UC Davis CTSA: Coming of Age

INTEGRATED PROGRAMS HELP PUT THE SPOTLIGHT ON CLINICAL AND TRANSLATIONAL SCIENCE

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The National Institutes of Health's (NIH) Clinical and Translational Science Award (CTSA) program has profoundly impacted clinical research and training at the University of California, Davis (UC Davis). UC Davis was among the first 12 institutions to receive this award and created its Clinical and Translational Science Center (CTSC) in 2006. The funding accelerated and further integrated an existing conscientious and careful planning effort for translational research with a stepwise approach to gradually increase our institutional competencies, capabilities, and resources in this area. Establishing our CTSC has led us to develop new ways of bringing together a diverse faculty and facilitating research and has created an integrated academic home for clinical and translational science with the resources and infrastructure to train and advance multi- and interdisciplinary investigators and research teams. In this article, we highlight the development of 2 of our CTSC programs, Participant and Clinical Interactions Resources (PCIR) and Pilot and Collaborative Studies. We view these programs as outstanding opportunities to engage a wide spectrum of faculty both in the transition of the General Clinical Research Center (GCRC) to a CTSC and to educate faculty and trainees about the many opportunities that an NIH-supported CTSC can provide to our partners and research community.

The Journey from GCRC Model to Integrated CTSC

To meet the challenges and opportunities to advance and promote clinical and translational research, we adopted an innovative approach to create a diverse and functional PCIR program from our very young General Clinical Research Center (GCRC), founded in 2004. The journey from a GCRC to the PCIR program was greatly facilitated by integration with an institution-initiated Clinical Research Investigator Services Program (CRISP), conceived to physically and administratively co-localize key resources to support clinical and translational research. The institutional support in establishing CRISP proved critical in building the framework to implement the CTSC.

Although highly engaged in clinical research, UC Davis was one of the few academic centers that lacked a GCRC. The foundation to create a GCRC at UC Davis involved a long-standing and collaborative research relationship between the university and the VA Northern California Health Care System (VANCHCS). When the VA was planning a new hospital in Sacramento, VANCHCS and UC Davis agreed to include plans for a clinical research facility in the new hospital, which was completed in 2003 and this became home to the UC Davis GCRC in 2004.

A CTSA with an innovative framework and flexible approach has allowed clinical and translational research to grow and thrive at UC Davis.

From the inception of the GCRC at UC Davis, we took steps to increase the flexibility of traditional GCRC functions by aligning the GCRC with CRISP. To take full advantage of these resources, we co-located many of the traditional GCRC support service functions (e.g., Informatics, Biostatistics, Education) within the CRISP facility at the UC Davis Medical Center, approximately 10 miles from the Sacramento VA Medical Center where the GCRC patient unit is located.

To promote the spirit of the CTSA and to reduce the time that it takes for research to move from bench to bedside, it was clear that we needed to implement processes to accelerate the initiation of research studies. We began this process with the GCRC and have markedly improved these capabilities with the CTSC. A very important step in this process was to transform the GCRC Advisory Committee (GAC).

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Transformation of the GAC

In agreement with the rules regulating the GCRCs, the UC Davis GCRC constituted a GAC in December 2002, prior to the formal NIH funding in September 2004. From its inception, the GAC was coordinated with committees overseeing other research infrastructure resources, including the School of Medicine's Research Resource Advisory Committee, the UC Davis Health System Clinical Research Compliance and Oversight Committee, and the VA Research and Development (R&D) Committee.

The flexibility afforded by CTSC funding allowed us to transform the GAC into the CTSC Resource Review Committee (CRRC), which improved operational efficiencies and removed redundancy. For example, many protocols had undergone 2, if not 3, scientific reviews prior to yet another one by the GAC. Thus, the most important change in scope was to operate this committee less as a study section (which formerly included detailed review of research proposals focused on scientific merit, patient safety, and facility use) and more as a council, where the committee oversees overall use of PCIR resources and helps provide strategic direction and guidance. The CRRC assumed an important role as an advisory and regulatory body whose membership was expanded to represent key stakeholders in the entire clinical and translational research spectrum at UC Davis and included key representatives of each PCIR program unit. To preserve important review functions, we delegated these reviews to key faculty and staff and other committees as outlined further in this article.

