

California Initiative to Advance **2021**

2021 ANNUAL REPORT PREPARED BY THE

GOVERNOR'S OFFICE OF

California Initiative to Advance Precision Medicine

2021 Annual Report to the California Legislature

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EXECUTIVE SUMMARY

The California Initiative to Advance Precision Medicine (CIAPM) was launched in 2014 to coordinate public, private, and nonprofit precision medicine stakeholders and foster the creation of new technologies and therapies that can improve the health of Californians while prioritizing equity. CIAPM funds precision medicine research demonstration projects that address a variety of California's most pressing health issues. CIAPM's projects are collaborations between some of the world's leading research institutions and community-based clinics and organizations that serve California's most vulnerable populations. CIAPM also has a statutory mandate to maintain an inventory of precision medicine resources to aid the development of cross-sector partnerships.

In 2021, CIAPM continued to fulfill its duties to push the boundaries of knowledge in the field of precision medicine and provide services to California's precision medicine community. Specifically, CIAPM's 2021 accomplishments include:

- Selecting and initiating seven projects that use a precision medicine framework to address Adverse Childhood Experiences (ACEs).
- Holding briefings to share information about the seven ACEs projects with legislative staff and other external stakeholders.
- Supporting the continued progress of three research teams working to combat cancer disparities in California's Latinx communities through work in molecular biology and community engagement.
- Generating content and conducting outreach for a future website that encourages diversifying participants in biomedical research

to improve applicability of research findings to underserved subpopulations.

- Supporting California's ongoing efforts to integrate social determinants of health data into medical records to maximize clinical utility and optimize the potential for new research findings.
- Serving on the Governor's COVID-19 Testing Task Force.
- Launching a new website to better convey CIAPM's mission, successes, and ongoing efforts, with a section devoted to accessible precision medicine educational resources.
- Revamping the California Precision Medicine Asset Inventory with an improved user interface.
- Participating in the Capitol Collaborative on Race and Equity to build racial equity capacity among CIAPM staff.

2022 Priorities

- Support ongoing demonstration projects for ACEs and cancer disparities.
- Advance the California Precision Medicine Advisory Council working group projects.
- Act as a hub for new ideas and collaborations among precision medicine stakeholders.
- Refine communications and public engagement.
- Leverage expertise in service of the state.
- Infuse racial equity into every programmatic approach.

MESSAGE FROM THE DIRECTOR

Honorable Members of the State Legislature,

On behalf of the Governor's Office of Planning and Research (OPR), we proudly present to you California Initiative to Advance Precision Medicine's (CIAPM's) 2021 Annual Report to the California Legislature. As in previous years, CIAPM worked beyond what is required by its statutory responsibilities to make California healthier, more equitable, and more resilient to challenges like the COVID-19 pandemic.

The small but nimble CIAPM team continued to facilitate groundbreaking, cross-sector, community-focused precision medicine research that addresses health disparities while pushing the boundaries of knowledge and generating new research networks. CIAPM-funded demonstration projects also create transformational change and augment the capacity of community-based organizations and research institutions by offering valuable training opportunities for community health workers, graduate students, and others.

Also in 2021, under the guidance of the California Precision Medicine Advisory Council which includes one member recommended by the Senate President pro Tempore and another by the Speaker of the Assembly, CIAPM pursued two working group projects. The first aims to better integrate health data—specifically data about the social determinants of health—in a way that optimizes clinical utility and allows researchers to access and analyze the data safely and ethically to uncover new correlations and patterns that could inform their work. The second project is curating information about the importance of diversity, equity, and inclusion in biomedical research. Once concluded, this project will provide resources and best practices to precision medicine stakeholders so that research is more applicable across subpopulations.

2021 demonstrated the need for cross-cutting, innovative, and part-

ner-driven solutions that center communities and help advance equity while addressing California's needs. I invite you to learn more about CIAPM's unique approach and collaborative nature, the milestones it has accomplished, and the numerous exciting projects that serve California's communities.

We thank you for your continued support of CIAPM's important work. Sincerely,

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Samuel Assefa Director, Governor's Office of Planning and Research

BACKGROUND

What is Precision Medicine?

Modern technology has opened the floodgates of health-related data. With an abundance of fresh information, scientists, physicians, and other health care providers can understand and respond to people's needs as individuals, rather than seeing them as statistical averages. From one's genetic makeup to one's housing status, working conditions, or recreational activities, information from multiple sources can be as relevant to health as vital signs, and should be incorporated into today's healthcare system. This new, data-driven approach, called precision medicine, has the potential to transform the delivery of health care, disease prevention, and the quality of targeted interventions beyond a one-size-fits-all approach.

For researchers developing cutting–edge strategies, tools, and therapeutics, the field of precision medicine is an opportunity to reexamine underlying causes of poor health. For example, rather than basing diag– noses on symptoms, which can differ from one patient to the next, dis– eases can be more accurately characterized through molecular profiling, artificial intelligence–driven image analysis, and integration of the social determinants of health. Additionally, wearable technology offers new techniques for measuring health, and the walls of the traditional clinic no longer confine a physician's ability to monitor and care for a patient.

We encourage interested readers to visit the CIAPM website, which features an <u>educational primer</u> that introduces new audiences to precision medicine.

About CIAPM

To help guide the emerging field of precision medicine toward health equity goals, in 2014 California established CIAPM, the first-in-thenation state-level precision medicine initiative. CIAPM's primary activities are to: administer precision medicine demonstration projects; provide the legislature with annual reports and expert evaluations for each demonstration project; and develop an inventory of precision medicine assets within California. In addition to these activities, CIAPM also:

- Regularly convenes cross-sector leaders, mostly through the activities of the California Precision Medicine Advisory Council.
- Supports fellow public agencies with new and ongoing projects.
- Delivers presentations to public and expert audiences.
- Maintains an educational website to introduce new audiences to precision medicine.
- Provides science policy training opportunities to California-based graduate students.

Until February 2019 the program was administered in close partnership with the University of California, San Francisco (UCSF). UCSF developed and managed CIAPM's grantmaking and organized precision medicine

Budget Year	Appropriation for Precision Medicine	Demonstration Projects Funded	Demonstration Project Topics
2014-15	\$3M	2	 Pediatric cancer Infectious disease genetics
2016-17	\$10M	6	 Traumatic brain injury Remote heart monitoring Genomic sequencing Mobile mental health Multiple sclerosis Prostate cancer
2017-18	\$10M	3	Cancer health disparities
2018-19	\$30M	4	 Adverse Childhood Experiences (\$10M)
2020	-\$18.2M		
2021-22	\$12.42M	3	Adverse Childhood Experiences

Table 1. Allocation of CIAPM Funds

conferences on behalf of the state. From February 2019 to present, OPR directly manages CIAPM.

To date, the legislature has invested \$65.4 million in support of CIAPM across its seven-year history. The COVID-19 recession in 2020 paused further research activities and reallocated \$18.2 million to support essential needs across state government. In 2021, Governor Gavin Newsom and the legislature made transformative investments in California's youth, including \$12.4 million for CIAPM to expand its four ACEs research projects and fund an additional three teams.

In summary, the CIAPM's total budget to date is \$47.2 million.

DEMONSTRATION PROJECTS

The pursuit of precision medicine is an inherently collaborative effort, requiring access to large data sets and diverse technologies and expertise. One of the major goals of CIAPM is to foster such collaborations by supporting demonstration projects that leverage the state's diverse research capabilities, clinical expertise, and other public and private resources.

With the launch of seven new research demonstration projects in 2021, CIAPM has eighteen projects total in its portfolio.

CIAPM's portfolio of demonstration projects comprises broad collaborative efforts across institutions and sectors. The activities range from discovery-based science to clinical implementation. All aim to enable more precise and individually targeted prevention, diagnosis, and treatment of disease, and to illustrate that precision medicine is making a difference **now**.

With the launch of seven new research demonstration projects in 2021, CIAPM has eighteen projects total in its portfolio: ten currently funded and eight completed. Funds are awarded based on criteria designated in statute, including:

- The potential to reduce health disparities.
- 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 clinical and commercial potential of the project.

- The potential to develop the use of tools, measurements, and data, including publicly generated and available data.
- The prospects for efficient and effective data integration and analysis.
- The resources available for the project outside of the Initiative, including the potential for leveraging nonstate funding.
- The potential to scale and leverage multiple electronic health records systems.

Adverse Childhood Experiences Research

Adverse Childhood Experiences, or ACEs, refer to 10 types of adversity faced by children ages 0–17, categorized into three domains: 1) child abuse (physical, emotional, or sexual); 2) neglect (physical or emotional); and 3) household challenges (having a caregiver with untreated mental illness, a family member with substance dependence or who is incarcerated, parental separation or divorce, or witnessing intimate partner violence). ACEs can trigger toxic stress, which is an excessive and persistent activation of the physiological stress response system during development. Toxic stress can lead to long-term biological changes that contribute to poor health and social challenges throughout the lifespan.

In 2021 CIAPM awarded seven precision medicine research projects to address the health impacts of Adverse Childhood Experiences. All projects are co-led by researchers and community partners and will take place over the next three years. Start dates ranged from summer 2021 to winter 2022.

SELECTION PROCESS

The ACEs Request for Proposals was released on December 3, 2019. The release was supported by the launch of the revamped California Precision Medicine Asset Inventory and informational webinar. The three-stage selection process followed National Institutes of Health standards. Applicants first submitted letters of intent (LOIs), followed by concept proposals, and finally full proposals.

Based on the scientific specialties represented within the 39 sub-

CIAPM ACEs Selection Committe



California Initiative to Advance Precision Medicine



Chair Melissa T. Merrick, PhD



Saida Abdi, PhD, MSW, LICSW



Larissa Avilés-Santa, MD, MPH



Zulfaqir A. Bhutta, PhD, MBBS



Keith Dobson, PhD



Willarda Edwards, MD, MBA



Dylan G. Gee, PhD



Jacob Ham, PhD



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Patricia Kerig, PhD



Liliana J. Lengua, PhD



Lloyd Michener, MD



Charles A. Nelson III, PhD



Kenneth S. Ramos, MD, PhD



Arash Shaban-Nejad, PhD, MPH

mitted LOIs, CIAPM staff recruited a 15-member, out-of-state selection committee, following a solicitation of nominations from the legislature. Experts represented the fields of precision medicine, ACEs, community engagement, big data, trauma, and more.

The ACEs Selection Committee reviewed the concept proposals and invited 12 teams to submit full proposals. In March 2021, the selection committee reviewed the full proposals and recommended seven for funding. Due to limited funds at the time, the four top-scoring awardees were announced on March 30. Governor Newsom and the State Legislature allocated supplemental state funds on July 1, which allowed three additional projects to be funded. CIAPM published a <u>press release</u> on July 9.

ACES RESEARCH PROJECTS

Advancing a Precision Population Health Approach to ACEs to Reduce Health Disparities (2021-2024)

Lead Principal Investigator: Dr. Gary S. Firestein, UC San Diego Partners: American Academy of Pediatrics, California Chapter 3; Chicano Federation; Comité Organizador Latino de City Heights; Family Health Centers of San Diego; Kitchenistas; Olivewood Gardens and Learning Center; Poder Popular; San Diego County Childhood Obesity Initiative; San Diego County Health and Human Services; San Diego County Promotores Coalition; San Diego State University; South Bay Community Services; StreetWyze; Vista Community Clinic; We Support You; YMCA Childcare Resource Service; and others

In collaboration with Latino communities, *promotores*, community health workers, and Family Health Centers of San Diego and other community clinics, UC San Diego researchers are creating a family-based approach to improve individual and community-wide resiliency against the health impacts of stress and obesity. The project team is developing targeted ACEs and toxic stress family-based interventions focused on strengthening the caregiver-child relationship, developing healing-centered prevention, and designing individually tailored therapies. To identify the best ways to provide care, researchers are measuring and comparing biomarkers and environmental influences to the response to therapy. This community-researcher network strengthens communications and improves the design and delivery of preventive and treatment services.

During the first months of the project, the team engaged various underserved communities to understand which interventions might meet their needs most effectively and which measures should be used to evaluate success. All partners, including co-investigators from San Diego County Promotores Coalition, Vista Community Clinics, and Family Health Centers of San Diego (FHC) worked together to:

- Describe current barriers to providing culturally tailored, evidence-based care to families experiencing ACEs and obesity.
- Conduct literature reviews examining different evidence-based programs that could be useful for addressing ACEs and toxic stress, given the unique needs of Latino families.
- Identify likely social, environmental, and behavioral determinants of ACEs and obesity for Latino families.
- Identify current standard practices, best practices, and gaps in care within FHC, with a particular focus on developing a multicomponent intervention that could potentially continue after the project has ended.
- Identify gaps in the safety net system (e.g., food assistance, housing, etc.) that could undermine the care and support families receive at FHC.

The research team established three working groups to tackle the main components of the project: Community, Interventions, and Measurements. Each group includes community members, researchers, clinicians, and key institutional stakeholders. This further demonstrates the desire for inclusive collaboration and proactive community engagement for precision medicine. The team developed and submitted a protocol to the UC San Diego Institutional Review Boards (IRB) for evaluation and plans to launch the clinical trial evaluating the various approaches in 2022.

The Collaborative Approach to Examining Adversity and Building Resilience(CARE) Program (2021-2024)

Lead Principal Investigator: Dr. Neeta Thakur, University of California, San Francisco

Partners: Futures Without Violence; Harvard University; LifeLong Medical; Santa Barbara Neighborhood Clinics; UC Santa Barbara; UCSF Benioff Children's Hospital Oakland; University of Delaware; William Jenkins Health Center

While there has been tremendous growth in knowledge about ACEs and their impact on health across the life course, critical questions persist: Which biological pathways are most affected by ACEs during early childhood and might help identify those children at greatest risk for future poor health and how might child and family resilience be improved across the care continuum to mitigate the negative health effects of ACEs? These gaps in knowledge limit providers' ability to effectively identify children at high risk for future poor health and to intervene before it occurs. This project draws upon clinical intervention, stress-biology science, and community partnership to help understand which children are most vulnerable to the effects of ACEs, what family and community-level factors provide the most buffering protection, and which interventions most improve child and family outcomes.

Through the Collaborative Approach to Examining Adversity and Building Resilience (CARE) Program, the research team is leveraging existing California-based ACEs longitudinal research studies that collected measurements of demographic, health outcome, and biomarker data. Preliminary results have already identified differences in biomarkers of toxic stress and in health outcomes.

The research team is building upon these studies and aligning efforts across Northern and Central California. Applying a precision medicine approach, they are expanding upon the existing Pediatric ACEs and Resiliency Study (PEARLS) cohort by adding a three-year follow-up biomarker testing and analysis point. This will allow them to look for early effects of adversity at a genetic level, with a focus on identifying characteristics that are protective. Researchers will follow up with patients after one year to look for cumulative stress responses across biological systems and examine the predictive effect of baseline childhood adversity at one- and three-year follow-ups.

To examine the behavioral, psychosocial, and biological impact of supportive interventions associated with primary care, the UCSF, UC Santa Barbara, and Santa Barbara Neighborhood Clinics teams have piloted three resilience-promoting, caregiver-child interventions they are applying to this study. Across the three participating sites, the UCSF and Futures Without Violence (FWV) teams will interview front line staff, nurses, clinicians, health system leaders, and administrators. They will also conduct focus groups with caregivers of children aged two to five years to learn more about barriers to access and resources, community experience with screening, and offer feedback on resilience-promoting interventions targeted at child-caregiver relationships and caregiver stress.

The goal is to identify best practices for implementing resilience-promoting interventions across the care continuum and pilot a resilience-promoting toolkit for use in low-resource, primary care settings. Community partners at FWV will lead the development of and pilot the Resilience Toolkit. The UCSF, FWV, and Lifelong Medical teams will work to ensure implementation methods address barriers and fit local conditions. The result will be a toolkit that is ready for use and further study in a larger community-based collaboration.

Pediatric Early Adversity and Related Life Effect Screen (PEARLS)

The Pediatric Early Adversity and Related Life Effect Screen (PEARLS) is a pediatric ACEs screen developed by investigators from UCSF Benioff Children's Hospital Oakland and the UCSF School of Medicine, as a collaborative effort with the Center for Youth Wellness. PEARLS is a 17item screen that assesses ACEs in children from 0 to 12 years of age. With the results obtained from this screen, clinicians can provide practical recommendations on how parents can build resilience in their children.¹

Identifying Social, Molecular, & Immunological Processes for Mitigating Toxic Stress & Enhancing Personalized Resilience (2021-2024) Lead Principal Investigator: Dr. George Slavich, UC Los Angeles Partners: Burnham Benefits; Donna Jackson Nakazawa; Los Angeles County Department of Health Services; Palo Alto University; Stanford University; UC Berkeley; UC Health; UCSF; Yale University

Stress is among the leading causes of disability and death in California, especially if experienced early in life. However, doctors rarely assess stress levels, and it is not clear exactly how stress impacts individuals' health. This project combines the best of stress science and precision medicine to address the health impacts of ACEs.

The overall goal of this project is to harness the power of cutting-edge tools from psychology, immunology, multi-omics, and translational bioinformatics to identify social, molecular, and immunological processes that can be targeted to reduce toxic stress effects and enhance personalized resilience. The UCLA team is creating a network of scientists, academic institutions, healthcare providers, public and private clinics, businesses, spokespeople, and advisors focused on stress, health, and resilience in California, to be called the California Stress, Trauma, & Resilience (CAL STAR) Network. The network has four main objectives:

- Conduct collaborative research at the intersection of stress science and precision medicine.
- Create a Massive Open Online Course on Stress, Health, and Resilience to educate students, professionals, and the public.
- Develop the framework for a clinical research training program to prepare postdoctoral trainees to conduct cutting-edge research on stress, precision medicine, and resilience.
- Engage all major stakeholders, including patients, hospitals, advocacy groups, and insurance companies to understand opportunities and challenges and address privacy, ethical, and acceptability issues, and guide the team's ongoing work and impact.

To determine lifetime stress burden and study the mechanisms linking ACEs and health, the UCLA team will collect the early life and total lifetime stress burden of a representative sample of adults across California. They will also examine how prior life stress exposure and current stress levels are associated with differences in health outcomes for all participants at baseline. The team will then identify associations between stress levels and health by collecting participants' self-reported data and information from their electronic health records. The team will also utilize non-invasive blood microsampling and smart watches to record participants' biological, physical, and mental states.

With these data, the team will develop a Personal Health Dashboard that will show participants their results and deliver personalized feedback. All participants will be trained how to use the Personal Health Dashboard, and the research team will provide up to 100 smartphones with data plans.

The anonymized, aggregated data from all Personal Health Dashboards will be used to build Stress Tracker, a public stress surveillance website. Stress Tracker will display real-time stress summary charts, which could be used to predict population-level risk for stress-related health events (e.g., heart attack, stroke) or to inform hospitals, government officials, policymakers, and the public.

The team will also develop the CAL STAR Intervention, in which each person's most dysregulated biobehavioral process is targeted using a virtual coach. In 2022, the team is starting participant recruitment, data collection, and beta testing of the Stress Tracker. They are also planning the Massive Open Online Course on Stress, Health, and Resilience and the training program to prepare postdoctoral trainees to conduct cutting-edge research on stress, precision medicine, and resilience.

A Multi-Component Intervention to Strengthen Families and Build Youth Resilience (2021-2024)

Lead Principal Investigator: Dr. Ariane Marie–Mitchell, Loma Linda University

Partners: El Sol; Help Me Grow Inland Empire; Inland Empire Health Plan; San Bernardino City Unified School District and Preschool Services; Social Action Community Health System; UCLA; Walden Family Services

Children with ACEs may benefit from interventions that mitigate the negative health effects of prior trauma. The challenge for many communities, especially those that are underserved, is that health and education systems are fragmented and often fail to accommodate families' level of need. The research team led by Dr. Marie-Mitchell brings together pediatricians, community health workers, and parenting educators to improve the delivery of information and resources to a diverse population of families throughout the Inland Empire. Service providers will be trained with an established technique known as Families Implementing Resilience Together (FIRST), which focuses on strengthening families and building youth resilience. During several follow-ups over twelve months, researchers stay in touch with children and families to determine which intervention is most effective at decreasing toxic stress associated with ACEs, improving health outcomes, and reducing health disparities. Research visits will include the measurements of biomarkers of toxic stress and other psychosocial indicators which, in combination with ACE scores, will be used to better understand the biopsychosocial changes that lead to poor health.

