

California Initiative  
to Advance  
Precision Medicine

# 2019 ANNUAL REPORT



GOVERNOR'S OFFICE *of* PLANNING AND RESEARCH

California Initiative to Advance Precision Medicine  
2019 Annual Report to the California Legislature

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# CONTENTS

Executive Summary	i
Background	1
Project Highlights	3
Program Highlights	12
Next Steps	16
Conclusion	17
Appendices	18
A. 2019 Publications, Presentations, and Press about CIAPM-funded Projects	18
B. Outreach Efforts: CIAPM Representation at External Events	21
C. Key Personnel in 2019	22
D. Meeting Overviews	22
E. 2019 Request for Proposals	24
F. Community-Researcher Partnership Guidance	33

# EXECUTIVE SUMMARY

California is a world leader in the fields of medicine, biotechnology, and computational systems. The burgeoning field of precision medicine combines cutting-edge medical research with large data sets in order to individualize care. The California Initiative to Advance Precision Medicine (CIAPM) was established to capitalize on California's technical strengths for the benefit of all Californians, particularly populations that are disadvantaged by health disparities.

2019 was a year of transformation for CIAPM. The administration of the program transitioned fully to the Governor's Office of Planning and Research (OPR), which prompted the hiring of new staff and establishment of a framework for a permanent Precision Medicine Advisory Council. Over the course of the year, the Initiative's accomplishments included the following:

- Participation in the first-ever Assembly Select Committee on Biotechnology Informational Hearing on Precision Medicine
- Commencement of three-year demonstration projects by three newly funded cancer research teams, amounting to a \$9.5 million investment
- Facilitation of a formal evaluation by out-of-state experts and publication of the 2019 Evaluation Report on the eight completed CIAPM demonstration projects
- Launch of a request for proposals (RFP) to address Adverse Childhood Experiences (ACEs), in coordination with the Office of the Surgeon General
- Migration of the RFP process to a cloud-based submission and administration portal
- Facilitation of a convening of current and formerly funded CIAPM research teams
- A revamp and online launch of the California Precision Medicine Asset Inventory
- Outreach activities to fellow state agencies, departments, and programs, as well as external partners within and outside the state
- Representation of CIAPM at numerous conferences and meetings

Plans for 2020 include the following:

- Awarding of \$9 million to support demonstration projects in the field of ACEs
- Inaugural meeting of the new Precision Medicine Advisory Council
- Determination of the next priority research area and launch of an RFP to address it
- Continuous updates to and modernization of the California Precision Medicine Asset Inventory
- Fostering networking opportunities for current and formerly funded research teams and precision medicine leaders
- Extensive outreach to new and current partners from industry, nonprofit

- research institutions, and community groups
- Continued integration of legislative and executive priorities into CIAPM activities

# BACKGROUND

## WHAT IS PRECISION MEDICINE?

Over ten years ago, the U.S. President's Council of Advisors on Science and Technology defined precision medicine as: "The tailoring of medical treatment to the individual characteristics of each patient...to classify individuals into subpopulations that differ in their susceptibility to a particular disease or their response to a specific treatment."

20<sup>th</sup> century health care delivery was a one-size-fits-all system where treatment plans and clinical trials were almost universally designed for the "average patient." With the support of rapidly developing biotechnology and high-performance computing, the future will see advancements in prevention, diagnosis, measurement, and treatment of disease based on health-related data that is individualized and precise.

Until recently, health care providers have had few tools and limited capacity to understand what makes each patient unique, but emerging medical research and data science have unleashed an array of powerful instruments that make such characterization possible, including genetic sequencing, artificially intelligent medical imaging analysis, molecular biomarker profiling, and mobile health devices. Modern devices and algorithms are granting clinicians and researchers never-before-imagined windows into the mechanisms of health and illness and are generating information that can impact essential medical decisions, optimize treatment strategy, and inform more accurate prognoses.

The improvement of health across whole communities, however, also depends on cross-sector partnerships that aim to reduce health disparities and prioritize equity among research and clinical outcomes. Toward that goal, the field of precision medicine encourages a culture change whereby patients are engaged as active partners in health care and medical research.

## BRIEF HISTORY OF CIAPM AND ALLOCATION OF FUNDS

In the Governor's 2014 State of the State address, he postulated that California could "pioneer the new field of precision medicine, which uses genomics, medical devices, computer sciences, and other fields to treat individual patients, instead of broad populations." That same year, the FY 2014-2015 budget included \$3M for the Office of Planning and Research (OPR) to use for precision medicine. In the following months, the Governor's Office worked with OPR, UC Health, and UC San Francisco (UCSF) to fund two UC-based collaborative research teams to demonstrate the promise of precision medicine.

In 2016, the California Initiative to Advance Precision Medicine (CIAPM) was officially established in statute by Assembly Bill 1602. The enacting legislation states, among other mandates, that CIAPM is to:

- Develop, implement, award funding to, and evaluate demonstration

projects on precision medicine

- Use a peer-review process to select the proposals that are funded
- Collaborate with public, nonprofit, and private entities
- Develop an inventory of precision medicine assets, including projects, data sets, and experts

That same year, an additional \$10M was allocated to precision medicine in the FY 2016-2017 budget. With those funds, six additional precision medicine demonstration projects were launched, and all finished by the end of December 2018. A \$10M budget allocation for FY 2017-2018 funded three more research teams that are currently working to address cancer health disparities in California with a precision medicine approach. Those projects will conclude in fall 2022. Summaries of the first eight projects and three current projects can be found in the Project Highlights section of this report. Additionally, a detailed description and formal analysis of the first eight projects can be found in the Evaluation Report, which is discussed in the Program Highlights section.

In the budget for FY 2018-2019, the Legislature allocated \$30M to OPR for CIAPM. Senate Bill 82, statutes of 2019, extended the encumbrance date of the funds through December 31, 2025.

# PROJECT HIGHLIGHTS

## CURRENT DEMONSTRATION PROJECTS

### **Addressing Disparities in Breast Cancer in Latinas: A multi-tiered approach (2019-2022)**

**Lead Principal Investigator** Dr. Elad Ziv, UC San Francisco

**Partners** Bay Area Cancer Connections, City of Hope, Latino Cancer Institute, Pomona Health, Stanford University, UC Davis, Vision y Compromiso, Zuckerberg SF General

Breast cancer is the leading cause of cancer death among Latinas in California, but mortality may be decreased by improved screening and earlier detection. Understanding hereditary cancer risk can help improve screening and detection by identifying women at particularly high risk who should start screening at an earlier age, more often, and with better technologies (e.g., MRI). This project aims to better understand which genetic variants cause Latinas to develop breast cancer, and to increase community awareness of hereditary cancer and genetic testing.

### **Integrated Machine-Learning Platform to Inform Precision Therapy in Underrepresented Triple-Negative Breast Cancer Patients (2019- 2022)**

**Lead Principal Investigators** Dr. William Kim and Dr. Pablo Tamayo, UC San Diego

**Partners** American Cancer Society, Cancer Resource Center of the Desert, El Centro Regional Medical Center, Michigan State University, Moores Cancer Center, Quality Partners, Rady Children's Hospital, San Diego State University, Sanford Burnham Prebys Medical Discovery Institute, Tri-City Medical Center, University of Guadalajara

Despite recent progress in the development of new cancer drugs, Triple-Negative Breast Cancers (TNBCs) remain largely untreatable. TNBC is more prevalent among Hispanic women, resulting in a major health disparity in cancer diagnosis and treatment. This project has brought together a community of researchers, clinicians, patients, and community advocates who have begun to apply genomic profiling to identify novel treatments and implement a more precise system to match TNBC tumors with cancer therapies.

### **Reducing Cancer Disparities Through Innovative Community-Academic Partnership to Advance Access and Delivery of Precision Medicine in Santa Clara County (2019-2022)**

**Lead Principal Investigator** Dr. Manali Patel, Stanford University

**Partners** Cancer Patients Alliance, Clinica de Salud del Valle de Salinas, Community Hospital of Monterrey Peninsula, Latino Cancer Institute, Natividad Medical Center, Pacific Cancer Care

Low-income and minority populations experience a disproportionately greater burden of cancer incidence and mortality, lower rates of evidence-based cancer

care, and increased rates of untreated symptoms compared with non-minority patients. Precision medicine has the potential to worsen these existing cancer care disparities if minority and low-income populations cannot access such innovative approaches. The objective of this project is to develop, implement, and evaluate a Community Health Worker (CHW) intervention that increases access to precision medicine approaches across the cancer care continuum, from prevention and screening to diagnosis, treatment, survivorship, and end-of-life care. The hypothesis is that this approach is feasible and acceptable in the community (in part due to the language and cultural appropriateness of the CHWs) and can improve patients' quality of life and reduce disparities in receipt of precision medicine cancer care services.

## EVALUATION REPORT OF COMPLETED DEMONSTRATION PROJECTS

CIAPM funded eight collaborative demonstration projects between 2015 and 2018 that targeted specific disease areas, in addition to improving general tools that could be applied to a wide range of disorders and integrated into preventative, diagnostic, and/or therapeutic strategies. To evaluate the quality and significance of the projects' scientific achievements and clinical contributions, formal assessments were conducted by expert scientists and clinicians recruited from outside the state. Evaluators were granted access to the research teams' materials and original proposals to determine how well the projects both fulfilled their anticipated milestones and furthered the respective scientific fields, in line with the state's ambitious goals.

