision medicine: biotechnology, technology, health systems, health disparities, population health, cancer, bioinformatics, ethics, genomics and patient engagement.

PMAC was created to advise the Governor's Office on emerging precision medicine policy issues, such as data sharing and data privacy within and across technology platforms and tools; clinical utility of precision medicine approaches to care; patient and provider engagement and education; and economic impact and sustainability of precision medicine-based treatments. The committee was also tasked with providing recommendations on further actions the public and private sectors can take to integrate precision medicine into health care.

The Governor's Precision Medicine Advisory Committee conducted its first meeting on November 22, 2017, by teleconference. Five meetings are scheduled for 2018 (three in-person and two teleconference). PMAC is developing its work plan for the year, with initial focus on data challenges and opportunities in precision medicine.

VI. Impact Beyond CIAPM

California continues to have a role in the national and international dialogue in precision medicine. Several demonstration project team leads, CIAPM staff and OPR staff are presenting at academic and policy-oriented conferences nation-wide and multiple publications have been accepted into the academic literature from the 2015 demonstration projects. California's role to advance precision medicine serves as a model for other states as well as enables the partnerships needed across sectors and expertise to realize precision medicine. This work is important so that California continues to be a global leader in technological innovation, health promotion, and health care.

In order to raise awareness about the State's involvement in precision medicine in stakeholder communities, California's Precision Medicine work has been represented at several meetings (Appendix I).

The demonstration project teams often present their work at national and international conferences, and in 2017, demonstration project team members delivered over 30 talks and panel contributions at national conferences, and 12 talks at international conferences about their CIAPM-funded work. Many investigators also communicate their work to educate and inform the public about their work and how it contributes to advancing health and healthcare. For instance, Dr. Chiu's work on rapidly and accurately diagnosing infectious diseases was featured in the cover story "The World Is Not Ready for the Next Pandemic" of the May 4,

2017 issue of Time Magazine. Furthermore, the two 2015 projects have already published some of their CIAPM-funded findings in the scientific literature (Appendix J).

VII. Conclusion

In under three years CIAPM has grown from a $3 million to a $23 million state initiative. This work has attracted more than $10 million in private, foundation, and other matching funds. The demonstration project teams have started to publish and present their work globally, and their projects are already having an impact in the healthcare delivery system.

The state's initial investment has spurred unique collaborations between the State of California, academia, non-profit, and private sectors. Continuing to support this emerging field of precision medicine will be vital to making important advances to improve health and healthcare for Californians.

Appendices

A. CIAPM Limited Competition for Supplemental Funds: Request for Proposals, 2017
B. Selection Committee 2017
C. Peer Review Process 2017
D. List of Eight Demonstration Projects
E. CIAPM - inventory list
F. Agenda, CIAPM Annual Meeting
G. CIAPM Academic Committee
H. Governor Precision Medicine Advisory Committee
I. CIAPM outreach
J. Publications by Demonstration Project Teams

Endnotes

[i] CIAPM's working definition of precision medicine:

> *Precision medicine aims to use advanced computing tools to aggregate, integrate, and analyze vast amounts of data from research, clinical, personal, environmental, and population health settings to better understand diseases and develop and deliver more precise diagnostics, therapeutics, and prevention measures.* This definition is informed by the National Academy of Sciences "Toward Precision Medicine: Building a Knowledge Network for Biomedical Research and a New Taxonomy of Disease".

[ii] An additional consultant was recruited as requested by the team in both review rounds to complete the expertise, consistent with National Institutes of Health Review practices.

[iii] An additional consultant was recruited as noted in endnote ii.

[iv] AB 1602, Chapter 24, Statutes of 2016, which establishes Article 6. *California Initiative to Advance Precision Medicine* under Chapter 1.5 of Division 1 of Title 7 of the Government Code.

California Initiative to Advance Precision Medicine

CIAPM Limited Competition for Supplemental Funds: Request for Proposals

Eligibility	Principal investigators of current and completed CIAPM demonstration projects
Request for Proposals announced	July 28, 2017
Proposals deadline	**September 5, 2017**
Awardees announced	First week of October, 2017
Supplemental work begins	Early November 2017
Supplemental works ends	August 31, 2018
Available Funding	~ 3-4 projects to be funded, up to $500,000 total per project; no indirect costs

I. Precision Medicine

Precision medicine holds promise to profoundly transform health, healthcare and biomedical research. As envisioned in the 2011 National Academy of Sciences' (NAS) report, "Toward Precision Medicine: Building a Knowledge Network for Biomedical Research and a New Taxonomy of Disease," precision medicine aims to use advanced computing tools to aggregate, integrate and analyze vast amounts of data from research, clinical, personal, environmental and population health settings, to better understand diseases and develop and deliver more precise diagnostics, therapeutics, and prevention measures.

II. California Initiative to Advance Precision Medicine

The California Initiative to Advance Precision Medicine (CIAPM) was established by the State of California to help coordinate public, private, and non-profit partners to advance precision medicine approaches and foster the creation of new technologies and therapies that can improve the health of diverse populations. The initiative brings together state precision medicine leaders and supports projects aimed at demonstrating the power and application of precision medicine to the people of California.

III. CIAPM Supplemental Funds

Background

Based on a rigorous peer review process, CIAPM selected eight demonstration projects that aim to illustrate the potential of precision medicine. The projects, awarded at $1.2 million each, are under contract to be completed in 18-20 months. The CIAPM 2015 projects have been completed and have provided valuable results and insight into hurdles and solutions for precision medicine (their formal evaluation is under way). The six demonstration projects selected in 2016 have completed their first progress report and are achieving early milestones.

Objective

One of the goals of CIAPM, and specifically of the demonstration projects, is to build partnerships, and attract funding and other support from third parties to leverage state funds. Projects have been able to attract matching funds in the form of capital, in kind services, and additional leveraged funds. Funding for this limited RFP will be offered through a competitive process, open to all currently or previously funded CIAPM demonstration projects (parent awards), to expand the capacity of selected teams. Inclusion of additional funds (matching funds) by third parties is highly encouraged. Projects will be rated based on specified review criteria (see Section VI.B and Instruction for Peer Review Process), and approximately three to four of the most competitive projects will be awarded supplemental funding. The scope and funding level for each awarded supplemental project will be determined based on available funds, requested amounts and number of awarded proposals.

IV. Guidelines

Eligibility Criteria

- Principal Investigators of all eight CIAPM demonstration projects (current and complete) are eligible to compete for supplemental funding.
- Currently active projects must be in good standing, with progress reports submitted according to agreed upon schedule, and adequate progress on milestones.

Principal Investigator / Team

The principal investigator (PI) of a supplemental funding award has to be the same as the PI on the original award; inclusion of additional team members, particularly new partners, is encouraged to ensure ability to complete additional work proposed.

Matching Funds

For matching funds to be considered for the purposes of this competitive round, the date of matching funds committed must be July 1, 2017 or later (i.e., previous commitments, while viewed favorably, will not be deliberately considered as factor for selection of supplemental award). Any non-State source is eligible to match funds. A dated letter of commitment detailing the amount and nature of the matching funds and funding period must be included and signed by an appropriate official.

Additional considerations

- *As set forth in Section 65058 of the California Government Code,* the awards will be made to "public institutions in both northern and southern California".
- Maximum of one supplemental funding award is allowed per host institution.
- Successful teams' host institutions need to commit to contracting timeline, to ensure that work can begin as specified.
- CIAPM may discuss with reviewers any significant issues related to progress on specific projects, if applicable.

V. Application process

Applicants are asked to submit proposals to CIAPM as outlined in this RFP. As was the case for the parent awards, supplemental awards should advance greater understanding in one or more focus areas, significantly enhancing a focus area(s) already addressed in the parent award, or addressing a focus area(s) not yet addressed in a parent award.

The focus areas are set forth in Sections 65057 and 65058 of the California Government Code as follows:

- The application of precision medicine to specific disease areas.
- The challenges of system interoperability.
- Economic analysis.
- Standards for sharing data or protocols across institutions.
- The federal and state regulatory environment.
- The clinical environment.
- Challenges relating to data, tools, and infrastructure.
- The protection of privacy and personal health information.
- The potential for reducing health disparities.
- Methods and protocols for patient engagement.

A. Proposals

Please prepare a maximum five-page proposal; minimum Arial 11 font; 0.5 inch margins; no appendices. For questions, please contact ciapm@ucsf.edu.

The five-page proposal should cover the following points:

1) Accomplishments on parent CIAPM project to date
   - Briefly outline your current or completed CIAPM-funded work, and describe your progress to date in relation to milestones.
   - Explain delays and / or changes, and their anticipated effects on overall project goals and impact.

2) Proposed activities, milestones and timeline
   - Describe the components of your proposed CIAPM-funded supplemental project (specific aim(s) and research strategy). If you are including matching funds, clearly indicate what activities are to be conducted with CIAPM funds.
   - If you are including matching funds, identify and describe the activities to be accomplished with those funds.
   - Create a table, listing milestones, timeline and metrics to assess completion of milestones. **Clearly indicate which milestones will be achieved using CIAPM funds.** The end date for CIAPM-funded activities is August 31, 2018. Work supported by third party funds can extend beyond the CIAPM project period.
   - Describe anticipated challenges and proposed solutions.
   - If you propose new or expanded human subject research, describe and justify your approach to protection of human subjects from research risks, and the inclusion (or exclusion) of individuals on the basis of sex/gender, race, and ethnicity, as well as the inclusion (exclusion) of children.

3) Rationale and impact
   - Provide an explanation of added value, such as addressing RFP 2016 focus areas (see section V. top) not yet covered in the parent project or significant enhancement of an existing aim.
   - Explain how your supplemental work will likely advance precision medicine. Describe the impact your proposed work will likely have on patients/participants, participant engagement,

healthcare costs and/or health disparities, as applicable.
- Emphasize any innovative aspects of your proposed supplemental work.

4) Project team and resources
   - Describe existing or added personnel, facilities and access to resources, and their role in achieving the added goals(s) within the CIAPM project period. Cross-institutional partnerships are highly valued.

5) Budget
   - Propose a CIAPM supplemental budget of up to $500,000. If you request more than $200,000 from CIAPM, indicate what you would do with less. Note: no indirect costs will be provided with CIAPM funds.
   - Provide a budget for matching funds, if proposed (spending from matching funds can begin and/or extend beyond the CIAPM project end date, i.e. August 31, 2018.)
   - Describe other supportive funding available to your project.
   - Briefly outline how CIAPM funds will be used and how other resources will be leveraged.
   - Comment on why CIAPM funds are needed as opposed to other funding sources such as federal or philanthropic grants.

