# CIRM Diversity Workshop: Report




The CIRM Diversity Workshop was held February 26, 2010 at Charles Drew University of Medicine and Science Los Angeles

Report Available at: http://www.cirm.ca.gov/MeetingReports

Suggested citation:

California Institute for Regenerative Medicine. 2010. *CIRM Diversity Workshop Report*. San Francisco, California: http://www.cirm.ca.gov/MeetingReports

## *Introduction*

The California Institute for Regenerative Medicine (CIRM) sponsored a workshop in February 2010, which was hosted at Charles Drew University. The workshop included participants with a range of expertise and experience in the clinical, laboratory and social sciences and provided an opportunity to discuss scientific, social and policy considerations salient to the successful development of stem cell-based therapies for all Californians. The workshop's goals were (1) to gain a greater understanding of how population diversity affects, benefits and advances CIRM's mission and (2) to use this knowledge to ensure that CIRM's funding initiatives support diversity in regenerative medicine.

The workshop was divided into two panels addressing diversity issues in (1) regenerative medicine basic and translational research and (2) clinical trials. Prior to the workshop CIRM commissioned a study titled, *Supporting Diversity in Research Participation: A Framework for Action*. This report examines issues related to enrollment in clinical trials among different segments of California's population and provides recommendations for enhancing participation. Workshop participants were able to review the report in advance and commented on its recommendations.

## *Regenerative Medicine Basic Research*

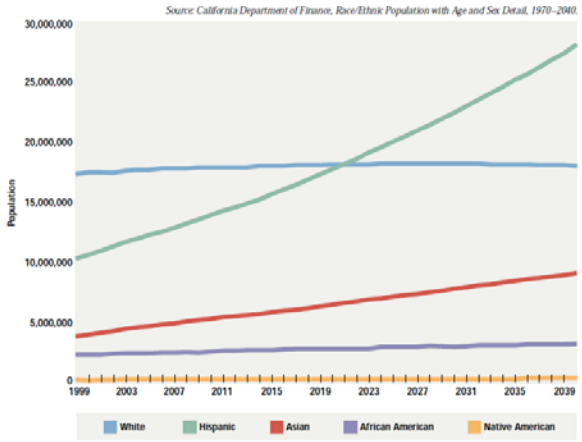


Figure 1: Population diversity in California

### *Unique California Opportunities*

The California population is the most diverse among the nation's 50 states. California's extraordinary population diversity creates opportunities for the development of regenerative medicine. For example, one critical concern in the development of cell-based therapies is the potential for a patient's immune system to respond negatively to treatment.

Experience with bone marrow transplant demonstrates the importance of matching the donor and recipient according to their immune profile so transplanted cells are tolerated by the patient. There is general consensus among scientists that immune system matching will play a role in the development of cell-based therapies. Developing a diverse stock of cells, incorporating racial and ethnic variability, appears to be an effective strategy for addressing differences in immunological tolerance.

Induced pluripotent cells (iPS) offer great potential for developing a diverse collection of cells for research, and a previous CIRM workshop (http://www.cirm.ca.gov/pub/pdf/CIRM_Predictive_Tox.pdf) discussed the value if iPS cells as tools for testing the toxic effects of new drugs on diverse populations.

Workshop participants presented research suggesting the need for greater population diversity among donors of cells used to create human iPS cell lines. For example, Dr. Louise Laurent of UC San Diego presented results from genetic analysis indicating there is restricted genetic diversity in established human embryonic stem cell lines. The UC San Diego team is currently developing a genetically diverse collection of human iPS cell lines. The success of this effort depends, in part, on the ability to recruit a genetically diverse group of donors to participate in the project.

The ability to involve diverse groups in research in general and stem cell research in particular was a theme developed by Dr. Maria Pallavicini of UC Merced. Dr. Pallavicini drew on her experience in developing successful research and training programs at a new, emerging university to offer insights to supporting diversity in regenerative medicine. Dr. Maria Pallavicini described how UC Merced had to educate the population of this historically underserved population in the San Joaquin Valley about the nature and value of research. This has been a challenge in a region with relatively high rates of poverty and low levels of educational achievement, as compared to the statewide averages. Recognizing these socioeconomic factors, UC Merced has taken a number of steps to convey the value of research in a manner that is **meaningful** and **relevant** to individuals, families and the community. These efforts even include innovative community outreach efforts such as sponsoring booths at flea markets where students discuss UC Merced's research efforts and programs.