In 2021, FIRST was rolled out as a collaborative effort between community health workers (CHWs), the Nurturing Parent Program (NPP), and pediatric and family medicine resident clinics at the Social Action Community Health System (SACHS) in San Bernardino. The research team trained seventy-five service providers from clinical, community health, and educational settings. The training was refined over time using feedback from participants.

Clinicians referred families to CHWs and the NPP. The research team established a database to collect demographics, ACE scores, and other



Community health workers met with families throughout the pandemic, sometimes finding creative ways to get much-needed concrete resources and psychosocial support to families. All photos shared with permission.

health information about the referred patients. The researchers continue to track referrals to CHWs and the NPP. They also keep primary physicians informed about their referred patients, and encourage them to apply lessons from their FIRST training. Of the study's youth participants so far, 40% have a total ACE score of four or more, which is more than double the state and national average. The most common ACEs in the cohort are parent mental health issues and parental divorce/separation.

The research team developed information materials in Spanish and English about ACEs and resilience, stress management, and healthy relationships. They distributed materials to providers, CHWs, and parenting educators to share with patients and families. Family Voices, the participant-led advisory board, convened two meetings, and the research team adopted the board's recommendations on language and framing for the parenting education materials and program strategy.

In 2022, the team will continue to complete and expand the collaborations related to clinical interventions, begin recruitment for research evaluations, and obtain IT support to plan and develop a secure information system that will support and sustain a biopsychosocial dataset for the community.

Scalable Measurement and Clinical Deployment of Mitochondrial Biomarkers of Toxic Stress (2021–2024)

Lead Principal Investigator: Dr. Pat Levitt, Children's Hospital Los Angeles Partners: Fiesta Educativa, Inc.; Kaiser Permanente of Southern California; Karsh Family Social Service Center; Para Los Niños; St. Anne's; University of Southern California; Ventura County Medical Center

The very best health outcomes can be achieved by identifying infants at greatest risk for ACEs and toxic stress and intervening early to reduce the chronic stress response. This project is improving early screening by combining a questionnaire with innovative laboratory tests that detect disruptions in metabolic health, a key indicator of toxic stress. This project is a collaboration between experts in precision medicine, laboratory test development, child development, stress-related health risks, and health equity improvement. The project is bringing a greater understanding of infant-caregiver well-being, and uses screening to close the equity gap in access to quality behavioral health programs.

ACEs can cause body and brain disturbances associated with poor health and educational outcomes across a person's lifespan. Developmental delays are often the first detectable consequence of ACEs. However in California nearly 40% of children are not screened with any developmental tool. There are significant racial/ethnic disparities among those who are screened. For some infants and toddlers, ACE-associated health conditions may not be caught during developmental or other clinical screens, making it difficult to fully understand and respond to the impact of ACEs.

The Children's Hospital Los Angeles (CHLA) research program is addressing these challenges by improving the power of toxic stress screening with a biomarker that reliably reveals early life stress: mitochondrial allostatic load. CHLA and its partners, including Kaiser Permanente of Southern California and Ventura County Medical Center, are recruiting and retaining 300 mother-infant pairs, seen at six and twelve months to:

• Measure maternal health and well-being and infant development with currently available evaluation tools.

Mitochondrial Allostatic Load

Mitochondria are the energy generators in cells. Long- and short-term stress can change the structure and function of mitochondria, and cause damage to a mitochondria's DNA. These stress-induced changes, also known as the Mitochondrial Allostatic Load, can interfere with the ability of the body to respond appropriately to stress, which may contribute to disease.²

- Determine a child's ACE score with the PEARLS questionnaire.
- Monitor attention circuits using eye movement.
- Collect physical samples (via cheek swab) to measure mitochondrial allostatic load.

The research team has incorporated standard operating procedures to refer participant families with high ACE scores, limited resources, or maternal depression to intervention services. Trained community navigators and a hospital-wide behavioral health program with expertise in family-centered mental health provide referrals.

The combined strategy brings precision to identifying infants and toddlers who are both at greatest risk for developmental harm from toxic stress and who are less likely to have been identified by screening questionnaires. A multi-pronged approach provides opportunities for early detection of stress in infants, which means interventions can be more scalable, affordable, and ultimately most effective. The immediate impact for the study participants is the connection with family-centered, evidence-based infant mental health services at CHLA. The lessons learned from this project's approach of combining biological measures with existing tools will inform future efforts to integrate precision medicine techniques into current clinical practice.





Take vital signs Tomar signos vitales

Cheek swab sample (required)

Muestra de mejilla (requerida)



Mom-baby interaction Interacción madre-bebé

Mother Madre



Blood sample (optional) Muestra de sangre (opcional)



Use of samples for future research (optional)

futuro (opcional)

El uso de las

Eye tracking

Rastreo de ojo

es en el

Questionnaires . Cuestionarios

Confidencialidad

All health information and immigration status will be kept confidential. In the rare instance of suspected child abuse or neglect, this information will need to be shared.

Confidentiality

Se mantendrá confidencial toda la información de salud y estatus inmigratorio. En el caso poco frecuente de sospecho de abuso infantil o negligencia, será necesario compartir esta información.

Informational flier in English and Spanish developed by the CHLA team

Systems-based, Multidisciplinary Assessment of Adversity and Toxic Stress for Individualized Care (The SYSTEMAATIC Project) (2022-2025) Lead Principal Investigator: Dr. Sayantani Sindher, Stanford University Partners: Center for Youth Wellness/Safe and Sound; Central Valley Community Foundation; Every Neighborhood Partnership in Fresno; Sean N. Parker Center for Allergy & Asthma; South San Francisco Clinic; Stanford Precision Health for Ethnic and Racial Equity; The Primary School in Palo Alto

Currently, the impacts of ACEs and toxic stress are detected by symptoms like depression or anxiety rather than the underlying root changes to a person's neurologic, endocrine, metabolic, and immune system functions. While there is a large body of scientific literature demonstrating the link between ACEs, toxic stress, and poor health outcomes, there is no widely agreed-upon strategy to diagnose toxic stress nor evaluate intervention effectiveness at improving physiologic disruptions. Current assessment tools and interventions for ACEs and toxic stress are rarely integrated across mental health, physical health, protective factors, and community experiences. The SYSTEMAATIC Project will use machine learning and artificial intelligence to create a clinical diagnostic tool for toxic stress by combining multiple disciplines for an approach that addresses organ systems as a whole, rather than a symptoms-based approach. The results will be earlier detection and more targeted clinical recommendations to address the root causes of toxic stress.

The goal of the SYSTEMAATIC Project is to use precision medicine approaches to:

- Develop a multidisciplinary Toxic Stress Assessment Profile that identifies disruptions in the neurological, endocrine, and immune pathways under stress.
- Pilot the feasibility, adaptability, and validity of the Toxic Stress Assessment Profile and the impact of interventions within partner clinics and organizations. Researchers will also speak with focus groups to learn community-specific barriers and enablers in the context of diagnostic strategies and feasible interventions.

This innovative approach will incorporate into the Toxic Stress Assessment Profile machine learning techniques and scoring algorithms to improve validity, account for prior experiences including discrimination and racial bias, address individual vulnerabilities, and identify coping, protective, and supportive factors.

The goal will be to create a Toxic Stress Assessment Profile that can be implemented in clinical practice. Individualized intervention recommendations may include methods for improving sensory integration (massage, movement, music), self-regulation (breathing techniques, Eye Movement Desensitization and Reprocessing, neurofeedback), relational health (parent-child, family, or couples therapy), and cognitive function (cognitive behavioral therapy). It will also recommend general strategies to counter toxic stress physiology and improve health, such as sleep, exercise, mindfulness, access to nature, and nutrition. Pre- and post-testing of the assessment profile will provide opportunities to evaluate the effects of the interventions and the integrated, multidisciplinary approach to care.

The team will develop a series of tests leveraging the expertise and past research of their scientific advisory council and academic collaborators. They will gather participants' history of adversity, perceived stress, attachment and relationship security, and medical history. Additional data on 100 individuals will be collected via blood sampling, wearable devices, and neuroimaging.

For participant engagement and recruitment, the team will turn to the expertise of partners at the Center for Youth Wellness (CYW)/Safe and Sound, and other partnerships. The CYW will organize regional

Eye Movement Desensitization and Reprocessing

Eye Movement Desensitization and Reprocessing, or EMDR, was developed for the treatment of posttraumatic stress disorder. EMDR is a structured therapy that encourages the patient to briefly focus on a traumatic memory while simultaneously moving their eyes back and forth (or use other methods such as tones, vibrations, or taps), which is associated with a reduction in the vividness and emotion associated with the traumatic memories.³ Community Advisory Councils (CAC)/Health Navigator Teams that will be involved with coordinating, recruiting, and advising on the best practices related to research with communities. Prioritizing community input, the CYW and CACs will provide input on recruitment and assessment strategies, developing protocols, and community resources for interventions. The researchers will recruit participants through clinics and neighborhood institutions. This project will commence in early 2022.

Using Precision Medicine to Tackle Impacts of Adverse and Unpredictable Experiences on Children's Neurodevelopment: The SoCal Kids Study (2021– 2024)

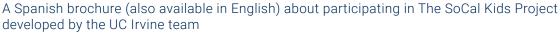
Lead Principal Investigator: Dr. Tallie Z. Baram, University of California, Irvine

Partners: Chapman University; Children's Hospital of Orange County Primary Care Network; Children's Hospital of Orange County (CHOC); CHOC Health Center Garden Grove; Clínica CHOC Para Niños; First 5 Orange County; Illumina, Inc.; Illumination Foundation; Orange County Health Care Agency; Santa Ana Boys & Girls Club; Sea View Pediatrics; the Simms/Mann Family Foundation; Syntropy Technologies, LLC

The burden of ACEs is not equally distributed, with greater risk of exposure among low socioeconomic and racial/ethnic minority communities. This project has two goals. First, it seeks to better understand the role of a novel ACE—unpredictability of caretakers and environment—in influencing neurodevelopment. Second, it aims to discover a marker that predicts a child's intrinsic level of vulnerability or resilience to all ACEs. This information would help providers quickly determine which children with ACEs are most at risk of poor health outcomes so that interventions can be delivered where needed most urgently. The researchers are screening 100,000 children across Orange County and analyzing the findings through lenses of neuroscience, community engagement, epigenetics, data science, brain development, emotional health, health disparities, and database design and sharing.

In 2021, the team's primary goals were to obtain approval to conduct the study from the relevant IRB, hire staff, finalize protocols, and





begin screening. The team received IRB approval and hired new staff at Children's Hospital of Orange County (CHOC) and Chapman University. Providers and clinic staff from five primary pediatric clinics gathered to discuss implementation of the Questionnaire of Unpredictability in Childhood (QUIC) screen and the PEARLS tool. Screening for unpredictability (QUIC) and ACEs (PEARLS) is now occurring at every well-child visit at the CHOC primary care clinics.

The investigators overseeing the biomarker study met weekly to discuss how to optimize collection, handling, processing, and analyses of DNA samples. Findings from samples of a pilot cohort (external to the project) demonstrated associations between exposures to unpredictability, ACEs, and epigenetic profiles in the first year of life. In partnership

Community Engagement Studios

The Meharry-Vanderbilt Community-Engaged Research Core developed Community Engagement Studios (CES) in 2009 as a structured approach for community engagement, and a process by which researchers obtain community and patient input to improve research design, implementation, and dissemination. CES relies on experienced faculty and staff to work with the research team, identify community stakeholders, and facilitate interactions and communications, minimizing investigator burden and maximizing efficiency.⁴

with the CHOC clinics, the research team initiated DNA sample collection and recruitment of newborn infants.

The SoCal Kids Community Advisory Board (CAB) was established to conduct outreach to regional stakeholders including physicians, psychologists, health care advocates, non-profit leadership, and Orange County Health Care Agency representatives that address health equity. CAB members provide guidance to the researchers and anchor the study within regional priorities and needs.

Building on the expansive community engagement plan, the researchers are conducting Community Engagement Studios (CES) to obtain community and parent input to improve research design, implementation, and dissemination. The UC Irvine Institute for Clinical and Translational Sciences helped develop informational materials and study approaches for the CES. The CES plans to convene CHOC pediatricians, CHOC pediatric clinic staff, English-speaking parents, and Spanish-speaking parents in 2022 for data collection.

Cancer Disparities Research Projects

Three precision medicine demonstration projects addressing cancer disparities in California's Hispanic and Latinx communities launched in late 2019. All projects were initially slated to last 36 months, but inevitable delays caused by COVID-19 necessitated no-cost extensions for each project; they will now conclude in 2023. All three projects are co-hosted by an academic research institution and at least one community clinic or community-based organization that provides patient services for populations that suffer from cancer health disparities.

A highlight of 2021 was a mini symposium in which the three cancer disparities research teams met virtually to network, provide updates on their progress, and discuss common themes and challenges.

Addressing Disparities in Breast Cancer in Latinas: A multi-tiered approach (2019-2023)

Lead Principal Investigator: Dr. Elad Ziv, UC San Francisco Partners: Bay Area Cancer Connections; City of Hope; Pomona Health; Stanford University; The Latino Cancer Institute; UC Davis; Vision y Compromiso; Zuckerberg SF General Hospital

Breast cancer is the leading cause of cancer death among Latinas in California. Understanding hereditary cancer risk can help improve screening and detection by identifying women who should start screening at an earlier age and be screened more often with more accurate methods. 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.

Another project goal was to implement a bilingual education program on hereditary genetics, risk, and genetic testing. As a first step the team recruited and trained 24 *promotores*, or community health workers, to talk to community members about genetics and heritability, cancer and risk, and the importance of screening. By the end of 2021 the trained *promotores* had held educational sessions with over 800 Latina women. Almost 700 of those women completed family health histories designed to assess their familial risk for developing breast cancer; of those over 40 met the criteria to be referred to genetic counselors, and most of these women have started to work with health navigators to set up counseling appointments.

In 2021, Dr. Ziv and his team also made progress toward their goal of improving hereditary breast cancer risk assessment in Latina women

by sequencing the DNA of breast cancer patients and controls, and then comparing them to find out if certain variations in specific genes are associated with an increased risk of developing breast cancer. The researchers used existing datasets to analyze more than 8,000 samples and continued to add to the sample size by incorporating data from additional sources. These sources included the Hispanic Community Health Study/ Study of Latinos, the Women Informed to Screen Depending On Measures of risk (WISDOM) trial, and UC Davis Medical Center. The team also enrolled new study participants compiled from the California Cancer Registry, as well as patients who received treatment at City of Hope, UCSF Breast Care Center, and Zuckerberg San Francisco General Hospital. By the end of 2021, the team collected samples from 450 women.

Dr. Ziv and his team collaborated with the genomic sequencing company Foundation Medicine to determine if certain mutations that arise during the process of cancer development, known as somatic mutations, are found more commonly among women of certain ancestry. From a database containing sequences from 30,000 breast tumors, there were about 2,000 samples from women of African ancestry, 2,000 from women with East Asian ancestry, and about 2,000 from women with mixed indigenous American ancestry. Dr. Ziv and his team successfully identified the genes that are most and least likely to be mutated in women with specific ancestral backgrounds.

Furthermore, the team is also working to determine if certain genes that are not yet known to be important in cancer may be mutated among Latina women. To do this they are sequencing all the genes in breast tumors from Latina patients, a process known as whole exome sequencing. By the end of 2021, the team had collected 187 matched tumor and blood samples, as well as treatment data. The team also sequenced 142 tumors, with many more samples in the queue.

In 2022, Dr. Ziv and the research team plan to continue to recruit participants, and collect and analyze DNA from patients and tumors. The team will compare the sequencing data to patients' treatment histories and clinical outcomes like metastasis and mortality to further determine the relationship between DNA and disease. Integrated Machine-Learning Platform to Inform Precision Therapy in Underrepresented Triple-Negative Breast Cancer Patients (2019-2023) 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; University of Guadalajara

Despite recent progress in the development of new cancer medications, Triple-Negative Breast Cancers (TNBCs) remain largely untreatable. TNBC tumors grow faster and are more likely to metastasize than other breast cancers, leading to higher mortality rates. TNBCs are prevalent among Hispanic women, representing a major health disparity in cancer diagnosis and treatment. This project brings together researchers, clinicians, patients, and community advocates, joining forces as Project CELSUS to apply precision medicine genomic profiling to identify new treatments and implement a more precise and rational system to match TNBC tumors with existing cancer therapies. The project is named after Aulus Cornelius Celsus, an early pioneer of evidenced-based medicine in the first century.

In 2021, Drs. Kim and Tamayo continued to lead Project CELSUS toward the goal of using patient and tumor data to help oncologists recommend precision treatment for their TNBC patients.

In order to assess the lived experiences of Latina women with breast cancer the research team, in partnership with the Institute for Public Health at San Diego State University, completed 48 interviews with physicians, patients, patient navigators, social workers, caregivers, research staff, support group facilitators, and other stakeholders. Key findings included:

 The diagnosis of breast cancer was particularly overwhelming for those who had limited English proficiency and lower levels of health literacy. In-person certified medical interpreters and Spanish language materials are critical to their care but are often unavailable.

- Many patients did not know or understand key components of their care, including what type of breast cancer they had and what type of treatment they received.
- Some Hispanic patients felt that their concerns were dismissed or not fully heard. Many experienced long delays in receiving an appropriate diagnosis and felt that their symptoms had been minimized.
- Support groups for Hispanic women played a key role in education and navigation.
- Many Hispanic women faced economic barriers to timely and consistent treatment.
- Patients were commonly mistrustful of the medical system.
- It was challenging for some providers to discuss the role of racism in the disparities experienced by Hispanic patients. However, when asked directly many providers acknowledged racism within the medical system. Patients and providers agreed that racism needs to be acknowledged and openly discussed.
- Hispanic women were less likely to participate in clinical trials due to geographic and financial barriers, not being offered the opportunity, fears about experimentation, and fears about immigration status being recorded.
- Many providers viewed "equity" in terms of what treatment is provided, i.e., every woman with a similar breast cancer profile receives the same chemotherapy regimen, and so they believed that Hispanic women with breast cancer had the same experience as other women.
- Providers often felt helpless to address social determinants of health. They know these impact patient outcomes, but do not have the time or the resources to address them.

The team also used several established datasets to compile clinical data about breast tumors. They are now adding data from patient samples collected both before and after treatment to learn why some tumors become resistant to treatment. Once these data are fully generated and incorporated the team will share the aggregated data compendium with stakeholders and the public.

The combined data strengthened their computational model that classifies cancer cells according to their molecular signatures, or cellular states. The research team compared cellular states of samples from Hispanic patients with those of non–Hispanic patients to test whether differences in cellular states might be partially responsible for the dis– parity in TNBC diagnoses. Their initial findings suggest that there may be some interesting differences in the types of TNBCs prevalent in Hispanic patients, but warrant further study.

To identify what drugs are most effective at fighting cancer cells in a particular state, the project team is treating cells in different states with drugs, alone and in combination. Drug and cellular state combinations that look promising are tested using Hispanic patients' cells that have been cultured in three dimensions to mimic the cellular architecture of a tumor, which is a more accurate model than was used in the initial screen. Analysis of these three-dimensional organoids will eventually help further elucidate the biology of distinct cellular states.

Drs. Kim and Tamayo also successfully established the infrastructure and protocols to obtain tissue samples from patients treated at El Centro Medical Center. This collaboration has so far yielded eleven biospecimens from Hispanic TNBC patients. These samples, along with others from patients at UC San Diego, will ultimately be used to generate profiles of cellular states that provide new information about TNBC tumors.

In 2022, Drs. Kim and Tamayo plan to launch an animal experimentation model and continue studying tumors from TNBC patients.