   Note: CIAPM funds are intended to be used exclusively in California. If the project necessitates the use of CIAPM funds outside of California, provide a brief justification and estimate of the funding that will leave the state. The amount of funds that can leave the state will be subject to the final award agreement.

Submission of additional documents
- Dated letter from third party sponsor(s), if proposed, detailing the amount and nature of the matching funds and funding period and signed by an appropriate official.
- Biographical sketches of additional personnel, not covered in original proposal.
- Updates to biosketch for PI (optional)
- Letters of support from new collaborators / partners.
- Institutional support letter

Note: The parent award proposal and negotiated milestones will be made available to reviewers. For completed projects, the evaluation reports will also be made available to reviewers.

B. Submission – Proposals must be submitted electronically as a single PDF to ciapm@ucsf.edu by 5:00pm PT on Tuesday, September 5, 2017.

C. Submission of updates prior to review meeting

Applicants may submit updates 5 days prior to the review meeting (date to be determined). Allowed submissions:
- Maximum one page of text, minimum Arial 11 font; 0.5 inch margins (additional information may be allowed at discretion of CIAPM)
  - Information provided may include description of matching funding secured, a

milestone reached in parent project, additional partnership or collaboration formed, a manuscript accepted for publication or additional expertise included.

- Letter(s) from new third party sponsor(s), specifying the contributed funds and the commitment to the project.
- Biographical sketches of additional personnel, not covered in original supplemental proposal
- Letters of support from new collaborators / partners.

VI. Selection

A. Reviewers

Members of the CIAPM 2016 Selection Committee will be recruited to review the proposals submitted in response to this RFP. Depending on availability and expertise needs, additional experts may be included.

Reviewers will be screened for conflict of interest consistent with NIH procedures.

B. Review criteria

The proposals will be rated on the following review criteria:

1) Accomplishments on parent CIAPM project to date
2) Innovation and potential for impact of added activities
3) Rationale and approach
4) Demonstrated ability to attract and leverage matching funds
5) Ability to achieve expanded CIAPM-funded project within the contract period. (Note: activities funded by third parties may continue beyond the CIAPM funding period.)

The assessment of the projects according to the review criteria will be guided by the following criteria used in selecting the parent awards *as set forth in Section 65057 of the Government Code:*

- The potential for tangible benefit to patients within two to five years, including the likelihood that the study will have an immediate impact on patients.
- The depth and breadth of data available in the disease focus areas across institutions.
- The prospects for efficient and effective data integration and analysis.
- The expertise of potential team members.
- The resources available for the project outside of the initiative, including the potential for leveraging non-state funding.
- The clinical and commercial potential of the project.
- The potential to reduce health disparities.
- The potential to scale and leverage multiple electronic health records systems.
- The potential to develop the use of tools, measurements, and data, including publicly generated and available data.

The reviewers may also consider additional factors in reviewing the proposals such as:

- The potential for positive economic impact of the proposed intervention or platform, if implemented into clinical practice.
- The quality and extent of patient engagement.
- Where the project is located in California to ensure that at least one proposal each from a public institution in northern and in southern California is included.
- The host institution, as a maximum of one supplemental funding award is allowed per host institution.

C. Review process

Reviewers will be instructed to follow CIAPM-provided procedures for reviewing the proposals and making award recommendations. This process is consistent with NIH practices to ensure proposals are evaluated in a manner that is fair, equitable, timely and free of bias. Reviewers will recommend to the Governor's Office of Planning and Research (OPR) a number of supplemental projects for funding, based on available funds, merit and guidelines (see section IV). They may adjust budgets to accommodate competitive proposals. OPR will make and announce the final funding decision.

VII. Applicants of those proposals that are selected for supplemental funding will be asked to amend their existing agreement with CIAPM through the University of California, San Francisco. For completed projects, a new agreement will be negotiated. The amended / new agreement will address project implementation, including the following:

A. Indirect Costs: Due to statutory limits of funding, no indirect costs will be provided with CIAPM funds. Awardees are asked to waive indirect expenses.

B. Intellectual Property Agreement: Agree to terms of previously established patent agreement for existing CIAPM projects.

C. Start Date: Complete contracting such that work can be initiated within 30 days of receiving the award notification.

D. Reporting: Provide progress information on supplemental work as part of the quarterly progress reports scheduled for the parent project. The final progress report for supplemental work is due September 15, 2018. CIAPM is obligated to perform an evaluation of each demonstration project and report the results to the State Legislature. The final progress report will be comprehensive, covering the entire project period, and will be used as a basis for the demonstration project evaluations; any activities and milestones resulting from a supplemental award will be included in the project evaluation process.

Work with CIAPM staff throughout the project, if funded, on milestone and budget development and adjustments, and participate in conference calls and convening activities. If awarded, precise post-award expectations will be specified in amended award agreements.

E. Use of Data: Investigators and demonstration project teams are expected to share data and research findings consistent with academic standards.

F. Protection of Privacy and Health Information: Investigators and demonstration project teams are expected to follow state and federal law to protect privacy and personal health information, and rights of human subjects.

Appendix B: Selection Committee 2017

California Initiative to Advance Precision Medicine

CIAPM Limited Competition for Supplemental Funds: Request for Proposals

Selection Committee

Overview by Expertise

Selection Committee Member	Institution	Expertise
Nancy Cox - Chair	Vanderbilt University	Genomics / Statistics
Elaine Mardis	Nationwide Children's Hospital, The Ohio State University College of Medicine	Genomics / Cancer
Stanley Shaw	Harvard University	Digital Health
Rachel Ceballos	Fred Hutchinson Cancer Research Center	Health Disparities / Behavioral Health
Timothy Coetzee	National Multiple Sclerosis Society	Patient Engagement, Neuroscience
Margaret Anderson	Deloitte Consulting	Patient Engagement

Listed in alphabetical order

Margaret Anderson
Managing Director
Deloitte Consulting

Margaret Anderson is Managing Director at Deloitte Consulting, where she engages across federal health, nonprofit, and the life science sectors to advance treatments and interventions for patients and to help improve the outcomes and efficiency of the research and delivery systems. Prior to her role at Deloitte, she was the executive director of FasterCures, a Milken Institute center that works to speed up the process of getting new medicines from discovery to patients. She is a founding board member and past-president of the Alliance for a Stronger FDA, a member of the NIH National Center for Advancing Translational Sciences Advisory Council and Cures Acceleration Network Review Board, the National Health Council Board of Directors, United for Medical Research Steering Committee, and the Institute of Medicine's Forum on Drug Discovery, Development and Translation. Previously, Anderson was the deputy director and team leader of the Center on AIDS & Community Health at the Academy for Educational Development; program director at the Society for Women's Health Research; health science analyst at the American Public Health Association; and analyst and project director at the Congressional Office of Technology Assessment in the Biological Applications Program. Anderson holds a bachelor's degree from the University of Maryland and a master's degree in science, technology, and public policy from George Washington University.

Rachel Ceballos, PhD
Assistant Member, Public Health Sciences Division
Fred Hutchinson Cancer Research Center
Affiliate Assistant Professor, School of Public Health
University of Washington in Seattle

Dr. Ceballos is currently an Assistant Member in the Division of Public Health Sciences at the Fred Hutchinson Cancer Research Center and Affiliate Assistant Professor in the School of Public Health at the University of Washington in Seattle, WA. Her research focuses on the development of culturally appropriate interventions to improve emotional well-being and health education opportunities for Latino and African-American cancer survivors. This includes examination of underserved Latinos' interests, beliefs, and preferences for biomedical research participation. Her research methods emphasize community based participatory research practice, which engages in reciprocal learning and community collaboration at all levels of the research process. She is the recipient of a career development award funded by the National Cancer Institute. Dr. Ceballos received her doctoral degree from the Department of Biobehavioral Health at Penn State University. She is trained as an interdisciplinary scientist with both laboratory and community-level research experience. Dr. Ceballos is a Steering Committee Member for the National Latino Cancer Summit, an Advisory Board member for the Susan G. Komen Puget Sound LGBTQ Initiative, and is a Board Member for Cancer Lifeline (a Seattle-based community cancer support center).

Tim Coetzee, PhD
Chief Advocacy, Services, and Research Officer
National Multiple Sclerosis Society

Timothy Coetzee, Ph.D., is the Chief Advocacy, Services and Research officer at the National Multiple Sclerosis Society (NMSS) in New York. Dr. Coetzee has been engaged in multiple sclerosis research and advocacy work throughout his career. He leads the Society's federal and state activism programs, manages its investment in basic, clinical and commercial research, and oversees the delivery of nationwide educational programs and services for people living with MS. He has also helped launch and served as president of Fast Forward, an initiative of the NMSS to speed the commercial development of new treatments for multiple sclerosis. He earned his Ph.D. at Albany Medical College in New York, pursued postdoctoral training at the University of North Carolina at Chapel Hill. Prior to joining the Society, he was a faculty member of the Departments of Microbiology and Neuroscience at the University of Connecticut Health Center.

Nancy J. Cox, PhD
Director, Vanderbilt Genetics Institute
Director, Division of Genetic Medicine
Mary Phillips Edmonds Gray Professor of Genetics
Vanderbilt University

Nancy J. Cox, PhD is a quantitative human geneticist with a long-standing research program focused on identifying and characterizing the genetic component to common human diseases. Dr. Cox earned a BS in Biology from the University of Notre Dame in 1978, a PhD in

Human Genetics at Yale in 1982 and did post-doctoral research at Washington University and the University of Pennsylvania before joining the University of Chicago in 1987. She spent 28 years at the University of Chicago rising to Professor and Chief of the Division of Genetic Medicine before moving to Vanderbilt University in 2015 to become the Mary Phillips Edmonds Gray Professor of Genetics and inaugural Director of the Vanderbilt Genetics Institute, and Director of the Division of Genetic Medicine. Dr. Cox is the President-elect of the American Society of Human Genetics (2016-18), a Fellow of the AAAS, was part of a team winning the Landon Award in 2008 from the American Association for Cancer Research, and achieved the Leadership Award in 2010 from the International Genetic Epidemiology Society. Dr. Cox's current research is now focused largely on integrating data on genome variation and genome function with electronic health records to push the next round of translation of genome discovery into healthcare. Currently funded research projects on which Dr. Cox is PI or co-PI include using these data integration approaches to analyze whole genome sequence data generated by the Centers for Common Disease Genomics, and developing the new Center of Excellence in Health Disparities for Personalized Medicine and Population Health at Vanderbilt.