Dr. Pallavicini suggested the lessons-learned from the Merced experience are applicable to stem cell research and regenerative medicine. She amplified the themes of meaning and relevance in describing a number of approaches that can be taken to convey the significance of stem cell research to the local community. Dr. Louise Laurent echoed similar themes in her discussion or recruiting strategies.

## *Linking Basic and Clinical Research*

Dr. Keith Norris of Drew University discussed strategies for translating basic research into clinical research for patients and communities. Dr. Norris highlighted the importance of having research scientists engage with doctors and clinical researchers. The goal of this interaction should be to relate research to broader community health concerns. This interaction may also be important for creating context for individual patients so they can understand the meaning and relevance of participation in research or clinical trials.

Dr. Norris also emphasized that there are challenges when it comes to engaging community participation in research studies. He indicated there is limited understanding of clinical research. Further, problems with functional illiteracy (48% of US adults

cannot fill out job application) and concerns about the time and expenses (travel, child care, lost income) limit people's ability to participate.

Dr. Norris emphasized the important role smaller institutions can play in supporting interactions between basic and clinical research and the community. He discussed Drew's experience building an academic-community partnered network for research. The network serves to simultaneously relate research to the health needs of the community and vice versa. Drew has developed a framework for this interaction with the primary goal of improving the community health outcomes.


Presentation by Dr. Keith Norris of Drew University

This framework is designed to build institutional capacity that connects researchers and clinicians with patients and community members. Dr. Norris suggested this approach applied by smaller health science institutions is an effective mechanism for educating diverse communities about regenerative medicine. Given the importance of including diversity in regenerative research from embryonic and iPS cells, Dr. Norris suggested smaller mission based and/or minority-serving institutions may be uniquely positioned to increase minority community participation in research.

## *Discussion Themes*

Diversity of Cell Lines: California has the opportunity to address specific disease areas, build programs around endemic diseases and support the development of population specific cell lines. Developing cell lines and disease-in-a-dish models could offer important insights into underlying mechanisms by population group. Practically, this will require obtaining cells from a diverse population of donors. Further, once derived, there may be a need to develop banks to support the maintenance and distribution of cell lines. Participants suggested CIRM might consider working with established cell and tissue repositories to support the banking and distribution of cell lines.

Barriers to Participation in Basic Research: Participation barriers discussed in the CIRM-commissioned report apply to basic research as well as clinical trials. To overcome these barriers, community-based physicians could be involved as colleagues. Recruiters who come from the community are particularly effective. Further, researchers should be able to relate the goals of basic research to community health needs.

Niche Roles for Institutions: Drew faculty suggested the challenge for small institutions is limited resources/facilities to compete for CIRM awards. Participants discussed the value of developing niche institutional capacity. UC Merced's Stem Cell Foundry served as an example a smaller institution that was able to develop unique expertise to advance techniques for single cell analysis. Participants suggested developing a niche role is particularly valuable for developing capacity at smaller institutions.

Other Points of Entry: There was also discussion of other points of entry for institutions with a community orientation. For example, the CIRM Bridges and Shared Laboratory programs were cited as mechanisms where capacity has been developed for research and training. Initiatives that leverage this capacity may be an efficient means of expanding institutional involvement in regenerative medicine. Resource sharing is valuable because, as participants emphasize, a critical level of resource is necessary to support laboratory programs. Human resources may be a particular challenge. For example, if faculty have a major time commitment to teaching it may be difficult to run a lab. The Shared Laboratory Program serves as a capacity development program and it is worth considering ways to expand the utilization of shared facilities.

Dr. Louise Laurent of UC San Diego

## *Clinical Research Participation Report Summary*

Emily Friedman summarized her report *Supporting Diversity in Research Participation: A Framework for Action*. The full report is available [provide link or attach a appendix].

