

Promoting translational research at Vanderbilt University's CTSA institute

As part of a national consortium to efficiently advance patient care, Vanderbilt University is approaching translational medicine in creative new ways. **Kristin Kain** investigates.

How would you use US\$40 million to create a healthier community? At Vanderbilt University Medical Center (Fig. 1), such funds created the new Vanderbilt Institute for Clinical and Translational Research (VICTR) in partnership with the nearby campus of Meharry Medical College. VICTR aims to cut through administrative burdens, promote multidisciplinary education and sponsor the clinical research that is necessary to improve patient care.

Clinical and Translational Science Awards (CTSAs)

VICTR is part of a growing NIH initiative that is designed to push experimental findings into clinically meaningful practices and advance translational medicine through the creation of Clinical and Translational Science Awards (CTSAs). In the past two years, 38 new CTSAs have been put in place to address this key objective in the NIH roadmap for medical research, and to hopefully bring patients new treatments in a more efficient manner. Institutions are using CTSA funds to test new ideas for removing the hurdles that currently prevent the fluid exchange of ideas between research and clinical practice. Eventually, NIH-funded CTSA grants are expected to link 60 institutions together to form a consortium with coordinated efforts to improve societal health. The desire is that these academic health centers will learn from one another and create an overarching vision to advance health care and train a new generation of clinical and translational researchers.

What makes VICTR unique from other CTSAs?

Before establishing a CTSA, Vanderbilt's mission was aligned with NIH objectives. A few years before Vanderbilt became a CTSA grant recipient, the institution



Fig. 1. Vanderbilt University Medical Center.

began reorganizing the often-burdensome administrative duties associated with clinical research. "We could see that we needed a centralized organizational structure" said Dr Gordon Bernard, Vanderbilt's Assistant Vice Chancellor for Research and primary investigator for VICTR (Fig. 2) "...all aspects of clinical research needed to be going through one place so when there is a problem in the system, there is somebody in a position to know about the needs and fix them." The current Vanderbilt system puts administrative issues, such as the institutional review board, grants, contracts, and radiation safety, under the direct guidance of a practicing clinician-scientist who understands the needs of the clinical research community. The intention is to create an administrative system that allows research investigators to remain focused on their work, enabling the institution's research enterprise.

Vanderbilt administrators also try to recognize and provide incentives for clinical researchers, whose work is often overlooked during promotion reviews owing to the 'dilution effect' caused by long author

lists on publications. "Clinical research doesn't get as much attention for tenure and promotion as basic science research" Dr Bernard acknowledges, "because you can almost never do a single investigator project, and instead you need an army. It's hard to tell who did what and most people want to immediately discount it". Vanderbilt was creating a career advancement program to reward faculty for their research contributions even before their CTSA was granted.

Because the University had already begun to implement a new organizational structure and incentives to facilitate clinical research, it stood out as a center with policies that were concordant with the goals outlined for the NIH's CTSA programs.

VICTR uses seed money to stimulate new ideas and bring long-term projects to conclusion

A poll of the Vanderbilt faculty determined that pilot funds, intended to cover the costs of obtaining small amounts of data that are crucial to submit a grant or finish a manuscript, were in the greatest demand and the

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Fig. 2. Gordon Bernard, MD, VICTR director and primary investigator.

most difficult to obtain. Regarding these 'seed money' funds, Dr Bernard says, "We want to pick up those leads so that someone is not stopped prematurely in the progress of taking something from the bench to the bedside".

VICTR focuses on speed and efficiency for seed money grants. Expedited vouchers for up to \$2000 are made available online within 48 hours following request submission, and the funds or resources become available immediately upon approval. To date, most of these award types have been funded but, if they are not, revised proposals can be submitted and reconsidered immediately. Larger grants are often needed to bring significant numbers of patients into the Clinical Research Center and during these early days of VICTR the average request includes hospital stays and is approximately \$50,000, with funding rates of better than 90%. Although many grants involve cash support, a large part of what the CTSA provides includes clinical laboratory testing and other hospital-related services.

Since a primary goal of VICTR is to stimulate new ideas in clinical research, funding approval is determined primarily by the innovation of the idea and the feasibility of the project. "To qualify for VICTR funding the

project is what we look at, not the individual [applicant]" comments Dr Bernard. "If the project is using human tissues, human information or humans, then it is eligible... We have a few hybrids in the mix, for example where literally an animal has human tissues implanted. The terms of the federal grant greatly limit spending outside of these rules so that for now we cannot support pure animal research."

Expert round table discussions of research projects promote success through 'studios' The combined minds of experts are more powerful than each alone when addressing complex issues. Thus, VICTR does not fund investigators or staff salaries, but supports their projects through studios that bring together professionals with unique perspectives and skill sets to help guide work from hypothesis generation to analysis of results. Unlike meetings that might result from sending e-mails to a few of your colleagues, these studios are orchestrated by administrators who are skilled in arranging meetings that involve significant numbers of very busy people. They bring together well-experienced people with backgrounds in basic science, clinical medicine, statistics and bio-informatics. Studios are most effective in the early stages of a research project and can be requested by any clinical or translational investigator at Vanderbilt University or Meharry Medical College at any time in their project. The resulting brainstorming sessions typically stimulate major improvements and can save valuable time and money.