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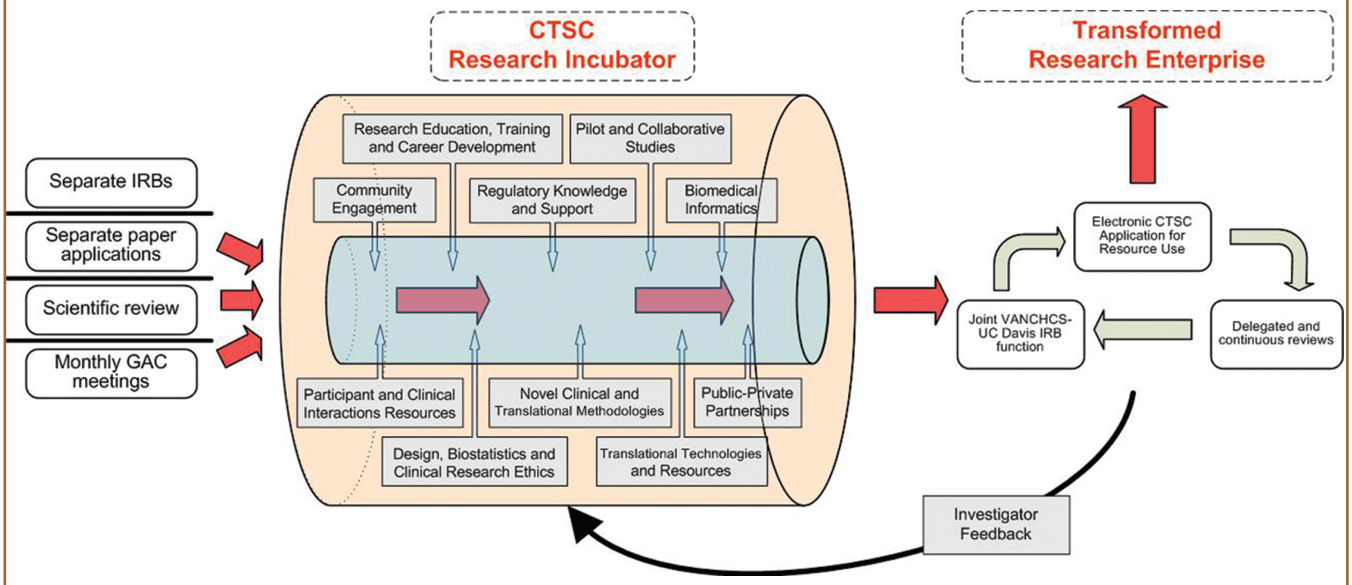
To realize the gains made possible by the flexibility of the CTSA program, we implemented a number of other changes in concert with changing the GAC, including: 1) delegated and continuous reviews by staff and program leadership; 2) a joint VANCHCS–UC Davis IRB function; and 3) an online and simplified application for CTSC use. We adapted our research incubator model to enable these changes (*Figure 1*).

The first transformative step was to dissociate protocol review from the GAC while still maintaining the GAC's oversight function and ensuring a continued high level of scrutiny for scientific rigor and patient safety. We approached this in a stepwise fashion, initially collaborating with the Scientific Review Committee of the UC Davis Cancer Center as a test bed to reduce redundancies. This process worked satisfactorily and increased the strong collaboration between the CTSC and the UC Davis Cancer Center, identifying oncology studies that would benefit from CTSC resources. We were then able to apply the use of a combined review system more widely, and the UC Davis IRB and the CTSC integrated their respective review processes. Briefly, the IRB assumed a delegated responsibility from GAC to include an element of scientific review in addition to patient safety aspects, and the CTSC made the decision to utilize the IRB for its scientific review. Further, the IRB agreed to incorporate a requirement of a data safety and monitoring plan (DSMP) for each application, indicating use of the CTSC in addition to existing requirements in the Common Rule. For the investigators, this alignment of reviews eliminated an element of uncertainty, ensuring there rarely would be conflicts between GAC and IRB reviews.