Elaine R. Mardis, PhD
Co-Executive Director, Institute for Genomic Medicine, Nationwide Children's Hospital
Professor of Pediatrics, The Ohio State University College of Medicine

Elaine Mardis, PhD is co-Executive Director of the Institute for Genomic Medicine at Nationwide Children's Hospital. She also is Professor of Pediatrics at The Ohio State University College of Medicine. Dr. Mardis joined Nationwide Children's Hospital in 2016. Educated at the University of Oklahoma with a B.S. in Zoology and a Ph.D. in Chemistry and Biochemistry, Dr. Mardis did postgraduate work in industry at BioRad Laboratories. She was a member of the faculty of Washington University School of Medicine from 1993-2016. Dr. Mardis has authored over 330 articles in prestigious peer-reviewed journals and has written book chapters for several medical textbooks. She serves as an associate editor for three peer-reviewed journals and is Editor-in-Chief of Molecular Case Studies, published by Cold Spring Harbor Press. Dr. Mardis has given lectures at scientific meetings worldwide, and was awarded the Morton K Schwartz award from the American Association for Clinical Chemistry in 2016. She has been listed since 2013 as one of the most highly cited researchers in the world by Thompson Reuters. Dr. Mardis has been a member of the American Association for Cancer Research (AACR) since 2007, serves on its Board of Directors, and is the program committee chair for the 2018 AACR Annual Meeting.

Stanley Shaw, MD, PhD
Assistant Professor of Medicine, Harvard Medical School
Associate Member of the Broad Institute of Harvard and MIT
Co-Director, Center for Assessment Technology and Continuous Health

Stanley Shaw, MD PhD is the co-founder and co-director of the Center for Assessment Technology and Continuous Health (CATCH) at Massachusetts General Hospital (MGH), Associate Dean for Executive Education at Harvard Medical School, an Associate Member of the Broad Institute of Harvard and MIT, and a founding Principal Investigator in the MGH Center for Systems Biology.

His research seeks to better assess human wellness and disease through new phenotypes (measurable traits), including patient-derived cells, Electronic Medical Records (EMR), the gut microbiome in human disease, and digital health. Dr. Shaw recently led the development of GlucoSuccess, an iOS ResearchKit app for type 2 diabetes patients, in partnership with Apple.

Dr. Shaw received his AB in Chemistry & Physics from Harvard College, and his MD and PhD (Biophysics) from Harvard. He is a practicing cardiologist in the Corrigan Minehan Heart Center at Massachusetts General Hospital.

Additional Expertise

Expert Consultant	Institution	Expertise
Pingkun Yan	Rensselaer Polytechnic Institute	Medical Imaging Informatics / Machine Learning

Pingkun Yan, PhD
Assistant Professor, Department of Biomedical Engineering
Rensselaer Polytechnic Institute

Dr. Pingkun Yan is an Assistant Professor at the Department of Biomedical Engineering at Rensselaer Polytechnic Institute (RPI). Before joining RPI, he was a Senior Scientist of Philips Research working at the clinical site at the National Institutes of Health (NIH). His research interests are in translational medicine focusing on medical imaging informatics and interventional oncology guidance using machine learning and computer vision techniques. Dr. Yan has published over 80 peer reviewed articles in well recognized journals including Medical Image Analysis, J. Urology, IEEE T-CSVT, IEEE T-BME, IEEE T-ITB, Medical Physics, and top international conferences including MICCAI, ISBI, ICCV, CVPR. His publications have been cited for more than 2,700 times with H-index of 28 (according to Google Scholar by 08/2017). His research work has also been recognized by a number of awards including MICCAI 2005 best paper award and IJCARS-MICCAI 2016 best paper award. Dr. Yan is currently serving as an associate editor of multiple international journals, including Machine Vision and Applications and Neurocomputing. He co-organized 6 international workshops and 4 international journal special issues, and have served as a program committee member for more than 40 international conferences. He is also a regular reviewer of a large number of international journals and conferences.

Appendix C: Peer Review Process 2017

California Initiative to Advance Precision Medicine

CIAPM Limited Competition for Supplemental Funds: Request for Proposals Instructions for Peer Review Process

Overview

The CIAPM Limited Competition for Supplemental Funds: Request for Proposals (RFP) is posted at ciapm.org. The CIAPM peer review process is modeled on the NIH peer review process, and is designed to ensure that applications are evaluated in a manner that is fair, equitable, timely and free of bias.

The application process is outlined in the RFP. A Selection Committee will evaluate the proposals and will make recommendations for supplemental awards to the Governor's Office of Planning and Research (OPR). The Selection Committee is composed of experts who have expertise in disciplines relevant to this RFP and the proposals. The composition of the Selection Committee, once established, can be viewed at ciapm.org.

The scientific review meeting is closed to the public as it is a deliberative process in which the committee will review and rank proposals. Everyone who will have access to proposals or who will attend the review meetings will be required to maintain confidentiality and NIH conflict screening rules will apply.

Review of Proposals

The RFP specifies the review criteria and other considerations that will be used in the evaluation and selection of proposals.

A. Peer Review Roles

The Selection Committee process is overseen by a Scientific Review Officer (SRO). The SRO is responsible for ensuring that each application receives an objective and fair peer review, and that the process described herein is followed.

Scientific Review Officer:

- Analyzes the content of each application, and checks for completeness.
- Documents and manages conflicts of interest.
- Assigns applications to reviewers for critique preparation and assignment of individual criterion scores.
- Attends and oversees administrative aspects of peer review meetings.
- Keeps detailed minutes of all the meetings

Selection Committee Members

Chair:

- Serves as moderator of the discussion of merit of the applications under review.
- Is also a peer reviewer.

Reviewers:

- Declare Conflicts of Interest with specific applications according to NIH conflict screening rules.
- Receive access to the applications prior to the peer review meeting.
- Prepare a brief written critique for each application assigned, based on review criteria and judgment of merit.
- Assign a numerical score to each scored review criterion.
- Make recommendations concerning the scientific and technical merit and the potential to enhance the goals and impact of the parent award and advance precision medicine, in the form of final numerical scores.
- Submit a rank order of proposals to OPR where the final decision will be made for funding.
- Submit recommendations concerning appropriateness of budget requests to OPR.

Other CIAPM affiliated individuals:

- CIAPM affiliated individuals are permitted to attend closed review meetings.
- These individuals may provide administrative and programmatic input during the review meeting.

B. Peer Review Meeting Procedures

- Applications are reviewed based on established review criteria (see RFP and section C below).
- Assigned reviewers summarize their prepared brief written critiques for the group.
- A discussion with Selection Committee members follows.
- Final scoring of overall impact scores is conducted by private ballot.

C. Review Criteria

Proposals are submitted to CIAPM and are evaluated for their scientific and technical merit and their potential to enhance the goals and impact of the parent project and to advance precision medicine.

Scored Review Criteria. Reviewers will be asked to consider the review criteria listed in the RFP in the determination of merit. Reviewers will be asked to give a separate score for each of the five review criteria.

Detailed considerations for review criteria are as follows:

1. **Accomplishments on parent CIAPM project to date.** For currently active projects, has the parent project made adequate progress toward its milestones to date? If there have been delays or changes, do they jeopardize achieving the goals of the project? If the project is complete, has it achieved its overall goals? Has it had an impact on precision medicine?

2. **Innovation and potential for impact of added activities.** Does the supplemental proposal use innovative concepts, approaches or methodologies, instrumentation, or interventions to advance precision medicine? Does it add substantial value to the parent project, either by addressing a focus area(s) not yet covered in the parent project or significantly enhancing an existing aim(s)? Will the proposed activities likely have a substantial impact on advancing precision medicine?

   Note: Although innovation is highly valued, it is not required for a project to be competitive as long as the proposed activities are likely to have a substantial impact on advancing precision medicine.

3. **Rationale and Approach.** Are the overall strategy, methodology, and analyses well reasoned and appropriate to accomplish the proposed supplemental activities? Are potential problems and alternative strategies presented? Are the proposed milestones, timeline and success metrics well thought out?

If additional human subject research is proposed, have the investigators presented adequate plans to address relevant biological variables, such as sex, for studies in human subjects? Are the plans to address the protection of human subjects from research risks, and the inclusion (or exclusion) of individuals on the basis of sex/gender, race, and ethnicity, as well as the inclusion (exclusion) of children, justified in terms of the scientific goals and research strategy proposed?

4. **Demonstrated ability to attract and leverage matching funds.** Has the team attracted matching funds from third parties since July 1, 2017 (sponsor letter dated 7.1.17 or later)? If so, are those funds significant both in amount and in their ability to enhance project goals?

5. **Ability to achieve expanded CIAPM-funded project within the contract period.** Can the project plan for the CIAPM-supported supplemental activities be achieved within the proposed timeline? If proposed, are activities supported by matching funds achievable? (Note: activities supported by matching funds may continue beyond the CIAPM funding period.)

   Are the PI, collaborators, and other team members well suited to conduct the supplemental activities? If new collaborators or partners have been added, do they add critical expertise or needed effort?

   Will the professional environment in which the supplemental work will be conducted contribute to the probability of success? Are the institutional support, equipment and other resources available to the investigators adequate for the proposed supplemental activities? Will the supplemental activities benefit from unique features of the professional environment, subject populations, collaborative arrangements or access to additional funds?

The assessment of the projects according to the five review criteria will be guided by the following criteria used in selecting the parent awards *as set forth in Section 65057 of the Government Code:*

- The depth and breadth of data available in the disease focus areas across institutions.
- The prospects for efficient and effective data integration and analysis.
- The expertise of potential team members.
- The resources available for the project outside of the initiative, including the potential for leveraging non-state funding.
- The clinical and commercial potential of the project.
- The potential to reduce health disparities.
- The potential to scale and leverage multiple electronic health records systems.
- The potential to develop the use of tools, measurements, and data, including publicly generated and available data.

The reviewers may also consider additional factors in reviewing the proposals such as:

- The potential for positive economic impact of the proposed intervention or platform, if implemented into clinical practice.
- The quality and extent of patient engagement.
- Where the project is located in California to ensure that at least one proposal each from a public institution in northern and in southern California is included.
- The host institution, as a maximum of one supplemental funding award is allowed per host institution.

Overall Impact. In consideration of the above review criteria, reviewers will provide an overall impact score to reflect their assessment of the likelihood that the supplemental activities will enhance the goals and impact of the parent project and advance precision medicine. A supplemental proposal does not need to be strong in all categories to be judged likely to have a major impact.

D. Scoring

Scores will be used to guide the review process, they will not be provided to the applicants. CIAPM will use the NIH scoring system, which utilizes a 9-point rating scale (1 = exceptional; 9 = poor) for overall impact scores. (NOT-OD-09-024). A modified system, using letters (a= exceptional; e=poor), will be used for criterion scores.