Organoids

Organoids are simplified, miniature organs that scientists make in laboratories to study the structure and activity of organs, including tumors. Organoids begin as a few cells that then grow and self-organize in three-dimensional tissue cultures. This better matches the biological environment than if the cells were grown in a single layer. Researchers can use tumor organoids to test the efficacy of drugs on different types of cancer.⁵

Reducing Cancer Disparities Through Innovative Community-Academic Partnership to Advance Access and Delivery of Precision Medicine in Monterey County (2019-2023)

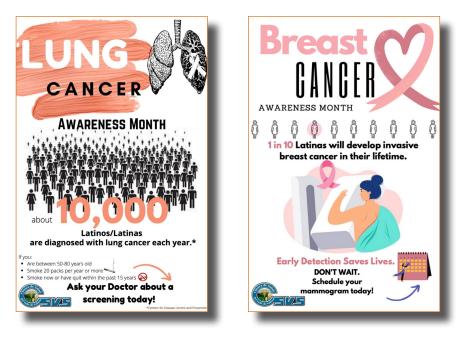
Lead Principal Investigator: Dr. Manali Patel, Stanford University Partners: Cancer Patients Alliance; Clinica de Salud del Valle de Salinas; Community Hospital of Monterrey Peninsula; Natividad Medical Center; Pacific Cancer Care; The Latino Cancer Institute

Low-income and minority populations experience disproportionately high rates of cancer incidence and mortality, lower rates of evidence-based cancer care, and increased rates of untreated symptoms compared with non-minority patients. The objective of this project is to develop, implement, and evaluate a CHW or Community Health Advocate (CHA) approach that increases access to precision medicine at every stage of cancer care.

In 2021 Dr. Patel and her team built on their previous work in which they established a CAB and conducted several focus groups and interviews with key stakeholders in cancer care including community members, patients, health system executives, and healthcare providers. Using the feedback obtained in those interviews Dr. Patel and her team developed projects at two sites: Clinica de Salud del Valle de Salinas (CSVS), a Federally Qualified Health Center that provides comprehensive care with an emphasis on farm worker families and the agricultural community, and Pacific Cancer Care (PCC), the largest oncology and hematology community practice on the Central Coast in California.

Clinica de Salud del Valle Salinas

At CSVS the team used the findings from the interviews and focus groups to design a CHA-facilitated cancer prevention and screening program. In the experimental group, CHAs engage patients about tumor testing and the risks and benefits of precision medicine and targeted therapies, explain clinical trials, serve as patient navigators, introduce and assist patients with advance directives and other palliative care topics, take family health histories, and educate community members



Informational materials developed by the team at Clinica de Salud del Valle Salinas

about cancer prevention, screening, and treatment, with a focus on risk factors for Latinx communities. The control group receives the current standard of care without the CHA interventions.

The CHAs and research team created educational posters and flyers for patients about several types of cancers to raise awareness of risk and preventative measures. The posters were placed in exam rooms at CSVS clinic sites; the flyers were placed in CSVS waiting rooms and shared at community outreach events.

In 2021 the researchers also developed a HIPAA-compliant database to store the information they collect during the study.

Pacific Cancer Care

Dr. Patel and her team are also using the feedback from the focus groups and interviews to evaluate the effectiveness and acceptability of intervention activities to improve cancer patients' engagement, understanding of diagnosis and treatment options, knowledge of precision medicine, and access to advance care planning. These interventions are different than those offered at CSVS in that they are specifically designed for patients who have already been diagnosed with cancer, as opposed to the broader community at CSVS where prevention is emphasized. In the experimental group CHWs are discussing with participants their goals of care and the basics of treatment, explaining how precision targeted therapies work and assisting them with completing advance directives and identifying surrogate decisionmakers. The CHWs are also screening for and identifying complications from social determinants of health and providing wrap-around services to overcome these challenges. These services include:

- Provision of translation for clinic visits.
- Assistance with insurance questions, access, and coverage.
- Help with registering for state and federal programs, such as CalFresh, for participants who have food insecurity.
- Referrals to Spanish-language support groups.
- Provision of care navigation between healthcare organizations (e.g., county health departments and PCC).

The team developed recruitment materials including a brochure in plain language (English and Spanish) that contains information about the study, the risks and benefits of participating, the estimated time commitment, and how to enroll. They also produced an animated twominute recruitment video to introduce the study to potential research participants. In addition to participant-facing materials, the team created postcards with the study's purpose, inclusion criteria, and referral phone number, and provided the postcards to physicians at PCC.

This study has already screened over 400 participants and enrolled over 55 participants from low-income households who self-identify as Latinx, are mostly Spanish-speaking, and have less than a high school degree. The team has conducted a series of interviews with all stakeholders participating in the study including participants, their caregivers and/ or family members, and staff and clinicians at PCC to assess the perceived effectiveness of the study's protocols and procedures.

Throughout their work Dr. Patel and her team continue to engage their CAB. The CAB has been instrumental in sharing with the community relevant resources, events, and job openings. Board members were also invited to attend the Stanford Office of Community Engagement's series of monthly COVID-19 virtual town halls to learn about important resources and recommendations that could be distributed to their own networks. A new CAB partner added in 2021, The Food Bank for Monterey County, is assisting with the team's newly funded grant to train CHWs to screen for and mitigate food insecurity.

In 2022 Dr. Patel and the research team will launch the prevention and screening project at CSVS and test the program's effectiveness on research participants' understanding of cancer risk; their health literacy; their knowledge, skill, and confidence for managing their health and health care; and their diet and exercise habits. They will also continue the randomized controlled trial at PCC.

Former Projects Overview

Eight of the 18 collaborative research projects funded by CIAPM since its establishment in 2015 have concluded. CIAPM worked with outside evaluators on a formal process to examine project milestones and outcomes, culminating in a report presented to the legislature in 2019. Recognizing that research builds on preceding work and that not all longrange results can be seen within a defined project period, the Initiative stays up to date with its former teams' new discoveries that may have been based on work supported by CIAPM. It is only through this continued communication that we can measure CIAPM's full impact. Further details about the first eight projects are listed in Appendix B.

Publications, Presentations, and Press

To date, CIAPM-funded research has generated 123 publications (57 in 2021), 150 presentations (52 in 2021), 61 press events (29 in 2021) or articles, and 5 patents or patent extensions. To view all publications, presentations, and articles from 2021, see Appendix A. Previous works are detailed in the 2019 evaluation report and the 2020 Annual Report.

IMPACT ASSESSMENT

CIAPM was launched in 2014 to support California's precision medicine community and accelerate the science and application of precision medicine in California.

To date, the initiative has funded 18 community-based research projects, and continues to support cross-sector collaborations and build public resources.

All of these activities share a common goal: to encourage a more equitable and patient-centered precision medicine ecosystem. Summarized below are the state funds, matching funds and leveraged resources, and institutions engaged by CIAPM-funded research. Data collection has been the first step of CIAPM's efforts to assess the full impact of the program which will be published as a dynamic webpage in 2022, released in phases, and then regularly updated as projects are funded and completed.

Current Projects

Advancing a Precision Population Health Approach to ACEs to Reduce Health Disparities (2021-2024)

Lead Institution: University of California, San Diego

Partner Institutions: American Academy of Pediatrics, California Chapter 3; Chicano Federation; Comité Organizador Latino de City Heights; Family Health Centers of San Diego; Kitchenistas; Olivewood Gardens and Learning Center; Poder Popular; San Diego County Childhood Obesity Initiative; San Diego County Health and Human Services; San Diego County Promotores Coalition; San Diego State University; South Bay Community Services; StreetWyze; Vista Community Clinic; We Support You; YMCA Childcare Resource Service; and others

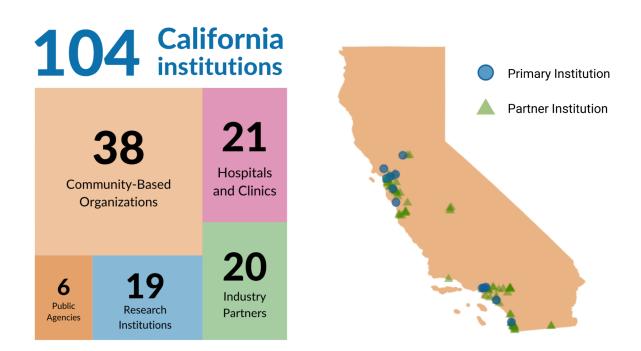
State Funds: \$2,999,749 Non-state Funds: \$1,000,000 Total Funds: \$3,999,749

The Collaborative Approach to Examining Adversity and Building Resilience (CARE) Program (2021-2024)

Lead Institution: University of California, San Francisco

Partner Institutions: Futures Without Violence; Harvard University; LifeLong Medical; Santa Barbara Neighborhood Clinics; UC Santa Barbara; UCSF Benioff Children's Hospital Oakland; University of Delaware; William Jenkins Health Center

State Funds: \$2,988,695 Non-state Funds: \$1,480,000 Total Funds: \$4,468,695



Current Projects

Identifying Social, Molecular, & Immunological Processes for Mitigating Toxic Stress & Enhancing Personalized Resilience (2021-2024)

Lead Institution: University of California, Los Angeles

Partner Institutions: Burnham Benefits; Donna Jackson Nakazawa; Los Angeles County Department of Health Services; Palo Alto University; Stanford University; UC Berkeley; UC Health; UCSF; Yale University

State Funds: \$3,000,000 Non-state Funds: \$2,823,292 **Total Funds: \$5,823,292**

A Multi-Component Intervention to Strengthen Families and Build Youth Resilience (2021-2024)

Lead Institution: Loma Linda University

Partner Institutions: El Sol; Help Me Grow Inland Empire; Inland Empire Health Plan; San Bernardino City Unified School District and Preschool Services; Social Action Community Health System; UCLA; Walden Family Services

State Funds: \$2,852,430 Non-state Funds: \$2,050,000 **Total Funds: \$4,902,430**

Scalable Measurement and Clinical Deployment of Mitochondrial Biomarkers of Toxic Stress (2021-2024)

Lead Institution: Children's Hospital Los Angeles

Partner Institutions: Fiesta Educativa, Inc.; Kaiser Permanente of Southern California; Para Los Niños; St. Anne's; Karsh Family Social Service Center; University of Southern California; Ventura County Medical Center

State Funds: \$2,462,755 Non-state Funds: \$2,400,000 Total Funds: \$4,862,755

Systems-based, Multidisciplinary Assessment of Adversity and Toxic Stress for Individualized Care (The SYSTEMAATIC Project) (2022-2025)

Lead Institution: Stanford University

Partner Institutions: Center for Youth Wellness/Safe and Sound; Central Valley Community Foundation; Every Neighborhood Partnership in Fresno; Sean N. Parker Center for Allergy & Asthma; South San Francisco Clinic; Stanford Precision Health for Ethnic and Racial Equity; The Primary School in Palo Alto

State Funds: \$2,970,081 Non-state Funds: \$1,000,000 **Total Funds: \$3,970,081**

Current Projects

Using Precision Medicine to Tackle Impacts of Adverse and Unpredictable Experiences on Children's Neurodevelopment: The SoCal Kids Study (2021-2024)

Lead Institution: University of California, Irvine

Partner Institutions: CHOC Health Center Garden Grove; Chapman University; Children's Hospital of Orange County Primary Care Network; Children's Hospital of Orange County; Clínica CHOC Para Niños; First 5 Orange County; Illumina, Inc.; Illumination Foundation; Orange County Health Care Agency; Santa Ana Boys & Girls Club; Sea View Pediatrics; the Simms/Mann Family Foundation; Syntropy Technologies, LLC

State Funds: \$2,899,783 Non-state Funds: \$3,433,352 Total Funds: \$6,333,135

Addressing Disparities in Breast Cancer in Latinas: A multi-tiered approach (2019-2023)

Lead Institution: University of California, San Francisco

Partner Institutions: Bay Area Cancer Connections; City of Hope; Pomona Health; Stanford University; The Latino Cancer Institute; UC Davis; Vision y Compromiso; Zuckerberg SF General Hospital

State Funds: \$3,000,000 Non-state Funds: \$900,000 Total Funds: \$3,900,00

Integrated Machine–Learning Platform to Inform Precision Therapy in Underrepresented Triple–Negative Breast Cancer Patients (2019–2023)

Lead Institution: University of California, San Diego

Partner Institutions: 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; University of Guadalajara

State Funds: \$3,000,000 Non-state Funds: \$120,000 Total Funds: \$3,120,000

Reducing Cancer Disparities Through Innovative Community-Academic Partnerships (2019-2023)

Lead Institution: Stanford University

Partner Institutions: Cancer Patients Alliance; Clinica de Salud del Valle de Salinas; Community Hospital of Monterrey Peninsula; The Latino Cancer Institute; Natividad Medical Center; Pacific Cancer Care

State Funds: \$3,000,000 Non-state Funds: \$495,000 Total Funds: \$3,495,000

Completed Projects

Artificial Intelligence for Imaging of Neurological Emergencies (2017-2018)

Lead Institution: University of California, San Francisco

Partner Institutions: 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; UC Berkeley; Zuckerberg San Francisco General Hospital and Trauma Center

State Funds: \$1,200,000 Non-state Funds: \$300,000 Total Funds: \$1,500,000

California Kids Cancer Comparison (2015-2018)

Lead Institution: University of California, Santa Cruz

Partner Institutions: Alex's Lemonade Stand Foundation; Amazon Services, Inc.; Azure, Inc.; Children's Hospital Orange County; Children's Mercy Hospital in Kansas City; DNAnexus, Inc.; Jacob's Heart; Key for a Cure; Kids v Cancer; Live for Others Foundation; Microsoft, Inc.; NuMedii, Inc.; Pacific Pediatric Neuro-Oncology Consortium; Philanthropist George Kraw; Sanford University of South Dakota Medical Center; Seven Bridges Genomics, Inc.; Stanford University Hospital; St. Baldrick's Foundation; Team Finn; Team G Foundation; UC San Francisco; University of British Columbia Cancer Agency; University of Michigan; University of Pittsburg; Unravel Pediatric Cancer

State Funds: \$1,690,533 Non-state Funds: \$4,198,500 Total Funds: \$5,889,033

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

Lead Institution: Cedars-Sinai Medical Center

Partner Institutions: Agilent, Inc.; AliveCor, Inc.; Beckman Coulter, Inc.; DocuSign, Inc.; Fitabase, Inc.; Fitbit, Inc.; HealthLoop, Inc.; Neoteryx, Inc.; SCIEX, Inc.; Tasso, Inc.; Thermo Fisher Scientific, Inc.; UCLA

State Funds: \$1,423,261 Non-state Funds: \$704,431 **Total Funds: \$2,127,692**

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

Lead Institution: University of California, Irvine

Partner Institutions: Ambry Genetics Corporation; Cedars-Sinai Medical Center; GenomeDx Biosciences, Inc.; Vanderbilt University; Veterans Affairs Los Angeles; UCLA Medical Center

State Funds: \$1,446,205 Non-state Funds: \$4,126,031 **Total Funds: \$5,572,236**

Completed Projects

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

Lead Institution: Children's Hospital Oakland Research Institute Partner Institutions: GenomeOne, Inc.; Human Longevity, Inc.; Illumina, Inc.; UC Berkeley; UC San Francisco; UCSF Benioff Children's Hospital Oakland

State Funds: \$1,200,000 Non-state Funds: \$350,000 Total Funds: \$1,550,000

Personal Mobile and Contextual Precision Health (2017-2018)

Lead Institution: University of California, Davis Partner Institutions: *Overlap Health, Inc.; UC Berkeley; UC San Francisco* State Funds: \$1,200,000 Non-state Funds: \$440,000 **Total Funds: \$1,640,000**

Precision Diagnosis of Acute Infectious Diseases (2015-2018)

Lead Institution: University of California, San Francisco

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

State Funds: \$1,700,000 Non-state Funds: \$8,975,000 Total Funds: \$10,675,000

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

Lead Institution: Sutter Health

Partner Institutions: National Multiple Sclerosis Society; Palo Alto Medical Foundation; Plan Language Health, Inc.; Roche/Genentech, Inc.; Sutter's Jordan Research and Education Institute; Sutter Philanthropy; UC San Francisco

State Funds: \$1,200,000 Non-state Funds: \$805,000 Total Funds: \$2,005,000

PROGRAM HIGHLIGHTS

Pandemic Response

GOVERNOR'S COVID-19 TESTING TASK FORCE

At the onset of the pandemic, the California Department of Public Health (CDPH) enlisted leaders from government, industry, and communities to stand up a COVID-19 Testing Task Force (TTF). Since April 2020, four staff members of CIAPM have served on the task force. The TTF's mission is to reduce transmission of COVID-19 by addressing supply chain challenges, promoting test accessibility, evaluating test efficacy, and tracking the spread and mutations of the novel coronavirus. The TTF website captures the primary goal of the task force as pursuing "the right test, for the right situation, at the right time," reflecting the principles of precision medicine.

In 2021, CIAPM Co-Director Dr. McCall and Policy Fellow Hyunsoo Gloria Kim contributed to the Testing Innovations Workstream, which focused on analyzing new diagnostic technologies. Led by Dr. Sharon Messenger of CDPH, frequent meetings gathered experts from academia, health care, local public health departments, and state government to address topics related to novel techniques, logistical barriers, supply concerns, and future needs. Among other roles, CIAPM staff generated regular literature reviews of research studies, reports, and news articles, coordinated meetings, and provided synopses of relevant national and international meetings and webinars.

CIAPM staff answered numerous invitations to speak to public and expert audiences about the state's pandemic response, and how a precision medicine lens could be used to better understand the impacts of and public health responses to the spread of the virus. The interest in innovative approaches demonstrated why precision medicine is so important to meeting the state's needs, especially during public health crises.

CIAPM PUBLIC PRESENTATIONS ON COVID-19

- Stanford University COVID-19 Community Town Hall: Vaccine Readiness On January 21, Dr. McCall joined State Epidemiologist Dr. Erica Pan for a panel on vaccine readiness for a general audience, with live interpretation in Spanish.
- Precision Medicine World Conference: 21st Century Precision Medicine in the Age of COVID-19 On January 27, Dr. McCall was a member of a panel titled "Tackling the Mental Health Crisis in the Wake of COVID-19," during which she discussed with academic and industry experts the challenges of balancing youth mental health with public safety in schools and the community.
- Launch of the California Council on Science and Technology Disaster Resilience Initiative On February 18, Dr. McCall served on a panel of policymakers that addressed an audience of academic researchers as part of the launch of the California Council on Science and Technology Disaster Resilience Initiative.

California Precision Medicine Advisory Council

CIAPM launched the California Precision Medicine Advisory Council in spring of 2020 to advise and make recommendations to OPR on matters related to CIAPM. The Council, including a member recommended by the Senate and another by the Assembly, is comprised of eleven advisors who represent a broad range of sectors and expertise. The full Council Guidelines can be found in Appendix F.

In 2021 the Advisory Council's two working groups, Data Integration and Equitable Consent, made progress toward their goals which are based on recommendations from CIAPM's 2018 report, *Precision Medicine: An Action Plan for California.*

California Precision Medicine Advisory Council



California Initiative to Advance **Precision Medicine**



Nadine Burke Harris, MD, MPH



Oliver Keown, MD



Fatima Muñoz, MD



Chair Clara Lajonchere, PhD



Samar Muzaffar, MD



Kenneth Kim, MD



Hakan Sakul, PhD



Vice Chair Keith Yamamoto, PhD



Ysabel Duron



Yvonne (Bonnie) Maldonado, MD



Mary Anne Schultz, PhD, MBA, MSN, RN

DATA INTEGRATION WORKING GROUP

There is enormous momentum in California, as well as across the nation, to uplift social determinants of health alongside biological determinants as critical data that can be stored in electronic health records to guide clinical decision-making and improve quality of care. Decades of evidence linking socioeconomic circumstances to health outcomes have guided the development of strategies to tailor prevention and responses to underlying conditions that drive illness and disability, such as food insecurity, housing instability, and poor access to health care. Rather than forever treating the symptoms of poor health, a system built upon principles of precision medicine meets the challenges where they are and treats the root causes, physical or otherwise.

In 2021 the Data Integration Working Group gathered information from experts and connected with several state agencies and external entities working at the cutting-edge of data interoperability. Among the public efforts explored were the California Health and Human Services Data Exchange Framework, the California Department of Health Care Access and Information's All Payer Claims Database, and the Coleridge Administrative Data Research Facility. CIAPM facilitated meetings with the California Institute for Regenerative Medicine to consider overlapping goals and potential partnership.

EQUITABLE CONSENT WORKING GROUP

The Equitable Consent Working Group aims to increase the number of underrepresented minorities that participate in biomedical research so that advances in precision medicine are equitably distributed across people from different ancestries, genders, cultures, geographies, and age groups. For many reasons medical diagnostics, drugs, devices, and other interventions often are not tested on a wide variety of patients, which can lead to decreased efficacy or increased side effects in some subpopulations.

