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# The Institute for Clinical and Translational Science at UC Irvine: Building an Inquisitive Environment Where Everything Is Questioned and There Is No *Status Quo*

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## Introduction

**T**he University of California, Irvine, is one of the prestigious University of California family of campuses. It is a young and dynamic institution with a student population of 22,000 undergraduates and 5,000 graduates. The *Times of London* selected UC Irvine in both 2012 and 2013 as one of the top five young (less-than-50-years-old) universities in the world. Academic development in the past decade has been particularly robust with the addition of new Schools of Law and Education, and Programs in Nursing Science, Pharmaceutical Science, and Public Health. The School of Medicine and the UC Irvine Health clinical enterprise comprise the only academic health center in the central region of southern California. We are emerging as a catalyst for healthcare reform and clinical translational investigation, both regionally and globally.

We are situated in one of the most ethnically and socioeconomically diverse, vibrant, and rapidly growing population centers (approximately 3 million people) in the United States—an ideal platform for the National Center for Advancing Translational Sciences (NCATS), our parent organization at the National Institutes of Health [NIH] vision of translational research that begins in the laboratory and reaches out to all aspects of the community. In this review, we briefly describe the concerted efforts of our Clinical Translational Science Award (CTSA), funded originally in 2010 to harness the energy of what had been loosely interconnected hubs of biomedical research excellence, training, and health care, and to transform these into a creative, flexible, and proactive home for clinical translational science.

## Our Mission and Guiding Principles

We have embraced the NCATS mission “to catalyze the generation of innovative methods and technologies that will enhance the development, testing, and implementation of diagnostics and therapeutics across a wide range of human diseases and conditions.” The ICTS vision is straightforward, “To become a global leader in advancing healthcare discovery through translational science.” This vision is guided by a set of key principles and strategies:

(1) Establishing a nimble infrastructure that facilitates new and existing technology to provide novel, frequent, and effective support for the translational connection, be it in the laboratory, hospital, clinic, or community.

- (2) Facilitating the formation of teams of investigators that transcend traditional silos, include physicians, nurses, basic scientists, and community partners, and share information openly and frequently.
- (3) Providing, perhaps most importantly, in the words of Dr. George Gregory (one of the discoverers of continuous positive airway pressure that revolutionized the respiratory care of critically ill patients), “an inquisitive environment where everything is questioned and there is no *status quo*.”<sup>1</sup>

## The UC Irvine ICTS “Ecosystem”

### Within the university—“crossing boundaries”

When the NIH announced its plans to radically reconfigure its vision and support for translational research almost 10 years ago,<sup>2</sup> the task of bringing together the elements necessary for a successful CTSA application was daunting for a comparatively small academic health center such as ours. Our challenge was to uncover and coalesce a wide range of skill and talent, ranging from expertise in mining the electronic health record for cohort discovery to engaging faculty skilled in translational research bioethics, study design, and statistics. We addressed these challenges by crossing traditional academic boundaries and integrating key concepts of multi-, trans-, and interdisciplinary team science into our organizational ethos from its inception. Examples of this include:

- (1) Our designation as a UC Irvine campus-wide center, which facilitated our ability to interact with schools, institutes, and centers outside of the School of Medicine.
- (2) Strong collaboration with the UC Irvine Program in Nursing Science and Public Health.
- (3) Initial leadership in study design, bioinformatics, and biostatistics through the UC Irvine Donald Bren School of Information and Computer Science.
- (4) An integrated medical informatics unit that engaged existing leaders of the electronic health records management of the UC Irvine Medical Center with researchers and scholars in academic departments.
- (5) Technology incubation infrastructure that brought together faculty from diverse schools including Physical Sciences, Engineering, and Social Ecology.

### Health centers in our region

We recognized early on that our success as leader in translational science would depend in no small measure on our ability to partner with existing health centers in our region. The ICTS has strengthened translational research relationships with existing clinical enterprise partners, such as Memorial Health Center, Miller Children's Hospital, and the Veterans Administration Healthcare Center, which are located nearby Long Beach, California. Long Beach is one of the most ethnically and socioeconomically diverse cities in the United States. Newly developed partnerships include:

- (1) Children's Hospital of Orange County (CHOC Children's). The ICTS was substantially involved in the creation of a formal UC Irvine-CHOC Children's Translational Research Strategic plan leading to a blossoming of collaborative pilot studies focused on child health.
- (2) US Naval Hospital, Camp Pendleton Marine Corps Base. As part of UC Irvine's broader efforts to support translational research addressing the "invisible wounds of war," a pilot-grant program was initiated last year that required research collaborations between UC Irvine and Naval Hospital physicians.