- Before the peer review meeting, each reviewer assigned to an application gives a separate score for each of the scored review criteria categories.
- In addition, each reviewer assigned to an application gives a preliminary overall impact score for that application.
- During the review meeting, a final impact score is given for each proposal by each eligible reviewer (without conflicts of interest) including the assigned reviewers.
- Each reviewer's score reflects his/her evaluation of the overall impact that the supplemental activities are likely to have on enhancing the goals and impact of the parent project and advancing precision medicine, rather than being a calculation of the reviewer's scores for each criterion.
- The final overall impact score for each discussed application is determined by calculating the mean score from all the eligible reviewers' impact scores, and multiplying the average by 10. Thus, the final overall impact scores range from 10 (high impact) through 90 (low impact).

E. Decision Process

Merit as determined by the final overall impact scores will be the main determinant of supplemental proposal selection and final award recommendations. However, OPR aims to fund a balanced portfolio that represents diversity in several areas, including but not limited to, approaches, disease areas, focus areas, types of partners, and types of patient populations. Furthermore, a maximum of one supplemental funding award is allowed per host institution and statute requires that public institutions in both northern and southern California are included.

The Selection Committee will be asked to select approximately 3-4 proposals to recommend for funding, based primarily on rank order while also ensuring that at least one proposal each from a public institution in northern and in southern California is included and that a maximum of one supplemental award is recommended per host institution. The Selection Committee may also choose to adjust the list of recommended proposals to achieve a balanced portfolio as described above.

During the decision making process, Robert's Rules of Order will be used to take actions.

F. Review Results

Scores will be used to guide the review process, they will not be provided to the applicants.

Based on the review discussions for the supplemental proposals, feedback from reviewers for the selected proposals may be implemented during the agreement negotiations.

Appendix D: CIAPM Portfolio of Demonstration Projects

Year of award	Supp. award	Principal Investigator	Lead institution	Project title	Disease focus
2015	2017	David Haussler	UC Santa Cruz	California Kids Cancer Comparison	Childhood Cancer
2015	2017	Charles Chiu	UC San Francisco	Precision Diagnosis of Acute Infectious Diseases	Acute Infectious Disease
2016		Nicholas Anderson	UC Davis	Personal Mobile and Contextual Precision Health	Hypertension, Depression
2016	2017	Sheldon Greenfield	UC Irvine	Early Prostate Cancer: Predicting Treatment Response	Prostate Cancer
2016		David Martin	Children's Hospital Oakland Research Institute	Full Genome Analysis to Guide Precision Medicine	Severe Genetic Disorders in Children
2016		Pratik Mukherjee	UC San Francisco	Artificial Intelligence for Imaging of Brain Emergencies	Traumatic Brain Injury, Aneurysm, Stroke
2016	2017	Brennan Spiegel	Cedars-Sinai Medical Center	Early Prediction of Major Adverse Cardiovascular Events Using Remote Monitoring	Heart Disease
2016		Walter Stewart	Sutter Health	Precision Medicine for MS: Making It Work	Multiple Sclerosis

Appendix E: List of inventory asset tags

The data collected in the Precision Medicine inventory catalog is defined below and was collected from public web sources.

- First and Last Name: as publically listed
- Organization Name: name of the organization that the individual is associated with or organization separate from any individuals.
- Type of Organization (727): this was narrowed down to 4 categories.
    - Academia/.edu (430): the environment or community concerned with the pursuit of research, education, and scholarship.
    - Government/.gov (18): any person or agency that if part of the governing body of the city, state or nation. These include individuals that work within city or state departments.
    - Industry/.com (211): for profit companies that work in the fields related to Precision Medicine. These include biotechnology, pharmaceutical and technology.
    - Non-profit/.org (68): not established for the purpose of making a profit; not entered into for money. These include patient advocacy, life sciences education and granting organizations.
- Degree (505 advanced degrees): advanced academic degrees as listed publically
- Title: professional title as listed publically
- Website Link: web link to public site that describes in additional detail the work of the individual or organization listed. If an organizational profile was unavailable a LinkedIn profile was added.
- Type of Organization - detailed: a listing of 18 different categories to better describe the work of the individual or organization.
    - Academia (54): education and research institution that is not a UC.
    - Academia – UC (334): education and research that is part of the University of California system.
    - Biotechnology (102): the exploitation of biological processes for industrial and other purposes, especially the genetic manipulation of microorganisms for the production of antibiotics, hormones, etc.
    - Business Strategy (8): a long term plan of action designed to achieve a particular goal or set of goals or objectives.
    - Government (18): any person or agency if part of the governing body of the city, state or nation. These include individuals that work within city or state departments.
    - Health IT (8): (health information technology) is the area of IT involving the design, development, creation, use and maintenance of information systems for the healthcare industry.
    - Healthcare Organization (9): the administration and organization of health care systems, hospital networks, and other health care settings

    - High Technology (73): advanced technological development, especially in electronics and computing.
    - Legal (1): of, based on, or concerned with the law.
    - Life sciences policy / public education (8): individual or group which aims to make educated decisions within political, economic, and social systems and institutions through education and policy making.
    - Patient foundation / advocacy (10): an area of specialization in health care concerned with advocacy for patients, survivors, and carergivers.
    - Pharmaceutical (11): discovers, develops, produces, and markets drugs or pharmaceutical drugs for use as medications.
    - Philanthropy (1): discovers, develops, produces, and markets drugs or pharmaceutical drugs for use as medications.
    - Research (19): engaged primarily or exclusively in scientific research.
    - Research / hospital (60): a designated medical facility used to conduct clinical research, such as at a hospital or medical clinic.
    - Trade Organization (3): an association of organizations in the same trade formed to further their collective interests.
    - Venture capital (8): capital invested in a project in which there is a substantial element of risk, typically a new or expanding business.

- Disease area (281): individual or organizations that are focused on specific illness or disorders. Many listed are disease agnostic and work across multiple disciplines. Example: Cancer.
- Disease Area – detailed: work focused on a specific disease or disorder. Example: Breast Cancer
- City: the city in which and an individual or organization is publically listed at.
- Zip code: the geographical postal code in which and an individual or organization is publically listed at.
- County: the county in California in which the zip code is associated.
- Name of Initiative: a specific research/academic activity that an individual or organization is associated with.
- Keywords: additional words that help describe the work being conducted by specific individual and organizations.

California Initiative to Advance Precision Medicine

2017 CIAPM meeting
October 12th & 13th, La Jolla, CA

Data in Precision Medicine
Where are we going and how do we get there?

San Diego Marriott La Jolla

California has made a strong commitment to precision medicine, launching CIAPM in 2015. Our goal for the initiative, and specifically for the annual meeting, is to build community amongst California's thought leaders and stakeholders in precision medicine, to help them discover and pursue opportunities in precision medicine.

The focus of this year's annual meeting is on data - data needs, safe and effective data sharing, transformative technologies and ethical considerations in data generation and use - in the context of the changing health care paradigm, including the shifting relationship between research and clinical practice.

General questions addressed by panels throughout the meeting

- What will/should precision medicine (and the data landscape) look like in 5yrs? In 20yrs?
- How do we get there?
- What can CIAPM, the State of California, or other stakeholders, do to help advance precision medicine?
- Who are the stakeholder groups; what are their needs/how do they differ? How can one stakeholder group help solve (or avoid creating) problems for other stakeholders, i.e., how do we re-align incentives to support the new paradigm?

October 12th, 2017

9:00 AM	**Registration — Coffee and light breakfast**
10:00 AM	**Welcome and Introductory Remarks** • Atul Butte, MD, PhD, Director, Institute for Computational Health Sciences, UCSF, CIAPM Principal Investigator • David Brenner, MD, Vice Chancellor for Health Sciences and Dean of the School of Medicine, UCSD
10:30 AM	**Session 1: Overview of the Data Landscape in Precision Medicine – the Changing Paradigm** • Atul Butte, MD, PhD, Director, Institute for Computational Health Sciences, UCSF, CIAPM Principal Investigator

10:45 AM	**Session 2: Data Needs for Precision Medicine** *Overview of data landscape, types of data, sources of data needed and available - from Molecular to Clinical to Population - Importance of integrating multiple data sources for discovery and application* **Session Moderator:** Jill Mesirov, PhD, MA, Associate Vice Chancellor for Computational Health Sciences, UCSD, Member of CIAPM Academic Committee **Speakers / panelists:** • Dawn Barry, MBA, VP, Applied Genomics, Illumina • Marti Head, PhD, Senior Director, GlaxoSmithKline Pharmaceuticals • Arash Naeim, MD, PhD, CMO Clinical Research, UCLA • Tom Insel, MD, Founder and President, Mindstrong Health • Neal Halfon, MD, MPH, Founding Director, Center for Healthier Children, Families and Communities, UCLA
12:15 PM	**CIAPM Demonstration Project:** Early Prediction of Major Adverse Cardiovascular Events Using Remote Monitoring • Brennan Spiegel, MD, MSHS, Director of Health Services Research, Cedars-Sinai Medical Center
12:30 PM	**Lunch and Networking**
1:15 PM	**CIAPM Demonstration Project:** Personal Mobile and Contextual Precision Health • Nicholas Anderson, MS, PhD, Director of Informatics Research, UC Davis
1:30 PM	**Session 3: Data Needs for Precision Medicine - Cohorts** *Building cohorts and data resources, making use of California's data – opportunities and barriers* **Session Moderator:** Kelsey Martin, MD, PhD, Dean, David Geffen School of Medicine, UCLA, Member of CIAPM Academic Committee **Speakers / panelists:** • Hoda Anton-Culver, PhD, Professor & Chair, Epidemiology, School of Medicine, UC Irvine; Co-PI, All of US- California Consortium • Sumitra Muralidhar, PhD, Director, Million Veteran Program, U.S. Department of Veterans Affairs • Claudia Williams, MS, CEO Manifest MedEx