The Evaluation Report was published in July 2019 and is available on the CIAPM website. In addition to project-by-project analyses of results, the report includes contextual background of the projects' targeted scientific fields and diseases, detailed methods of the evaluation process, and biographical profiles of the contributing expert evaluators. The report highlights the high quality and impactful research that was conducted using CIAPM funds, citing great progress across several fields with significant achievements toward the state's goals for health and precision medicine in California.

The diseases addressed by CIAPM-funded projects through 2018 included pediatric cancer, infectious diseases, brain damage, heart disease, rare childhood genetic disorders, high blood pressure, depression, prostate cancer, and multiple sclerosis. The technologies that were developed and/or refined included artificial intelligence for medical imaging analysis; remote biosensors; automated genomic analysis; networked databases to foster data sharing, computation, and collaboration; a clinical portal to engage patients; mobile health apps; and others.

In terms of matching funds to support the work of CIAPM projects, research teams attracted over \$12 million in monetary support and were sustained by in-kind institutional support valued over \$6.4 million. Thirty-four publications detailing study results have been included in scientific journals or are currently in preparation. Eighteen articles and press releases have highlighted the projects, including a Time magazine cover story, and at least 80 presentations have been delivered to public and professional audiences. According to

the expert evaluators, the work of the eight completed projects has already helped shape the field of precision medicine and the future of biomedical research and clinical practice.

Each completed project is summarized below, including a brief list of each research team's most prominent achievements.

### **California Kids Cancer Comparison (2015-2018)**

**Lead Principal Investigator** Dr. David Haussler, UC Santa Cruz

**Partners** Stanford University Hospital, Children's Hospital Orange County, Pacific Pediatric Neuro-Oncology Consortium, UC San Francisco, 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, DNAnexus, Microsoft, NuMedii, Seven Bridges Genomics, Philanthropist George Kraw, University of British Columbia Cancer Agency, Children's Mercy Hospital (Kansas City), Sanford University of South Dakota Medical Center, University of Michigan, University of Pittsburgh

Despite research advances in cancers affecting adults, pediatric cancer treatments have changed very little over the past 50 years, and cancer remains the most common cause of death from disease in children. In California alone, 500 of the 1,700 children diagnosed with cancer every year either do not respond to treatments or lack standard therapies to treat their condition.

Since DNA testing and analysis only provides useful information for less than 10% of pediatric cancer patients, the California Kids Cancer Comparison (CKCC) project sought to analyze a more comprehensive genetic profile of each tumor by sequencing RNA, which indicates which genes are active. Unlike DNA, RNA provides insight into how the tumor is functioning, and which genes and pathways might contribute to the cancer growth. CKCC sought to improve pediatric cancer care by using RNA to profile patient tumors and find new targets for therapeutic intervention and treatment.

CKCC's RNA-based approach gave the researchers new information in 100% of the pediatric cancer cases, far exceeding their goal of new information for 20% of pediatric cases. The team also established a registry of the tumor RNA profiles for physicians to use when diagnosing and treating pediatric cancer patients. Overall, CKCC's RNA approach was able to discover new treatment options when DNA-based diagnoses did not provide useful treatment information and can be scaled to more pediatric and adult cancers for a broader impact.

#### *Notable Accomplishments*

- Established a consortium of hospitals and research institutions
- Suggested new treatment options based on data analyses
- Reported findings to molecular tumor boards
- Optimized computational approaches and created a tumor data catalog
- Engaged patients in the research process and clinical decision-making
- Created an early-phase patient registry study to validate usefulness of data

## **Precision Diagnosis of Acute Infectious Diseases (2015-2018)**

**Lead Principal Investigator** Dr. Charles Chiu, UC San Francisco

**Partners** UC Los Angeles, UC Davis, UC Berkeley, UC San Diego, California Department of Public Health, Synapse, DNAnexus, Quest Diagnostics, Illumina, Google, Abbott Laboratories, American Tissue Culture Collection, Children's Hospital Los Angeles, Children's Hospital Colorado/University of Colorado, Children's National Medical Center at Washington D.C., Oxford Nanopore Technologies, St. Jude Children's Research Hospital (Vanderbilt, TN), University of Maryland, U.S. Food and Drug Administration, Zuckerberg San Francisco General Hospital and Trauma Center

Rare bacterial infections are costly and difficult to diagnose. Often, patients with suspected infections receive general therapies like antibiotics, instead of a specific diagnosis and treatment for their particular infection. This non-specific approach leads to increased healthcare costs as well as risks of antibacterial resistance and death.

To improve precise diagnosis and treatment of brain infections in patients, the Precision Diagnosis of Acute Infectious Disease (PDAID) team at UCSF developed a genomic test, called metagenomic sequencing, to find microbial DNA in patients' samples, such as their spinal fluid or blood. Genetic profiling of these patient samples enabled the team to identify the DNA of bacteria and microbes in the patient and confirm if bacteria were the cause of infection.

The research team used their metagenomic test on patients with brain infections and identified 14 previously undiagnosed infections among the patients enrolled. The team also demonstrated the cost-saving measures provided by this precision medicine approach through the use of their test on a 14-year-old boy who was unable to receive a diagnosis for months after numerous tests were inconclusive. The new test quickly identified the cause of his infection, and if used earlier, could have significantly reduced suffering and medical costs by avoiding the need for multiple hospitalizations and uninformative diagnostic tests. Overall, the research represents an excellent precision medicine approach with a potential to scale to other diseases.

### *Notable Accomplishments*

- Developed clinical grade software
- Confirmed the experimental metagenomics test in a clinical laboratory for diagnosing the causes of brain inflammation
- Confirmed the test in a clinical laboratory for diagnosing infections through blood plasma
- Initiated clinical studies of critically ill hospitalized patients to compare conventional and metagenomic-based approaches
- Established and regularly convened a clinical microbial sequencing board, a multidisciplinary group that meets to discuss complex patient cases
- Pursued additional efforts to make the test widely and affordably available

## **Artificial Intelligence for Imaging of Brain Emergencies (2017-2018)**

**Lead Principal Investigator** Dr. Pratik Mukherjee, UC San Francisco

**Partners** UC Berkeley, Brain Trauma Foundation, Community Regional Medical Center in Fresno, Stanford University, TBI Endpoints Development Project, Transforming Research and Clinical Knowledge in Traumatic Brain Injury Consortium, Zuckerberg San Francisco General Hospital and Trauma Center

Irreversible brain damage can occur within minutes of brain injury. Diagnosis depends upon skilled radiologists to evaluate brain scans, limiting the ability of doctors to quickly help patients with treatment during this small immediate window of time.

The research team at UCSF and UC Berkeley developed a state-of-the-art technology capable of automating Computed Tomography (CT) brain scan analysis, to test the use of image recognition software and Artificial Intelligence (AI) to detect brain injury. After training on over 100,000 CT scans, the technology successfully identified brain injury in over 99% of CT scans, with accuracy equal to that of board-certified radiologists.

The team developed a cloud-based platform that, once FDA-approved, can be used in areas without sufficient radiologists on hand, such as rural or remote locations.

### *Notable Accomplishments*

- Demonstrated the promise of AI automated image analysis of neurologic injuries for application in routine clinical use, research studies, and drug trials
- Developed a computer vision AI tool to identify and quantify biomarkers of brain injury
- Analyzed thousands of patient images with an accuracy of diagnosis greater than 99%
- Optimized the AI tool for cloud-based, multi-scanner use, working towards FDA-approval for mass-system integration
- Aggregated data from multiple medical centers with various electronic health records

## **Precision Medicine for Multiple Sclerosis: Making It Work (2017-2018)**

**Lead Principal Investigator** Dr. JB Jones, Sutter Health

**Partners** UC San Francisco, Roche/Genentech, Sutter's Jordan Research and Education Institute, Palo Alto Medical Foundation, Plain Language Health, National Multiple Sclerosis Society, Sutter Philanthropy

Multiple sclerosis (MS) is a chronic neurological disease that affects the brain and spinal cord when the body's immune system mistakenly attacks healthy cells, causing neurodegeneration. Although symptoms onset between 20 and 40 years of age, disease progression varies greatly between patients and is difficult to predict or treat.

To address this lack of knowledge about MS progression, the research team at Sutter Health and UCSF developed an interactive tool, called neuroSHARE.

The neuroSHARE application was designed to support access to clinical and patient-reported data, predict disease management to slow progression and address symptoms, as well as enable shared decision making between the patient and physician. The design of neuroSHARE simplifies and uses the latest research on MS as a resource for patients, in addition to interpreting data from patients to ensure their individual concerns were addressed at their next medical appointment.

As a result of this study, neuroSHARE was successfully used in multiple real-world neurology practice settings. The concept of this application, which provided a precision medicine connection from the patient's bedside to the doctor's office, could be easily applied to a variety of other conditions. Tools like neuroSHARE demonstrate the power of bringing patient data into the conversation between clinician and patient, and integration with electronic health records.