Stimulation of education and career development supports the future of clinical research

To improve clinical medicine, "We really need to develop scientists who are capable of translating discovery into human beings" says Dr Nancy Brown, a co-director of VICTR, professor of Medicine and Pharmacology, and associate dean for Clinical and Translational Scientist Development in education and training at Vanderbilt (Fig. 3).

VICTR funds individual educational grants to support undergraduate medical scholars and has developed its own educational programs. These include a new track within Vanderbilt's MD/PhD program, the Clinical Investigator Track, which allows students to conduct patient-oriented re-

search and provides an alternative entry point during fellowship, career development support for clinical and translational scientists, and training programs for research nurses.

As with its seed money program, VICTR tries to pick up key pieces that other programs leave untouched, including providing an oversight to junior investigators. Every young grant awardee, whether within VICTR or an external K award recipient, is a member of Vanderbilt's Newman society that provides a scientific community of interactive young faculty. "They participate in a career development seminar series that deals with everything from promotion and tenure to how you run a lab or how you resolve conflicts or authorship issues... all of those things that you really need to know" says Dr Brown.

Additional VICTR programs provide intellectual resources to research scientists applying for external funding. Dr Brown credits Vanderbilt's K award (K08 and K23) funding rate of 80% on good mentorship and the use of studios and internal review to help new investigators design and focus their aims. In addition, more senior researchers are on the winning end of these programs as there is also an internal review process available for new R01 applications.



Fig. 3. Nancy Brown, MD, VICTR co-director in charge of education and training.

An extensive resource of information and statistics creates a strong foundation for research projects

The accessibility and extent of information within VICTR stands out among CTSA. Vanderbilt has the largest department of bioinformatics in the country with 55 members, which is headed by Dr Dan Masys, co-director of VICTR and professor and chair of Biomedical Informatics (Fig. 4). His group provides sophisticated electronic medical record systems to clinical researchers.

There are two functions of Vanderbilt's record keeping system that are particularly useful with respect to facilitating translational medicine. First, Vanderbilt's record system encourages practicing physicians to implement the most current treatment for their patients. The Vanderbilt bioinformatics system alerts physicians when new therapeutic approaches are advisable based on the patient's chart information, and presents the care provider with the original research data to assist them in determining the best course of action for the situation. The presiding physician still makes the final decision, but not without the most current research information to guide their decision. This initiative is designed to overcome the recognized lag between the publication of improved clinical practices and their implementation, which often takes more than a decade.

The second advantage of the bioinformatics system at Vanderbilt, for translational medicine, is the wealth of patient data it contains for retrospective and prospective research studies. The Vanderbilt system has been collecting data since the 1960s and has genome-phenotype correlations dating from the early 1990s. To ensure patients' confidentiality, records are 'scrubbed', or depleted of any personal identification, and as a further measure to ensure confidentiality, these de-identified records can only be accessed by researchers within the Vanderbilt Medical Center or VICTR. Authorized clinical researchers can use this information to validate or discard hypotheses that can be tested prospectively or in real time. They can also analyze data with respect to peer treatment groups

within the system. This allows researchers to efficiently test hypotheses and provides an extensive resource with which to organize pilot data for new projects.

Researchers within VICTR also have access to the largest patient DNA database in the world, called VGER (a name which Star Trek fans might recognize as honoring the Voyager Probe that seeks all knowledge). This database is built from DNA sequencing of excess blood from patient samples and thus avoids the exorbitant costs of collecting blood for the sole purpose of creating a DNA databank. DNA information is linked to de-identified clinical data to help identify correlations between genotypes and important factors such as phenotypes, advent of disease, disease progression and manifestation or response to therapeutics. Patients can opt against having their leftover blood used for the biobank; however, over 800 samples are added per week to this ever-growing resource.

How can the efficacy of CTSA projects be measured?

To evaluate the effectiveness and impact of VICTR programs, two seemingly impossible targets must be evaluated. First, what is the impact of the programs on the health of the Vanderbilt and Meharry community? Second, are the effects of these programs maximized relative to the money spent? Harry Jacobson MD, Vanderbilt University Medical Center's vice chancellor for health affairs, wants to go beyond traditional definitions of success for an academic medical center and determine the ability of Vanderbilt to improve the health of people within its reach, whether or not they actually use Vanderbilt facilities.

Dr Bernard points out that the NIH is also implementing an extensive evaluation system that is consistent with the pre-existing goals within the University. "They want you to show that you have improved societal health [as a CTSA]". But how do you really measure it? "We will move away from using some traditional scoring metrics and NIH rankings as our primary target, but we must find a way to define our influence on overall patient health. Just how exactly the effects of the broader



Fig. 4. Dan Masys, MD, VICTR co-director in charge of bioinformatics.

University effort will be measured out in the community remains to be seen," says Dr Bernard. It seems that identifying ways to measure and track the impact of money spent on human health is a particular challenge for CTSA in general.

CTSAs as part of a larger community

As the CTSA NIH initiative expands, the communities affected by CTSA will become a broad and diverse network. Information between the CTSA is shared in meetings of the investigators within each award program. These meetings includes separate focused meetings for primary investigators as well as specialized, highly focused committees, made up of experts from each CTSA, that tackle more specific health concerns. Dr Bernard is encouraged by this nationwide effort, "Now, all of a sudden, we have the best and most appropriate people available to work on national clinical research strategy together in one place. We have never had that before."

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