3:00 PM	**CIAPM Demonstration Project:** Precision Medicine for MS: Making It Work • Riley Bove, MD, Assistant Professor, UCSF
3:15 PM	**Afternoon Break and Networking**
3:45 PM	**Session 4: Enabling Safe and Effective Data Sharing** *Changing the Culture: What are the benefits and risks of data sharing for various stakeholders, e.g., researchers, patients/consumers, clinicians, industry/pharma, payers, academic institutions? How do we change incentives?* **Session Moderator:** Mary Maxon, PhD, Associate Laboratory Director for Biosciences, Lawrence Berkeley National Laboratory, Member of CIAPM Academic Committee **Speakers / panelists:** • David Shaywitz, MD, PhD, CMO, DNAnexus • Darshak Sanghavi, MD, CMO, OptumLabs • Hakan Sakul, PhD, VP & Head of Diagnostics, Worldwide R&D, Pfizer • David Neal, MD, SVP of Global Research, Elsevier • Keith Yamamoto, PhD, Vice Chancellor for Science Policy and Strategy, UCSF
5:15 PM	**CIAPM Demonstration Project:** California Kids Cancer Comparison • David Haussler, PhD, Director, UC Santa Cruz Genomics Institute
5:30 PM	**Adjourn to Keynote Presentation**
Shuttle Service to UCSD Skaggs School of Pharmacy and Pharmaceutical Sciences	
Public Event	
5:30 PM	**Reception**
6:30 PM	**Keynote Presentation - *Toward Individualized Medicine*** • Eric Topol, MD, Founder & Director, Scripps Translational Science Institute **Fireside Chat** • Eric Topol and Atul Butte
7:30 PM	**Reception**
8:30 PM	**Adjourn for the day**

California Initiative to Advance Precision Medicine

October 13th, 2017

8:00 AM	**Arrival and Light Breakfast**
9:00 AM	**Welcome and Observations from Day 1** • Atul Butte, MD, PhD, Director, Institute for Computational Health Sciences, UCSF, CIAPM Principal Investigator
9:10 AM	**CIAPM Economic Study: Impact and Potential of Precision Medicine in California** • Patrick Kallerman, Research Director, Bay Area Council Economic Institute
9:15 AM	**Session 5: In What Direction Will Precision Medicine Bend the Cost Curve?** *Tracking cost impacts, anticipating pain points, possible solutions* **Fireside chat:** • Arnold Milstein, MD, MPH, Director, Clinical Excellence Research Center, Stanford University, Member of CIAPM Academic Committee • Richard Kronick, PhD, Professor, Department of Family Medicine and Public Health, UCSD • Robert Kaplan, PhD, Research Director, Clinical Excellence Research Center, Stanford University
9:45 AM	**CIAPM Demonstration Project:** Full Genome Analysis to Guide Precision Medicine • David Martin, MD, Senior Scientist, Children's Hospital Oakland Research Institute
10:00 AM	**Morning Break and Networking**
10:30 AM	**Session 6: Ethical Considerations in Data Generation and Use** *Addressing data ownership, diversity/inclusion, trust, reducing health disparities, access; achieving health justice through precision medicine* **Session Moderator:** Fred Meyers, MD, MACP, Associate Dean, Precision Medicine, UC Davis, Member of CIAPM Academic Committee **Speakers / panelists:** • Barbara Koenig, PhD, Director, UCSF Bioethics • Nazneen Aziz, PhD, Executive Director, Kaiser Permanente Research Bank • Ted Chan, MD, Chair of Emergency Medicine, UCSD • Camille Nebeker, EdD, MS, Director, Research Ethics, All of Us Research Program, Scripps Translational Science Institute

12:00 PM	**CIAPM Demonstration Project:** Early Prostate Cancer: Predicting Treatment Response • Sheldon Greenfield, MD, Executive Co-Director, Health Policy Research Institute, School of Medicine, UC Irvine
12:15 PM	**Lunch and Networking**
1:15 PM	**CIAPM Demonstration Project:** Artificial Intelligence for Imaging of Brain Emergencies • Pratik Mukherjee, MD, PhD, Professor, UCSF
1:30 PM	**Session 7: Mapping Technology Opportunities** *This session will explore emerging technologies and innovative approaches for precision medicine, especially with respect to data sharing, management and security, analysis and visualization.* **Session Moderator:** John Carpten, PhD, Director, Institute for Translational Genomics, University of Southern California, Member of CIAPM Academic Committee **Speakers / panelists:** • Iya Khalil, PhD, Co-Founder & Chief Commercial Officer, GNS Healthcare, Inc. • Anthony Joseph, PhD, Chancellor's Professor, UC Berkeley • Tara Maddala, PhD, Head of Biostatistics and Data Management, GRAIL • Sara Radcliffe, MPH, MA, President & CEO, California Life Sciences Association
3:00 PM	**CIAPM Demonstration Project:** Precision Diagnosis of Acute Infectious Diseases • Charles Chiu, MD, PhD, Director, UCSF-Abbott Viral Diagnostics and Discovery Center, UCSF
3:15 PM	**Closing remarks**
3:30 PM	**Adjourn**

Appendix G: CIAPM Academic Committee

California Initiative to Advance Precision Medicine

CIAPM Academic Committee

Committee Member	Title	Institution
Atul Butte	Director, Institute for Computational Health Sciences	University of California, San Francisco
John Carpten	Director, Institute For Translational Genomics	University of Southern California
Kelsey Martin	Dean, David Geffen School of Medicine	University of California, Los Angeles
Mary Maxon	Biosciences Area Principal Deputy	Lawrence Berkeley National Laboratories
Jill Mesirov	Associate Vice Chancellor for Computational Health Sciences	University of California, San Diego
Fred Meyers	Associate Dean, Precision Medicine	University of California, Davis
Arnold Milstein	Director, Clinical Excellence Research Center	Stanford University

Biographies of CIAPM Academic Committee Members

Atul Butte, MD, PhD
Priscilla Chan and Mark Zuckerberg Distinguished Professor
Director, Institute for Computational Health Sciences
University of California, San Francisco

Dr. Butte has been principal investigator of the California Initiative to Advance Precision Medicine, director of the Institute for Computational Health Sciences, and Priscilla Chan and Mark Zuckerberg Distinguished Professor at the University of California, San Francisco since 2015. Butte has been a founder and scientific advisor at NuMedii Inc. since 2009 and at Personalis Inc. since 2011. He held several positions at the Stanford University School of Medicine from 2005 to 2015, including assistant professor, professor of pediatrics and division chief. Butte earned a Doctor of Medicine degree from the Brown University School of Medicine and a Doctor of Philosophy degree in health sciences and technology from the Massachusetts Institute of Technology and Harvard Medical School.

John Carpten, PhD
Professor and Chair of Translational Genomics
Director, USC Institute For Translational Genomics
University of Southern California

Dr. Carpten currently serves as Professor and Chair for the Department of Translational Genomics, and Director of the Institute for Translational Genomics, Keck School of Medicine, University of Southern California, Los Angeles, CA. Previously he was Professor and Deputy Director of Basic Sciences, Translational Genomics Research Institute, Phoenix, AZ. Dr. Carpten's research background spans a very broad range of topics including work in germ-line genetics, tumor genome analysis, cancer cell biology, and health disparities. His research program centers around the development and application of cutting edge genomic technologies and bioinformatics analysis in search of germ-line and somatic alterations that are associated with cancer risk and tumor biology, respectively. His work spans many of the known cancer types including but not limited to prostate cancer, breast cancer, colon cancer, brain cancer, multiple myeloma, and pediatric cancers.

Dr. Carpten has an intense focus on understanding the role of biology in disparate cancer incidence and mortality rates among underrepresented populations. Through his leadership, the African American Hereditary Prostate Cancer Study (AAHPC) Network was conceived. This study has become a model for genetic studies in underrepresented populations and led to the first genome wide scan for prostate cancer susceptibility genes in African Americans. Dr. Carpten also has a very active program in sporadic tumor research. His laboratory participated in and led several high impact studies including the identification of NF-□B pathway mutations in Multiple Myeloma, which was published in *Cancer Cell*. He also led a landmark study, which culminated in the discovery of the AKT1(E17K) activating mutation in human cancers, published in *Nature*. He also has research published in *Science, Nature Genetics, Genome Research, and New England Journal of Medicine.*

To improve the discovery of important alterations associated with cancer, Dr. Carpten co-led the implementation, development, and application of Next Generation Sequencing (NGS) technologies at TGen. These technologies offer the opportunity to comprehensively interrogate cancer genomes to uncover the lexicon of somatic events within tumors. Currently, the largest efforts of the Carpten laboratory are in applying NGS for Precision Medicine approaches, where cancer genomes and transcriptomes are sequenced and used to identify targetable events for select therapeutics. He and clinical partners performed a precision medicine study using whole genome and transcriptome sequencing on 14 metastatic triple negative breast cancers to identify therapeutically actionable events that were used for treatment recommendations. The resulting paper was the most cited article in the journal Molecular Cancer Therapeutics in 2014. Furthermore, he coordinated the development of a CLIA-certified genomic testing laboratory at TGen, which was later commercialized as Ashion Analytics, LLC. He is recognized as a thought leader in precision medicine, as shown by a number of papers describing the results of clinical cancer sequencing studies in cancer patients. It is his hope that this work will one day lead to improvements in knowledge based therapeutics toward improvements in outcomes for cancer patients.

Finally, Dr. Carpten has received research funding awards from various sources to support his research including NIH, NCI, Prostate Cancer Foundation, Susan G. Komen for the Cure, Multiple Myeloma Research Foundation, and a number of pharmaceutical companies.

Kelsey Martin, MD, PhD
Dean, David Geffen School of Medicine at UCLA
Professor, Departments of Biological Chemistry and Psychiatry and Biobehavioral Sciences
University of California, Los Angeles

Dr. Kelsey Martin is the Dean for the David Geffen School of Medicine at UCLA, where she is also a Professor in the Departments of Biological Chemistry and Psychiatry and Biobehavioral Sciences. Dr. Martin is very active in the medical community. She serves on the editorial board of Cell, the board of directors for the Burroughs Wellcome Fund, the selection committee of the McKnight Scholar Awards, and the board of directors for the McKnight Endowment Fund for Neuroscience. In 2016, she became a member of the American Academy of Arts and Sciences and a member of the National Academy of Medicine.

Dr. Martin received her B.A. in English and American Language and Literature at Harvard University. After serving as a Peace Corps volunteer in the Democratic Republic of the Congo, she entered the M.D., Ph.D. program at Yale University, where she studied influenza virus-host cell interactions in the laboratory of Ari Helenius, Ph.D., receiving her Ph.D. in Molecular Biophysics and Biochemistry and her medical degree in 1992. She went on to complete her postdoctoral training in neurobiology with Dr. Eric Kandel at Columbia University, and joined the UCLA faculty in 1999.