#### *Notable Accomplishments*

- Developed a tool for efficient and effective patient data management
- Made progress toward reducing health disparities
- Utilized partnerships to encourage clinical and commercial use, with great potential to scale toward other diseases/conditions

### **Early Prediction of Major Adverse Cardiovascular Event Surrogates (2017-2018)**

**Lead Principal Investigator** Dr. Brennan Spiegel, Cedars-Sinai Medical Center

**Partners** UC Los Angeles, Agilent, AliveCor, Beckman Coulter, DocuSign, Fitbase, Fitbit, HealthLoop, Neoteryx, SCIEX, Tasso, Thermo Fisher Scientific

Cardiovascular disease is the leading cause of death in men and women in California, occurring more often in younger women and racial/ethnic minorities. Early signs of disease are easily overlooked, and lack of consistent healthcare can result in detrimental disease progression.

The research team at Cedars-Sinai Medical Center sought to understand whether cardiovascular threats can be detected early enough for effective treatment or prevention by measuring physical, biochemical, and psychosocial indicators to predict Major Adverse Cardiac Events (MACEs). They remotely monitored 200 patients diagnosed with ischemic heart disease by using wearable biosensors for twelve months. Their activity, sleep, heart rate, stress levels, self-reported mental health, and finger-prick blood samples were recorded and used to determine if monitoring these factors helped to predict MACEs.

The team's remote monitoring system demonstrated the capacity of this method to monitor patients outside the doctor's office, and potentially help predict and prevent MACEs. For example, when one of the participants, a 64-year-old man, noted chest pain and a cardiac abnormality detected by his remote wearable biosensor, the program prompted him to visit the emergency room to prevent a more serious cardiac event. The team has already published the success of the findings and will continue to publish additional results after

further analysis of the more than 500 potential biomarkers from the patients' blood samples.

#### *Notable Accomplishments*

- Demonstrated that remote blood collection at a patient's home results in quality samples for clinical analysis that are as good if not better than samples collected in-clinic
- 72% of patients adhered to the entire study, demonstrating feasibility and consistency of patient participation in this study model
- Linked lower physical activity and sleep with a higher risk of developing anxiety and depression in participants
- Discovered an association linking physical activity and overall health with increased cardiac health and lower risk of MACE

### **Early Prostate Cancer: Predicting Treatment Response (2017-2018)**

**Lead Principal Investigator** Dr. Sheldon Greenfield, UC Irvine

**Partners** Cedars-Sinai Medical Center, UC Los Angeles Medical Center, Veterans Affairs Los Angeles, Vanderbilt University, GenomeDx Biosciences, Ambry Genetics Corporation

Prostate cancer, the most common cancer in men in the United States, is diagnosed and treated based on a few tests which are not effective in predicting the tumor's response to treatment. Different levels of access to care, chronic stress, socioeconomic status, and environmental factors have all been implicated as important indicators of differences in prostate cancer outcomes. Despite this knowledge, such characteristics have not been considered when profiling prostate cancer and personalizing patient treatment.

The research team at UC Irvine addressed this care gap with an individualized risk profile to personalize care and reduce disparities in prostate cancer outcomes. The Comparative Effectiveness Analysis of Surgery and Radiation (CEASAR) Study sought to understand whether prostate cancer severity and patients' personal conditions help predict health outcomes after therapeutic radiation or surgery.

The models developed in this study to predict patient outcomes will increasingly inform treatment effectiveness and cancer recurrence in patients. As these models are finalized, the research team will share their findings with physicians in Southern California, beginning with urologists and radiation oncologists at the five partner institutions, where they plan to implement this model to improve patient care.

#### *Notable Accomplishments*

- Organized a network of collaborative clinicians, scientists, and industry partners to accomplish this study
- Created a Citizen Science Committee to review information and provide patient perspectives
- Designed a federated registry, enabling searches of the data collected to inform patient outcomes while strengthening health data privacy
- Correlated genetic risk with patient demographics and treatment, finding

African American and Latino men were generally at higher genetic risk of prostate cancer

### **Full Genome Analysis to Guide Precision Medicine (2017-2018)**

**Lead Principal Investigator** Dr. David Martin, Children's Hospital Oakland Research Institute

**Partners** UC San Francisco, UCSF Benioff Children's Hospital Oakland, UC Berkeley, Human Longevity, GenomeOne, Illumina

While much progress has been achieved in genetic testing over the last decade, most tests used in doctor's offices and hospitals focus on a narrow list of common genetic disorders rather than completely analyzing the patient's full genetic information, called the genome. Additionally, communities of color are largely underrepresented in these genetic tests, leaving many patients in this demographic underdiagnosed.

The research team at Children's Hospital Oakland Research Institute developed a method called Full Genome Analysis (FGA) to read the entire genome of children with potential genetic disorders. They tested 45 pediatric cases, from predominantly underserved backgrounds and identified the likely genetic cause of disorder for 40% of the cases.

This research demonstrated that FGA can give clinicians the ability to assess disease risk and potential therapies early for their pediatric patients. It also contributed to identifying genetic diseases which may otherwise have been overlooked in communities of color, improving the list of genetic diseases for clinicians to consider when diagnosing patients.

#### *Notable Accomplishments*

- Identified the likely genetic cause of disorder in 40% of pediatric patients in the study
- Confirms the use of Full Genome Analysis in clinical care of pediatric patients as a potential new standard of care for undiagnosed diseases
- Contributed genomic data from underrepresented communities to the catalog of disease information for clinicians to consider

### **Personal Mobile and Contextual Precision Health (2017-2018)**

**Lead Principal Investigator** Dr. Nicholas Anderson, UC Davis

**Partners** UC San Francisco, UC Berkeley, Overlap Health

Chronic diseases, such as hypertension and depression, can be difficult to monitor when patients leave the office and are not in constant contact with their health care providers. However, patients are constantly accumulating personal data on their mobile phones which could help them and their clinicians track their disease progression. While these data could be extremely useful for health records and patient care, most of these mobile phone applications do not enable clinicians to view or integrate data into electronic health records (EHRs).

The research team at UC Davis developed a HIPAA-compliant<sup>1</sup> mobile health application, designed to send alerts and collect, monitor, and report patient-generated data. This application integrated data from the patient's EHR, making it possible for both the clinical care team and the patient to interact with and view their health data in real time.

This project designed, implemented, and evaluated a multi-disciplinary system capable of linking two major hospital record systems with a private mobile health industry partner. The research team demonstrated the ability to link EHR data with applications that monitor daily lifestyle-generated data, providing a model for integrated precision medicine care both inside and outside of the clinic.

#### *Notable Accomplishments*

- Demonstrated the use of an integrated mobile phone application with EHRs for monitoring chronic disease
- Established a policy and privacy framework for linking data providers with clinical and personal data
- Evaluated patients' use of and engagement with the application

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1 Health Insurance Portability and Accountability Act, <https://www.hhs.gov/hipaa/for-professionals/privacy/laws-regulations/index.html>

# PROGRAM HIGHLIGHTS

## NEXT TARGET: ADVERSE CHILDHOOD EXPERIENCES

CIAPM issued a Request for Proposals (RFP) on December 3, 2019 to award \$9 million total for research demonstration projects that address the health impacts of Adverse Childhood Experiences (ACEs) through collaborative precision medicine approaches.

The RFP topic addresses a core priority of California Surgeon General Dr. Nadine Burke Harris by supporting research that uses a precision medicine approach to improve prevention, diagnosis, measurement, and treatment of ACEs. Children who experience high levels of stress and/or trauma demonstrate lifelong vulnerabilities to numerous physical and mental disorders, thus far linked to the effects of a disrupted physiological stress response on the neuro-endocrine-immune system and/or gene regulation.

Awards will be granted to three to five proof-of-principle demonstration projects, with the aim to address ACEs through collaborations between academic, community, public, nonprofit, and private partners. Additional funds may become available to awarded projects to examine and potentially select and use a common data-sharing platform.

At present, few studies have been conducted to unravel the complex roles ACEs play in human physiology and health throughout life. Outcomes of successful proposals may include, for example, new biomarkers predictive of individual risk for future negative health outcomes, understanding individual variation in response to therapeutic approaches, and impacts of ACEs on diverse communities reflective of California's population.

Projects must be located in California and co-hosted by at least one academic research institution and at least one nonprofit community or county institution that provides support for individuals with ACEs. Research teams are encouraged to engage additional nonprofit or for-profit organizations in the community as well as industry partners. Demonstration projects will be selected through a three-stage process, involving (1) submission of letters of intent to submit concept proposals; (2) submission of concept proposals; and (3) submission of full proposals, based on selected concept proposals, from which the final selection of awards will be made. After the selection committee makes its recommendations for awards, OPR will work with awardees to develop concrete metrics and goals to track the progress of the demonstration projects, examine and potentially select a common data-sharing platform, and enter into contracts with OPR.

### *ACEs RFP Communications & Outreach Resources*

- Dedicated website to the RFP
- Online Asset Inventory (interactive map of stakeholders)
- Live Informational Webinar, available as a recording on the OPR website
- Email Listserv announcements

- FAQ document updated weekly
- Plans to showcase the RFP during early 2020 precision medicine conferences
- Staff availability for questions from candidates and stakeholders

## RFP TECHNOLOGY UPGRADE

In time for the ACEs RFP, CIAPM invested in improving its grant application process by transitioning to a cloud-based submission portal. For the first time, CIAPM applicants and reviewers are able to manage their applications or review assignments through an online system. This will increase efficiency and provide a professional platform where all documents are transparently compiled and freely accessible by both applicants and administrators. Previously, all application materials were managed through email.