### *Participation Issues*

She summarized existing research describing how members of minority groups have often been underrepresented in clinical trials. Among the reasons given for low minority participation are:

- Lack of awareness by members of minority groups and their community-based physicians of clinical trials
- Limited recruitment of members of minority groups by trial sponsors
- A general lack of trust in the health care system and especially in clinical research
- Logistical barriers, such as lack of transportation, child care, and/or elder care; inability to take time off work; lack of means of communication; the time required; costs of participation not covered by other entities; and confusing processes
- Literacy issues, including lack of English-speaking ability, lack of health literacy, and lack of literacy in clinical jargon
- Cultural considerations, including lack of understanding or acceptance of concepts such as double-blind trials using placebos

Issues specific to certain groups were also identified. African-Americans tend to have the lowest level of trust in the health care system because of historical abuses. Chinese-Americans also have trust issues, as well as problems with English and, for older members of the community and recent immigrants, a lack of understanding of the underlying concepts of clinical research. Latinos also face language barriers, as well as a fear on the part of immigrants – legal or otherwise – that participation could bring negative consequences for them and their families. Southeast Asians share many of these issues, along with, for many groups, a fear of authority bred by a variety of traumas.

Given CIRM's commitment to supporting diversity in clinical research, it is suggested that opportunities for participation be enhanced by supporting the following activities in the context of clinical research supported by the institute:

- Early Outreach: Support grantees in engaging community partners at an early stage and perform a formative evaluation to identify possible literacy issues and understand the questions and preferences of potential study participants.

- Involve Familiar Faces: Use celebrities, community leaders or other credible spokespersons, including patient advocates, to facilitate communication.

- Involve Community-based Physicians: Support health care provider outreach and education to inform community-based physicians and health care workers of opportunities for trial participation • Community Advisory Boards: Establish advisory bodies, comprised of representatives from the above groups, to provide ongoing interaction with the research team to support educational material development, community outreach, recruitment, results interpretation and reporting.

- Patient Support: Provide support mechanisms to improve participant access including use of research funds for transportation, childcare, and compensation for lost wages.

- Provide Feedback: Synthesize results for all audiences and develop mechanisms to recognize the contributions of participants. Ensure that researchers do not "helicopter" in and out of projects. They must build relationships with community leaders and local physicians and provide them feedback. Build on existing CIRM communications strategies to make stories accessible and understandable to broad audiences.

For CIRM-funded clinical researchers, actions must be taken to ensure long-term partnerships with them, their community-based providers, and their communities.

## *Regenerative Medicine Clinical Research*

The second panel focused on strategies for attracting patients and physicians to stem cell clinical trials. Participants discussed their experience with recruiting participants and conducting trials.

### *Stem Cell Therapy Trials*

Gay Crooks considered how early stage trials involving stem cell based therapies would be conducted. She suggests such trials are likely to be targeted to a small, specialized population. Even trials for common diseases (e.g. Diabetes), are likely to be restricted to a highly select population initially. For example, selection criterion will likely target patients with specific clinical indicators. For rare diseases it is likely most participants will be recruited from tertiary referral centers.

The small number of subjects in early stage trials also has advantages. Initial stem cell therapy trials are likely to be complex involving highly innovative therapies, so the informed consent process will need to be rigorous. Working with small numbers of subjects should enhance each sponsor's ability to educate and clarify the consent process. Crooks suggests the risk:benefit equation may be less favorable in the first trials, so rigorous consent is essential. Further, the cost of participation will be high (travel, housing, time off work). Early trials will require lots of tests and close follow-up.

A discussion session during the workshop

Collectively, these factors – innovative therapies, small numbers of participants, disease status, referral mechanisms, intensive follow-up – may make ensuring diversity difficult in early trails. Given CIRM's current focus on advancing early stage trials, the institute should consider realistic objectives with regard to participant diversity. The institute might consider how early stage trials can serve to promote diversity in later trials involving larger numbers of participants. For example, outreach and consent efforts in early trials should be rigorously evaluated for efficacy.