Dr. Martin directs a productive research laboratory focused on understanding how experience changes connectivity in the brain to store long-term memories. While many aspects of brain circuitry are hardwired, it also is dynamic: the connections between neurons in the brain change with experience to store information, and in this way nature and nurture combine to define a person's identity. Conversely, experiences that produce maladaptive changes in brain circuitry underlie many neuropsychiatric disorders and age-related decreases in brain plasticity contribute to age-related memory disorders, such as Alzheimer's disease. Long-lasting changes in brain connectivity require new gene expression and Dr. Martin has discovered a role for specific signaling molecules that travel from stimulated synapses to the nucleus to change the transcription of DNA to RNA. Her research also has highlighted a central role for the localization of RNAs to synapses, where their synthesis into protein is regulated by neuronal activity, and has uncovered a role for local protein synthesis in autism spectrum disorders.

Mary Maxon, PhD
Biosciences Area Principal Deputy
Lawrence Berkeley National Laboratory

Mary Maxon is the Biosciences Area Principal Deputy at Lawrence Berkeley National Laboratory, where she is responsible for developing strategies for the use of biosciences to address national-scale challenges in energy and environment. She has extensive experience in both the public and private sectors, having served as the Assistant Director for Biological Research at the White House Office of Science and Technology Policy (OSTP) in the Executive Office of the President, where she developed the National Bioeconomy Blueprint, Director of the Marine Microbiology Program at the Gordon and Betty Moore Foundation, and in executive and management roles at Cytokinetics and Microbia, Inc. Maxon received her Ph.D. from the University of California, Berkeley and performed postdoctoral research in biochemistry and genetics at the University of California, San Francisco.

Jill Mesirov, PhD, MA
Associate Vice Chancellor for Computational Health Sciences
Professor of Medicine, UC San Diego School of Medicine
University of California, San Diego

Jill Mesirov is associate vice chancellor for computational health sciences and professor of medicine UC San Diego School of Medicine. As associate vice chancellor, Mesirov is responsible for the overarching strategy for computational health sciences and research computing at UC San Diego School of Medicine. She is a member of the UCSD Moores Cancer Center, where she serves as co-lead for the cancer genomes and networks research program.

Mesirov's research focuses on the application of machine-learning methods to functional genomics data in cancer. Her lab analyzes molecular data to determine the underlying biological mechanisms of specific tumor subtypes, to stratify patients according to their relative risk of relapse, and to identify possible new drug targets. In addition, Mesirov is committed to the development of practical, accessible software tools to bring the methods developed in her lab to the general biomedical research community. These tools are used by hundreds of thousands of investigators worldwide.

Before moving to UCSD in 2015, Mesirov served as associate director and chief informatics officer at the Broad Institute of MIT and Harvard, formerly the Whitehead Institute/MIT Center for Genome Research, where she directed the Computational Biology and Bioinformatics Program. She previously served as manager of computational biology and bioinformatics in the Healthcare/Pharmaceutical Solutions Organization, director of research at Thinking Machines Corporation and has also held positions in the mathematics department at the University of California at Berkeley and served as associate executive director of the American Mathematical Society.

Mesirov, a former president of the Association for Women in Mathematics, is a fellow of the American Association for the Advancement of Science (AAAS), the American Mathematical Society (AMS), and the International Society for Computational Biology (ISCB).

Mesirov received her B.A. in mathematics from the University of Pennsylvania. She earned her M.A. and Ph.D. in mathematics from Brandeis University.

Fred Meyers, MD, MACP
Associate Dean, Precision Medicine
Professor, Internal Medicine / Hematology-Oncology, UC Davis School of Medicine
University of California, Davis

Dr. Frederick Meyers is the Associate Dean for Precision Medicine and professor of internal medicine / hematology-oncology at UC Davis School of Medicine. He has served UC Davis as chief of hematology-oncology, chair of the Department of Internal Medicine and vice dean of the School of Medicine.

Dr. Meyers has a long-standing interest in cancer biology, with a focus on advanced and metastatic malignancies. His earliest publications in the molecular oncology of urologic cancers emphasized clinical trials with laboratory correlative studies. He recognized the inherent ethical conflict between early-phase cancer clinical trials and the need to deliver palliative and end-of-life care. Many of his early grants and publications highlighted this apparent paradox that he resolved by developing a model of simultaneous or concurrent care. The systems-based improvement of cancer-care delivery integrated cancer therapy and palliative care at the same time, rather than sequentially, and changed the paradigm of the care of patients with both advanced malignancy and nonmalignant illnesses, successfully introducing palliative care earlier in the trajectory of illness. This forms the basis for his ongoing commitment to quality of care improvement, and he has long been an advocate for integrating it into health sciences education.

Dr. Meyers is strongly committed to the career development of junior scholars, MD and PhD, pre-and postdoctoral. He directs the Research Education and Career Development core of the UC Davis NIH-funded Clinical Translational Science Center (CTSC). His commitment is reflected in his service as principal investigator of several training grants including the CTSC Mentored Clinical Research Training Program, a California stem cell research training grant and a grant from HHMI Integrating Medicine into Basic Sciences. He is principal investigator of the UC Davis NIH Common Fund Broadening Experiences in Scientific Training (BEST) award. His current focus is leading and integrating precision medicine across all of the colleges and schools at UC Davis and the communities it serves.

Arnold Milstein, MD, MPH
Director, Clinical Excellence Research Center
Professor of Medicine
Stanford University

Dr. Milstein is a Professor of Medicine, an Affiliated Scholar at the Philip R. Lee Institute for Health Policy Studies and directs Stanford's Clinical Excellence Research Center. The Center is a collaboration of the Schools of Medicine, Engineering and Business to design and demonstrate in multi-state locations innovative health care delivery models that safely lower per capita health care spending while improving patients' health and experience of their care.

Before joining Stanford's faculty, his career of applied research spanned private and public sector healthcare delivery and policy. After creating a healthcare performance improvement firm that he expanded globally following its acquisition by Mercer, he co-founded two nationally influential public benefit initiatives, the Leapfrog Group in 1998 and the Consumer-Purchaser Disclosure Project (now the Consumer-Purchaser Alliance) in 2001. He was appointed to a six year term as a Congressional MedPAC Commissioner, originating several subsequently enacted legislative changes. Since its inception, he has served as the Medical Director of the Pacific Business Group on Health (PBGH), the largest employer-led regional healthcare improvement coalition in the U.S.

Citing his national impact on innovation in health care policy and delivery methods, he was selected for the highest annual award of both the National Business Group on Health (NBGH) and of the American College of Medical Quality. Elected to the Institute of Medicine (IOM) of the National Academy of Sciences, he chaired the planning committee of its series on best methods to lower per capita health care spending and improve clinical outcomes. He was educated at Harvard (BA–Economics), Tufts (MD) and UC Berkeley (MPH Healthcare Evaluation).

Appendix H: Governor's Advisory Committee on Precision Medicine (PMAC)

GOVERNOR BROWN ANNOUNCES PRECISION MEDICINE ADVISORY COMMITTEE

10-5-2017

SACRAMENTO - Continuing the state's efforts to use advanced computing and technology to better understand, treat and prevent disease, Governor Edmund G. Brown Jr. today established the Governor's Advisory Committee on Precision Medicine.

"California is a world leader in medicine and technology. This committee of experts will help us think through how precision medicine can improve health and health care for Californians," said Governor Brown.

Precision medicine aims to use data-driven tools and analysis to develop new diagnostics, therapies and insights into health and disease. Governor Brown announced the California Initiative to Advance Precision Medicine (CIAPM) in April 2015 as the first-in-the-nation, state-level effort to fund focused precision medicine projects to improve care and treatment for specific diseases. Since the initial launch, CIAPM has supported several demonstration projects, led by California's renowned academic and medical institutions, which span the disease spectrum - from childhood cancer to traumatic brain injury, multiple sclerosis and heart disease. To date, California has invested $13 million out of the total $23 million in allocated state funding for precision medicine. Private companies and foundations have also provided additional funding and donated in-kind support directly to the projects.

The committee will advise the Governor's Office on emerging precision medicine policy issues, such as data sharing and data privacy within and across technology platforms and tools; clinical utility of precision medicine approaches to care; patient and provider engagement and education; and economic impact and sustainability of precision medicine-based treatments. The committee will also provide recommendations on further actions the public and private sectors can take to integrate precision medicine into health care.

The advisory committee members appointed by the Governor encompass the range of expertise necessary in precision medicine: biotechnology, technology, health systems, health disparities, population health, cancer, bioinformatics, ethics, genomics and patient engagement.

Governor's Advisory Committee on Precision Medicine Members:

Tomás J. Aragón, MD, MPH, DrPH, 57, of San Francisco, has been appointed to the Governor's Precision Medicine Advisory Committee. Aragón has been the health officer of the City and County of San Francisco and director of the Population Health Division at the San Francisco Department of Public Health since 2011. He has been an assistant adjunct professor of epidemiology (teaching R programming) at the University of California, Berkeley School of Public Health since 2004, where he directed a Centers for Disease Control and Prevention training and research center from 2003 to 2010. Aragón earned a Doctor of Medicine degree from Harvard Medical School, a Master of Public Health degree from the Harvard School of Public Health and a Doctor of Public Health degree from the University of California, Berkeley School of Public Health. He completed a primary care internal medicine residency and a clinical and research fellowship in infectious diseases at the University of California, San Francisco. Aragón has completed leadership training with the California Health Care Foundation and earned certification in Healthcare Strategic Decision and Risk Management from Stanford University. This position does not require Senate confirmation and there is no compensation.

Atul Butte, MD, PhD, 48, of Menlo Park, has been appointed to the Governor's Precision Medicine Advisory Committee. Butte has been principal investigator of the California Initiative to Advance Precision Medicine, director of the Institute for Computational Health Sciences, and Priscilla Chan and Mark Zuckerberg Distinguished Professor at the University of California, San Francisco since 2015. Butte has

been a founder and scientific advisor at NuMedii Inc. since 2009 and at Personalis Inc. since 2011. He held several positions at the Stanford University School of Medicine from 2005 to 2015, including assistant professor, professor of pediatrics and division chief. Butte earned a Doctor of Medicine degree from the Brown University School of Medicine and a Doctor of Philosophy degree in health sciences and technology from the Massachusetts Institute of Technology and Harvard Medical School. This position does not require Senate confirmation and there is no compensation.

John Carpten, PhD, 52, of Los Angeles, has been appointed to the Governor's Precision Medicine Advisory Committee. Carpten has been chair of the Department of Translational Genomics at the University of Southern California, Keck School of Medicine and co-director at the University of Southern California Institute for Translational Genomics since 2016. He was director of the Integrated Cancer Genomics Division at the Translational Genomics Research Institute from 2003 to 2015, where he was deputy director of basic sciences from 2012 to 2015. He was a tenure-track investigator at the National Institutes of Health's National Human Genome Research Institute from 1988 to1994. Carpten earned a Doctor of Philosophy degree in molecular, cellular and developmental biology from Ohio State University. This position does not require Senate confirmation and there is no compensation.