## ADMINISTRATIVE TRANSITION

CIAPM was launched in 2015 with a one-time allocation from the state general fund. OPR has had statutory authority over the program since its inception. In the first years of the program, OPR outsourced day-to-day management of the program to UCSF, due to a lack of internal capacity and limited one-time funding allocations. When CIAPM received new funding in subsequent budget years, the agreement with UCSF was amended to extend the expiration date to December 31, 2018, then again to January 31, 2019. On February 1, 2019, the program's management reverted fully to OPR. The increased budget and extended sunset date allow for long-range planning for the Initiative that had previously not been possible, and aids in the alignment of the program with the goals of newly elected Governor Newsom and his administration.

## ADVISORY COUNCIL

OPR is building on the solid foundation that UCSF put in place by continuing to ensure that the Initiative is transparent and guided by a variety of stakeholders from across the precision medicine landscape. The Office has initiated the creation of a Precision Medicine Advisory Council, which will help ensure that the Initiative continues to benefit from broad and diverse expertise, and that grant funds are leveraged strategically to maximize the benefit to California.

The State has had precision medicine advisory committees in the past. Those include the academic advisory committee that directed the operations of the Initiative while housed at UCSF, and Governor Brown's Precision Medicine Advisory Committee that was tasked with producing the report *Precision Medicine: An Action Plan for California*<sup>2</sup>. The framework for a public-facing Precision Medicine Advisory Council has been established, and members will be announced in early 2020. A public Call for Nominations was conducted through October 4, 2019 via website post and email listserv announcement that generated nearly one hundred nominations. Specifically, the Council will

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2 [http://opr.ca.gov/docs/20190107-Precision\\_Medicine\\_An\\_Action\\_Plan\\_for\\_California.pdf](http://opr.ca.gov/docs/20190107-Precision_Medicine_An_Action_Plan_for_California.pdf)

be comprised of the following:

- Seven members invited by OPR, in consultation with the Governor's Office
- One member recommended by the Speaker of the Assembly
- One member recommended by the Senate President Pro Tempore
- The Secretary of the California Health and Human Services Agency, ex officio
- The Surgeon General of California, ex officio

It is expected that members will have expertise in precision medicine, and represent multiple sectors and geographic regions of the state. A more permanent Council with this broad representation will be able to foresee trends in precision medicine and recognize emerging needs of the state while encouraging partnerships with the private sector and planning for the Initiative's future. Additionally, inclusion of the Surgeon General and the Secretary of the Health and Human Services will help to align State efforts in addressing priority health challenges.

The major responsibilities of the Council members may include but are not limited to the following:

1. Identifying and recommending research fields, total grant funding levels, timelines, and selection committee members for the RFP process, and expert project evaluators
2. Developing strategies to support sustainability of the Initiative, responding to changes in societal needs and opportunities, and stimulating adequate community engagement with CIAPM activities
3. Reviewing and providing feedback on documents including, but not limited to, annual legislative reports and project evaluation reports

OPR proposes that the Council should meet at least four times annually in person.

## ALL TEAMS MEETING

On May 1, 2019, OPR gathered Principal Investigators and other representatives from seven of the eight completed projects and all three 2019 projects for a half-day meeting in the Governor's Council Room in the State Capitol to discuss strategy and best practices around data infrastructure, community engagement, dissemination of research results, and many other topics. In total, 30 individuals participated from 14 institutions across the state. In addition to OPR staff, two members of Governor Newsom's administration joined: Surgeon General Dr. Nadine Burke Harris and Deputy Cabinet Secretary Richard Figueroa. Members of the 2017-2018 Governor's Precision Medicine Advisory Committee and other advisors also contributed to moderating discussion sessions. An abbreviated meeting agenda may be found in Appendix D.

## ASSEMBLY SELECT COMMITTEE ON BIOTECHNOLOGY INFORMATIONAL HEARING ON PRECISION MEDICINE

On August 27, 2019, the Assembly Select Committee on Biotechnology hosted the first Informational Hearing on Precision Medicine in California, chaired by Assemblymember Kevin Mullin (D-22). It granted an opportunity for CIAPM staff and awardees to demonstrate to the legislature both the importance and the caliber of the research that has been made possible because of California's investment. Testimony was provided by Dr. Shannon Muir, CIAPM Science Officer, Dr. Clara Lajonchere, Deputy Director for the Institute for Precision Health at UCLA, Dr. Brennen Spiegel, former CIAPM awardee and Director of Health Services Research in Academic Affairs and Clinical Transformation at Cedars-Sinai Medical Center, and Dr. Eleanor Duff, Global Head of Oncology R&D Corporate Affairs at AstraZeneca. Current grantee Ysabel Duron, Founder and President of the Latino Cancer Institute and current grantee for both the UCSF and Stanford cancer disparities projects, also testified, as did Dr. Laura Julian, Principal Medical Science Director at Genentech. A recording of the hearing is available online<sup>3</sup>, and the full agenda for the hearing can be found in Appendix D.

CIAPM staff provided all Select Committee members with a copy of *Precision Medicine: An Action Plan for California*, and the CIAPM 2019 Evaluation Report.

## WEBSITE UPDATE AND ASSET INVENTORY

The CIAPM website was updated for consistency and readability for the general public. A redesign is in the initial planning stages, part of a sitewide update for OPR.

The Initiative's enabling statute tasked the program with creating an "asset inventory" of precision medicine stakeholders and resources in California<sup>4</sup>, including data sets, researchers, and community groups. The goal is to foster collaboration and facilitate outreach efforts and cross-sector partnerships, such as between researchers, patient organizations, health care providers, and private companies. The initial build was provided pro bono by Lawrence Berkeley National Laboratory.

The beta version of the revamped California Precision Medicine Asset Inventory was launched in parallel with the ACEs RFP on December 3, and its curation and expansion are ongoing.

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3 [https://calchannel.granicus.com/MediaPlayer.php?view\\_id=21&clip\\_id=6533](https://calchannel.granicus.com/MediaPlayer.php?view_id=21&clip_id=6533)

4 Cal. Gov. Code § 65057(b)

# NEXT STEPS

## OUTREACH STRATEGY

Community voices and active engagement are critical to responsible health research to ensure that vital results are informed by and shared with those who need it most and in ways that are timely, relevant, and meaningful. CIAPM staff have compiled a document, “Guidance on Authentic Research-Community Partnerships,” that includes lists of free resources to help researchers implement highly interactive and proactive stakeholder models in which patients and families are represented in the governance, design, conduct, dissemination, and evaluation of CIAPM-funded research demonstration projects (see Appendix F). The guidance document identifies strategies to expand the reach of the program and ensure that communities across the state, especially those that have been historically underrepresented in medical research, are aware of upcoming funding and partnership opportunities.

In addition to community outreach, CIAPM has also created a plan to engage the following types of partners:

- Academic researchers
- Clinicians
- Industry (healthcare providers, biomedical research companies, pharmaceutical companies)
- Insurance providers
- Grant providers

The plan covers dissemination of the following information:

- Funding availability for collaborative demonstration projects
- Opportunities to partner across sectors and disciplines
- Availability of guidance for authentic community-researcher partnership

## FUTURE RFP TOPICS

Decisions regarding future RFP topics will be made by the new Advisory Council. *Precision Medicine: An Action Plan for California* lists particular diseases in which an immediate or near-term impact could be achieved using a precision medicine approach. The disease areas identified in the report include diabetes, depression, Alzheimer’s Disease, and environmental impacts on health. In support of the Advisory Council’s deliberations, CIAPM staff will be responsible for researching the aforementioned and other potential topics and prepare background reports.

# CONCLUSION

2019 marked the beginning of a new era for California and CIAPM. January saw a new governor inaugurated, as well as the appointment of California's first Surgeon General. CIAPM administration transitioned entirely to OPR, and access to funds was extended through 2025 to support several rounds of grant-making, creating an opportunity to strategically leverage the research investment over multiple years toward more ambitious goals. CIAPM has been able to coordinate closely with and align priorities across the Newsom administration, as seen through the recent release of the RFP for Adverse Childhood Experiences. CIAPM also worked in tandem with the California Legislature to hold the first-ever Informational Hearing on Precision Medicine, hosted by the Assembly Select Committee on Biotechnology. The revamp and launch of the California Precision Medicine Asset Inventory and online publication of "Guidance on Authentic Research-Community Partnership" serve to support all stakeholders, beyond the direct recipients of CIAPM research grants. Finally, the Initiative has in place a framework for an Advisory Council that will represent a broad range of strategic groups and help shape the Initiative for years to come.

# APPENDICES

## A. 2019 PUBLICATIONS, PRESENTATIONS, AND PRESS ABOUT CIAPM-FUNDED PROJECTS

All publications, presentations, and press that occurred between 2015 and 2018 are listed in the 2019 Evaluation Report, available on the CIAPM website. The following section summarizes only those from 2019.