### Community partners

Powered by both CTSA funding and an NIH American Recovery Act award focused on building university-community partnerships in translational research, the ICTS Community Engagement Unit (CEU) has been instrumental in ensuring that university-based researchers were aware of, and responsive to the needs and concerns of our community. Prior to our CTSA funding, we began a series of workshops and community researcher award presentations that were designed to build awareness and identify potential partners in community based participatory research (CBPR). Our ICTS Community Incubator Grants program has been remarkably successful in stimulating CBPR and has led to substantial numbers of extramurally funded research endeavors. Recent examples of incubator awards include:

- (1) Psychological and behavioral risk factors for type 2 diabetes (T2D) among Korean immigrants. Korean immigrants suffer one of the highest rates of T2D among Asians and have two to three times the likelihood of DM relative to Caucasians.
- (2) Effect of Maternal-Child Home Visitation on Birth Outcomes. This project highlighted a partnership with MOMS Orange County. MOMS provides access to prenatal care, health screenings, health education, and referral services to more than 3,500 low income pregnant women annually in underserved communities in Orange County.

### BRAID and BRAID-CH

The five UC medical campuses, in collaboration with the UC Office of the President (UCOP), have identified system-wide collaboration in biomedical research as an opportunity to enhance clinical and translational research efforts. In response, UCOP launched an initiative in 2010 to identify policy changes and areas of collaboration to accelerate biomedical research across the UC biomedical campuses. The UC Biomedical Research Acceleration, Integration, and Development (UC BRAID) consortium, led by the Principal Investigators of the five UC CTSA's (Davis, Irvine, Los Angeles, San Diego, and San Francisco), is part of the effort to accelerate clinical and translational research.

UC Irvine has played an instrumental role in many of BRAID's accomplishments to date. Among them are:

- (1) UC research exchange. A cohort discovery tool that enables researchers to mine the 12.5 million electronic health records throughout the UC Medical Centers.
- (2) Drug and Device Discovery and Development (BRAID D4). A consortium of centers and laboratories across the UC system that will collaborate to enhance the creation of new disease therapies.
- (3) BRAID Child Health. Established in response to the Institute of Medicine Report on the CTSA's released in June 2013, BRAID-CH is designed to support collaborative research among the UC Departments of Pediatrics. BRAID-CH was instrumental in finding resources for the first ever UC-wide Autism Translational Research Summit to be held in August 2014.

### The Continuous Process of Evaluation and Tracking

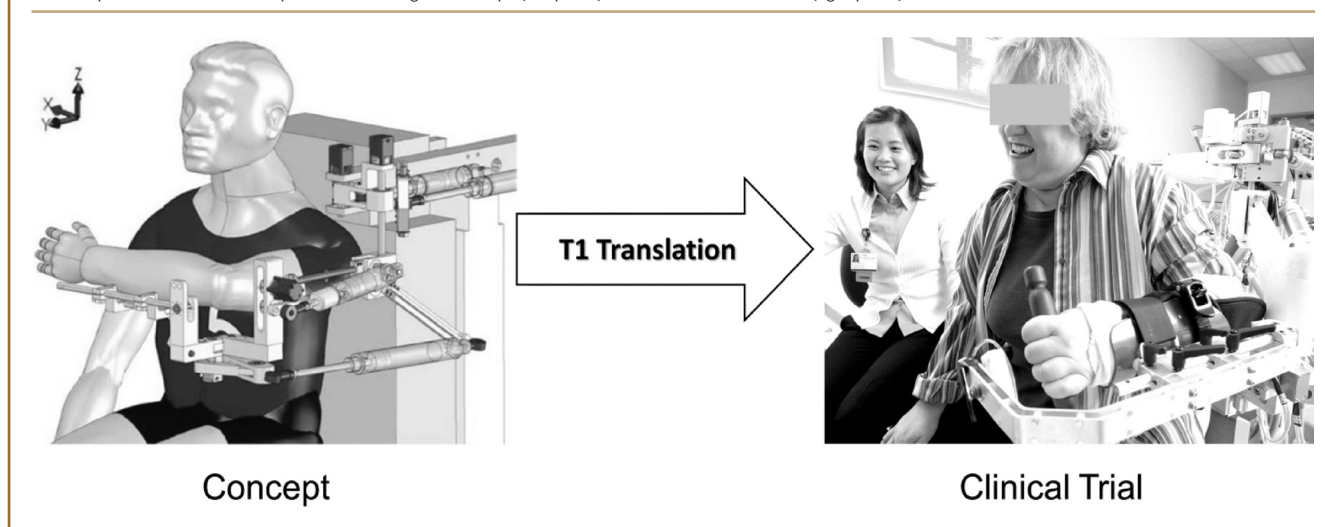
The goal of evaluation is to determine whether a planned set of activities is effective in achieving the desired outcome. Our evaluation plan is designed to create a framework of evaluation tools that will use a common methodology to assess each Unit's progress toward meeting its stated goals and objectives. This approach has been quite useful in actually modifying and ultimately improving key ICTS activities.