With the goal of diversifying biomedical research participation, the Equitable Consent Working Group is developing a website that will feature contextual information, toolkits, best practices, and other resources about equitable participation in research for biomedical research stakeholders including research sponsors, research staff, potential and existing research participants, and health care providers who may refer patients to studies.

In 2021 CIAPM staff generated and curated website content, and engaged pharmaceutical companies, academics, patient advocacy groups, and other organizations to identify needs, determine the scope of information presented, and map out a dissemination plan.

NETWORK ENGAGEMENT

When CIAPM was established the legislature envisioned the Initiative would help cross-pollinate the fields of data infrastructure, medicine, and biomedical research by coordinating the efforts of public, private, and nonprofit partners throughout California. This coordination includes staff contributions to scientific discourse, maintenance of the California Precision Medicine Asset Inventory, and frequent communication with its network through multiple mediums.

To meet this responsibility, CIAPM staff and fellows developed several resources providing multiple groups of stakeholders with information that improves their understanding of precision medicine and helps them identify potential precision medicine partnerships.

California Precision Medicine Asset Inventory

As required by statute, CIAPM maintains a public database and mapping tool of precision medicine assets in California. Assets include published data sets, researchers, academic and commercial laboratories, campus institutes, community-based organizations, and others. The goal of the Asset Inventory is to facilitate outreach efforts and collaborations by allowing California-based researchers, clinicians, community groups, and industry partners to search the assets and filter on criteria like research interest or location.

The Asset Inventory was initially built with pro bono support from Lawrence Berkeley National Laboratory and launched in parallel with the ACEs RFP in December 2019. As of September 2021, the Asset Inventory has been revamped to improve user experience and better meet our goals of hosting an accessible tool to maintain and raise awareness of precision medicine assets in California.

The revamp process transferred the Asset Inventory from the data

visualization platform Tableau to an ArcGIS ExperienceBuilder application. CIAPM chose this application for its flexible mapping interface, powerful search and filter capabilities, and ability for users to add or edit information about themselves within the inventory. Team members also created a tutorial video to introduce new users to the inventory's search, filter, and editing features.

CIAPM will continue adding information to the Asset Inventory in 2022, to build atop the nearly 500 assets currently featured.

Newsletter and Social Media

In 2021 CIAPM continued regular communications with its network through its newsletter and social media feeds. In July the newsletter was redesigned for a more contemporary audience, and CIAPM invited readers to provide feedback on content. The responses helped CIAPM staff realign newsletter topics and features to audience priorities.

CIAPM also worked closely with OPR's communications team to create social media content that keeps its network informed of important announcements, upcoming meetings, and general precision medicine news and research updates.

Website Update

In April 2021 CIAPM debuted a new website that improves the user experience and features more content. This includes a curated library of precision medicine educational resources for all audience levels; a calendar of conferences, webinars, and other events related to precision health and medicine; a list of pertinent external funding opportunities; and a primer on precision medicine. The primer was created to introduce new audiences to precision medicine, answering questions like *What is precision medicine?* or *How will data change health care?* The resource library provides additional information from reliable sources about these topics.

Invited Talks

CIAPM staff are regularly invited to present the program and speak to timely topics at various conferences, meetings, schools, and community events. Below is a selection of talks and presentations from 2021. CIAPM was additionally represented at other external events, including those listed in Appendix C.

- January 8 American Association for Precision Medicine Annual Meeting 2021, "Driving the Future of Precision Medicine," Dr. Muir
- January 21 Stanford University, "COVID-19 Community Town Hall: Vaccine Readiness," Dr. McCall
- January 27 Precision Medicine World Conference, "21st Century Precision Medicine in the Age of COVID-19, Tackling the Mental Health Crisis in the Wake of COVID-19," Dr. McCall
- **February 11** Van Horn Public Library Talks, "Precision Medicine and Alzheimer's Disease," Dr. McCall
- February 18 California Council on Science and Technology,
 "Launch of the CCST Disaster Resilience Initiative," Dr. McCall
- March 6 500 Women Scientists and Journal of Science Policy & Governance, "Intersectional Science Policy," Dr. McCall
- March 12 Portland State University, "Toward Health Equity," Dr. McCall
- **April 14** UC San Diego, "Science Policy for an Equitable California," Dr. McCall
- **April 16** Stanford University, "Advancing Neuroscience with Precision," Dr. McCall
- **May 18** National Science Policy Network, "Partnerships for Health Equity," Dr. McCall
- June 17 CIAPM 2020 Annual Report briefings delivered by CIAPM staff to state legislators, Capitol staff, and members of the public
- **June-July** Individual briefings to legislative offices about statefunded ACEs demonstration projects, Dr. McCall

- September 22 Precision Medicine World Conference: Pittsburgh, "Authentic Community Engagement in State-Sponsored Precision Medicine Research" and "Diversity, Inclusion, Equity, and Access in Community Engaged Precision Medicine Research and Clinical Implementation," Dr. Muir
- **October 15** UC Davis NIH Molecular and Cell Biology graduate program training grant retreat, "Precision Medicine," Dr. Muir
- November 5 International "Brain Bee" Neuroscience Olympiad, "Applying Science for Social Good: Precision Medicine and Health Equity," Dr. McCall

Capitol Collaborative on Race and Equity

OPR was part of the 2020-21 cohort of the Capitol Collaborative on Race and Equity (CCORE), a racial equity capacity-building program for state government employees. CIAPM staff attended monthly trainings to increase their capacity for operationalizing racial equity practices in every aspect of their work. The trainings included:

- A study of the foundational history and concepts of race in America.
- Exercises to frame and reframe the language used about race, personal history, and privilege.
- An introduction to the Results-Based Accountability[™] tool, developed by Mark Friedman.
- Analysis of the root causes of racism and inequities within participants' purview.

CIAPM will continue to embed into its work CCORE takeaways and best practices such as transformational change, root cause analyses, meaningful community engagement, and messaging that affirms shared values while directly countering harmful narratives about race.

Key Takeaways from the 2020-21 CCORE Cohort

Transactional vs. Transformational Change

Transactional change improves conditions but does so within existing structures and policies, even when those structures are harmful. Transformational policies and ideas seek to change the underlying structures so community gains are long lasting.

Root Cause Analysis

CIAPM determined that persistent underrepresentation of minorities in biomedical research was a key indicator for racial disparities, and that inadequate consenting processes and recruitment strategies in clinical trials composed a root cause. This analysis informed the mission of the Equitable Consent Working Group.

Spectrum of Community Engagement

The spectrum of community engagement describes community engagement methods frequently used by policy makers. They range from marginalizing or shutting groups out of the process to supporting community ownership. True ownership extends beyond collaboration on a single project; it means a community will retain capacity and resources after the project ends. CIAPM considers how the communities and people with which we engage are enriched in the long term.

Affirm, Counter, Transform

Affirm, Counter, Transform language guides CIAPM's messaging: affirming shared values, directly countering harmful narratives about race, and transforming the status quo with solutions.

Interagency Cooperation

Throughout 2021 CIAPM staff served several interagency efforts toward reducing health disparities and addressing top priorities of Governor Gavin Newsom's Administration, including:

- Governor's COVID-19 Testing Task Force (member) Seeks to reduce transmission of COVID-19 and support public health by improving accessibility, equity, timeliness, and sustainability of testing.
- CA Surgeon General's Trauma-Informed Primary Care Advisory Committee (member) Advises the Surgeon General and California Health & Human Services Agency on promising models, best practices, evolving science, and clinical expertise for the implementation of trauma-informed care systems in California.
- CA Essentials for Childhood Initiative Consortium (member)
 Addresses child maltreatment as a public health issue and aims
 to 1) raise awareness and commitment to promote safe, stable,
 nurturing relationships and environments; 2) create the context
 for healthy children and families through social norms change,
 programs, and policies; and 3) uses data to inform actions.
- CA Health in All Policies Task Force (member) Identifies
 priority programs, policies, and strategies to improve the health
 of Californians while advancing the goals of improving air and
 water quality, protecting natural resources and agricultural lands,
 increasing the availability of affordable housing, improving
 infrastructure systems, promoting public health, planning
 sustainable communities, and meeting climate change goals.

CONCLUSION AND LOOKING AHEAD

Amid the ongoing uncertainties and extraordinary challenges of 2021 CIAPM created opportunities for revitalization and growth, continuing to exceed its statutory responsibilities to better serve California.

CIAPM prioritized user experience and accessibility in the launch of its new website, new precision medicine educational resources webpage, and redesigned interactive asset inventory. These tools will facilitate relationship growth between stakeholder groups including patient and community partners, researchers, healthcare providers, and the biomedical industry.

CIAPM stands resolute to deliver to California promising public research and unique cross-sector projects.

CIAPM helped shape the state's ongoing pandemic response and disaster resilience efforts by continuing to serve on the Governor's COVID-19 Testing Task Force, and by contributing to agenda-setting discussions on the most critical policy and research challenges facing California as part of the California Council on Science & Technology's Disaster Resilience Initiative.

While supporting the ongoing cancer disparities demonstration projects, CIAPM expanded its efforts to promote equity in healthcare and precision medicine. CIAPM's funding for seven new multi-year, community-driven projects on Adverse Childhood Experiences aligns with priorities of the California Surgeon General and Governor Newsom, and contributes to innovative, scalable solutions for patients.

CIAPM engaged in racial equity capacity building at a programmatic level through the Capitol Collaborative on Race and Equity. Leveraging

the experts of the California Precision Medicine Advisory Council, the council's two working groups began ambitious projects aimed at ensuring precision medicine advances will be justly distributed across all Californians.

Looking forward, CIAPM stands resolute to deliver to California promising public research and unique cross-sector projects. It will continue to spark collaboration that yields innovative health and medicine solutions to help the most marginalized Californians. CIAPM looks to the future, and its main goals are to:

- Support ongoing demonstration projects including conducting site visits, convening meetings for researchers to network and collaborate, and sharing each project's emerging impact with its larger network and the public.
- Advance the projects of the advisory council's two working groups to better integrate social determinants of health into health records, and share resources to help stakeholder groups diversify participation in biomedical research.
- Continue to facilitate relationships and idea exchanges between external stakeholders.
- Refine communications and public engagement with strategic investments in additional resources.
- Continue learning about and grounding staff and council work in equitable practices, and contributing to the development of OPR's Racial Equity Action Plan.
- Leverage the expertise of California's scientists and health professionals to help the state meet challenges and optimize opportunities, including closing health equity gaps.

APPENDICES

A. PUBLICATIONS

Current Projects

Addressing Disparities in Breast Cancer in Latinas: A Multi-Tiered Approach (2019-2023) Lead Principal Investigator: Dr. Elad Ziv, UCSF

PUBLICATIONS

- Adedokun, B., Du, Z., Gao, G., Ahearn, T. U., Lunetta, K. L., Zirpoli, G., ... Huo, D. (2021). Cross-ancestry GWAS meta-analysis identifies six breast cancer loci in African and European ancestry women. *Nature communications*, 12(1), 1-8. https://doi.org/10.1038/s41467-021-24327-x
- Almeida, R., Lopez-Macha, A., Dugatkin, T., Joseph, G., Duron, Y., Hurtado de Mendoza, A., ... Fejerman, L. (2021). Community research collaboration to develop a promotores-based hereditary breast cancer education program for Spanish-speaking Latinas. *Health Education Research*, 36(3), 319-336. <u>https://doi. org/10.1093/her/cyab011</u>
- Borrell, L. N., Elhawary, J. R., Fuentes–Afflick, E., Witonsky, J., Bhakta, N., Wu, A. H., ... Burchard, E. G. (2021). Race and genetic ancestry in medicine—a time for reckoning with racism. *New England Journal of Medicine*, 384(5), 474–480. https://doi.org/10.1056/NEJMms2029562
- Herzog, J. S., Chavarri-Guerra, Y., Castillo, D., Abugattas, J., Villarreal-Garza, C., Sand, S., ... Weitzel, J. N. (2021). Genetic epidemiology of BRCA1-and BRCA2associated cancer across Latin America. *NPJ breast cancer*, 7(1), 1-8. :107 ; <u>https:// doi.org/10.1038/s41523-021-00317-6</u>
- Li, N., Zethoven, M., McInerny, S., Devereux, L., Huang, Y. K., Thio, N., ... Campbell, I. G. (2021). Evaluation of the association of heterozygous germline variants in NTHL1 with breast cancer predisposition: an international multi-center study of 47,180 subjects. *npj Breast Cancer*, 7(1), 1–12. <u>https://doi.org/10.1038/s41523-021-00255-3</u>
- Newman, L., Fejerman, L., Pal, T., Mema, E., McGinty, G., Cheng, A., ... Hunt, K. (2021). Breast cancer disparities through the lens of the COVID-19 pandemic. *Current breast cancer reports*, 13(3), 110–112. <u>https://doi.org/10.1007/s12609-021-00419-x</u>

Zavala, V. A., Bracci, P. M., Carethers, J. M., Carvajal–Carmona, L., Coggins, N. B., Cruz–Correa, M. R., ... Fejerman, L. (2021). Cancer health disparities in racial/ ethnic minorities in the United States. *British journal of cancer*, 124(2), 315–332. https://doi.org/10.1038/s41416–020–01038–6

PRESENTATIONS

- Nierenberg, J.L., Adamson, A., Ding, Y.C., Shieh, Y., Hu, D., Huntsman, S., ... Ziv, E. (2021, October). Breast cancer polygenic risk scores and rare variants in Latinas. *American Society for Human Genetics Annual Meeting*, Reviewers' Choice poster award.
- Nierenberg, J.L., Adamson, A., Ding, Y.C., Shieh, Y., Hu, D., Huntsman, S., ... Neuhausen, S.L. (2021, October).Pathogenic Variants in Breast Cancer Risk Genes in Latinas. *American Association for Cancer Research Disparities Conference.*
- Nierenberg, J.L., Adamson, A., Zavala, V., Lott, P., John, E., Hu, D., ... Ziv, E. (2021, March). Common RAD52 variants are associated with decreased breast cancer risk among US Latinas and Latin American women. *The Breast Oncology Program Scientific Retreat.*
- Perez, F., Fejerman, L., Robles-Garibay, E., Perez, A., Quino, E., Gonzalez, M., ... Duron, Y. (2021, October). Tu historia cuenta' online version: Promotores' experience and perspectives on the virtual adaption of a hereditary breast cancer education and risk identification program. *American Association for Cancer Research Disparities Conference.*
- Mak, A., Kachuri, L., Hu, D., Eng, C., Huntsman, S., Elhawary, J., ... Ziv, E. (2021, October). Genome-wide gene expression analyses reveals ancestry-specific genetic architecture in Latino and African American children. *American Society of Human Genetics.*

Advancing a Precision Population Health Approach to ACEs to Reduce Health Disparities (2021-2024)

Lead Principal Investigator: Dr. Gary Firestein, UC San Diego

PRESENTATIONS

Firestein, G., (2021, November). Showcase of Advancing a Precision Population Health Approach to ACEs to Reduce Health Disparities. *Showcases*. Presented at the UCSD Design & Innovation Building Grand Opening.

PRESS

- City News Service, KPBS. (2021, July 7). UC San Diego Gets \$3 Million To Reduce Latino Childhood Obesity. KPBS. <u>https://www.kpbs.org/news/2021/07/07/uc-san-diego-reduce-latino-childhood-obesity</u>
- City News Service. (2021, July 7). UCSD gets \$3 million to reduce Latino childhood obesity. CBS8 News. <u>https://www.cbs8.com/article/news/health/ucsd-gets-3-</u>

million-to-reduce-latino-childhood-obesity/509-c384e215-dee0-46af-a997-4f4333a2d5c2

- City News Service. (2021, July 7). UCSD receives \$3M to study, reduce Latino childhood obesity. FOX 5 San Diego. <u>https://fox5sandiego.com/news/health/ucsd-receives-3m-to-study-reduce-latino-childhood-obesity/</u>
- Coast News wire services. (2021, July 7). UCSD gets \$3 million to reduce Latino childhood obesity. The Coast News Group. <u>https://thecoastnews.com/ucsd-gets-3-million-to-reduce-latino-childhood-obesity/</u>
- Efe. (2021, July 7). California asigna 3 millones para investigar obesidad infantil en latinos. San Diego Union Tribune News En Español. <u>https://www.</u> <u>sandiegouniontribune.com/en-espanol/noticias/salud/articulo/2021-07-07/</u> <u>california-asigna-3-millones-para-investigar-obesidad-infantil-en-latinos</u>
- Efe. (2021, July 7). California asigna 3 millones para investigar obesidad infantil en latinos. The Los Angeles Times. <u>https://www.latimes.com/espanol/california/articulo/2021-07-07/california-millones-dinero-obesidad-infantil-latinos</u>
- KPBS Public Media. (2021, July 13). UC San Diego Gets \$3 Million To Reduce Latino Childhood Obesity. KPBS Midday Edition Radio. <u>https://www.kpbs.org/podcasts/ kpbs-midday-edition-segments/uc-san-diego-gets-3-million-reduce-latinochildhoo</u>
- LaFee S., UC San Diego Health. (2021, July 7). How to Reduce Obesity among Latino Children, with Precision [Press release]. <u>https://health.ucsd.edu/news/releases/</u> <u>Pages/2021-07-07-how-to-reduce-obesity-among-latino-children-with-</u> <u>precision.aspx</u>
- Noticias Ya San Diego (Director). (2021, October 05). Inversión millonaria para combatir la obesidad infantil en San Diego [Video file]. <u>https://www.facebook.</u> <u>com/watch/?v=593442171804591</u>
- Sklar, D. (2021, July 7). UCSD Gets \$3 Million to Reduce Latino Childhood Obesity. Times of San Diego News. <u>https://timesofsandiego.com/health/2021/07/07/</u> ucsd_gets_3-million_to_reduce_latino_childhood_obesity/

Identifying Social, Molecular, & Immunological Processes for Mitigating Toxic Stress & Enhancing Personalized Resilience

Lead Principal Investigator: Dr. George Slavich, UCLA

PUBLICATIONS

Allison, G. O., Kamath, R. A., Carrillo, V., Alqueza, K. L., Pagliaccio, D., Slavich, G. M., ... Auerbach, R. P. (2021). Self-referential processing in remitted depression: An event related potential study. *Biological Psychiatry Global Open Science*. <u>https:// doi:10.1016/j.bpsgos.2021.12.005</u>

Rahal, D., Fales, M. R., Haselton, M. G., Slavich, G. M., & Robles, T. F. (2021).

Achieving status and reducing loneliness during the transition to college: The role of entitlement, intrasexual competitiveness, and dominance. *Social Development*. <u>https://doi:10.1111/sode.12569</u>

- Senft Miller, A., Nop, O., Slavich, G. M., & Dumas, J. A. (2021). Lifetime stress exposure, cognition, and psychiatric wellbeing in women. *Aging & Mental Health*. https://doi:10.1080/13607863.2021.1958144
- Adeloye, D., Agarwal, D., Barnes, P. J., Bonay, M., van Boven, J. F., Bryant, J., ... Rudan, I. (2021). Research priorities to address the global burden of chronic obstructive pulmonary disease (COPD) in the next decade. *Journal of Global Health*, 11, 15003. <u>https://doi:10.7189/jogh.11.15003</u>
- Byrne, M. L., Lind, M. N., Horn, S. R., Mills, K. L., Nelson, B. W., Barnes, M. L., Slavich, G. M., & Allen, N. B. (2021). Using mobile sensing data to assess stress: Associations with perceived and lifetime stress, mental health, sleep, and inflammation. *Digital Health*, 7, 1–11. <u>https://doi:10.1177/20552076211037227</u>
- Rahal, D., Fales, M. R., Haselton, M. G., Slavich, G. M., & Robles, T. F. (2021). Cues of social status: Associations between attractiveness, dominance, and status. *Evolutionary Psychology*, 19, 14747049211056160. <u>https:// doi:10.1177/14747049211056160</u>
- Moseley, R. L., Turner-Cobb, J. M., Spahr, C. M., Shields, G. S., & Slavich, G. M. (2021). Lifetime and perceived stress, social support, loneliness, and health in autistic adults. *Health Psychology*, 40, 556–568.
- Milas, G., Martinović Klarić, I., Malnar, A., Saftić, V., Šupe-Domić, D., & Slavich, G. M. (2021). The impact of stress and coping strategies on life satisfaction in a national sample of adolescents: A structural equation modelling approach. *Stress and Health*, 37, 1026-1034. <u>https://doi:10.1002/smi.3050</u>
- Polick, C. S., Polick, S. R., Stoddard, S. A., Braley, T. J., & Slavich, G. M. (2021). The importance of assessing life stress exposure in multiple sclerosis: A case report. *Multiple Sclerosis and Related Disorders*, 54, 103145. <u>https://doi:10.1016/j.</u> <u>msard.2021.103145</u>
- Sichko, S., Bui, T. Q., Vinograd, M., Shields, G. S., Saha, K., Devkota, S., Olvera-Alvarez, H. A., Carroll, J. E., Cole, S. W., Irwin, M. R., & Slavich, G. M. (2021).
 Psychobiology of Stress and Adolescent Depression (PSY SAD) Study: Protocol overview for an fMRI-based multi-method investigation. *Brain, Behavior, and Immunity Health*, 17, 100334. https://doi:10.1016/j.bbih.2021.100334

PRESENTATIONS

Slavich, G. M. (2021, September). The psychobiology of social safety and health: During the COVID-19 pandemic and beyond. 5th Croatian Congress of Psychodermatology. Talk given in Zagreb, Croatia.

