DISEASE TEAM WORKSHOP: EXECUTIVE SUMMARY

The California Institute of Regenerative Medicine (CIRM) is charged with furthering the development of therapies, cures and diagnostics based on human stem cell research in California. To fulfill this ambitious mission, the CIRM developed a Scientific Strategic Plan in 2006 that defined the specific goals of the Institute and established a detailed blueprint for achieving these goals. Several funding programs targeting different aspects of biomedical research were proposed, among them the Disease Team Initiative that would support teams composed of basic, translational and clinical scientists working together to develop therapies and diagnostics for specific diseases. This initiative aims to "organize funding in new and unconventional ways in order to promote progress," and proposes testing novel research models such as requiring active team management and emphasizing defined milestones in order to better support the development of therapies based on stem cells. The program is meant to complement other CIRM funding mechanisms that support specific stages in the pathway to stem cell based therapies and diagnostics, such as the initiatives for Translational Research, Preclinical Product Development, and Clinical Investigation. Given the novelty of this particular funding model, two workshops were planned to explore different types of Disease Team projects and ways of implementing and managing them.

The first workshop, which took place in July of 2007, brought together scientists from industry and academia, patient advocates, and representatives from federal funding and regulatory agencies as well as from foundations that fund disease-targeted research. Participants considered how to best support teams of researchers translating human stem cell therapies and diagnostics to the clinic. The interim Chief Scientific Officer of the CIRM, Dr. Arlene Chiu, defined the goals of the workshop as "gathering information to help CIRM understand how best to support and fund targeted, team efforts in translational research" involving stem cells. She asked that participants discuss how functional teams are built, funded and managed, and present models for team-based development of therapies and diagnostics.

Major themes emerged from discussion of these successful team models, and the following were felt to be specific to team-based translational projects (compared to individual scientist projects). First, translational research does indeed benefit from team-based research, which encourages early consultation and cooperation with researchers of diverse skills and expertise. Second, strong scientific leadership and project management are essential for team recruitment, motivation, and success. Third, active management and oversight provided by the funding organization can increase the rate of successful translation to the clinic. Active oversight is resource intensive, and can be accomplished by: 1) direct staff involvement, 2) close communication with project managers, and 3) appointment to and use of independent scientific advisory boards. Periodic evaluation against defined milestones is the responsibility of the oversight body

in tracking project progress. Finally, most teams cited access to core services and regulatory expertise (beyond the scope of the core team) as helpful in streamlining the process of translation to the clinic. Leadership, management and oversight, and access to regulatory expertise were described as key to the success of Disease Teams. These themes replayed throughout the workshop discussion sessions.

In discussion of Scientific Scope and Stages, participants were asked to consider whether to focus the scope of Disease Team grants on specific diseases, and at what stage of development team-based research could operate most effectively. The overwhelming consensus was that the Request for Applications (RFAs) should invite team-based proposals that intend to address a disease-related issue, but that CIRM should not limit the RFA to specific diseases. Most felt that funding multidisciplinary teams would have a positive impact on therapy development, especially if stable funding for long-term projects were available. Opinions differed as to what stage of research warranted a team approach, but most favored funding preclinical research “within shouting range” of a development candidate, or at most 4-5 years from clinical testing.

Stable funding was identified as critical to attract the top scientific leaders to team-based research, given the institutional pressures to perform and to be competitive as individuals. An ideal scientific leader would function as “a leader among equals”, and would be responsible for motivating the team, establishing clear project ownership, and recognizing individual contributions to team goals. The scientific research plan would be a collaborative effort developed by the team members in a process orchestrated by the leader. Therefore, the leader would need to be a practicing scientist of good stature whose laboratory is involved in the project. Advisory committees could be assembled by the team, to further assist with scientific direction.

In the Project Management and Oversight, participants were asked to consider how teams might be managed and evaluated. Most agreed that active management would facilitate the rate of successful translation of scientific ideas into the clinic. A role for a project manager during preclinical research was recognized, but the description of potential roles, responsibilities and qualifications varied greatly among the participants. Most felt that active oversight provided by an expert committee is needed to advise on team progress, to provide executive oversight, and to make decisions at critical points in the projects. Oversight committees should consist of external (mainly third party) members who are willing to commit time to the project, and could be assembled by the funding organization with input from the team. CIRM must evaluate and track progress; formally, either via teleconference or biannual or annual review, and informally, via regular verbal communication with the project manager or project leader. Academic researchers do not like the term “milestones”, but all agreed that there must be checkpoints along the way for assessing project progress. Failure to meet critical milestones could result in project termination. The group favored having the Disease Team RFA list management and oversight mechanisms (including project management plans) as a requirement.

Throughout the workshop and in the Resources and Budgetary Considerations Session, participants identified resources that may be needed to support the complex endeavor of therapy discovery and development. Suggestions that would help teams meet key regulatory requirements included: establishing core services, increasing access to regulatory expertise, and encouraging the development of standard tools and techniques for stem cells. Assistance with outsourcing and development of a “toolbox” were also ways that the CIRM could facilitate therapy development.

The workshop satisfied two distinct goals (1) it contextualized the process of therapy and diagnostic development, highlighting issues specific to the use of human stem cells, and (2) it presented the CIRM staff with a number of current working models of team research aimed at developing therapies or diagnostics, and different funding mechanisms developed to support these teams. Consideration of the strengths and challenges of these concepts will assist CIRM in developing a successful Disease Team Initiative.