## *Population-Specific Trials*

Gay Crooks also reminded participants that the incidence of certain diseases might vary by population. She cited the example of sickle cell disease (SCD) that affects >70,000 in the US and disproportionately affects minorities: 1/500 African-Americans and 1/36,000 Hispanic-Americans. She described a Disease Team Grant awarded by CIRM to Dr Don Kohn (UCLA) in 2009 to develop a stem cell gene therapy for sickle cell disease. For that trial a multi-disciplinary team of hematologists, bone marrow transplant physicians, gene therapy investigators and clinical/regulatory managers that has been assembled to perform pre-clinical studies and develop clinical trial protocols, informed consent and other documents. The project's goal is to apply to the FDA for an IND for the clinical trial in 3-4 yrs.

The SCD trial illustrates the previous considerations related to stem cell trials. The treatment targets a specific population cared for by specialists who can participate in recruitment and education. The protocol includes community/lay members knowledgeable about the disease who are available to advise and assist. Conduct for gene therapy trials is well established with rigorous pre-clinical safety testing, consent process, oversight.

## *Working With Clinicians*

Dr. Lyndee Knox described the role Practice Based Research Networks (PBRNs) can play in supporting clinical research. PBRNs are groups of ambulatory practices devoted primarily to patient care affiliated with each other to investigate questions related to their practice. There are115 PBRNs in U.S. involving 8,475 practices or clinics with 44,134 providers (MDs, NPs, Pas other) who serve 2.5 million patients. The example of LA Net was discussed to illustrate the role PBRNs can play.

LA Net is a non-profit organization (501(c)3) involving 20 Community Health Clinics and 165 practices with over one million patient visits per year. LA Net's mission is to reduce health disparities by providing comprehensive primary care to poor/underserved pediatric and adult patients.

Dr. Knox described what LA Net members want potential collaborators to know about involving clinicians in research. First and foremost LA Net clinicians want to be engaged as team members and not simply viewed as recruitment sites. In considering participation, members will consider:

- Whether meaningful funding for participation is provided to the physician and the clinic
- Whether collaboration will support their internal research capacity and improve the care they deliver

- Whether collaboration will provide "ancillary" support that solves problems

Researchers should view the collaboration as an investment in research infrastructure not just single studies. Infrastructure includes relationships designed to enhance social networks. When possible, collaborators should not reinvent the wheel, instead partner with PBRNs and other groups already supporting the clinics – they've done the difficult work already.

Dr. Knox also emphasized that researchers must understand possible tradeoffs between primary care delivery and research recruitment. She detailed the opportunity costs of recruitment with the following breakdown:

- A provider has 15 minutes or less per patient visit;
- This figure translates to 32+ patients a day per provider;
- If 3 minutes per patient are added for research, then 96 minutes are not available for primary care;
- As a result 6.4 patients may not be seen in a day.

These figures are useful for illustrating why researchers should provide meaningful funding for research. Such funding could be used for staff that can work at the clinic and simultaneously support the research and the clinical operation. This funding can serve to prevent research recruitment from taking away from primary care; it can help build trust; and it can serve as a vehicle for providing continual feedback to the local staff about the impact of their research efforts.

Maria Alexander-Bridges, representing the Endocrine Society, amplified the value of CIRM promoting collaborative interactions between primary care providers, contract research organizations and community-based research partnerships.

She summarized findings from the RWJF program *Finding Answers: Disparities Research for Change*. The program was designed to identify, evaluate and disseminate interventions to reduce racial and ethnic disparities in the care and outcomes of patients with cardiovascular disease, depression and diabetes. RWJF funded the Endocrine Society to convene a taskforce and develop recommendations aimed at increasing minority representation in clinical trials. The taskforce suggested the following:

- There are potential advantages to using diversity-focused contract research organizations to recruit, train, and retain clinicians that serve diverse patients to clinical trials including:
  - Sustainable minority recruitment of diverse patients across multiple trials;
  - Cost-effective outreach and support of interactions between practicing physicians in diverse communities and institutions performing clinical research in academia and or the pharmaceutical industry;
  - Cost-effective patient education, recruitment and debriefing efforts.