Slavich, G. M. (2021, October). From social signal transduction to social safety:

Developing a biologically based understanding of depression and health. *Division of Child & Adolescent Psychiatry*. Talk given at Columbia University, New York, NY.

- Slavich, G. M. (2021, October). Social safety theory: From research to clinical practice. *Mediterranean Institute for Life Sciences.* Talk given in Split, Croatia.
- Slavich, G. M. (2021, November). Breaking traditional boundaries to foster scientific innovation and discovery. *18th annual meeting of Society in Science*. Talk given in Zurich, Switzerland.
- Burani, K., Brush, C. J., Shields, G. S., Slavich, G. M., Nelson, B., & Hajcak, G. (2021, September). Acute, but not chronic, lifetime stress exposure interacts with the RewP to prospectively predict increases in depressive symptoms. Paper presented at the 2021 annual meeting of the Society for Psychophysiological Research (virtual meeting).
- Patel, K., Pollak, O. H., Sheridan, M. A., Giletta, M., Hastings, P. D., Nock, M. K., Rudolph, K. D., ... Bryant Miller, A. (2021, September). Testing the comparative predictive validity of neural structure versus suicidal ideation history for prediction of Suicide Stroop Task performance. Paper presented at the 2021 annual meeting of the Flux Society (virtual meeting).
- Kim, S., Zhang, W., Pak, V., Spahr, C. M., & Slavich, G. M. (2021, November). How lifetime stress exposure, acculturative stress, and racism are related to anxiety and depression among Chinese and Korean Immigrants. Paper presented at the 2021 International Meeting of the Asian American Pacific Islander Nurses Association (virtual meeting).

PRESS

- UCLA Health Connect. (2021, September 2). Toxic stress to be studied, taught, with \$3 million state grant awarded to UCLA Health. <u>https://connect.uclahealth.org/2021/09/02/ucla-health-awarded-3-million-state-grant-to-study-and-teach-about-toxic-stress/</u>
- UCLA Health. (2021, September 3). UCLA Health researchers to study the impact of stress on health. <u>https://www.uclahealth.org/news/ucla-health-researchers-study-impact-stress-health</u>

Integrated Machine-Learning Platform to Inform Precision Therapy in Breast Cancer Patients (2019-2023)

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

PUBLICATIONS

Li, J., Xu, X., Tiwari, M., Chen, Y., Fuller, M., Bansal, V., ... Sen, G. L. (2021). SPT6 promotes epidermal differentiation and blockade of an intestinal-like phenotype through control of transcriptional elongation. *Nature communications*, 12(1), 1–15. https://doi.org/10.1038/s41467-021-21067-w

- Maynard, R. E., Poore, B., Hanaford, A. R., Pham, K., James, M., Alt, J., ... Raabe, E.
 H. (2021). TORC1/2 kinase inhibition depletes glutathione and synergizes with carboplatin to suppress the growth of MYC-driven medulloblastoma. *Cancer Letters*, 504, 137–145. <u>https://doi.org/10.1016/j.canlet.2021.02.001</u>
- Hahn, W. C., Bader, J. S., Braun, T. P., Califano, A., Clemons, P. A., Druker, B. J., ... Weissman, J. (2021). An expanded universe of cancer targets. *Cell*, 184(5), 1142– 1155. <u>https://doi.org/10.1016/j.cell.2021.02.020</u>
- Banerjee, S., Yoon, H., Ting, S., Tang, C. M., Yebra, M., Wenzel, A. T., ... Sicklick, J. K. (2021). KITlow Cells Mediate Imatinib Resistance in Gastrointestinal Stromal Tumor. *Molecular Cancer Therapeutics*, 20(10), 2035–2048. <u>https://doi.org/10.1158/1535–7163.MCT–20–0973</u>
- Pan, E., Cabal, A., Javier-DesLoges, J., Patel, D., Panian, J., Lee, S., ... McKay, R. R. (2021). Analysis of CDK12 alterations in a pan-cancer database. *Cancer Medicine*. https://doi.org/10.1002/cam4.4483
- Pouyanfard, S., Meshgin, N., Cruz, L. S., Diggle, K., Hashemi, H., Pham, T. V., ... Kaufman, D. S. (2021). Human induced pluripotent stem cell-derived macrophages ameliorate liver fibrosis. *Stem Cells*, 39(12), 1701–1717. <u>https://doi.org/10.1002/stem.3449</u>

PRESENTATIONS

- Tamayo, P. (2021, October). Cancer Archetypes: a Framework to Functionally Classify and Model Oncogenic Cellular and Tumor States. *Cell–NCI Symposium: Beyond Cancer Genomics Toward Precision Oncology.* Talk conducted virtually.
- Tamayo, P. (2021, October). Cancer Archetypes: a Framework to Functionally Classify and Model Oncogenic Cellular and Tumor States. *Delivering Discoveries: Updates in Oncology*. Talk conducted at Aventine, San Diego.

A Multi-Component Intervention to Strengthen Families and Build Youth Resilience (2021-2024)

Lead Principal Investigator: Dr. Ariane Marie–Mitchell, Loma Linda University Loma Linda University Health. (2021, April). Loma Linda University awarded more than \$2 million grant by state of California to address adverse childhood experiences. <u>https://news.llu.edu/research/loma-linda-university-awarded-</u> <u>more-than-2-million-grant-by-state-of-california-address-adverse-</u> <u>childhood-experiences</u>

Reducing Cancer Disparities Through Innovative Community-Academic Partnerships (2019-2023) Lead Principal Investigator: Dr. Manali Patel, Stanford University

PUBLICATIONS

- Rodriguez, G. M., Leach, M., Osorio, J., Wood, E., Duron, Y., O'Brien, D. G., ... Patel, M. I. (2021). Addressing cancer care needs for Latino adults: A formative qualitative evaluation. *American Journal of Clinical Oncology*, 39(28), 105. <u>https://doi:10.1200/JCO.2020.39.28_suppl.105</u>
- Rodriguez, G. M., Ferguson, J. M., Kurian, A., Bondy, M., & Patel, M. I. (2021). The Impact of COVID-19 on Patients with Cancer: A National Study of Patient Experiences. *American Journal of Clinical Oncology*, 44(11), 580. <u>https://</u> <u>doi:10.1097/COC.00000000000865</u>

PRESENTATIONS

- Duarte, V. & Garcia, Y. (2021, March). Factores de riesgo de enfermedades crónicas. Parent Health Workshop hosted by Migrant Education. Talk conducted virtually.
- Villicana, G. & Koontz, Z. (2021, November). Introducing the Precision Medicine in Monterey County Project in Collaboration with Stanford. *Tumor Board Meeting at the Community Hospital of the Monterey Peninsula.*
- Magaly Rodriguez, G. (2021, November). Is Community Health Equity Within Reach? The ALCANCE Study. Frontiers in Cancer Clinical Translation Series at Stanford Cancer Center.
- Goldman Rosas, L. (2021, November). What is at Stake? Ethical, Legal, and Social Implications (ELSI) of Community Engagement to Diversify the Human Reference Genome. *TAGRI-II Conference: Reducing Health Disparities: Actively Engaging the Community, Researchers, and Community Health Workers, Representatives, and Guides.* Panel presented virtually.
- Duron, Y. (2021, October). COVID, Cancer and Systemic Barriers to Latino Health. 3rd Annual National Latino Cancer Institute Forum. Talk conducted virtually.
- Garcia, M.R. & Garcia, Y. (2021, October). Cancer Prevention and Screening. CSVS Child/Adolescent Vaccine Clinic. Talk conducted in Salinas, California.
- Tenney, D. & Villicana, G. (2021, October and September). PINE (Plant-based Instant Pot Nutrition Education) Program, ALCANCE Announcement. *Pacific Cancer Care.*
- Rodriguez, G.M., Leach, M., Osorio, J., Wood, E.H., Duron, Y., O'Brian, D., ... Manali I. (2021, September). Addressing Cancer Care Needs for Latinx Adults: A Formative Qualitative Evaluation. *American Society of Clinical Oncology Quality Symposium*. Poster presented virtually.
- Magaly Rodriguez, G., (2021, September). Addressing Latinx Cancer Care Equity (ALCANCE) Study. Oncology/Hematology/BMT Research Retreat at Asilomar Conference Center. Talk presented virtually.
- Garcia, M. R. & Garcia, Y., (2021, August). Cancer Prevention and Screening. Breastfeeding Awareness Health Fair/Walk. Talk conducted in Salinas, California.

- O'Brien, D. G., Nkwocha, O., Agustin-Garcia, R., & Wood, E.H. (2021, July). Genetic Testing for Cancer Risk for Primary Care Providers: Common questions and practical applications. *Clinica de Salud del Valle de Salinas*. Talk presented in Salinas, California.
- Rodriguez Espinosa, P., Goldman Rosas, L., & Wood, E. H., (2021, July). Qualitative Interviewing Training. *Stanford University*. Presented virtually.
- Koontz, Z. & Patel, M. I. (2021, June). Precision Medicine in Monterey County Update. *Cancer Care Meeting at Pacific Cancer Care.* Talk presented in Monterey, California.
- Nkwocha, O. & Goldman Rosas, L. (2021, June). SPHERE Precision Health Equity in Primary Care Seminar. *Stanford University*. Presented virtually.
- Patel, M. I. (2021, May). Value Based Care Delivery The Influence of Data-Driven Community-Based Approaches to Improve Cancer Outcomes Equitably. *Northern California Kaiser Permanente Grand Rounds*. Talk conducted virtually.
- Patel, M. I. (2021, May). Ensuring Equity in Precision Cancer Care. American Society of *Clinical Oncology Virtual Roundtable.* Talk conducted virtually.
- Patel, M. I. (2021, August). Equity: Every Patient, Every Day, Everywhere. Association of Northern California Oncologists and the American Society of Clinical Oncology Meeting Highlights Annual Session. Talk conducted virtually.
- Patel, M. I. (2021, October). Reimaging a More Equitable Future Together. Invited Expert Panel Moderator. BMS Foundation Virtual Grantee Summit. Talk conducted virtually.
- Patel, M. I. (2021, November). Achieving Equity in Cancer Clinical Trials: Partnerships with Communities. Invited Lecturer and Coordinator. *Harvard Medical School's Addressing Health Disparities: Clinical Insights on Race and Social Justice Virtual Web Series*. Lecture given virtually.
- Patel, M. I. (2021, November). Cancer Health Disparities and Cancer Health Equity: A policy problem. Invited Keynote Speaker. *Florida Society of Clinical Oncology Cancer Disparities and Health Equity Summit.* Talk conducted in Hollywood, Florida.
- Patel, M. I. (2021, December). Disparities to Equity: Moving the Needle on Lung Cancer. Invited Keynote Conversation Virtual Panel Speaker. 5th Annual Meeting of the National Lung Cancer Roundtable. Talk conducted virtually.

PRESS

- Office of Community Engagement. (2021, July 22). ALCANCE PROJECT: Monterey County Addressing Latinx CANcer Care Equity. ALCANCE Project. <u>https://med.stanford.edu/oce/research-projectsnew/alcance.html</u>
- Community Advisory Board. (2021, August). August 2020 Community Advisory Board Newsletter.

Community Advisory Board. (2021, May). May 2021 Community Advisory Board Newsletter.

Using Precision Medicine to Tackle Impacts of Adverse and Unpredictable Experiences on Children's Neurodevelopment (2021–2024) Lead Principal Investigator: Dr. Tallie Z. Baram, University of California, Irvine

PUBLICATIONS

- Short, A. K., Thai, C. W., Chen, Y., Kamei, N., Pham, A. L., Birnie, M. T., Bolton, J. L., Mortazavi, A., Baram, T. Z. (2021). Single-cell transcriptional changes in hypothalamic corticotropin-releasing factor-expressing neurons after early-life adversity inform enduring alterations in vulnerabilities to stress. *Biological Psychiatry Global Open Science*. https://doi.org/10.1016/j.bpsgos.2021.12.006
- Glynn, L. M., Davis, E. P., Luby, J. L., Baram, T. Z., Sandman, C. A. (2021). A predictable home environment may protect child mental health during the COVID-19 pandemic. *Neurobiology of Stress*, 14, 100291. <u>https://doi.org/10.1016/j.ynstr.2020.100291</u>*

*This paper, focusing on the adverse impact of COVID-19 on California's preschoolers, and the protective role of predictability of the early-life environment, was cited by the U.S. Surgeon General in his Mental Health Advisory.

PRESENTATIONS

- Baram, T. Z., (2021, September) Sex-specific corruption of reward-seeking behaviors by early-life adversity: craving, anhedonia and mechanisms. *Early–life origins and sex-dependence of vulnerability to mental disorders*. Symposium presented at the 49th Meeting of the European Brain and Behaviour Society.
- Baram, T. Z., (2021, September) How early-life experiences shape our brain: signals, synapses circuits, behaviors. *Multidimensional Approaches to Early Adversity Across Species*. Symposium presented at the FLUX Congress.
- Baram, T. Z., (2021, October). Enduring Memory Deficits after Early–Life Adversity: Epigenetics, Imaging and Intervention. *Child Neurology Society 50th Annual Meeting.* Talk conducted in Boston, Massachussetts.
- Baram, T. Z., (2021, December). Patterned Sensory Signals During Sensitive Periods Enable Brain Circuit Maturation: Synapses, Microglia, Behaviors; The impact of the COVID-19 pandemic on child and adolescent mental health: The protective role of predictability. The impact of unpredictable parental and environmental signals on cognitive and emotional development: a trans-species approach. Symposium presented at the American College of Neuropsychopharmacology Annual meeting.
- Baram, T. Z., (2021, December). How established and newly recognized early-life adversities influence the developing brain: From the clinic to the back to the human--and to action & communication. Talk conducted at National Scientific

Council on the Developing Child, Harvard University.

- Glynn, L.M., (2021, December) The impact of the COVID-19 pandemic on child and adolescent mental health: The protective role of predictability. *The impact of unpredictable parental and environmental signals on cognitive and emotional development: a trans-species approach.* Symposium presented at the American College of Neuropsychopharmacology annual meeting.
- Glynn, L. M., (2021, September). Unpredictability in early life: A novel antecedent of psychopathology. *Crean College of Health and Behavioral Sciences*. Lecture given at Chapman University.

PRESS

Liu, S. R. (2021, December). Interview on ACEs, health, and health disparities. "Let's Talk About It" Radio Show/Podcast.

Past-funded Projects

All publications, presentations, press coverage, and patent submissions or updates that occurred between 2015 and 2020 are listed in the 2019 Evaluation Report (until July 2019) and earlier annual reports, all available on the CIAPM website. The follow-ing section summarizes only those from 2021.

Artificial Intelligence for Imaging of Neurological Emergencies Lead Principal Investigator: Dr. Pratik Mukherjee, UCSF

PUBLICATIONS

- Agtarap, S. D., Campbell–Sills, L., Jain, S., Sun, X., Dikmen, S., Levin, H., ... Stein, M. B. (2021). Satisfaction with Life after Mild Traumatic Brain Injury: A TRACK–TBI Study. *Journal of neurotrauma*, 38(5), 546–554. <u>https://doi.org/10.1089/neu.2020.7055</u>
- Agtarap, S., Kramer, M. D., Campbell–Sills, L., Yuh, E., Mukherjee, P., Manley, G. T., ... Nelson, L. D. (2021). Invariance of the Bifactor Structure of Mild Traumatic Brain Injury (mTBI) Symptoms on the Rivermead Postconcussion Symptoms Questionnaire Across Time, Demographic Characteristics, and Clinical Groups: A TRACK–TBI Study. Assessment, 28(6), 1656–1670. <u>https://doi.org/10.1177/1073191120913941</u>
- Boase, K., Machamer, J., Temkin, N. R., Dikmen, S., Wilson, L., Nelson, L. D., ... Manley, G. T. (2021). Central Curation of Glasgow Outcome Scale–Extended Data: Lessons Learned from TRACK–TBI. *Journal of neurotrauma*, 38(17), 2419–2434. https://doi.org/10.1089/neu.2020.7528
- Brett, B. L., Kramer, M. D., Whyte, J., McCrea, M. A., Stein, M. B., Giacino, J. T., ... Zafonte, R. (2021). Latent Profile Analysis of Neuropsychiatric Symptoms and Cognitive Function of Adults 2 Weeks After Traumatic Brain Injury: Findings From the TRACK–TBI Study. *JAMA network open*, 4(3), e213467. <u>https://doi.org/10.1001/jamanetworkopen.2021.3467</u>

- Huie, J. R., Mondello, S., Lindsell, C. J., Antiga, L., Yuh, E. L., Zanier, E. R., ... Ferguson, A. R. (2021). Biomarkers for Traumatic Brain Injury: Data Standards and Statistical Considerations. *Journal of neurotrauma*, 38(18), 2514–2529. <u>https://doi.org/10.1089/neu.2019.6762</u>
- Kreitzer, N., Jain, S., Young, J. S., Sun, X., Stein, M. B., McCrea, M. A., ... Nelson, L. D. (2021). Comparing the Quality of Life after Brain Injury–Overall Scale and Satisfaction with Life Scale as Outcome Measures for Traumatic Brain Injury Research. *Journal of neurotrauma*, 38(23), 3352–3363. <u>https://doi.org/10.1089/neu.2020.7546</u>
- Krishnamoorthy, V., Temkin, N., Barber, J., Foreman, B., Komisarow, J., Korley, F. K... Vavilala, M. S. (2021). Association of Early Multiple Organ Dysfunction With Clinical and Functional Outcomes Over the Year Following Traumatic Brain Injury: A Transforming Research and Clinical Knowledge in Traumatic Brain Injury Study. *Critical care medicine*, 49(10), 1769–1778. <u>https://doi.org/10.1097/</u> <u>CCM.00000000005055</u>
- Levin, H. S., Temkin, N. R., Barber, J., Nelson, L. D., Robertson, C., Brennan, J., ... Zafonte, R. (2021). Association of Sex and Age With Mild Traumatic Brain Injury– Related Symptoms: A TRACK–TBI Study. *JAMA network open*, 4(4), e213046. <u>https://doi.org/10.1001/jamanetworkopen.2021.3046</u>
- McCrea, M. A., Giacino, J. T., Barber, J., Temkin, N. R., Nelson, L. D., Levin,
 H. S., ... Zafonte, R. (2021). Functional Outcomes Over the First Year After
 Moderate to Severe Traumatic Brain Injury in the Prospective, Longitudinal
 TRACK-TBI Study. *JAMA neurology*, 78(8), 982–992. https://doi.org/10.1001/jamaneurol.2021.2043
- Nolan, A. L., Petersen, C., Iacono, D., Mac Donald, C. L., Mukherjee, P., van der Kouwe, A., ... Edlow, B. L. (2021). Tractography-Pathology Correlations in Traumatic Brain Injury: A TRACK-TBI Study. *Journal of neurotrauma*, 38(12), 1620–1631. <u>https://doi.org/10.1089/neu.2020.7373</u>
- Reber, J., Hwang, K., Bowren, M., Bruss, J., Mukherjee, P., Tranel, D., & Boes, A. D. (2021). Cognitive impairment after focal brain lesions is better predicted by damage to structural than functional network hubs. *Proceedings of the National Academy of Sciences of the United States of America*, 118(19), e2018784118. <u>https:// doi.org/10.1073/pnas.2018784118</u>
- Rincon, S. P., Mukherjee, P., Levin, H. S., Temkin, N. R., Mac Donald, C. L., Krainak, D. M., ... Yuh, E. L. (2021). Interrater Reliability of National Institutes of Health Traumatic Brain Injury Imaging Common Data Elements for Brain Magnetic Resonance Imaging in Mild Traumatic Brain Injury. *Journal of neurotrauma*, 38(20), 2831–2840. https://doi.org/10.1089/neu.2021.0138
- Stein, M. B., Yuh, E., Jain, S., Okonkwo, D. O., Mac Donald, C. L., Levin, H., ... Mukherjee, P. (2021). Smaller Regional Brain Volumes Predict Posttraumatic