The second major improvement in streamlining GAC functions was to achieve a joint UC Davis–VANCHCS IRB review system. Initially, UC Davis and VANCHCS had 2 independent IRBs, and investigators planning to use both UC Davis and VA resources had to face 2 independent and unaligned IRB reviews. This system hindered the streamlined approach envisioned by the CTSA program and made joint patient recruitment more difficult. The CTSC brokered an arrangement between UC Davis and the VANCHCS, allowing the UC Davis IRB to serve as the IRB of Record for all clinical trials carried out at the UC Davis CTSC PCIR unit. This involved the creation of a joint VA–UC Davis model consent form that includes: 1) standard language requirements for both the VA and UC Davis, approved by the VA Central Office in Washington D.C. and the UC Davis IRB; 2) required VA representation in the designated UC Davis IRB committee addressing CTSC-bound applications; and 3) a stipulation as to the submission of all such protocols to the VA R&D committee for scrutiny. A joint VA–UC Davis Health Insurance Portability and Accountability Act research authorization form was developed that satisfies the requirements for both the VA and UC Davis.

Finally, the UC Davis CTSC Informatics program developed a university-wide online system for a CTSC resource application process. The electronic form combines a resource request with the IRB application—including a scientific summary, the respective grant or investigator brochure, and the DSMP—and applications are approved using a real-time model. Routing of the application to specific CRRC reviewers is determined by the need of the investigators, as indicated in the form. The routing process begins immediately, and review and approval typically occurs within 14 days, which is a huge improvement from the previous process, which could take as long as 2 to 3 months. Collectively, these changes in the PCIR review process have greatly stimulated

Figure 1. UC Davis CTSC research incubator used as a model to transform the GCRC into the PCIR.



applications for use. Since the inception of the CTSC in September 2006, PCIR use has increased more than 3-fold, and the median time period from application to approval has decreased by more than a month (from 52 to 14 days). We are expanding the scope of the CRRC to an Advisory Committee for all CTSC functions.

New Paths Through Pilot and Collaborative Studies

The CTSC Pilot and Collaborative Studies program is a critical component for facilitating translational research at UC Davis. As such, we publicized our first call for pilot grants immediately upon receiving notice of our CTSC award. We were able to announce the first 6 awardees the same week that NIH announced the inaugural 12 CTSA institutions.

In keeping with the spirit of the CTSC as a translational research incubator and a partnership program, and to provide an impetus for prospective pilot grant applicants to use the full breadth of the CTSC program, we have closely linked our calls for pilot studies to ongoing activities in our translational program. For example, we have maximized and leveraged calls for pilot projects and planning grants by collaborating with other centers at UC Davis, such as the Alzheimer's Disease Center, the Cancer Center, and the Children's Miracle Network. This approach has served a 3-fold purpose. First, we increased the amount of pilot funding available to translational investigators. Second, it provided a partnership in which to encourage collaborative studies by requiring the formation of new teams and by joining in the evaluation process. We also have implemented targeted pilot calls in focused areas of translational research, such as inflammation and the application of novel technologies. Several of these calls were linked to collaborative workshops that encouraged multidisciplinary approaches and the attendance of investigators from a variety of disciplines. Finally, through full or partial matching from our partnering centers, we have more efficiently leveraged available funding in a challenging fiscal environment.