One of our most utilized CTSA activities, the Pilot Grant Program, has benefited particularly from rigorous evaluation. Following a series of interviews with pilot grant recipients, we are in the process of building a more continuous and interactive relationship between grantees, and the ICTS staff and faculty. We learned that beyond formal funding of pilot grants, many researchers wanted ongoing guidance and support regarding the availability of ICTS links to core laboratories, biostatistical consulting, information management, and potentials for team building. The ICTS evaluation team is using the commercially available Salesforce software ([www.salesforce.com](http://www.salesforce.com)) to engage in a continuous exchange of information with pilot grant awardees. In the most recent round of awards, grantees were informed of this new structure during an activation meeting and without exception expressed enthusiastic support for this innovation.

### Novel Accomplishments

- (1) *Exercise Medicine Initiatives*: The ICTS has been instrumental in the creation of several novel translational projects focused on exercise medicine. The Pediatric Exercise and Genomics Research Center (PERC) supports research on the use of exercise and physical activity in biomarker and therapy discovery in healthy children, and in children with chronic disease and disability. More recently, the ICTS has been working with a multidisciplinary group of UC Irvine investigators to create the Exercise Medicine and Sports Science institute (EMSSI). EMSSI has succeeded in bringing together abroad array of scientists and clinicians in an effort to focus on exercise as a tool for translational discovery of novel biomarkers and therapeutics.<sup>3</sup> EMSSI consists of faculty from disciplines such as orthopedics, pediatrics, neurology, rehabilitation medicine, physiology, comparative physiology, engineering, cognitive sciences, dance medicine, and athletics.
- (2) *Breath Biomarkers*: This collaboration between the ICTS and the UC Irvine Department of Chemistry's Volatile

**Figure 1.** The UC Irvine ICTS has supported researchers like Drs. David Reinkensmeyer (Department of Mechanical Engineering, School of Engineering) and Steven Cramer (Department of Neurology, School of Medicine) in developing novel uses of robots to improve rehabilitation in people with brain injury. Here we show an example of how the ICTS helped move an original concept (left panel) into an actual clinical trial (right panel).



Organic Chemistry Laboratory led by Dr. Don Blake and established by the late Nobel Laureate Dr. F. Sherwood Rowland, is targeting the use of biologic gases that can be measured in human breath as noninvasive disease biomarkers.<sup>4</sup>

- (3) *Robots to Rehabilitation in Stroke and Brain Injury (Figure 1)*: Robotic devices can benefit people with brain injury such as stroke through cost-effective and consistent performance of rehabilitative activities. Moreover, robots are programmable, can be adjusted with precision, provide an accurate record of usage, and have high potential for telerehabilitation.<sup>5</sup> However, many questions remain unanswered in the application of robotic devices in humans with neurological disease, including measures of safety, efficacy, and satisfaction. To address these knowledge gaps, the UCI ICTS has been instrumental in supporting the translational work of investigators like Drs. David Reinkensmeyer from the Department of Mechanical Engineering in the School of Engineering and Steven Cramer from the Department of Neurology in the School of Medicine.
- (4) *California State Summer School for Mathematics and Science (COSMOS)*: In addition to the ICTS KL2 and TL1 awards, we have developed a high school baccalaureate preparatory course sequence, and we have taken on the challenge of working with the State of California-supported program to introduce concepts of translational science to high school students from highly diverse backgrounds. COSMOS has as its mission to motivate the most creative minds of the new generation of prospective scientists, engineers, and mathematicians. For the past four years, the ICTS has supported a major COSMOS cluster at UC Irvine—*Clinical Translational Science: The Next Generation of Biomedical Research*. To date, over 100 high school students have benefitted from this hands-on laboratory and highly interactive program in which the participants gain a greater appreciation of team science, and how physicians and health care professionals can enhance basic research.

From many of the interviews and follow-up discussions we have had, it is clear that the UC Irvine COSMOS Translational Science cluster has been transformative for many of the students as they develop the next stages of their education and, ultimately, career plans.

#### Toward the Future

The CTSA at UC Irvine has led to a palpable reconfiguration of the clinical research enterprise at our university. NIH funding enabled us to provide novel “incubator infrastructure” that has stimulated collaborative initiatives throughout the institution and with our community partners. For example, the Dean of the School of Medicine provided funding for a “Triumvirate Pilot Grant” which was managed by the ICTS and required that lead investigators from three separate Schools within the university work together. Our task now is to continue to support discovery in translational science during this remarkably challenging period in which the national health care delivery system is being restructured, and new mechanisms for funding biomedical research and training must be developed. In its recent report, the Institute of Medicine concluded that the CTSA program “has made notable strides in accomplishing its initial goal of reshaping clinical and translational research at these institutions and has begun to build a national network that has the potential to catalyze further progress.”<sup>6</sup> At UC Irvine, in order to continue this progress we now must rededicate our efforts to:

- (1) Demonstrate to the leaders of the clinical enterprise in our region the clear necessity of relentlessly advancing basic and translational research.
- (2) Train both clinicians and investigators that real progress in human health has inevitably resulted from frequent, robust, and meaningful interaction among scientists, caregivers, and patients themselves.
- (3) Ensure that advances in healthcare discovery are rapidly integrated into the patterns of care in our community and beyond.

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