Stress Disorder at 3 Months After Mild Traumatic Brain Injury. Biological psychiatry. Cognitive neuroscience and neuroimaging, 6(3), 352–359. <u>https://doi.org/10.1016/j.bpsc.2020.10.008</u>

- Williams, J. R., Nieblas-Bedolla, E., Feroze, A., Young, C., Temkin, N. R., Giacino, J. T.,
 ... Mac Donald, C. L. (2021). Prognostic Value of Hemorrhagic Brainstem Injury on Early Computed Tomography: A TRACK-TBI Study. *Neurocritical care*, 35(2), 335–346. <u>https://doi.org/10.1007/s12028-021-01263-8</u>
- Xu, L. B., Yue, J. K., Korley, F., Puccio, A. M., Yuh, E. L., Sun, X., ... Mukherjee, P. (2021). High–Sensitivity C–Reactive Protein is a Prognostic Biomarker of Six–Month Disability after Traumatic Brain Injury: Results from the TRACK–TBI Study. *Journal of neurotrauma*, 38(7), 918–927. https://doi.org/10.1089/neu.2020.7177
- Yue, J. K., Phelps, R. R., Hemmerle, D. D., Upadhyayula, P. S., Winkler, E. A., Deng, H., ... Manley, G. T. (2021). Predictors of six-month inability to return to work in previously employed subjects after mild traumatic brain injury: A TRACK-TBI pilot study. *Journal of concussion*, 5 <u>https://doi.org/10.1177/20597002211007271</u>
- Yuh, E. L., Jain, S., Sun, X., Pisica, D., Harris, M. H., Taylor, S. R., ... Zafonte, R. (2021). Pathological Computed Tomography Features Associated With Adverse Outcomes After Mild Traumatic Brain Injury: A TRACK-TBI Study With External Validation in CENTER-TBI. JAMA neurology, 78(9), 1137–1148. <u>https://doi.org/10.1001/jamaneurol.2021.2120</u>

California Kids Cancer Comparison

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

PUBLICATIONS

- Beale, H. C., Roger, J. M., Cattle, M. A., McKay, L. T., Thompson, D. K., Learned, K., ... Vaske, O. M. (2021). The case for using mapped exonic non-duplicate reads when reporting RNA-sequencing depth: Examples from pediatric cancer datasets. *GigaScience*, 10(3). <u>https://doi.org/10.1093/gigascience/giab011</u>
- Reed, M. R., Lyle, A. G., De Loose, A., Maddukuri, L., Learned, K., Beale, H. C.,
 … Rodriguez, A. (2021). A functional precision medicine pipeline combines comparative transcriptomics and tumor organoid modeling to identify bespoke treatment strategies for glioblastoma. *Cells*, 10(12), 3400. <u>https://doi.org/10.3390/cells10123400</u>

Early Prediction of Major Adverse Cardiovascular Events Using Remote Monitoring Lead Principal Investigator: Dr. Brennan Spiegel, Cedars-Sinai Medical Center

PUBLICATIONS

- Fuller, G., Mouapi, K. N., Joung, S., Shufelt, C., van den Broek, I., Lopez, M., ...
 Robinson, A. (2021). Feasibility of Patient-Centric Remote Dried Blood Sampling: The Prediction, Risk, and Evaluation of Major Adverse Cardiac Events (PRE-MACE) Study. *Biodemography And Social Biology*, 65(313).
- Gresham, G., Tjoe, B., Joung, S., Arnold, C., Shawan, S., Fuller, G., ... Shufelt, C. (2021). Longitudinal Trajectories Of Remotely–Monitored Activity Data In Patients With Stable Ischemic Heart Disease (Sihd): A Report From The Prediction, Risk, And Evaluation Of Major Adverse Cardiac Events (PRE–MACE) Study. *Journal of the American College of Cardiology*, 77(18_Supplement_1), 3246–3246.
- Tjoe, B., Gresham, G., Joung, S., Arnold, C., Dhawan, S., Fuller, G., ... Shufelt, C. (2021). Remote Patient Monitoring For Predicting Major Adverse Cardiac Events (Mace) And Cardiovascular Hospitalizations In Patients With Stable Ischemic Heart Disease (Sihd): A Report From The Prediction, Risk, And Evaluation Of Major Adverse Cardiac Events (PRE-MACE)) Study. Journal of the American College of Cardiology, 77(18_Supplement_1), 3251–3251.
- Tjoe, B., Gresham, G., Joung, S., Arnold, C., Dhawan, S., Fuller, G., ... Shufelt, C. (2021). Patient Reported Functional Status As A Predictor For N-Terminal Pro-Brain Natriuretic Peptide (Nt-Probnp) And Cardiovascular Hospitalizations In Patients With Stable Ischemic Heart Disease: A Report From The Prediction, Risk, And Evaluation Of Major Adverse Cardiac Events (PRE-MACE) Study. *Journal of the American College of Cardiology*, 77(18_Supplement_1), 173–173.

ABSTRACTS

- Gresham, G., Tjoe, B., Joung, S., Arnold, C., Dhawan, S., Fuller, G., ... Shufelt, C. Longitudinal trajectories of remotely-monitored activity data in patients with stable ischemic heart disease: A report from the prediction, risk and evaluation of major adverse cardiac events (PRE-MACE) study. *Journal of the American College* of Cardiology. 2021 May; 77(18):3246. https://doi:10.1016/S0735-1097(21)0460
- Tjoe, B., Gresham, G., Joung, S., Arnold, C., Dhawan, S., Fuller, G., ... Shufelt, C. Remote patient monitoring for predicting major adverse cardiac events and cardiovascular hospitalizations in patients with stable ischemic heart disease: A report from the prediction, risk and evaluation of major adverse cardiac events (PRE-MACE) study. *Journal of the American College of Cardiology*. 2021 May; 77(18):3251. https://doi:10.1016S0735-1097(21)04605-2
- Tjoe, B., Gresham, G., Joung, S., Arnold, C., Dhawan, S., Fuller, G., ... Shufelt, C. Patient reported functional status as a predictor for N-terminal pro-brain natriuretic and cardiovascular hospitalizations in patients with stable ischemic heart disease: A report from the prediction, risk and evaluation of major adverse cardiac events (PRE-MACE) study. *Journal of the American College of Cardiology*. 2021 May; 77(18):173. https://doi:10.1016/S0735-1097(21)01532-1

PRESENTATIONS

- Tjoe, B., Gresham, G., Joung, S., Arnold, C., Dhawan, S., Fuller, G., ... Shufelt, C. (2021, September). Digital health for predicting cardiac hospital visits in menopausal women with stable ischemic heart disease. *North American Menopause Society Annual Meeting*. Presented in Washington, DC.
- Tjoe, B., Gresham, G., Joung, S., Arnold, C., Dhawan, S., Fuller, G., ... Shufelt, C. (2021, September). Correlation of remotely monitored sleep, exercise, and heart rate by Fitbit with self-reported psychosocial measures in menopausal women with stable ischemic heart disease. *North American Menopause Society Annual Meeting*. Presented in Washington, DC.

PRESS

Comstock, J. (Host), & Spiegel, B. (November 21, 2021) Predicting where virtual care will go next [The Virtual Care Paradigm]. In HIMSS. Los Angeles, CA: *Healthcare Finance.*

Early Prostate Cancer: Predicting Treatment Response Lead Principal Investigator: Dr. Sheldon Greenfield, UC Irvine

PUBLICATIONS

- Grover, A. & Greenfield, S. (2021). Genomic Signatures for Post-Operative Radiation Therapy and Androgen Deprivation Therapy Response in Prostate Cancer: A Precision Medicine Initiative. *Modern Pathology*, 34, 647-766. <u>https://doi.org/10.1038/s41379-021-00760-7</u>
- Homayounpour, P. (2021). Risk factors for prostate cancer recurrence in african american patients: VA versus non-VA healthcare recipients (Order No. 28721803). Available from Dissertations & Theses @ University of California; ProQuest Dissertations & Theses A&I. (2596065603). https://escholarship.org/uc/item/1pg8t6jt

Full Genome Analysis to Guide Precision Medicine Lead Principal Investigator: Dr. David Martin, Children's Hospital Oakland Research Institute

PUBLICATIONS

Shieh, J. T., Penon–Portmann, M., Wong, K., Levy–Sakin, M., Verghese, M., Slavotinek, A., ... Boffelli, D. (2021). Application of full–genome analysis to diagnose rare monogenic disorders. *NPJ genomic medicine*, 6(1), 77. <u>https://doi.org/10.1038/s41525-021-00241-5</u>

Precision Medicine for Multiple Sclerosis: Making It Work (MS NeuroShare) Lead Principal Investigator: Dr. J.B. Jones, Sutter Health

PUBLICATIONS

Bove, R., Bruce, C. A., Lunders, C. K., Pearce, J. R., Liu, J., Schleimer, E., ... Jones, J. B. (2021). Electronic health record technology designed for the clinical encounter. *Neurology: clinical practice*, 11(4), 318–326. <u>https://doi.org/10.1212/cpj.0000000000986</u>

PRESS

Fleming, K., & Madison, L. (2021, December 22). Researchers develop apps to help with complex healthcare needs. Vitals. Retrieved January 12, 2022, from <u>https://</u> <u>vitals.sutterhealth.org/researchers-develop-apps-to-help-with-complex-healthcare-needs/</u>

Precision Diagnosis of Acute Infectious Diseases Lead Principal Investigator: Dr. Charles Chiu, UCSF

PUBLICATIONS

- Deng, X., Garcia-Knight, M. A., Khalid, M. M., Servellita, V., Wang, C., Morris, M. K.,... Chiu, C. Y. (2021). Transmission, infectivity, and neutralization of a spike L452R sars-COV-2 variant. *Cell*, 184(13), 3426-3437. <u>https://doi.org/10.1016/j. cell.2021.04.025</u>
- Gu, W., Talevich, E., Hsu, E., Qi, Z., Urisman, A., Federman,... Chiu, C. Y. (2021). Detection of cryptogenic malignancies from metagenomic whole genome sequencing of body fluids. *Genome Medicine*, 13(1). <u>https://doi.org/10.1186/ s13073-021-00912-z</u>

PRESENTATIONS

UCSF School of Medicine. (2021, January 14). Covid-19: Update on Vaccines and Implications of the New Variants [Video]. YouTube. <u>https://www.youtube.com/</u><u>watch?v=uZranBw5VZM</u>

PRESS

- ABC News Network. (2021, December 1). 1st omicron case in US identified in California. ABC News. <u>https://abcnews.go.com/Health/live-updates/</u> <u>coronavirus/?id=81441585#81496201</u>
- Allday, E. (2021, December 3). 'you sure it's the real thing?' the dramatic story of S.F. scientists' all-night race to sequence first U.S. omicron variant. San Francisco *Chronicle*. <u>https://www.sfchronicle.com/bayarea/article/You-sure-it-s-the-real-thing-The-16669787.php</u>
- California Department of Public Health. (2021, January 17). Covid-19 variant first found in other countries and states now seen more frequently in California. CDPH. <u>https://www.cdph.ca.gov/Programs/OPA/Pages/NR21-020.aspx</u>
- Centers for Disease Control and Prevention. (2021, December 1). First Confirmed Case of Omicron Variant Detected in the United States. CDC Newsroom. <u>https://www.</u>

cdc.gov/media/releases/2021/s1201-omicron-variant.html

- Krieger, L. (2021, January 27). The hunt for covid-19 genomes that could worsen pandemic. Santa Cruz *Sentinel*. <u>https://www.santacruzsentinel.com/2021/01/03/</u> the-hunt-for-covid-19-genomes-that-could-worsen-pandemic/?fbclid=IwAR1 IW8JfupwAwDsg7RTyZ0T0cfbX3BaugvXv6ii8t4YRKtPnkfm0JzehXJ0
- Krieger, L. M. (2021, August 30). New UCSF study: Vaccine-resistant viruses are driving 'breakthrough' covid infections. *The Mercury News*. <u>https://www.</u> <u>mercurynews.com/2021/08/27/new-ucsf-study-vaccine-resistant-viruses-aredriving-breakthrough-covid-infections/</u>
- Stanley, S. (2021, May 26). A comprehensive profile of California's "Homegrown" coronavirus. Gladstone Institutes. <u>https://gladstone.org/news/comprehensive-profile-californias-homegrown-coronavirus</u>
- Tompkins, L., & Zimmer, C. (2021, January 18). As the U.S. surpasses 24 million cases, Los Angeles confronts a more contagious variant. The New York *Times*. <u>https://www.nytimes.com/2021/01/18/us/as-the-us-surpasses-24-million-cases-los-angeles-confronts-a-more-contagious-variant.html</u>
- Yahoo News. (2021, April 27). White House COVID briefing [Video]. YouTube. <u>https://www.youtube.com/watch?v=zUsx3gwhvMU&t=1657s</u>
- Zimmer, C. (2021, January 6). U.S. is blind to contagious new virus variant, scientists warn. The New York *Times*. <u>https://www.nytimes.com/2021/01/06/health/</u>

coronavirus-variant-tracking.html?smid=tw-share

B. COMPLETED CIAPM DEMONSTRATION PROJECTS

Artificial Intelligence for Imaging of Brain Emergencies

Lead Principal Investigator: Dr. Pratik Mukherjee Host Institution: UC San Francisco

Project Period: February 1, 2017 – December 31, 2018

Partners: 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; UC Berkeley; Zuckerberg San Francisco General Hospital and Trauma Center

Irreversible brain damage can occur within minutes of brain injury. However, 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 boardcertified radiologists.

The team developed a cloud-based, automated image analysis platform capable of detecting intracranial bleeding with over 99% accuracy, and equal to the performance of a board-certified radiologist. Once FDA approved, the technology can be used in areas without sufficient radiologists on hand such as rural or remote locations as well as third world countries.

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 a greater than 99% accuracy of diagnosis
- 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

California Kids Cancer Comparison

Lead Principal Investigator: Dr. David Haussler Host Institution: UC Santa Cruz Project Period: September 1, 2015 – December 31, 2018 Partners: Alex's Lemonade Stand Foundation; Amazon Services, Inc.; Azure, Inc.; Children's Hospital Orange County; Children's Mercy Hospital in Kansas City; DNAnexus, Inc.; Jacob's Heart; Key for a Cure; Kids v Cancer; Live for Others Foundation; Microsoft, Inc.; NuMedii, Inc.; Pacific Pediatric Neuro–Oncology Consortium; Philanthropist George Kraw; Sanford University of South Dakota Medical Center; Seven Bridges Genomics, Inc.; Stanford University Hospital; St. Baldrick's Foundation; Team Finn; Team G Foundation; UC San Francisco; University of British Columbia Cancer Agency; University of Michigan; University of Pittsburg; Unravel Pediatric Cancer

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.

Because DNA testing and analysis only provide useful information for fewer 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 guiding cellular activity. 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 large 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

Early Prediction of Major Adverse Cardiovascular Event Surrogates

Lead Principal Investigator: Dr. Brennan Spiegel

Host Institution: Cedars-Sinai Medical Center

Project Period: January 1, 2017 – December 31, 2018

Partners: Agilent, Inc.; AliveCor, Inc.; Beckman Coulter, Inc.; DocuSign, Inc.; Fitabase, Inc.; Fitbit, Inc.; HealthLoop, Inc.; Neoteryx, Inc.; SCIEX, Inc.; Tasso, Inc.; Thermo Fisher Scientific, Inc.; UCLA

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 measurements to predict Major Adverse Cardiac Events (MACEs). They remotely monitored 200

patients diagnosed with ischemic heart disease with 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 in patients helped to predict MACEs in patients.

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 a cardiac abnormality on his remote wearable biosensor, the program prompted him to visit the emergency room and 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 association of physical activity and overall health with increased cardiac health and lower MACE risk

Early Prostate Cancer: Predicting Treatment Response

Lead Principal Investigator: Dr. Sheldon Greenfield

Host Institution: UC Irvine

Project Period: January 1, 2017 – December 31, 2018

Partners: Ambry Genetics Corporation; Cedars-Sinai Medical Center; GenomeDx Biosciences, Inc.; Vanderbilt University; Veterans Affairs Los Angeles; UCLA Medical Center

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 are expected to continue to develop to 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 patient data privacy
- Correlated genetic risk with patient demographics and treatment, finding African American and Latino men were generally at a higher genetic risk of prostate cancer

Full Genome Analysis to Guide Precision Medicine

Lead Principal Investigator: Dr. David Martin

Host Institution: Children's Hospital Oakland Research Institute

Project Period: March 1, 2017 – December 31, 2018

Partners: GenomeOne, Inc.; Human Longevity, Inc.; Illumina, Inc.; UC Berkeley; UC San Francisco; UCSF Benioff Children's Hospital Oakland

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 with potentially genetic disorders.

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

This research demonstrated that FGA can give clinicians the ability to assess disease risk and potential therapies early in their pediatric patient treatment. It also

contributed to identifying genetic diseases which may otherwise be 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 the disorder in 40% of pediatric patients in the study
- Proof of 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

Lead Principal Investigator: Dr. Nicholas Anderson Host Institution: UC Davis

Project Period: January 1, 2017 – December 31, 2018

Partners: Overlap Health, Inc.; UC Berkeley; UC San Francisco

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 healthcare providers. However, patients are constantly accumulating personal data on their mobile phones which could help patients and their clinicians follow their disease progression. While this data could be extremely useful for health record and patient care, most of these mobile phone applications do not enable clinicians to view the data or integrate with their electronic health records.