- NIH Guidelines requiring inclusion of women and minorities in clinical trials should be widely adopted (note CIRM regulations already adopt the NIH Guidelines)
- Consider a small business innovative research program designed to develop new diversity-focused contract research organizations and to support diversification efforts of established CROs.
- Consider hosting a meeting to discuss complexities of developing methods to accurately identify race and ethnicity and set achievable goals for increasing diversity at each stage of the clinical development process.

## *Discussion Themes*

Limitations of Early Trials: Phase I and II trials will involve small numbers of participants. These participants will likely be referred from specialized centers. Further, the trial design may require participants with specific clinical indications. This combination of factors suggests early trials will have limitations with regard to the population served. Early trials should present an opportunity to test the efficacy of the complex informed consent process that will likely accompany cell-based therapies. CIRM should ensure early trials evaluate how best to educate and inform potential participants, so that this knowledge can be applied to larger trails.

Relationship Between Disease and Populations: California is the most populous and diverse state. There are diseases that may have higher incidence in specific populations and participation by those groups will be imperative. Sickle cell disease is one example. Other diseases are more broadly distributed but responses to specific treatments might vary between ethnic and racial groups. In those cases clinical research with cell-based therapies will require participation by a diverse populous.

Supporting Clinicians Involved in Research: The workshop described models for how research and primary care may interact at the community level. Included in this discussion were examples of how recruitment for research impacts primary care delivery. Practice Based Research Networks demonstrate mechanisms for simultaneously support research recruitment in a primary care environment. However, this requires commitments of time, personnel and money. CIRM's polices should support such mechanisms.

Workshop speakers Alexander-Bridges, Crooks and Knox (left to right) during a discussion session.

## *Workshop Participants*

Marie Alexander-Bridges, MD, PHD (speaker)

Vincent Anthony, CDU

Jorge Artaza, Assistant Professor, College of Medicine & College of Science & Health, CDU

Ricardo Azziz, ICOC

Richard Baker, Dean, College of Medicine, CDU

Pat Beaupre Becker, CIRM

Jackie Brown, CDU

Dorothy Chan Ochida, Principal, Health Care Strategies

Nate Clark, CDU

Lila Collins, CIRM

Gay Crooks, CHLA/UCLA (Speaker)

Mervyn Dymally, Director, Urban Health Institute, CDU

Ronald Edelstein, Dean, Academic Affairs, DREW, CDU

Arthur Fleming, CDU

Emily Friedman, Independent Health Policy & Ethics Analyst (Speaker)

Ted Friedman, Associate Professor, College of Medicine , CDU

Don Gibbons, CIRM

Gus Gill, Senior Advisor to the President, CDU

Tori Glenn, UCSD CIRM Intern

Nestor Gonzales-Cadavid, Professor, College of Medicine, CDU

Mathew Ho, Associate Professor, College of Medicine, CDU

Bob Klein, CIRM/ICOC

Lyndee Knox, USC (Speaker)

Ron Lau, CDU

Louise Laurent, UCSD (Speaker)

Geoff Lomax, CIRM

Charles F. Louis, UC Riverside

Ted Love, ICOC

Gloria McNeal, CDU

Keith Norris, Charles Drew University (Speaker)

Keith Norris, Charles Drew University (Speaker)

Gail Orum-Alexander, Dean, College of Science and Health, CEU

Maria Pallavicini, UC Merced (Speaker)

Christopher Reid, Assistant Dean, College of Science and Health, CDU

John Robson, CIRM

Gil Sambrano, CIRM

Wayne Taylor, Assistant Professor, College of Science & Health, CDU

Art Torres, CIRM/ICOC

Alan Trounson, CIRM

Jay Vadgama, Chief, Division of Cancer Research and Training, Endowed Professor, CDU

Nick Warshaw, CIRM

Claudia Wiggins, CDU

Michael Yaffe, CIRM

Todd Yancey, M.D., Senior Vice President Clinical Development , Onyx Pharmaceuticals