### Publications

Joung, Sandy, Eldin Dzubur, Irene Van Den Broek, Aubrey Love, Lori Martinez-Rubio, Mayra Lopez, Benjamin Noah, et al. 2019. "Early Detection of Atrial Fibrillation-Atrial Flutter Using Remote Patient Monitoring." *Journal of Medical Cases* 10, no. 2: 31–36. <https://doi.org/10.14740/jmc3151w>. **Monitoring Adverse Cardiac Events (MACE)**

Shufelt, Chrisandra, Susan Cheng, Garth Fuller, Sandy Joung, Mitra Mastali, Kelly Mouapi, Qin Fu, et al. 2019. "Relationship Between Patient-Reported Outcomes And Cardiac Biomarkers: The Prediction, Risk, And Evaluation Of Major Adverse Cardiac Events (Pre-MACE) Study Baseline Results." *Journal of the American College of Cardiology* 73, no. 9: 1831. [https://doi.org/10.1016/s0735-1097\(19\)32437-4](https://doi.org/10.1016/s0735-1097(19)32437-4). **MACE**

Shufelt, Chrisandra, Eldin Dzubur, Sandy Joung, Garth Fuller, Kelly N. Mouapi, Irene Van Den Broek, Mayra Lopez, et al. 2019. "A Protocol Integrating Remote Patient Monitoring Patient Reported Outcomes and Cardiovascular Biomarkers." *npj Digital Medicine* 2, no. 1. <https://doi.org/10.1038/s41746-019-0145-6>. **MACE**

Shufelt, Chrisandra. 2019. "A Protocol Integrating Remote Monitoring, Patient Reported Outcomes, and Cardiovascular Biomarkers." *npj Digital Medicine Community*, September 24. <https://npjdigitalmedcommunity.nature.com/users/305047-chrisandra-shufelt/posts/53100-a-protocol-integrating-remote-patient-monitoring-patient-reported-outcomes-and-cardiovascular-biomarkers>. **MACE**

Meng, Yiwen, William Speier, Chrisandra Shufelt, Sandy Joung, Jennifer E. Van Eyk, C. Noel Bairey Merz, Mayra Lopez, Brennan Spiegel, and Corey W. Arnold. 2019. "A Machine Learning Approach to Classifying Self-Reported Health Status in a Cohort of Patients with Heart Disease Using Activity Tracker Data." *IEEE Journal of Biomedical and Health Informatics*. <https://doi.org/10.1109/jbhi.2019.2922178>. **MACE**

Shufelt, Chrisandra, Kim A, Sandy Joung, Lili Barsky, Corey Arnold, Susan Cheng, Shivani Dhawan, Garth Fuller, Mayra Lopez, Mitra Mastali, Kelly Mouapi, William Speier, Janet Wei, Irene Van Den Broek, Brennan Spiegel, Jennifer E. Van Eyk, C. Noel Bairey Merz. "Biometric and Psychometric Remote Monitoring Predicts Cardiovascular Risk Biomarkers in Ischemic

Heart Disease.” Submitted 2019. **MACE**

Bjork, Isabel, Jennifer Peralez, David Haussler, Sheri L. Spunt, Olena M. Vaske. “Data Sharing for Clinical Utility.” *Molecular Case Studies* (2019). Accepted. **California Kids Cancer Comparison (CKCC)**

Learned, Katrina Towle, Ann C. Durbin, Robert M. Currie, Ellen C. Kephart, Holly R. Beale, Lauren M. Sanders, Jacob Pfeil, et al. “Barriers to Accessing Public Cancer Genomic Data.” *Scientific Data* 6, no. 1 (2019). <https://doi.org/10.1038/s41597-019-0096-4>. **CKCC**

Sanders, Lauren M., Arun Rangaswami, Isabel Bjork, Du Linh Lam, Holly C. Beale, Ellen Towle Kephart, Ann Durbin, Katrina Learned, Rob Currie, A. Geoffrey Lyle, Jacob Pfeil, Avanthi Tayi Shah, Alex G. Lee, Stanley G. Leung, Inge H. Behroozfard, Marcus R. Breese, Jennifer Peralez, Florette K. Hazard, Norman Lacayo, Sheri L. Spunt, David Haussler, Sofie R. Salama, E. Alejandro Sweet-Cordero, and Olena M. Vaske. “Comparative RNA-seq analysis aids in diagnosis of a rare pediatric tumor.” *Molecular Case Studies* (2019), Accepted. **CKCC**

### **Presentations and Posters**

Sanders, Lauren M. "Shared Long Non-coding RNA Dysregulation in Histone H3 K27M Gliomas and PF-A Ependymomas." Conference talk, 5th Pediatric Neuro-Oncology Basic & Translational Research Conference from Society for NeuroOncology, San Francisco, CA, May 3, 2019. **CKCC**

Vaske, Olena. "Approaches to Data Federation at Treehouse Childhood Cancer Initiative." Conference talk, Childhood Cancer Data Initiative Symposium from NIH National Cancer Institute, Washington, DC, July, 2019. **CKCC**

Martinez, Elena. "Ensuring Diversity in Precision Oncology." Presentation, Quality Care Symposium from American Society for Clinical Oncology, San Diego, CA, September 6, 2019. <https://practice.asco.org/event/20190906-2019-quality-care-symposium>. **CKCC**

Sanders, Lauren M., A. Geoffrey Lyle, Holly C. Beale, Ellen Towle Kephart, Katrina Learned, Jacob Pfeil, Jennifer Peralez, Norman Lacayo, Arun Rangaswami, Sheri L. Spunt, Isabel Bjork, David Haussler, Sofie R. Salama, Olena M. Vaske. *Comparative gene expression analysis for identification and prioritization of therapeutic targets in a cohort of childhood cancers*. Poster presentation, Advances in Pediatric Cancer Research Meeting from American Association for Cancer Research, Montreal, September 17-20, 2019. **CKCC**

Cheney, Allison, Lauren M. Sanders, Lucas Seninge, Holly C. Beale, Ellen Towle Kephart, Jacob Pfeil, Katrina Learned, A. Geoffrey Lyle, Isabel Bjork, David Haussler, Sofie R. Salama, Olena M. Vaske. *The Epithelial-Mesenchymal Transition in Diffuse Midline Gliomas with H3K27M mutation*. Poster presentation, Advances in Pediatric Cancer Research Meeting from American Association of Cancer Researchers, Montreal, September 17-20, 2019. **CKCC**

Spiegel, Brennan. "Evaluating Mitra® Microsampling Devices for Remote Monitoring of Apolipoproteins in Patients at Risk for Cardiac Events." Presentation, Western Medical Research Conference from International Humane Proteome Organization (Targeted Proteomics in Women's Health), Orlando, FL, January 24, 2019. **MACE**

Mouapi, Kelly. "Early Prediction of Cardiac Events via Remote Monitoring Coupled with an Apolipoprotein Targeted MRM Panel." Conference talk, 11th Annual Conference from The Association for Mass Spectrometry Applications to the Clinical Lab, Palm Springs, CA, March 7, 2019. **MACE**

Van Den Broek, Irene, Mitra Mastali, Qin Fu, Vidya Venkatraman, Noel Bairey Merz, Brennan Spiegel, Jennifer Van Eyk. "Quality Control Recommendations for MRM Proteomics on Dried Blood Spots Using Mitra® Microsampling Device." Oral presentation, 67th Annual ASMS Conference on Mass Spectrometry from American Society on Mass Spectrometry, Atlanta, GA, June 6, 2019; 68th Annual Scientific Session from American College of Cardiology, Atlanta, GA, March 16-18, 2019. **MACE**

Fu, Qin, Irina Tchernyshyov, Ronald Holewinski, Vidya Venkatraman, David Sarracino, Casey Johnson, Kelly Njine Mouapi, Susan Cheng, Chrisandra Shufelt, Brennan Spiegel, Noel Bairey Merz, Scott Peterman, Jennifer Van Eyk. *Case-Control Study: Expanded Proteomics and Lipidomic Profiling for Early Prediction of Adverse Cardiac Events*. Poster presentation, 67th Annual ASMS Conference on Mass Spectrometry from American Society on Mass Spectrometry, Atlanta, GA, June 6, 2019. **MACE**

Spiegel, Brennan. "Opportunities and Pitfalls of Using PROMIS in Clinical Practice: Implementation Experience at Cedars-Sinai Medical Center." Keynote, 5th Annual PROMIS Health Organization Conference from Promis Health Organization, San Diego, CA, October 24, 2019. **MACE**

## **Press**

Fikes, Bradley. 2019. "UCSD gets \$3 million to fight triple-negative breast cancer." *San Diego Union Tribune*, February 15. <https://www.sandiegouniontribune.com/business/biotech/sd-me-ucsd-triple-negative-breast-cancer-20190215-story.html>. Triple Negative Breast Cancer in Latinas

## **B. OUTREACH EFFORTS: CIAPM REPRESENTATION AT EXTERNAL EVENTS**

American Association for the Advancement of Science; Washington, DC; February 14-18, 2019.

UC Riverside and American Association for the Advancement of Science Joint Science Policy Event; Riverside, CA; March 14, 2019.

California Budget & Policy Center Policy Insights Conference; Sacramento, CA; March 27, 2019.

UC San Diego School of Medicine Biomedical Sciences Graduate Program; La Jolla, CA; April 4, 2019.

Steinberg Institute Capitol Briefing: Return on Investment of Early Intervention in Mental Health Care; Sacramento, CA; May 7, 2019.

State Scientist Day; Sacramento, CA; May 8, 2019.

Stanford Medicine Big Data for Precision Health; Palo Alto, CA; May 22-23, 2019.

Athena Breast Health Network WISDOM Study Anniversary Event; San Francisco, CA; May 24, 2019.