The research team at UC Davis developed a HIPAA-compliant1 mobile health application, designed to send alerts and collect, monitor, and report patient-generated data. This application integrated data from the patient's electronic health record (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 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 and clinical and personal data
- Evaluated the use of and engagement with the application

Precision Diagnosis of Acute Infectious Diseases

Lead Principal Investigator: Dr. Charles Chiu

Host Institution: UC San Francisco

Project Period: September 1, 2015 – December 31, 2018

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

Rare bacterial infections are costly and difficult to diagnose. Often patients with suspected infections will 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 the 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

Precision Medicine for Multiple Sclerosis: Making It Work

Lead Principal Investigator: Dr. JB Jones

Host Institution: Sutter Health

Project Period: March 1, 2017 – December 31, 2018

Partners: National Multiple Sclerosis Society; Palo Alto Medical Foundation; Plan Language Health, Inc.; Roche/Genentech, Inc.; Sutter's Jordan Research and Education Institute; Sutter Philanthropy; UC San Francisco

Multiple sclerosis (MS) is a chronic nervous system 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 to 40 years-old, 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 of an interactive tool, called neuroSHARE. The neuroSHARE application was designed to support access to clinical and patientreported 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 data management
- Provided progress toward reducing health disparities
- Utilized partnerships to encourage clinical and commercial use, with a great potential to scale toward other diseases/conditions

C. CIAPM REPRESENTATION AT SELECT EXTERNAL EVENTS

January 8 – American Association for Precision Medicine Annual Meeting 2021, "Driving the Future of Precision Medicine"

January 21 – Stanford University, "COVID-19 Community Town Hall: Vaccine Readiness"

January 27 – Precision Medicine World Conference, "21st Century Precision Medicine in the Age of COVID-19, Tackling the Mental Health Crisis in the Wake of COVID-19"

February 9 - National Academy of Sciences, Engineering and Medine Workshop, "Envisioning a Transformed Clinical Trials Enterprise for 2030"

February 11 – Van Horn Public Library Talks, "Precision Medicine and Alzheimer's Disease"

February 18 – California Council on Science and Technology, "Launch of the CCST Disaster Resilience Initiative"

March 6 – 500 Women Scientists and Journal of Science Policy & Governance, "Intersectional Science Policy"

March 12 – Portland State University, "Toward Health Equity"

March 19 – South by Southwest 2021, "Health Equity through Coordinated Care"

April 14 – UC San Diego, "Science Policy for an Equitable California"

April 14 - UCSF Office of Population Health and Health Equity, "Racism and Race: The Use of Race in Medicine and Implications for Health Equity"

April 16 – Stanford University, "Advancing Neuroscience with Precision"

April 21 – All In: Data for Community Health, "Building Community Capacity by Sharing Power, Storytelling, & Systems Change"

April 28-29 - National Academy of Sciences, Engineering, and Medine Workshop, "Changing the Culture of Data Management and Sharing"

May 18 – National Science Policy Network, "Partnerships for Health Equity" June 10 – Precision Medicine Leaders' Summit, "Precision Medicine and Rare Disease Conference"

June 17 – CIAPM 2020 Annual Report briefings delivered by CIAPM staff to state legislators, Capitol staff, and members of the public

June-July – Individual briefings to legislative offices about state-funded ACEs demonstration projects

July 13 – US Office of the National Coordinator for Health Information Technology, "Advancing Social Determinants of Health Data Use and Interoperability for Achieving Health Equity"

August 18 – Break Barriers California, "Masterclass on Data Sharing"

August 30-September 2 - International Network for Government Science Advice, "INGSA 2021: Build Back Wiser"

September 22 – Precision Medicine World Conference: Pittsburgh, "Authentic Community Engagement in State-Sponsored Precision Medicine Research" and "Diversity, Inclusion, Equity, and Access in Community Engaged Precision Medicine Research and Clinical Implementation"

September 30 – US National Institutes of Health Office of Minority Health, "COVID-19 Health Equity Task Force"

September 30 – Network for Regional Healthcare Improvement and Strategic Health Information Exchange Collaborative, "Social Determinants of Health & Interoperability Learning Lab"

October 15 – UC Davis NIH Molecular and Cell Biology graduate program training grant retreat, "Precision Medicine"

October 25 – UC Health, "Maternal and Infant Health Administrative Data Study" **October 26** – Executives for Health Innovation, "Using Evaluation Data to Drive Social Determinant of Health Program Improvement Strategies"

November 5 – International "Brain Bee" Neuroscience Olympiad, "Applying Science for Social Good: Precision Medicine and Health Equity"

November 8-10 – All In: Data for Community Health, "2021 Annual Meeting" December 8 - UC Davis Center for Healthcare Policy and Research, "Launching the Nation's Largest All-Payer Claims Database"

D. KEY PERSONNEL IN 2021

Sam Assefa, OPR Director (October 2021-present) Kate Gordon, OPR Director (January 2019-June 2021) Julianne McCall, Co-Director of CIAPM Shannon Muir, Co-Director of CIAPM Megan Varvais, Communication Specialist & Administrator Aiyana Emigh Cortez, Policy Fellow Hyunsoo Gloria Kim, Policy Fellow Jessica Lumian, Policy Fellow (May 2021-present) Affad Shaikh, Graduate Student Intern (May 2021-August 2021) Alexandra Blundell, Graduate Student Intern (August 2021-November 2021) Hannah Chu, Policy Fellow (November 2021-present)

E. MEETING AGENDAS

February 25 – <u>CA Precision Medicine Advisory Council Winter Meeting</u>
March 26 – <u>CIAPM ACEs Expert Selection Committee Meeting</u>
May 27 – <u>CA Precision Medicine Advisory Council Spring Meeting</u>
August 16, 20 – <u>CA Precision Medicine Advisory Council Summer Meeting</u>
November 19 – <u>CA Precision Medicine Advisory Council Fall Meeting</u>

F. COUNCIL GUIDELINES

Ratified 11/19/2021

ARTICLE 1. Purpose of the Council

The purpose of the Precision Medicine Advisory Council (Council) is to advise and make recommendations to the Governor's Office of Planning and Research (OPR) on matters related to the California Initiative to Advance Precision Medicine (CIAPM) (Gov. Code, §§ 65055 – 65059).

ARTICLE 2. Membership of Council and Desired Qualifications

- 1. The Council should consist of the following eleven members:
 - a. The Surgeon General of California, ex officio
 - b. The Secretary, or an Assistant Secretary, of the Health and Human Services Agency, ex officio
 - c. Seven members invited by the Governor's Office of Planning and Research
 - d. One member recommended by the Senate Pro Tem and one member recommended by the Speaker of the Assembly
- 2. Members should be experts in precision medicine representing, for example, physicians, private industry, patient advocacy and community groups, regulatory affairs specialists, health insurance providers, public policy experts, venture capital communities, or academia in the areas of data science, bioinformatics, bioethics, the microbiome, metabolomics, genomics, community engagement, wearable devices, or other related fields.
- 3. All members serve at the pleasure of OPR.
- 4. Members may not select alternates or designees.

ARTICLE 3. Council Organization

1. Expected term of service of Council members may be as follows:

a. In the first year

i. Three members may be invited by OPR to serve a three-year term

ii. One member may be invited by OPR to serve a two-year term

iii. Three members may be invited by OPR to serve a one-year term

iv. Both members recommended by the Legislature may be invited to serve a two-year term

b. Following the first year, all new terms may be three years.

c. Members should serve no more than six years total on the Council.

d. Members invited to fill vacancies should serve out the remainder of the position's term.

e. Vacancies that occur should be filled within 90 days after the occurrence of the vacancy, and should be filled in the same manner in which the vacating member was invited.

2. The Council will elect a Chair and a Vice Chair for a one-year term. The Vice Chair will be responsible for fulfilling the Chair's duties when the Chair is unavailable.

a. Nominations

Nominations do not need to be seconded.

A person can nominate himself or herself.

Nominations for Vice Chair will follow election of Chair.

b. Nominee Statements

Each nominee will have 2 minutes to make a statement to the Council prior to the first round of voting.

c. Elections

i. Elections will be conducted via secret ballot.

ii. Election ballots may not be submitted via email.

iii. If there is only one nominee, a 2/3 majority vote is required for the nominee to be elected.

iv. In the event of a tie:

A. If there are exactly two candidates, all eligible council members will vote again. The process will repeat until one candidate receives a majority B. If there are more than two candidates, a winner will be chosen via ranked choice voting.

3. Quorum is achieved with seven Council members.

4. Six affirmative votes are needed for procedural motions to pass.

5. Ex officio members may vote and are counted toward quorum.

6. All motions that do not receive at least six affirmative votes during a meeting part are held open for 48 hours after that meeting part adjourns.

7. Council members who were not present at the time a motion was made may submit their votes for open motions up to 48 hours after that meeting part adjourns.

8. If a Council member cannot attend a meeting, they may, prior to a meeting, submit written comments that may be read aloud by staff during the meeting. Comments should be no longer than a half page per agenda item.

9. Council members who voted for a motion during a meeting may not change their vote via email.

10. Non-election votes submitted by email are subject to public posting.

11. Council members will be reimbursed for travel consistent with OPR's travel policies.

12. Any member of the Precision Medicine Advisory Council should be ineligible to apply for funding as a Principal Investigator from project grants during his or her term of service on the Council, and for one year immediately following his or her term of service on the Council.

13. The Council should meet at least four times annually in person and the meetings should be held in locations that allow stakeholders in different regions of the state to participate.

ARTICLE 4. Responsibilities

Responsibilities of the Council may include but are not limited to:

1. Identifying and recommending research fields, total funding levels, timelines, and selection committee members for the RFP process, and expert project evaluators

2. Preparing for and attending Council meetings

3. Developing strategies to support sustainability of the Initiative, respond to changes in societal needs and opportunities, and stimulate adequate community engagement with CIAPM activities

4. Reviewing and providing feedback on documents including, but not limited to, annual legislative reports and project evaluation reports

G. CALIFORNIA PRECISION MEDICINE ADVISORY COUNCIL MEMBERS

Chair Clara Lajonchere, PhD

Dr. Clara Lajonchere's background reflects a wide range of professional, clinical, and research activities across Central Nervous System disorders. She has spent her career on cross-cutting issues in psychiatric genetics and translational medicine. Through the Institute for Precision Health at UCLA, Dr. Lajonchere is working collaboratively with thought leaders across the state of California to advance precision medicine and improve outcomes for patients. Prior to UCLA, Dr. Lajonchere held faculty appointments at USC and Keck School of Medicine where she served as Director of the NIH Center for Genomic and Phenomic Studies in Autism and conducted research on models for dissemination of scientific information to underserved populations, including the Latino community. She also served as VP of Clinical Programs for Autism Speaks for over a decade where she oversaw a diverse portfolio of basic science and clinical programs. She currently consults for several tech start-ups in the autism space focused on AI, robotics, and targeted therapeutics.

Vice Chair Keith Yamamoto, PhD

Dr. Keith R. Yamamoto is Vice Chancellor for Science Policy and Strategy, and Director of Precision Medicine at UCSF. A UCSF researcher since 1973, he is a leader in determination of gene regulatory mechanisms. He has led or served on national committees focused on public and scientific policy, public understanding of science, science education, open science, and peer review. He chairs the Coalition for the Life Sciences and sits on the National Research Council Governing Board Executive Committee, the Board of Directors of Research!America, the Board of Directors of the Public Library of Science, the Governing Board of the California Institute for Regenerative Medicine, and the Advisory Board for Lawrence Berkeley National Laboratory. As Chair of the NAS Board on Life Sciences, Dr. Yamamoto created the study committee that produced the report "Toward Precision Medicine," which enunciated the precision medicine concept, and he helped lead efforts in the White House, in Congress, in Sacramento and at UCSF to implement it. Dr. Yamamoto was elected to the National Academy of Sciences, the National Academy of Medicine, the American Academy of Arts and Sciences, and is a fellow of the American Association for the Advancement of Science.

Nadine Burke Harris, MD, MPH

Dr. Nadine Burke Harris is an award-winning physician, researcher and advocate dedicated to changing the way our society responds to one of the most serious, expensive and widespread public health crises of our time: childhood trauma. She was appointed as California's first-ever Surgeon General by Governor Gavin

Newsom in January 2019. Her career has been dedicated to serving vulnerable communities and combating the root causes of health disparities.

Dr. Burke Harris founded the Center for Youth Wellness in one of San Francisco's most underserved communities, Bayview-Hunters Point, an organization leading the effort to advance pediatric medicine, raise public awareness, and transform the way society responds to children exposed to Adverse Childhood Experiences (ACEs) and toxic stress. She also founded and led the Bay Area Research Consortium on Toxic Stress and Health, to advance scientific screening and treatment of toxic stress.

Ysabel Duron

Ysabel Duron is the Founder/CEO of the California based Latino Cancer Institute working to eliminate the Latino cancer burden nationwide by driving equitable access, research and policy.

Duron was an award-winning TV journalist for 43 years in the San Francisco Bay Area and elsewhere, but stepped away in 2013 to continue her role as a patient advocate and voice for the Latino community.

A cancer survivor, she serves both on the Institutional Review Board of the NIH All of Us Research Program, and most recently joined the Board of California Institute for Regenerative Medicine, a state taxpayer funded initiative to support stem cell research.

She was inducted into the National Association of Hispanic Journalists Hall of Fame in 2009, named one of the 25 most outstanding Hispanics in the Bay Area in 2005 and honored with the W.E.B. DuBois from the SJ Chapter of the NAACP in 2011, amongst other honors that reflect her community engagement.

Oliver Keown, MD

Dr. Oliver Keown is a UK-trained physician, scientist and former policy advisor turned healthcare and medical technologies venture capital investor with Intuitive Ventures. Prior to joining Intuitive, he was a VC investor with GE Ventures, driving startup deal-flow in the Bay Area and beyond across HealthTech, life science and MedTech domains.

In past roles Dr. Keown has advised and supported a range of US and international healthcare innovation projects across technology, policy, commercial, and academic fields. Early in his career he worked as a junior doctor in the UK National Healthcare Service across a variety of medical and surgical disciplines. He holds an MD and a Bachelor's degree in Pharmacology from the University of Edinburgh, Scotland.

Kenneth Kim, MD

Dr. Kenneth Kim received his MD from Harvard Medical School, completed a fellowship at the MIT Sloan School of Management, and received internal medicine and allergy/immunology training at UCLA. He has served on the clinical faculty both at UCLA and UC Irvine for over 15 years. He has been a medical monitor,

consultant, and investigator on over 600 clinical trials, having published over 30 research articles and 50 abstracts in peer-reviewed journals. Dr. Kim is a nationally recognized expert in the areas of early stage clinical research, ethnobridging drug development strategy, influenza challenge, mold allergy, and latex allergy.

He has founded numerous health care services businesses, including a 200+ employee clinical research organization which he transitioned to private equity. He is currently the medical director of Ark Clinical Research and a strategic investor in a variety of startups, while also maintaining a private allergy and asthma practice in Southern California.

Yvonne Maldonado, MD

Dr. Yvonne (Bonnie) A. Maldonado is Professor in the Departments of Pediatrics and Epidemiology and Population Health, Chief of the Division of Infectious Diseases, and Senior Associate Dean for Faculty Development and Diversity at Stanford University School of Medicine. Her international research activities have included the epidemiology and prevention of viral infections such as rotavirus, measles, mumps, rubella, polio and pediatric HIV infection. She has written over 200 articles in peerreviewed journals, and 50 book chapters on these topics. In 1989, Dr. Maldonado received the Epidemic Intelligence Service Alumni Award from the Centers for Disease Control and Prevention, and she was inducted into the Multicultural Alumni Hall of Fame at Stanford University in 2001 and the Stanford Medical Alumni RISE (Reach, Inspire, Serve and Engage) award in 2018. Dr. Maldonado is a Fellow of the American Academy of Pediatrics, a member of the Society for Pediatric Research, the Pediatric Infectious Disease Society and the American Public Health Association. Dr. Maldonado has devoted substantial effort to teaching and training activities at Stanford University as well as in the national and international setting. Throughout her career, she has invested heavily in her commitment to improving cultural and gender diversity at all levels.

Fatima Muñoz, MD

Dr. Fatima Muñoz is the Director of the Department of Research and Health Promotion at San Ysidro Health (SYHealth), a high performing Federally Qualified Health Center (FQHC) providing care to over 105,000 patients throughout San Diego County. Fatima completed her medical training in Mexico and earned a Master's in Public Health from Universidad Autónoma de Baja California. She possesses over 15 years of clinical research experience working in health promotion programs and epidemiological research studies, specifically among underserved populations. Dr. Muñoz's expertise in public health issues spans both sides of the U.S.-Mexico border with emphasis in the elimination of health disparities. Her award winning research portfolio includes: chronic disease, HIV prevention and treatment, cervical and breast cancer, and the impact of bi-national access to care on health policy. Most recently, SYHealth was awarded the All of Us Research Program from the National Institute of Health. It is only one of six FQHCs west of the Mississippi that is part of the Program and Dr. Muñoz is the Principal Investigator for SYHealth. In this capacity, she and her team have been contributing in the development and implementation of the program Spanish speaking participants.

Samar Muzzafar, MD, MPH

Dr. Samar Muzaffar is an assistant secretary at the California Health and Human Services Agency. Prior to her appointment she was a population health and health systems design consultant for Integrated Health Solutions LLC. Dr. Muzaffar previously served as chief medical officer at the Missouri Department of Social Services for Missouri's Medicaid program and was the Emergency Medical Services medical director at the Missouri Department of Health and Senior Services. She served as an adjunct instructor at Washington University's Brown School, and was a clinical instructor and clinical assistant professor at the University of Missouri – Columbia University Hospital. Dr. Muzaffar is a member of the American College of Preventive Medicine's Board of Regents and Health Systems Transformation Task Force, and the American Academy of Pediatrics Institute for Healthy Childhood Weight TEAM UP Payer Advisory Board. She earned a Master of Public Health degree from Johns Hopkins University and a Doctor of Medicine degree from the University of Missouri–Columbia School of Medicine.

Hakan Sakul, PhD

As VP and Head of Diagnostics, Dr. Hakan Sakul leads Pfizer's company-wide Diagnostics efforts. Dr. Sakul worked in the biotech industry in human genetics and statistical genetics fields early in his career before moving to Parke–Davis Pharmaceuticals to direct human genetics, statistical genetics and pharmacogenetics programs. Following the merger of Parke–Davis with Pfizer, he has held positions of increasing responsibility, including Director/Site Head for Clinical Pharmacogenomics, Senior Director roles in Molecular Profiling and Translational Oncology, and most recently as Executive Director of Diagnostics. After receiving BS and MSc degrees from Ankara University in Turkey, and a PhD in Quantitative Genetics from the University of Minnesota as a Rotary Foundation Scholar, Dr. Sakul conducted postdoctoral studies at UC Davis. He is the author of over 30 refereed scientific articles as well as many other papers, abstracts, and book chapters. Dr. Sakul is keenly interested in diagnostics and related medical technologies to advance precision medicine for the improvement of individualized healthcare.

Mary Anne Schultz, PhD, MBA, MSN, RN

Dr. Mary Anne Schultz is an accomplished Senior Executive and Consultant with more than 40 years of success across the nursing service, nursing education, informatics, and clinical/business intel venues. Her broad areas of expertise include data analysis, program evaluation, and evidence-based practices customized to a system's health care client. Throughout her executive career, Dr. Schultz has held faculty and leadership positions within the California State University and University of California systems, and \$chultz & Associates. Dr. Schultz is a Professor, Informaticist and former Chair for the Nursing Department at California State University, San Bernardino. She holds a PhD in Nursing Systems and Economics from UCLA, an MBA from Claremont Graduate University, and a certificate in Health Informatics from UC Davis.

H. ACES EXPERT SELECTION COMMITTEE

Melissa T. Merrick, PhD

President & CEO, Prevent Child Abuse America

Areas of expertise: Child Abuse/Early Adversity Prevention

Dr. Merrick has nearly 20 years of clinical, research, and leadership experience related to the etiology, course, and prevention of child abuse and neglect. She is currently the President and CEO of Prevent Child Abuse America, the nation's oldest nonprofit organization dedicated to the primary prevention of child abuse and neglect.

Previously, Dr. Merrick was a senior epidemiologist at the National Center for Injury Prevention and Control at the Centers for Disease Control and Prevention (CDC), in Atlanta, and served on a detail in the Office of the Commissioner at the Children's Bureau in the Administration for Children and Families. In partnership with the U.S. Department of Health and Human Services' Office of Child Abuse and Neglect, she served as the lead scientist for the Adverse Childhood Experiences (ACE) study at CDC for 8 years. Dr. Merrick successfully leverages her clinical and research experiences to communicate and disseminate the critical public health importance of preventing early adversity to key stakeholders with diverse priorities, backgrounds, and knowledge, including legislators, business and civic leaders, and members of the academic and medical communities.

Dr. Merrick received her BA in Psychology, magna cum laude, from the University of Pennsylvania, and her master's and doctoral degrees in Clinical Psychology from the San Diego State University/UC San Diego joint doctoral program in clinical psychology, where she served as a program coordinator for the San Diego site of the Longitudinal Studies on Child Abuse and Neglect Consortium. Dr. Merrick was a National Institutes of Health-funded postdoctoral fellow at the University of Miami Child Protection Team (CPT), where she was involved in a multi-site program of research that examined child maltreatment risk and protective factors in families evaluated by CPTs across the state of Florida.

Dr. Merrick is married and has two young children who keep her grounded, thankful, and hopeful for a brighter future for all children.

Saida Abdi, PhD, MSW, LICSW

Assistant Professor of Social Work, University of Minnesota

Areas of expertise: *Refugees, Trauma Systems Therapy, Resilience* Dr. Abdi is a Clinical Social Worker and an expert in refugee trauma and resilience. She has worked for more than 20 years with refugee youth and families in the diaspora. Her areas of focus include building individual, family, and community resilience, improving systems of care responsiveness to the needs of refugee and immigrant communities, trauma systems therapy, and culturally responsive interventions. She is the co-developer of Community Connect, a multidisciplinary team-based intervention that worked with youth up to the age of 24 years of age who are at risk for violence of any type. She is also the Primary Investigator of the project, RAJO (Somali for hope) in Canada, funded by the Public Safety Agency in Canada to support positive outcomes for Somali-Canadian youth. This 5-year, multi-million-dollar project will be evaluated to test the impact of the intervention on youth outcomes.