Jay Gellert, 63, of Woodland Hills, has been appointed to the Governor's Precision Medicine Advisory Committee. Gellert was president and chief executive officer at Health Net Inc. from 1998 to 2016. Gellert was president and chief operating officer of Health Systems International Inc. (HSI) from 1996 to 1998 and was a member of the Health Systems International Inc. Board of Directors and chairman of the board for HSI's principal operating subsidiaries, Health Net and QualMed, from 1996 to 1998. Gellert directed Shattuck Hammond Partners Inc.'s strategic advisory engagements from 1990 to 1996, was president and chief executive officer of the Bay Pacific Health Corporation from 1988 to 1991 and was senior vice president and chief operating officer for California Healthcare System from 1985 to 1988. Gellert is a member of the Ventas, Inc. Board of Directors. He was as chairman of the America's Health Insurance Plans Board of Directors and served in several positions at the Council for Affordable Quality Healthcare, including co-chair of the Provider Council, chairman of the Administrative Simplification Committee and member of the Board of Directors and the Executive Committee. This position does not require Senate confirmation and there is no compensation.

Kim Goodwin, 46, of Oakland, has been appointed to the Governor's Precision Medicine Advisory Committee. Goodwin has worked with PatientsLikeMe - a social network, decision-support tool and medical research platform dedicated to connecting patients and analyzing patient-shared data - in various capacities since 2011, including as vice president of product and user experience and as a consultant to guide the development of software tools as well as the patient experiences of longitudinal research. Goodwin is the bestselling author of "Designing for the Digital Age" and speaks around the world about designing human-centered experiences. Goodwin was vice president and general manager at Cooper from 1998 to 2009, where she led consulting projects with Cardinal Health, Varian Medical Systems, Merck Medco, Mayo Clinic and Abbott Labs, as well as consumer brands such as Lexus and NBC. Her 24 years of product design and strategy have included work on electronic health records, personal health records, pharmacy websites, consumer glucose meters and insulin pumps and clinical medical devices. This position does not require Senate confirmation and there is no compensation.

Sol Lizerbram, DO, 69, of Rancho Santa Fe, has been appointed to the Governor's Precision Medicine Advisory Committee. He was co-founder and chairman at HealthFusion Inc., a web-based award winning national electronic health records software firm, from 1998 to 2016. The software collects and analyzes data, assisting physicians in meeting quality objectives. Lizerbram was medical director at The Prudential Insurance Company, San Diego from 1986 to 1992. He was appointed to the State of California Workers' Compensation Insurance Rating Bureau Board of Governors in 1993 and served on the California State Insurance Commissioner's Advisory Council from 1991 to 1993. Lizerbram served as chairman of the U.S. Senator John Rockefeller, Health Care Advisory Committee from 1989 to 1991. Lizerbram has served as chairman of the California Expanded Choice Program's Provider Advisory Board and as a member of the California Medical Assistance Commission and California Health Policy and Data Advisory Commission. He is a fellow of the American Osteopathic College of Allergy and Immunology and received the Nathaniel J. Loeb award for outstanding achievement in medicine. He is president of the Jewish

National Fund for the U.S. and a member of the University of California, San Diego Foundation Board of Trustees. Lizerbram earned a Doctor of Osteopathic Medicine and Surgery degree from the Philadelphia College of Osteopathic Medicine. This position does not require Senate confirmation and there is no compensation.

Stephen H. Lockhart, MD, MPhil, PhD, 59, of Oakland, has been appointed to the Governor's Precision Medicine Advisory Committee. He has been chief medical officer for Sutter Health since 2015, where he has held several positions, including East Bay regional chief medical officer from 2010 to 2015. Lockhart was chief administrative officer at the St Luke's campus of the California Pacific Medical Center from 2008 to 2010, where he was the medical administrative director of surgical services from 2003 to 2008 and had a long-standing practice of 20 years. A Rhodes Scholar, Lockhart earned a Master of Philosophy degree in economics from Oxford University and Doctor of Medicine and Doctor of Philosophy in biostatistics degrees from Cornell University. This position does not require Senate confirmation and there is no compensation.

Kelsey Martin, MD, PhD, 59, of Los Angeles, has been appointed to the Governor's Precision Medicine Advisory Committee. Martin has served as dean of the David Geffen School of Medicine at the University of California, Los Angeles since 2016, where she has served as a faculty member in the departments of Biological Chemistry and Psychiatry and Biobehavioral Sciences since 1999. She served as co-director of the University of California, Los Angeles-California Institute of Technology Medical Scientist Training Program from 2005 to 2013 and was chair of the University of California, Los Angeles Department of Biological Chemistry from 2010 to 2015. Martin is a member of the Cell Editorial Board, Burroughs Wellcome Fund Board of Directors and the McKnight Endowment Fund for Neuroscience Board of Directors. She is a member of the American Academy of Arts and Sciences and the National Academy of Medicine. After serving as a Peace Corps volunteer in the Democratic Republic of the Congo from 1980 to 1982, she earned a Doctor of Medicine degree and Doctor of Philosophy degree in molecular biophysics and biochemistry from Yale University. Martin completed postdoctoral training in neurobiology with Eric Kandel at Columbia University. This position does not require Senate confirmation and there is no compensation.

Mary E. Maxon, PhD, 55, of San Francisco, has been appointed to the Governor's Precision Medicine Advisory Committee. Maxon has been associate laboratory director for biosciences at Lawrence Berkeley National Laboratory since 2017, where she was biosciences area principal deputy from 2012 to 2017. Maxon is responsible for developing strategies for the use of biosciences to address national-scale challenges in energy, environment, health and biomanufacturing. She has extensive experience in both the public and private sectors. Maxon served as assistant director for biological research at the White House Office of Science and Technology Policy from 2009 to 2012, where she developed the National Bioeconomy Blueprint. Maxon was director of the Marine Microbiology Program at the Gordon and Betty Moore Foundation from 2007 to 2009 and held executive and management roles at Cytokinetics as associate director and as leader of the Anti-infective Program from 2001 to 2004. She was scientist II and project lead at Microbia Inc. from 1999 to 2001. Maxon served as deputy vice chair at the California Institute for Regenerative Medicine from 2004 to 2006. She earned a Doctor of Philosophy degree in molecular cell biology from the University of California, Berkeley and completed postdoctoral research in biochemistry and genetics at the University of California, San Francisco. This position does not require Senate confirmation and there is no compensation.

Jessica Mega, MD, MPH, 43, of Portola Valley, has been appointed to the Governor's Precision Medicine Advisory Committee. Mega has been chief medical officer at Verily Life Sciences since 2015. She led large, international, randomized trials evaluating novel cardiovascular therapies as a senior investigator with the TIMI Study Group and a cardiologist at Brigham and Women's Hospital from 2008 to 2015, and as a faculty member at Harvard Medical School, where she is currently on leave. Mega directed the TIMI Study Group's Genetics Program from 2011 to 2015, focusing on applications for precision medicine. Her research findings have been published in the New England Journal of Medicine, Lancet, JAMA and elsewhere. Mega earned a Doctor of Medicine degree from the Yale School of Medicine and a Master of Public Health degree from the Harvard School of Public Health. She completed an internal medicine residency at Brigham and Women's Hospital and a cardiovascular fellowship at Massachusetts General

Hospital. She has won the Laennec Society, Samuel A. Levine and Douglas P. Zipes awards and is a fellow of the American Heart Association and the American College of Cardiology. This position does not require Senate confirmation and there is no compensation.

Jill P. Mesirov, PhD, MA, 67, of Solana Beach, has been appointed to the Governor's Precision Medicine Advisory Committee. Mesirov has been associate vice chancellor for computational health sciences and professor of medicine at the University of California, San Diego School of Medicine since 2015. Mesirov served as associate director and chief informatics officer at the Broad Institute of MIT and Harvard - formerly the Whitehead Institute/MIT Center for Genome Research - from 1997 to 2015, where she directed the Computational Biology and Bioinformatics Program from 1997 to 2015. She was manager of computational biology and bioinformatics at IBM's Healthcare-Pharmaceutical Solutions Organization from 1995 to 1997 and director of research at Thinking Machines Corporation from 1985 to 1995. Mesirov was an instructor in the University of California, Berkeley Department of Mathematics from 1974 to 1976, a member of the research staff in the Communications Research Division of the Institute for Defense Analyses from 1976 to 1982 and associate executive director of the American Mathematical Society from 1982 to 1985. She earned Master of Arts and Doctor of Philosophy degrees in mathematics from Brandeis University. This position does not require Senate confirmation and there is no compensation.

Frederick J. Meyers, MD, 66, of Sacramento, has been appointed to the Governor's Precision Medicine Advisory Committee. Meyers has been associate dean for precision medicine at University of California, Davis Health since 2016, where he has served in several leadership positions since 1992, including chairperson of the Department of Internal Medicine and vice dean of the School of Medicine. He was one of the first in the country to develop the concept of simultaneous care, a system of patient-family centered caring that provides both treatment for advanced cancer using investigational clinical trials as well as intensive palliative care. Meyers has been an active medical oncologist at the University of California, Davis Comprehensive Cancer Center since joining the University of California, Davis faculty in 1982. Meyers earned a Doctor of Medicine degree from the University of California, San Francisco School of Medicine. He is a Master of the American College of Physicians. This position does not require Senate confirmation and there is no compensation.

Michael Milken, MBA, 71, of Los Angeles, has been appointed to the Governor’s Precision Medicine Advisory Committee. Milken co-founded the Milken Family Foundation in 1982 to formalize his previous philanthropy. He has long been at the forefront of successful initiatives in medical research, education, public health and access to capital. Fortune magazine called him "The Man Who Changed Medicine" and Forbes listed him among "Visionaries Reimagining Our Children's Future." He is chairman of the Milken Institute, which hosts more than 200 annual events including major conferences in Los Angeles, London, Singapore, Washington, D.C. and Abu Dhabi. As chairman of the Institute’s FasterCures center, he has worked to advance precision medicine for more than a decade. The Milken Institute School of Public Health at George Washington University was renamed to recognize an Institute gift. As a financier, Milken is often said to have revolutionized modern capital markets by pricing and rewarding risk more efficiently. The thousands of companies he financed created millions of jobs. He earned a Master of Business Administration degree at the University of Pennsylvania, Wharton School. He is a member of the Giving Pledge and a founding donor of the National Museum of African American History and Culture. This position does not require Senate confirmation and there is no compensation.