State Government Leaders' Site Visit of AstraZeneca; South San Francisco, CA; May 31, 2019.

Assembly Biotechnology Select Committee Informational Hearing on Precision Medicine; Sacramento, CA; August 27, 2019.

Capitol Briefing on Chronic Pain Management and Research Strategy; Sacramento, CA; August 14, 2019.

UC Davis FUTURES Program; Davis, CA; August 15, 2019.

2019 Brain Bee World Championship; Daegu, South Korea; September 21-24, 2019.

OPR and Department of Finance Site Visit of Lawrence Livermore National Laboratory; Livermore, CA; September 26, 2019.

XPOMET Medicinale 2019; Berlin, Germany; October 10-14, 2019.

Society for Neuroscience Annual Meeting; Chicago, IL; October 18-23, 2019.

TED at the National Academies of Sciences, Engineering, and Medicine; Washington, DC; November 1, 2019.

World Alliance Forum Health Care Changemakers; San Francisco, CA; October 29-30, 2019.

Healthcare Leadership Exchange; San Francisco, CA; October 30, 2019.

American Association for Precision Medicine Annual Meeting; Santa Clara, CA; November 8, 2019.

Breaking Barriers 2019 Interagency Symposium: Building California's Future: Breaking Barriers to Care; Sacramento, CA; November 20-21, 2019.

Rural Poverty and Health Equity Summit; Delano, CA; November 22, 2019.

American Geophysical Union Annual Meeting; San Francisco, CA; December 12, 2019.

## C. KEY PERSONNEL IN 2019

### OPR

Kate Gordon, Director (January 2019 – Present)

Elizabeth Baca, Senior Health Advisor and Deputy Director (April 2015 – July 2019)

Julianne McCall, Science Officer (February 2019 – Present)

Shannon Muir, Science Officer (April 2019 – Present)

Megan Varvais, Science Communication Specialist & Administrator (May 2019 – Present)

Nichole Holm, Policy Fellow (April – December 2019)

Ken McCullough, CCST Science & Technology Policy Fellow (December 2019 – Present)

April Booth, Graduate Student Intern (December 2019 – Present)

### UC Davis

Chris Wang, Financial Officer (January 2018 – Present)

### UCSF

Atul Butte, UC Health Chief Data Scientist (April 2015 – January 2019)

India Hook-Barnard, CIAPM Executive Director (April 2015 – January 2019)

David Paquette, CIAPM Science Officer (April 2018 – May 2019)

Ben Rubin, CIAPM Science Officer (April 2018 – January 2019)

## D. MEETING OVERVIEWS

### All Teams Meeting (May 1, 2019)

#### *Former Teams Showcase*

Each formerly funded research team provided a brief, high-level overview of their project. Afterward, discussion was moderated by Dr. India Hook-Barnard, UC San Francisco.

### *Current Teams Showcase*

Each currently funded research team delivered a presentation about their project. Afterward, discussion was moderated by Dr. Fred Meyers, UC Davis.

*CIAPM Presentation on Data Systems, Dr. Shannon Muir, OPR*

### *Shared Data Platform Brainstorm*

All teams were engaged in a discussion moderated by Dr. Clara Lajonchere, UC Los Angeles, to lay the foundation for the data sharing platform teams can select. Discussion prompts included:

- What resources are currently most useful?
- How could existing resources be improved?
- Is there a need for a new platform? What would that look like?

### *Community Partnerships Discussion*

All teams were engaged in a discussion moderated by Dr. Mark Cullen, Stanford University, regarding strategies for effective community partnership, existing resources, and opportunities for improvement.

### *Discussion on Next Steps*

All teams participated in a discussion moderated by OPR Deputy Director Dr. Elizabeth Baca. The main ideas were that patients and communities should be at the center of the research, and social determinants of health are key. Teams were encouraged to share with CIAPM patient successes stemming from their research.

## **Assembly Select Committee on Biotechnology Informational Hearing (August 27, 2019)**

OPR Science Officer Dr. Shannon Muir testified first and gave background about both precision medicine and CIAPM. Dr. Clara Lajonchere, Deputy Director for the Institute for Precision Health at UCLA, then summarized key policy recommendations from the report, *Precision Medicine: An Action Plan for California*, for which she served as support staff. Later in the hearing, former CIAPM awardee Dr. Brennen Spiegel, Director of Health Services Research in Academic Affairs and Clinical Transformation at Cedars-Sinai, spoke about his research, including his CIAPM project Early Prediction of Major Adverse Cardiovascular Events Using Remote Monitoring. Following, Ysabel Duron, Founder and President of the Latino Cancer Institute, and current grantee for both the UCSF project (Addressing Disparities in Breast Cancer in Latinas: A multi-tiered approach) and the Stanford project (Reducing Cancer Disparities Through Innovative Community-Academic Partnership to Advance Access and Delivery of Precision Medicine in Santa Clara County), addressed the need to include a diverse population in precision medicine research and the hurdles that underserved communities

face when attempting to access precision health resources. CIAPM was instrumental in the inclusion of all four of these presenters. Other presenters at the hearing included Dr. Laura Julian, Principal Medical Science Director at Genentech and collaborator on the CIAPM project Precision Medicine for Multiple Sclerosis, Dr. Eleanor Duff, Global Head of Oncology R&D Corporate Affairs at AstraZeneca, and OPR Science Officer Dr. Julianne McCall.

CIAPM staff provided all Select Committee members with a copy of *Precision Medicine: An Action Plan for California*, and the CIAPM 2019 Evaluation Report.

## E. 2019 REQUEST FOR PROPOSALS

### CIAPM Request for Proposals 2019: Addressing Health Impacts of Adverse Childhood Experiences through a Collaborative Precision Medicine Approach

#### I. Overview

The California Initiative to Advance Precision Medicine (CIAPM) will award \$9 million total across three to five independent research teams (\$1.8 to \$3.0 million per team) over a 3-year project term to address the health impacts of Adverse Childhood Experiences (ACEs) and toxic stress. The field of Precision Medicine continues to emerge as a modern application of scientific data and clinical practice toward the individualization of prevention, diagnosis, measurement, and treatment of disease. This funding opportunity aims to drive innovation in applying a Precision Medicine approach to understanding the biological mechanisms of and improving clinical means of addressing toxic stress from ACEs, particularly as a path toward reducing health disparities.

Research teams must be co-hosted by at least one academic research institution and one nonprofit community/patient organization or county institution that provides support to people with ACEs. Projects must be located in California, and funds may not be used for indirect costs. Additional matching funds and in-kind contributions are highly encouraged and will be considered as part of the selection process. Additional funding may become available for awarded project teams to examine and potentially select and use a common data-sharing platform.

All proposal materials will be accepted electronically by the Governor's Office of Planning and Research (OPR) via the online CIAPM Submission Portal, according to the timeline below. Letters of Intent to Submit a Proposal are not scored during the selection process but must be received by the noted deadline and reflect the general theme of a forthcoming concept proposal.

## II. Timeline

Request for Proposals Announced	12/3/2019
Informational Webinar	12/11/2019 at 3:00 PM
Due: Letters of Intent to Submit a Proposal	2/5/2020 by 11:59 PM
Due: Concept Proposals	4/22/2020 by 11:59 PM
Notification of Finalists	5/28/2020
Due: Full Proposals	7/22/2020 by 11:59 PM
Awardees Announced	8/31/2020
Anticipated Project Start	11/1/2020 – 11/30/2020
Duration of Projects	36 months

*All times listed are in Pacific Time.*

## III. Background

### *Precision Medicine*

Precision Medicine holds promise to profoundly transform health, health care, and biomedical research. As envisioned in the National Academy of Sciences (NAS) 2011 report, “Toward Precision Medicine: Building a Knowledge Network for Biomedical Research and a New Taxonomy of Disease,” the modern approach to health and disease 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 wellbeing and develop and deliver more precise diagnostics, therapeutics, and preventative measures.

While Precision Medicine approaches will likely bring about powerful insights, creating models of access for all communities will be just as important to address health disparities and positively impact clinical outcomes across socioeconomic groups.

### *California Initiative to Advance Precision Medicine*

CIAPM was established by the State of California pursuant to passage by the Legislature to help coordinate public, private, and nonprofit 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 is administered by the Governor’s Office of Planning and Research (OPR) to bring together state Precision Medicine leaders and support research projects that demonstrate the power and promise of Precision Medicine to the people of California.

### *Research on Adverse Childhood Experiences*

This Request for Proposals (RFP) addresses a core priority of California Surgeon General

Dr. Nadine Burke Harris by supporting research of toxic stress from ACEs

with a Precision Medicine approach, improving targeted prevention, diagnosis, measurement, and treatment throughout the lifespan. Children who experience high levels of stress and/or trauma demonstrate lifelong vulnerabilities to numerous physical and mental disorders, thus far linked to the effects of a disrupted physiological stress response on the neuro-endocrine-immune system and/or genetic regulation.

Recommendations from the 2019 NAS Report, “Vibrant and Healthy Kids: Aligning Science, Practice, and Policy to Advance Health Equity,” underscore structural and policy barriers to data integration, cross-sector collaboration, and screenings for early detection of trauma and adversity that collectively prevent patients from receiving holistic health care. Improvement in clinical outcomes relies upon, in part, the creation and expansion of referral systems, rapid coordination of cross-sector expertise, and routine training for trauma-informed care and social determinants of health.