Dr. Abdi previously served for over 12 years as Associate Director for Community Relations of the Refugee Trauma and Resilience Center at Boston Children's Hospital and Adjunct Professor of Boston College. She earned her PhD in Sociology and Social Work and a Master's degree in Social Work from Boston University and a second Master's degree in Communications and Media Studies from Carleton University in Ottawa, Canada.

She is the co-author of the recently published book, *Mental Health Practice with Immigrant and Refugee Youth: A Socioecological Framework* (APA, 2019).

Larissa Avilés-Santa, MD, MPH

Director, Division of Clinical and Health Services Research, National Institute on Minority Health and Health Disparities

Areas of expertise: Latinx/Women's Health, Healthcare Systems

Dr. Larissa Avilés-Santa is the Director of the Division of Clinical and Health Services Research at National Institute on Minority Health and Health Disparities (NIMHD) at the National Institutes of Health (NIH). In her current role, she works with her great team on fostering research aimed at improving health outcomes of health disparities populations within the context of healthcare systems.

Prior to joining NIMHD, she worked at the National Heart, Lung, and Blood Institute from 2006 to 2019 as the Project Director for the Hispanic Community Health Study/ Study of Latinos. In addition, she has participated in multiple NIH-wide committees and working groups addressing minority health, diabetes mellitus and its complications, and women's health. In 2015, she founded the NIH Hispanic Health Research Scientific Interest Group.

She has coauthored multiple publications on different Hispanic health topics and is a frequent guest lecturer at academic and other scientific venues within and outside of the NIH. In 2017, Dr. Avilés-Santa was the field coordinator of the post-hurricanes Irma and María recovery of the health and social services of the entire country of Puerto Rico. She worked in this capacity during the first six and a half months of recovery work coordinated by the HHS.

Dr. Avilés–Santa earned her medical degree from the University of Puerto Rico School of Medicine, and completed a residency in internal medicine at the University Hospital in San Juan. She completed her fellowship in endocrinology at the University of Texas (UT) Southwestern Medical Center, where she joined the faculty of the Endocrine Division. She also earned a Master's degree at the UT School of Public Health.

Zulfiqar A. Bhutta, PhD, MBBS

Inaugural Robert Harding Chair in Global Child Health, The Hospital for Sick Children Inaugural Ibn Sina Scholar in Global Child Health, The Hospital for Sick Children Co-Director of the SickKids Centre for Global Child Health

Founding Director of the Centre of Excellence in Women and Child Health, Aga Khan University

Areas of expertise: Global Child/Community Health, Nutrition

In addition to his leadership roles at the Hospital for Sick Children, the SickKids Centre for Global Child Health, and Aga Khan University in Pakistan, Dr. Bhutta holds adjunct professorships at several universities, including Johns Hopkins University and the London School of Hygiene & Tropical Medicine. Dr. Bhutta is a Distinguished National Professor of the Government of Pakistan, Co–Chair of the Maternal and Child Health Oversight Committee of the World Health Organization Eastern Mediterranean Region, Chairman of the Coalition of Centres in Global Child Health, Past President of the International Pediatric Association, and a leading voice for health professionals supporting integrated maternal, newborn, and child health globally.

Dr. Bhutta leads large research groups in Toronto, Karachi, and Nairobi with a special interest in scaling up evidence-based, community setting interventions and implementation of RMNCAH&N interventions in humanitarian contexts. His work with community health workers has influenced maternal and newborn outreach programs for marginalized populations internationally, and his group's work with the WHO and PMNCH is guiding global policy on essential interventions for women, children, and adolescents.

Dr. Bhutta obtained his MBBS from the University of Peshawar and his PhD from the Karolinska Institute. He is a Fellow of the Royal College of Physicians, the Royal College of Paediatrics and Child Health, and the Pakistan Academy of Sciences. He was recently awarded the honour of Fellow of the Royal Society and honorary Fellow of the American Academy of Pediatrics. Among many honors, in 2016, Dr. Bhutta received the World Academy of Sciences 2016 prize in Medical Sciences.

Keith Dobson, PhD

Professor of Clinical Psychology, University of Calgary

Areas of expertise: *Psychological Interventions, Depression, Professional Ethics* Dr. Keith Dobson is a professor of Clinical Psychology who leads University of Calgary's Depression Research Laboratory. His research interests are in Clinical Psychology, Cognitive Behaviour Therapy, Depression and stigma. Dr. Dobson also examined psychological approaches and treatments for adults in primary care with Adverse Childhood Experiences. Further, he has written about developments in professional psychology and ethics, and has been actively involved in organized psychology in Canada, including a term as President of the Canadian Psychological Association. Dr. Dobson is also a Principal Investigator for the Opening Minds program of the Mental Health Commission of Canada, with a focus on stigma reduction related to mental disorders in the workplace. His work has yielded more than 300 peer-reviewed published articles, 80 chapters, 17 books, and presentations in many parts of the world. He is a Past-President of both the Academy of Cognitive Therapy and the International Association for Cognitive Psychotherapy. Among other awards, he has been given the Canadian Psychological Association's Award for Distinguished Contributions to the Profession of Psychology, the Donald O. Hebb Award for Distinguished Contributions to the Science of Psychology, and the Award for Distinguished Contributions to the International Development of Psychology. Dr. Dobson received a PhD and Master's degree in Psychology from the University of Western Ontario, London and a Bachelor's degree in Psychology/Sociology from the University of Alberta, Edmonton.

Willarda Edwards, MD, MBA

Internal Medicine Physician

Member of the Board of Trustees, American Medical Association

Areas of expertise: Health Equity, Trauma, Migrant Communities

Dr. Edwards has been committed to organized medicine for over 30 years, holding prominent positions in local, state, and national associations. She is past president of the National Medical Association, MedChi, Baltimore City Medical Society, and Monumental City Medical Society.

Putting patients first has been this physician's mission in her 10-year tenure on the board of CRISP, the regional health information center in Maryland.

Joining AMA in 1994, Dr. Edwards was appointed to the inaugural governing council of the Women Physicians Congress and has served on reference committees, task forces and chaired the AMA Council on Constitution and Bylaws.

After completing active duty in the Navy, Dr. Edwards founded an internal medicine practice in Baltimore, where she is the managing partner. She retired from the U.S. Navy Reserves at the rank of commander after 24 years of service. In addition to her busy private practice and AMA responsibilities, Dr. Edwards held senior management positions at the National Association for the Advancement of Colored People Health Advocacy Division and at the Sickle Cell Disease Association of America.

Elected to the Board of Trustees in 2016 and re-elected in 2020, Dr. Edwards has demonstrated hard work, leadership skills, and consensus building. She chaired the Task Force on Health Equity, resulting in the establishment of the AMA Center on Health Equity.

Dr. Edwards knows the balance needed in a physician's work life and the need to always be an advocate for patients in the delivery of quality care.

Dylan G. Gee, PhD

Assistant Professor of Psychology and Psychiatry, Yale University

Areas of expertise: Child Development, Stress, Mental Health

Dr. Gee directs the Clinical Affective Neuroscience and Development Laboratory at Yale University. She received her BA in Psychological and Brain Studies from Dartmouth College and her PhD in clinical psychology from UCLA. Prior to joining the faculty at Yale, Dr. Gee completed her clinical internship and postdoctoral training at Weill Cornell Medical College. Her research focuses on child and adolescent mental health, with primary goals to delineate typical and atypical trajectories of brain development, elucidate how early adversity influences sensitive periods of development, and translate knowledge of the developing brain to optimize interventions for children and adolescents with anxiety and stress-related disorders. Dr. Gee's research is funded by the National Institutes of Health, the Brain & Behavior Research Foundation, the Jacobs Foundation, and the American Psychological Association. She has received broad recognition for her work, including an NIH Director's Early Independence Award, the Janet Taylor Spence Award for Transformative Early Career Contributions from the Association of Psychological Science, and the American Psychological Association's Early Career Award for Outstanding Contributions to Children, Youth, and Families.

Jacob Ham, PhD

Director of the Center for Child Trauma & Resilience, Icahn School of Medicine at Mount Sinai

Areas of expertise: Trauma, Child Development, Psychotherapy, Evaluation Dr. Ham is a Clinical Psychologist, Associate Professor in Psychiatry, and Director of the Center for Child Trauma and Resilience at the Icahn School of Medicine at Mount Sinai. He receives federal and local grants to create and advance trauma-informed practices throughout multiple service systems including education, foster care, medical health, and criminal justice. His most recent funding from SAMHSA, the NYC DOE, and the Manhattan District Attorney's office are being used to create a trauma-informed adolescent substance abuse recovery and prevention program, a complex trauma treatment program inside the Mount Sinai Health System, crime victims treatment centers and trauma-informed community schools. He is a highly sought trainer and consultant on trauma-informed engagement and maintains an active clinical practice at Mount Sinai Beth Israel for children, families, and adults with a particular focus on using moment-to-moment relationship-based interventions that enhance attachment to overcome trauma and improve mental health. He received his PhD at the University of Massachusetts Boston and completed an internship at Massachusetts General Hospital and a fellowship at Children's Hospital Boston, both of which were also part of Harvard Medical School.

H. Eugene Hoyme, MD

Medical Director of the Sanford Children's Genomic Medicine Consortium Professor of Pediatrics and Medicine, University of Arizona Senior Advisory in Genetics/Genomic Medicine, University of South Dakota Sanford School of Medicine **Areas of expertise:** Pediatric Genetics, Fetal Alcohol Syndrome Dr. Hoyme serves as Senior Advisor in Genetics/Genomic Medicine at Sanford Health, the University of South Dakota Sanford School of Medicine, and the University of Arizona Health Sciences. He also serves as Medical Director of the Sanford Children's Genomic Medicine Consortium, a formal collaborative in pediatric precision medicine among ten major children's hospitals. Previously, he functioned as Department Chair of Pediatrics at the Sanford School of Medicine, President of Sanford Research and Chief Academic Officer for Sanford Health. He has held academic and leadership posts at the Stanford University School of Medicine, Lucile Packard Children's Hospital, and the University of Vermont College of Medicine.

He earned his BA summa cum laude from Augustana University in Sioux Falls and his MD from the University of Chicago Pritzker School of Medicine. He completed his residency in Pediatrics and Clinical Genetics fellowship training at UC San Diego. He is board certified in Pediatrics, Clinical Genetics, and Clinical Cytogenetics.

He is the recipient of myriad awards in research, teaching, and mentorship, including the Western Society for Pediatric Research's Joseph W. St. Geme Jr. Education Award, the National Organization on Fetal Alcohol Syndrome Excellence Award, the American Academy of Pediatrics David W. Smith Education and Mentorship Award, and the Fetal Alcohol Spectrum Disorders Study Group's Henry Rosett Award for Lifetime Contributions to FASD Research. His research focuses on Pediatric Genetics/Precision Medicine and Fetal Alcohol Spectrum Disorders (FASD). Recently, he was first author of revised expert consensus diagnostic guidelines for FASD based on evaluation of over 10,000 children world-wide spanning more than 20 years.

Patricia Kerig, PhD

Director of the Risk to Resilience Laboratory, University of Utah Professor of Clinical Psychology, University of Utah

Co-Director of the Center for Trauma Recovery and Juvenile Justice, University of Utah Areas of expertise: Trauma, Juvenile Justice, Developmental Psychopathology Dr. Kerig received her doctorate in Clinical Psychology from the University of California at Berkeley with a specialization in children and families and currently is a Professor in the Clinical Psychology program at the University of Utah where she directs the Risk to Resilience Laboratory. She also serves as the Editor in Chief of the Journal of Traumatic Stress. Dr. Kerig is an author of over 185 scholarly journal articles, books, chapters, and journal special issues devoted to understanding the developmental psychopathology of risk, recovery, and resilience among children, adolescents, and families coping with adversity in the context of a range of traumatic stressors, including childhood maltreatment, exposure to interparental conflict and violence, and intimate partner abuse. Her current program of research is focused on investigating the mechanisms accounting for the link between childhood trauma exposure and adolescent delinquency, with attention to potential underlying psychophysiological, cognitive, emotional, and interpersonal processes. She has a special interest in risk factors specific to traumatized girls in the justice system and the roles of intersectionality in regard to gender, race, class, and sexual minority

status. Dr. Kerig also is a co-Director of the Center for Trauma Recovery and Juvenile Justice, a National Child Traumatic Stress Network center whose mission is to develop and disseminate trauma-informed assessment and intervention strategies to the systems that serve at-risk youth, while protecting staff from the potential adverse effects of secondary traumatic stress.

Liliana J. Lengua, PhD

Director of the Center for Child and Family Well-being, University of Washington Maritz Family Professor of Psychology, University of Washington

Areas of expertise: Adversity, Stress, Child Social-Emotional Development Dr. Lengua is a Child Clinical Psychologist studying the effects of stress and adversity on children, examining risk and protective factors that contribute to children's resilience or vulnerability. She examines children's neurobiological stress responses, temperament, coping, parenting, and family contexts as risk and protective factors that account for the effects of adversity on children's social, emotional, and academic well-being.

Dr. Lengua has been an investigator on several federally-funded projects examining the development of executive function (NICHD), the effects of low income, neighborhood, family, and parenting on neurobiological systems of self-regulation, and their effects on preschool and preadolescent children's social, emotional and academic development (NICHD, NIMH), neighborhood, family and peer effects on adolescent substance use (NIDA), and childhood risk factors for the emergence of adult mental health problems (NIDA). Dr. Lengua is the author of over 100 published papers. She serves on the steering committee for the CDC-funded Washington State Essentials for Childhood Initiative, collaborated with the Harvard Center for the Developing Child's Frontiers of Innovation, and has served on the Board of Trustees for Neighborhood House, a nonprofit anti-poverty organization.

Lloyd Michener, MD

Professor of Family Medicine & Community Health, Duke School of Medicine Areas of expertise: Community Engagement, Family Health, Equity Dr. Lloyd Michener serves as a Professor of Family Medicine and Community Health at Duke School of Medicine; Clinical Professor at Duke School of Nursing; and Adjunct Professor at UNC Gillings School of Public Health. He also serves as Chair of the Board of the Foundation for Health Leadership and Innovation and is a member of the National Academies of Medicine Workgroup on Assessing Meaningful Community Engagement.

He has served as Director of the "Practical Playbook", with the support of the deBeaumont Foundation, CDC, and HRSA, linking health care, public health, and communities across the country. In addition, he served as Chair of the Department of Community & Family Medicine at Duke for more than two decades and was the founding director of the Duke Center for Community Research.

Nationally, Dr. Michener has served as the founding Co-Chair of the Community

Engagement Steering Committee for the Clinical and Translational Science Awards of the NIH, and as President of the Association for Prevention, Teaching and Research (APTR). He has been a member of the National Academies Institute of Medicine Committee on Integrating Primary Care and Public Health, the Board of Directors of the Association of Academic Medical Colleges, and the NIH Council for Complementary and Alternative Medicine. Awards include Phi Beta Kappa, Alpha Omega Alpha, the Mead–Johnson Award from the American Academy of Family Physicians, and the Duncan Clark Award from APTR.

Dr. Michener is a graduate of Oberlin College, Harvard Medical School, and residency and fellowship in Family Medicine at Duke.

Charles A. Nelson III, PhD

Professor of Pediatrics and Neuroscience, Harvard Medical School Professor of Psychology, Department of Psychiatry, Harvard Medical School Professor of Education, Harvard Graduate School of Education Richard David Scott Chair in Pediatric Developmental Medicine Research, Boston Children's Hospital

Director of Research, Division of Developmental Medicine, Boston Children's Hospital Areas of expertise: Developmental Cognitive Neuroscience, Childhood Adversity Dr. Nelson's research interests center on a variety of problems in Developmental Cognitive Neuroscience, including the development of social perception; developmental trajectories to autism; and the effects of early adversity on brain and behavioral development. He chaired the John D. and Catherine T. MacArthur Foundation Research Network on Early Experience and Brain Development and served on the National Academy of Sciences (NAS) panels that wrote From Neurons to Neighborhoods, and New Directions in Child Abuse and Neglect Research. In total, Dr. Nelson has published over 400 peer-reviewed journal articles and book chapters, has edited eight books, and written three books. Among his many honors he has received the Leon Eisenberg award from Harvard Medical School, an honorary Doctorate from Bucharest University (Romania), and the Ruane Prize for Child and Adolescent Psychiatric Research from the Brain & Behavior Research Foundation. He was a resident fellow at the Rockefeller Foundation Bellagio Center (Italy) and has been elected to the American Academy of Arts and Sciences, the National Academy of Medicine, and the British Academy.

Kenneth S. Ramos, MD, PhD

Alkek Chair of Medical Genetics, Texas A&M Institute of Biosciences and Technology Professor of Translational Medicine, Texas A&M College of Medicine Professor of Oncology, Houston Methodist Research Institute Executive Director, Institute of Biosciences and Technology, Texas A&M University Health Science Center Associate Vice President, Texas A&M Health Assistant Vice Chancellor for Health Services, Texas A&M University System **Areas of expertise:** Precision Medicine, Genomics, Clinical Pharmacology Kenneth S. Ramos, MD, PhD, is an accomplished physician-scientist and transformational leader, with designations in the National Academy of Sciences and National Academy of Medicine. He is recognized throughout the world for his scientific contributions in the areas of Genomics, Precision Medicine, and Toxicology.

With formal training in Pharmaceutical Sciences, Chemistry, Biochemistry, Pharmacology, and Medicine, Dr. Ramos is helping to steer the changing landscape of medicine and healthcare. He leads several translational, clinical, and educational programs that integrate diverse approaches to elucidate genomic mechanisms of disease. Dr. Ramos has provided academic, executive, administrative, and scientific leadership in Genetics and Genomic Medicine and Toxicology at several institutions, and over the course of his career has influenced the career of numerous clinicians and scientists engaged in medical, veterinary, and pharmaceutical practice. He is committed to initiatives that advance modern technological applications to improve quality of healthcare and reduce disease burden and health–associated costs.

Dr. Ramos's research has paved the way for groundbreaking research on LINE-1 retroelements and their role in chromatin remodeling, DNA damage and repair, and genetic reprogramming. His group was the first to establish a role for retinoblastoma proteins as master regulators of epigenetic silencing of LINE-1 and later characterized novel targets for regulation of cancer cells. He is currently examining the utility of circulating LINE-1 protein as prognostic and diagnostic biomarkers of lung cancer, which combined with imaging may improve precision for early cancer detection. This knowledge is being used to develop targeted therapies for lung cancer.

Arash Shaban-Nejad, PhD, MPH

Assistant Professor, Center for Biomedical Informatics, University of Tennessee Health Science Center and Oak Ridge National Lab

Assistant Professor, Department of Pediatrics, University of Tennessee Health Science Center

Areas of expertise: Precision Medicine, ACEs, Big Data

In addition to his work at the Center for Biomedical Informatics at UTHSC-ORNL, Dr. Shaban-Nejad is also an adjunct faculty at the Bredesen Center for Interdisciplinary Research and Graduate Education, at the University of Tennessee, Knoxville. Before joining the faculty at UTHSC, he was a Postdoctoral Fellow of the McGill Clinical and Health Informatics Group at McGill University. Dr. Shaban-Nejad received his PhD and MSc in Computer Science from Concordia University, Montreal and Master of Public Health from the University of California, Berkeley. Additional training was received at the Harvard School of Public Health.

Dr. Shaban-Nejad's primary research interest is Population Health Intelligence, Precision Health and Medicine, Epidemiologic Surveillance, and Big-Data Semantic Analytics using tools and techniques from Artificial Intelligence, Knowledge Representation, and Semantic Web. Dr. Shaban-Nejad is an associate editor of BMC Medical Informatics and Decision Making and a guest editor of Nature – Digital Medicine, Artificial Intelligence in Medicine, and IEEE Journal of Biomedical and Health Informatics journals. His research has been supported by the Canada Institute for Health Research (CIHR), National Institutes of Health (NIH), the Gates Foundation, Microsoft Research, and Memphis Research Consortium (MRC). Dr. Shaban-Nejad is the Co-Chair of Health Intelligence workshops, which has been an integral part of the Association for the Advancement of Artificial Intelligence annual conference since 2014.

ENDNOTES

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