Arnold Milstein, MD, MPH, 71, of San Francisco, has been appointed to the Governor's Precision Medicine Advisory Committee. Milstein has been a professor of medicine and director of the Clinical Excellence Research Center at Stanford University since 2010. The Center designs and demonstrates scalable health care delivery innovations that provide better care with less health care spending. His research spans positive value outlier analysis, human experience of health care and, in partnership with Stanford's Artificial Intelligence Lab, the development of artificial intelligence systems to assess and support care for medically fragile populations in home and institutional settings. In 1984, Milstein founded a national health care performance improvement firm, National Medical Audit, which he expanded globally after its acquisition by Mercer. He also co-founded three nationally influential public benefit initiatives, the Leapfrog Group in 1998, the Pacific Business Group on Health in 1985 and the Consumer-Purchaser Alliance in 2001. As a member of the congressional Medicare Payment Advisory Commission

from 2004 to 2010, he originated two legislative changes to align health care provider revenue with value to patients. He served as chair of the National Academy of Medicine Planning Committee series on improving the efficiency of U.S. care delivery. Milstein earned a Doctor of Medicine degree from the Tufts University School of Medicine and a Master of Public Health degree from the University of California, Berkeley. This position does not require Senate confirmation and there is no compensation.

Hakan Sakul, MS, PhD, 55, of San Diego, has been appointed to the Governor's Precision Medicine Advisory Committee. Sakul has been vice president of diagnostics at Pfizer since 2016, with responsibility for development of companion diagnostics across Pfizer's pharmaceutical portfolio. He has held several positions at Pfizer since 2002, including executive director and head of diagnostics for Worldwide R&D; senior director of translational oncology in the Oncology Business Unit; senior director, global head of diagnostics and oncology leads for the Molecular Medicine Group and Clinical R&D; senior director of the Molecular Profiling Group and diagnostics lead for Clinical R&D; and director and site head of the Clinical Pharmacogenomics Group. He led Pfizer's flagship program in companion diagnostics for Xalkori(R), a non-small cell lung cancer drug that received FDA approval in 2011 along with its diagnostics test. He was director of the Human Genetics, Statistical and Pharmacogenetics Department at Parke-Davis Pharmaceuticals from 1998 to 2001. Sakul is a member of the Board of Personalized Medicine Coalition, and author of over 30 referred scientific articles. Sakul earned a Doctor of Philosophy degree in quantitative genetics from the University of Minnesota and a Master of Science degree from Ankara University. This position does not require Senate confirmation and there is no compensation.

Lisa Suennen, MA, 52, of Tiburon, has been appointed to the Governor's Precision Medicine Advisory Committee. Suennen has spent nearly 30 years as an entrepreneur, venture investor and advisor in the health care industry. She has been senior managing director at GE Ventures since 2016, leading the firm's health care venture fund. Suennen was managing partner of Venture Valkyrie, LLC from 2013 to 2016 and a partner at Psilos Group, a health care venture capital firm, from 1998 to 2013. She was senior vice president and general manager at Merit Behavioral Care, formerly American Biodyne, from 1989 to 1998. Suennen has been a faculty member at the University of California, Berkeley Haas School of Business since 2008 and a co-founder and chairman of CSweetener.org since 2016. Suennen is a member of the board of directors of Evidation Health, Health Reveal, Gravie, Dignity Health Foundation and Heart to Heart International. She is a member of the advisory boards of the California Health Care Foundation Innovation Fund, American Heart Association Innovation Think Tank, HealthXL, and the NASA Translational Research Institute. Suennen is a fellow of the inaugural class of the Aspen Institute's Health Innovators Fellowship. She earned a Master of Arts degree in political science from the University of California, Berkeley. This position does not require Senate confirmation and there is no compensation.

Appendix I: CIAPM outreach in 2017

CIAPM representation at scientific meetings

In order to raise awareness about the State's involvement in precision medicine in stakeholder communities, CIAPM has been represented at several meetings in 2017:

- Precision Medicine World Conference, Mountain View, January 23-25, 2017: CIAPM-hosted panel "CIAPM: Accelerating Precision Medicine Advances in California", moderated by Uta Grieshammer, scientific program director for CIAPM, panelists were team members from three demonstration projects, i.e, Olena Morozova (UCSC), Nicholas Anderson (UC Davis) and Brennan Spiegel (Cedars-Sinai), and also Rowan Chapman, Head of Johnson & Johnson Innovation, California
- Healthcare Information and Management Systems Society (HIMSS), February 21, 2017: Elizabeth Baca, Senior Health Advisor, Governor's Office of Planning and Research, "Meeting the Challenges of Precision Medicine: Enhancing Innovation and Mitigating Risk"
- San Jose Health IT Summit, April 14, 2017: Elizabeth Baca, Senior Health Advisor, Governor's Office of Planning and Research, "California Initiative to Advance Precision Medicine"
- Precision Medicine World Conference, Duke University, May 24 & 25, 2017: India Hook-Barnard, Executive Director for CIAPM, invited presentation, CIAPM's vision and efforts
- California Israel Medical Technology Summit, Oracle, Redwood City, June 7, 2017: India Hook-Barnard, Executive Director for CIAPM, panelist in precision medicine discussion
- Personalized Medicine Summit, Vancouver, Canada, June 12, 2017: Elizabeth Baca, Senior Health Advisor, Governor's Office of Planning and Research, "Advancing Precision Medicine in California Next Steps and Lessons Learned"
- BIO International Convention, San Diego, June 19-22, 2017: India Hook-Barnard, Executive Director for CIAPM, panelist in Personalized Medicine Coalition-hosted discussion
- BIO International Convention, San Diego, June 19-22, 2017: CIAPM-hosted session at the California Pavilion, moderated by India Hook-Barnard, Executive Director for CIAPM, panelists were team members from two demonstration projects, i.e., Sheldon Greenfield (UCI) and Dario Boffelli (CHORI)
- Connected Health Conference, Healthcare Information and Management Systems Society (HIMSS), Boston, October 25 - 27, 2017: India Hook-Barnard, Executive Director for CIAPM delivered a presentation
- Precision Medicine Leaders Summit, San Diego, August 21-24, 2017: CIAPM-hosted panel "High Resolution in the Clinic – Building a Scalable, Diverse and Contextualized Precision Medicine Design Framework", moderated by Elizabeth Baca, Senior Health Advisor, Governor's Office of Planning and Research, panelists were demonstration project lead Walter Stewart (Sutter Health) and three additional members of that team
- World Alliance Forum San Francisco, November 29 & 30, 2017: Elizabeth Baca, Senior Health Advisor, Governor's Office of Planning and Research, panelist in discussion "Government's Role in Innovation"

- World Alliance Forum San Francisco, November 29 & 30, 2017: Uta Grieshammer, scientific program director for CIAPM, moderated discussion on “Precision Medicine - the Power of Data”, panelists included demonstration project lead Walter Stewart (Sutter Health)
- Health 2.0, San Francisco, December 12, 2017: Elizabeth Baca, Senior Health Advisor, Governor's Office of Planning and Research, “Business models and investing in precision health”
- Elizabeth Baca, Senior Health Advisor, Governor's Office of Planning and Research, participated in two panel discussions on health and innovation for the World Economic Forum to inform the Davos Agenda in 2018.

Book

Case study on CIAPM Demonstration projects highlighted in Demystifying Big Data and Machine Learning for Healthcare (HIMMS Book) 1st Edition by Prashant Natarajan, John C. Frenzel, and Detlev H. Smaltz . The HIMSS #1 Best seller for 2017.

Contributing authors include:
Elizabeth Baca, MD, Senior Health Advisor, Governorʾs Office of Planning and Research, California; Lark Park, Senior Advisor, Governorʾs Office, California; Terri OʾBrien, PhD, Associate Chancellor, UCSF; Uta Grieshammer, PhD, Program Director, CIAPM; India Hook-Barnard, PhD, Director of Research Strategy, UCSF, all CIAPM team and demonstration partners

Journal

The Journal of Precision Medicine, August edition: ‘‘California Paves the Way for State Efforts in Precision Medicine’’

CIAPM discussions

Many companies and international initiatives are developing in the emerging precision medicine space and CIAPM is actively engaged in these discussions. In 2017, Discussions and interest with aligning programs included:

- Federal Department of Health and Human Services (HHS) and the Food and Drug Administration (FDA) with the Anderson CIAPM demonstration project team (UC Davis) and the Martin CIAPM demonstration project team (CHORI)
- Thermo Fisher Scientific, Precision Medicine group
- AllSeq (San Diego), Illumina (San Diego), Biocom (San Diego)
- Omnity, a company that uses associative semantic search technology to identify related documents
- Paladin Healthcare Alliance, USA
- Geoffrey Ginsburg, Duke University
- Ambry Genetics
- Indiana University precision medicine initiative
- California Radiotherapy Quality and Outcomes Initiative, Siris-Medical & UCSF radiology
- UC BRAID
- Chan Zuckerberg Initiative, Science
- Sutter demonstration project & Roche/Genentech Precision Medicine Collaboration Meeting
- University of California Office of the President, Strategy and Planning
- Horizon Government Affairs, Washington, DC
- UCSD Design Lab

Appendix J: CIAPM – funded scientific publications

Precision Diagnosis of Acute Infectious Diseases (PDAID)
Principal Investigator: Charles Chiu, UCSF

- Chiu CY, Coffey LL, Murkey J, Symmes K, Sample HA, Wilson MR, Naccache SN, et al. Diagnosis of Fatal Human Case of St. Louis Encephalitis Virus Infection by Metagenomic Sequencing, California, 2016. Emerg Infect Dis. 2017 (10), 1694-1698. PMID:28930022

- Murkey JA, Chew KW, Carlson M, Shannon CL, Sihori D, Sample HA, et al., Hepatitis E Virus-Associated Meningoencephalitis in a Lung Transplant Recipient Diagnosed by Clinical Metagenomic Sequencing. Open Forum Infect Dis. 2017, 4(3):ofx121. PMID: 28721353

- Mongkolrattanothai K, Naccache SN, Bender JM, Samayoa E, Pham E, Yu G, et al. Neurobrucellosis: Unexpected Answer from Metagenomic Next-Generation Sequencing. J Pediatric Infect Dis Soc. 2017, 6(4), 393-398. PubMed PMID: 28062553

California Kids Cancer Comparison (CKCC)
Principal Investigator: David Haussler, UC Santa Cruz

- Newton Y, Novak AM, Swatloski T, McColl DC, Chopra S, Graim K, et al. TumorMap: Exploring the Molecular Similarities of Cancer Samples in an Interactive Portal. Cancer Res. 2017 77(21):e111-e114. PMID: 29092953