At present, limited studies and interventions have been conducted to better comprehend ACEs from a biological and health perspective. This funding opportunity seeks to inspire collaborative research throughout the state into the broad field of ACEs, using Precision Medicine approaches to improve our understanding of, for example, new biomarkers predictive of individual risk for future negative health outcomes, individual variation in response to therapeutic approaches, and impacts of toxic stress from ACEs on communities reflective of the diverse California population.

#### **IV. Purpose: Collaborative Demonstration Projects**

Both NAS reports emphasize the need for strong partnerships and collaboration to achieve the vision of a healthier and more equitable society. As part of that process, pilot projects should be undertaken at various levels to identify barriers, define effective practices, and achieve some early, albeit modest scale, successes. Therefore, one of OPR’s primary approaches is to support collaborative demonstration projects that leverage the state’s expansive and diverse patient data, research expertise, and technological capabilities to advance Precision Medicine for ACEs and toxic stress.

For this RFP, up to \$9 million will be provided by the State for three to five proof-of-principle demonstration projects with the aim to address ACEs through collaborations between academic, community, public, nonprofit, and private partners. Additional funds may become available to awarded demonstration projects to examine and potentially select and use a common data-sharing platform.

Projects should be co-led by Principle Investigators (PIs) from at least one public or private academic institution and at least one nonprofit community/patient organization or county institution that provides support for people with ACEs. Successful proposals will also leverage contributions from other nonprofit or for-profit organizations in the community as well as industry

partners.

Demonstration projects will be selected through a three-stage process, involving (1) submission of Letters of Intent to Submit a Proposal; (2) submission of Concept Proposals; and (3) submission of Full Proposals, based on selected Concept Proposals, from which the final selection of awards will be made. Once the out-of-state expert Selection Committee delivers its recommendations for awards, OPR will announce and work with awardees to develop concrete metrics and goals to track the progress of the demonstration projects and enter into contracts with OPR.

## **V. Application Instructions**

### *Application process*

All application materials must be submitted electronically by the deadlines listed in Section II.

#### Stage 1: Letter of Intent to Submit a Proposal

Applicants should submit a brief Letter of Intent by February 5, 2020 via the online CIAPM Submission Portal at [opr.ca.gov/ciapm](http://opr.ca.gov/ciapm). The webform will require the following information: (i) a tentative title, (ii) Primary Institution, (iii) Lead PI, (iv) other PIs, (v) tentative project description (maximum 5 sentences), and (vi) tentative total budget. Letters of Intent are not scored during the selection process but must be received by the deadline and reflect the general theme of the forthcoming Concept Proposal. An institutional cover letter is not required at this stage. Applications may be re-opened by the applicant any time before the submission deadline.

#### Stage 2: Concept Proposals

On or before April 22, 2020, applicants should submit a three-page Concept Proposal in PDF format. Applicants must upload an additional PDF file with Biographical Sketches (resumes, in the format of the National Institutes of Health, NIH) of PIs and team members. Detailed parameters are presented in the Concept Proposal section, below. All Concept Proposal titles will be made public on the OPR website following the selection process. An institutional cover letter is not required at this stage; however, all PIs must confirm that their institutions/organizations have committed to support the project, if awarded funding.

#### Stage 3: Full Proposals

The out-of-state expert Selection Committee will identify a subset of submitted Concept Proposals by May 28, 2020 to move on to the Full Proposal stage. In parallel, instructions for electronic submission of Full Proposals will be made available. Institutional cover letters will be required. Full Proposals are due July 22, 2020.

The Selection Committee will recommend between three and five projects to award, and OPR will announce awardees by August 31, 2020. The three-year projects are anticipated to begin between November 1 and November 30, 2020.

### *Eligibility*

1. Applicant teams must designate a Lead Principal Investigator (Lead PI) from a public or private academic research institution, considered the “Primary Institution.” The Lead PI will serve as the main contact throughout the application process, demonstration project, and post-award evaluation. Up to ten additional PIs may also be designated. At least one PI must represent a nonprofit community/patient organization or county health institution that provides support to people with ACEs. Additional collaborations with other nonprofit and for-profit organizations and industry partners are encouraged.
2. Only one proposal per team will be accepted. An individual may serve as Lead PI for only one application; otherwise, individuals may contribute to multiple proposals.
3. There will not be more than one award per Primary Institution.
4. Demonstration projects must be located in California. Partners may be located outside of California if they provide their own funding.
5. Research teams may only use funds for direct costs. Indirect costs will not be supported.
6. Demonstration projects should aim to validate the utility of Precision Medicine approaches to improve outcomes through better prevention, diagnostics, measurements, and/or treatments for toxic stress from ACEs.

### *Concept proposals*

Each application should address all topics listed below in maximum three pages total in PDF format; minimum Arial 11 font; and minimum 0.5-inch margins. Biosketches (in NIH format) of all PIs and team members must also be submitted as a single PDF and will not be included in the 3-page limit. Proposal materials will be accepted via the online CIAPM Submission Portal at [opr.ca.gov/ciapm](http://opr.ca.gov/ciapm).

### *Impact on health outcomes and health disparities*

Describe how the proposed project will improve health outcomes and reduce disparities among populations affected by ACEs. Provide rationale for the project by outlining existing strengths, resources, and opportunities available (e.g., ability to study biomarkers, collect informative data, or integrate data from various sources; access to existing biobanks, databases, or medical records; an engaged participant community; or established mechanisms for responsible data sharing). Describe why the topic was selected and why the approach is impactful.

### *Project plan*

Describe the components of the proposed project, including specific aims and research strategy.

### *Data*

Each proposal should demonstrate its commitment to the use of robust data. Use of multiple data sets is encouraged (e.g., electronic medical records, mobile health device data, registries, and research databases). Briefly describe the data set(s) you propose to use or create, the rationale for integrating the selected data, and how the data set(s) may contribute to better outcomes by improving preventative, diagnostic, measurement, and/or treatment approaches. Please provide a rationale for use of designated standards that are already recognized, for example, by the American Academy of Pediatrics.

### *Precision Medicine capabilities*

Describe the Precision Medicine capabilities that will be developed as a result of this project, such as infrastructure and tools that will be built, including new consortia, collaborations, personnel competencies, databases, datasets, applications, software, intellectual property, patient cohorts, participant communities and networks, and models for responsible data sharing.

### *Participant engagement*

Describe strategies to engage patients, families, and communities for authentic partnership, such as developing opportunities to build trust, approaches to ensuring consent, or practical principles for data sharing, privacy, and security. For example, projects may integrate a community advisory board, employ patient navigators, host focus groups to better understand patient/community issues, or describe efforts to allow patients access to their medical data and/or opportunities to contribute data from this demonstration project to other research studies.

### *Impact for patients*

To the extent it is applicable to the project, describe opportunities to improve patient outcomes within the 36-month project timeframe—and beyond.

### *Approaches to improving training and/or education*

Describe how the proposal will develop or amplify quality opportunities for trainees and/or students to better apply Precision Medicine approaches to clinical care, for example, by creating or updating a curriculum for a graduate course or occupational certification program, engaging trainees in the implementation of the project, or assessing current training methods in

clinical ACEs screenings.

#### *Anticipated challenges and proposed solutions*

Describe potential barriers to the project's success, especially those that could delay the launch, progress, or completion (e.g., human subjects, health literacy barriers, or mobile patient populations), and describe potential solutions to these challenges.

#### *Project team*

Describe collaborations between at least two California-based institutions/ organizations as part of the proposal. Additional partners are highly encouraged. Describe the nature and strength of any existing collaborations. Provide biosketches for each PI and team member. Biosketches will not count toward the 3-page proposal limit.

#### *Budget overview*

Briefly outline how project funds (approximately \$1.8 million to \$3 million per project) will be used and how other resources will be leveraged, including total amount of matching funds from partners and third-party entities. Comment on why CIAPM funds are needed as opposed to other funding sources, such as federal or philanthropic grants. Examples of other resources that may be leveraged include the following: experts' time; molecular/genetic characterization; access to computational platforms, including data visualization, innovative databases, data sharing, data privacy and security, or high-performance computing; and mobile platforms to reach patients between medical encounters and/or track their health outcomes.

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 would leave the state. The amount of funds that can leave the state will be subject to the final award agreement.

#### *Data-Sharing Work Group*

Teams must express a willingness to attend coordination meetings with fellow grantees, share lessons learned, discuss the use of designated data standards, and agree to examine and potentially select and use a common data-sharing platform.

#### *Submission*

Concept Proposals must be submitted electronically through the online CIAPM Submission Portal on or before April 22, 2020 at [www.opr.ca.gov/ciapm](http://www.opr.ca.gov/ciapm). Applications may be re-opened and edited by the applicant any time before the submission deadline.

## VI. Selection

### *Selection Committee*

A committee will be comprised of out-of-state individuals that includes subject matter experts representing the breadth of stakeholders involved in the overall initiative. Nominations for the Selection Committee will be considered from the Legislature, public, and research communities. Selection Committee members shall be deemed to be free of conflicts of interest in any contract with an applicant and will be screened according to NIH procedures. The names of Selection Committee members will be provided on the OPR website. The Selection Committee will use a process consistent with NIH procedures for reviewing the proposals and making award recommendations. OPR will use a process consistent with NIH practices to ensure proposals are evaluated in a manner that is fair, equitable, timely, and free of bias.