Pilot Funding Calls and Collaborative Workshops

We highlight 3 examples where our collaborative calls for pilot funding included formal collaborations with other UC Davis centers and were linked to workshops focused on the topic of interest. The first example involves a partnership between the CTSC and the National Cancer Institute–designated UC Davis Cancer Center to promote studies focused on the broad topic of inflammation and cancer. This initiative resulted in 14 applications, of which 3 projects were funded. Subsequent to the pilot funding call, we organized a CTSC–Cancer Center-sponsored Inflammation Collaborative Workshop, which brought together more than 200 researchers from the Schools of Medicine and Veterinary Medicine and Colleges of Engineering, Agricultural and Environmental Sciences, Biological Sciences, and Letters and Science. The workshop included 2 prominent keynote speakers from outside UC Davis and presentations from UC Davis faculty with the goal of engaging the extensive expertise across our campus in systems biology, biomarkers, therapeutic targets, and models of disease related to inflammation. Participants, including

trainees, presented posters on a range of subjects, and break-out sessions focused on topics such as predictive biomarkers; the need for technologies, cores, and resources; and approaches to identify anti-inflammatory agents, to name a few. The workshop was coupled with a call for planning grants for new collaborative teams, resulting in 2 funded proposals.

The second example involved a CTSC partnership with the UC Davis Center for Health Care Policy and Research and the Center for Reducing Health Disparities. A workshop was organized that focused on community partnerships in the areas of obesity, cancer, and mental health. The workshop included a keynote speaker, faculty presentations, and discussion groups. Similar to the inflammation workshop, this workshop sought applications from investigators who were collaborating to plan new research proposals that could lead to funding in the focus areas. As a result, we were able to support 7 pilot projects.

The third example was a Translational Technologies workshop that was hosted in partnership with the UC Davis Center for Biophotonics, Science, and Technology, aimed at highlighting new research technologies developed at UC Davis. Again, the workshop was linked to a CTSC call for pilot funding on this topic, resulting in 4 funded projects, of which several represented collaborations between faculty in the College of Engineering and the School of Medicine. We now encourage similar collaborative research projects through a new pilot funding opportunity that will support 2 to 4 proposals to develop new medical devices or tools for patient care. School of Medicine faculty will partner with College of Engineering faculty to mentor a team of senior undergraduate students in the development of device prototypes. These projects will be conducted under the direction of College of Engineering "Capstone Senior Design" course faculty from the Departments of Mechanical and Aeronautical Engineering and Biomedical Engineering.

In addition to formal pilot and planning grant calls, we have pursued collaborative opportunities with other UC Davis centers to develop several workshops with cross-cutting themes to foster or stimulate collaborations on common mechanisms that reach across different diseases, including the trans-UC Davis Foods for Health Initiative. We also have partnered with 2 existing symposia, the Pediatric Telehealth Colloquium and the National Heart, Lung, and Blood Institute-sponsored Gene Therapy Symposium for Heart, Lung, and Blood Diseases.

Beyond engaging a wide range of UC Davis faculty in the Pilot and Collaborative Studies program, we have consistently encouraged the involvement of CTSC trainees at the graduate student, fellow, and junior faculty levels. We are very pleased that a number of alumni from our Mentored Clinical Research Training Program as well as our CTSC K12 trainees have successfully applied to our program. These pilot awards have enabled junior faculty to secure subsequent funding from the NIH and other extramural sources.

The Pilot and Collaborative Studies Program has brought together faculty from across the campus and encouraged the participation of researchers throughout all career stages to participate in collaborative translational research. We are particularly pleased by the multidisciplinary nature of these grants, and most awards have gone to teams combining senior and junior faculty members and trainees. The Pilot and Collaborative Studies Program has made an important impact on the manner in which research is performed across the entire UC Davis campus, and it has been an excellent vehicle for promoting the CTSC to our research community.

> Connecting research teams with the resources they need allows them to reconnect with the excitement of curiosity and the joy of discovery that initially led them to careers in science and health care.

Summary

The UC Davis CTSC has affected clinical and translational research at our institution, and, in its first 2 years, markedly transformed the ease and ability of UC Davis researchers to engage in clinical and translational research. We have summarized here 2 vehicles by which this transformation has been accelerated: our PCIR program, where we have greatly reduced previously existing barriers to performing clinical and translational research; and our Pilot and Collaborative Studies program, where we have aided in generating new, collaborative interdisciplinary research projects. These 2 key programs have provided a solid foundation for continuing efforts at UC Davis to impact human health and biomedical research. **CTS**