### *Selection criteria*

Section 65057 of the Government Code sets forth the following selection criteria:

- 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 potential to reduce health disparities.
- 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 leveraging of non-state funding.
- The clinical and commercial potential of the project.
- 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 Selection Committee will also consider the following additional factors in reviewing the proposals:

- The innovative concepts, approaches, methodologies, instrumentation, or interventions to advance Precision Medicine.
- The feasibility of the project (can the project be achieved within the proposed timeline).
- The quality and extent of patient/participant engagement.
- Approaches to protect privacy and personal health information.
- Methods to increase access and inclusion of populations that experience disparities.

- System interoperability.
- The quality and extent of training and educational contributions to improve the integration of Precision Medicine approaches in clinical settings.
- Sharing data and/or protocols across institutions.
- Where the project is located in California to balance geographic equity of awards and diversity of awarded institutions.
- Diverse expertise and background of team members, including those underrepresented in research, including underrepresented racial and ethnic groups, persons with disabilities, and women.
- Overall impact to advance Precision Medicine.

### *Results*

The Selection Committee will report on the justification for selecting the demonstration projects that are awarded funding and will provide a list of the demonstration projects that were not selected on the OPR website, as required by statute. Therefore, do not include in the project title any proprietary or confidential information or details that could identify the PI and applicant institution, unless there are no reservations against being identified.

## **VII. Terms and Conditions of Funding Awards**

Applicants of proposals that are selected will be asked to enter into an agreement with OPR. Terms and conditions will be based on UTC for UC/CSU/CSU auxiliary institutions. All agreements will include the following terms:

- **Indirect Costs** No indirect costs will be supported.
- **Intellectual Property Agreement** Agree to terms of patent and copyright agreements that balance the State's interests with the needs of the research team.
- **Funds** Funds will be disbursed monthly.
- **Start Date** Initiate work within 30 days of agreement execution.
- **Reporting** Submit biannual progress reports, work with OPR staff throughout the project on milestone and budget development and adjustments, and participate in conference calls and convening activities. Post-award expectations will be specified in award agreements, including a formal evaluation of the outcomes of the demonstration project.
- **Use of Data** Investigators and demonstration teams are expected to share data and research findings consistent with academic and state open-access standards.
- **Protection of Privacy and Health Information** Investigators and demonstration project teams are expected to follow state and federal law to protect privacy, personal health information, and rights of human subjects.

## VIII. RFP Administration and Contact Information

During the solicitation process, questions may be directed to CIAPM staff:

Julianne McCall, PhD  
Governor's Office of Planning & Research  
1400 Tenth Street, Sacramento, CA 95814  
Telephone: (916) 323 – 9912  
Email: [ciapm@opr.ca.gov](mailto:ciapm@opr.ca.gov)

Applicants may submit written questions via email or mail. All technical questions must be received by April 4, 2020. Non-technical questions (e.g., questions concerning format requirements or submission instructions) may be submitted to CIAPM staff at any time prior to the April 22, 2020 deadline for Concept Proposals. On a weekly basis, or as necessary, CIAPM staff will update a list of Frequently Asked Questions on the website.

Any verbal communication with CIAPM staff concerning this solicitation is not binding on the State and will in no way alter a specification, term, or condition of the solicitation. Therefore, all communication should be directed in writing, as indicated above.

If an ambiguity, conflict, discrepancy, omission, or other error is discovered in the solicitation at any time prior to a deadline, the proposer may notify CIAPM staff in writing and request modification or clarification of the solicitation. OPR, at its discretion, may provide modifications or clarifications either by an addendum to the solicitation or by a written notice to all parties who participate in the solicitation. At its discretion, OPR may re-open the technical question period to provide all applicants the opportunity to seek any further clarification required. Any change would be reflected on the CIAPM website.

## F. COMMUNITY-RESEARCHER PARTNERSHIP GUIDANCE

### CIAPM Guidance on Authentic Research-Community Partnerships Updated December 3, 2019

A significant mission of the California Initiative to Advance Precision Medicine (CIAPM) is to reduce health disparities, in part by orienting the vast health research infrastructure and the emerging field of Precision Medicine toward addressing inequitable medical challenges that persist across time and geographies. In order to foster research outcomes that address the needs and concerns of patients, family members, and health care providers, authentic research-community partnerships are critical.

According to the Institute of Medicine, community-based participatory research enhances community understanding of the issues under study and improves researchers' ability to understand community priorities, the

importance of addressing community priorities, and the need for culturally sensitive approaches and outreach<sup>1</sup>. Part of ensuring the success of CIAPM in demonstrating the promise of Precision Medicine is ensuring vital research results are informed by and shared with those who need it most and in ways that are timely, relevant, and meaningful.

This guidance aims to provide resources for researchers, communities, clinicians, and other project partners to encourage high quality, interactive, and proactive stakeholder models, where patients and families are represented in the governance, design, conduct, dissemination, and evaluation of CIAPM-funded research demonstration projects.

To facilitate cross-sector partnerships, CIAPM created the California Precision Medicine Asset Inventory, an online, interactive mapping tool that provides a dynamic view of private, public, and nonprofit entities working within areas relevant to Precision Medicine and community health. All researchers, patient advocacy and community organizations, health care providers, and others are invited to submit their basic information to be included in the Inventory. Information may be included by submitting the Asset Inventory Form.

#### *Resources for authentic research-community partnerships*

Successful CIAPM demonstration project proposals will exemplify a thoughtful strategy to developing and facilitating authentic cross-sector partnerships. The following resources are freely available and recommended:

- The Practical Playbook II: Building Multisector Partnerships That Work, Edited by J. Lloyd Michener, Brian C. Castrucci, Don W. Bradley, Edward L. Hunter, Craig W. Thomas, Catherine Patterson, and Elizabeth Corcoran; published May 21, 2019 by Oxford University Press.
- “Patient and Public Involvement in Research: Enabling Meaningful Contributions,” Written by Sarah Ball, Amelia Harshfield, Asha Carpenter, Adam Bertscher, and Sonja Marjanovic; published in 2019 by RAND Corporation.
- “Precision Medicine Initiative Cohort Program – Building a Research Foundation for 21st Century Medicine,” published September 17, 2015, p. 38-44.
- “Chapter 1. The vision, valley, and victory of community engagement.” Written by Loretta Jones, Kenneth Wells, Keith Norris, Barbara Meade, and Paul Koegel; published Autumn 2009; *Ethnicity & Disease*, 19 (4 Suppl 6), S6–7.
- “Applying a community-based participatory research framework to patient and family engagement in the development of patient-centered outcomes research and practice.” Written by Simona C. Kwon, Shiv Darius Tandon, Nadia Islam, Lindsey Riley, and Chau Trinh-Shevrin; published October 2018 in *Translational Behavioral Medicine*, 8;8(5):683-691.

- Principles of Community Engagement, Second Edition, Written by the Clinical and Translational Science Awards Consortium Community Engagement Key Function Committee Task Force on the Principles of Community Engagement; published June 2011 by the National Institutes of Health.
- “Community Engagement in Research: Frameworks for Education and Peer Review,” Written by Syed M. Ahmed and Ann-Gel S. Palermo, published August 2010 in the American Journal of Public Health, 100(8): 1380-1387.

### *Resources on Adverse Childhood Experiences*

The Office of the California Surgeon General has developed a website with many resources on ACEs that will become publicly available on December 4, 2019: [www.acesaware.org](http://www.acesaware.org).

### *Health Disparity Research Resources*

Applicants for CIAPM funds are encouraged to learn about health disparities and establish new collaborations through the California Precision Medicine Asset Inventory. Additional resources are available via the following links:

- National Institute on Minority Health and Health Disparities Community-Based Participatory Research Initiative, <https://www.nimhd.nih.gov/programs/extramural/community-based-participatory.html>
- Health Resources and Services Administration (HSRA) Office of Minority Health: Search for health disparity programs at <https://www.hrsa.gov/index.html>
- U.S. Centers for Disease Control and Prevention Office of Minority Health and Health Equity, <https://www.cdc.gov/healthequity/index.html>
- National Institutes of Health (NIH) Research Portfolio Online Reporting Tool (NIH RePORTER): Search for NIH awards at <https://projectreporter.nih.gov/reporter.cfm>
- National Library of Medicine, NIH, PubMed: Search for investigators publishing studies on health disparities at <https://www.ncbi.nlm.nih.gov/pubmed>
- U.S. Department of Education: Search for institutions that may have increased access to disproportionately affected populations at <https://www2.ed.gov/about/offices/list/ocr/edliteminorityinst.html>
- National Coalition for LGBT Health: For more information on programs focused on lesbian, gay, bisexual, and transgender (LGBT) research, policy, education, and training, search <http://www.healthlgbt.org>
- Indian Health Services, <https://www.ihs.gov/>
- National Alliance for Hispanic Health, <https://www.healthyamericas.org/>
- National Medical Association, <https://www.nmanet.org/>
- National Rural Health Association, <https://www.ruralhealthweb.org/>
- California Department of Public Health Office of Health Equity, <https://www.cdph.ca.gov/Programs/OHE/Pages/OfficeHealthEquity.aspx>