Translational Intention and CTSC Projects

CTSC projects are directed towards Translational Research.

**What is Translational Research?** Translational research describes a process of transforming scientific discoveries found in the laboratory, or through clinical and population studies, into interventions or treatments that will reduce morbidity and mortality from disease as well as provide prevention programs to improve the health of the general population. It includes two interrelated processes:

- Bench and preclinical studies that inform and shape studies and trials in humans
- Studies and trials in humans that leads to adoption of best practices in clinical practice and in the community including cost-effectiveness of prevention and treatment strategies.

Following the lead of the Tufts CTSI, translational science as a multidisciplinary collaboration accelerates the application of findings across four steps or levels of human research: T1 $\leftrightarrow$ T2 $\leftrightarrow$ T3 $\leftrightarrow$ T4." However, the power of translational research is that it is an iterative process, allowing room for the returning to a prior translational stage to respond to treatment strategy barriers or address the underlying mechanisms. In the CTSC program we expand Tufts definition to include a fifth step, called it T0, in recognition of a role for basic science in the process of understanding, informing, and defining clinical medicine now and in the future: T0 $\leftrightarrow$ T1 $\leftrightarrow$ T2 $\leftrightarrow$ T3 $\leftrightarrow$ T4.

**T0 Research** incorporates a broad area of pre-clinical approaches designed to inform an investigator about a pathway, pathophysiology, or treatment approach. Examples of experimental methods used for this purpose are animal models of human disease, human blood or cell lines, development of questionnaires, computational models, and human physiological studies, all which are directed at mechanisms and presentations of human disease. For the purposes of CTSC program, these disparate approaches are assigned as “bench” research and may or may not require approvals from human or animal use committees.

T0 research can:

- Identify the functional significance and mechanisms of genomic polymorphisms that are identified by human genome wide association studies
- Study mechanisms or derive modifications of cells, proteins and DNA that are present in human disease processes
- Develop a novel test or instrument for detection of disease that addresses new mechanisms
- Collect and subject human tissue from disease and control subjects to define, describe, or inform clinical studies and trials

Page 1 of 3
**T1 Research** translates discoveries made at the bench to first testing in humans. Typically these studies (case studies, phase 1 and 2 clinical trials) take place at the patient bedside in an academic medical center. The focus of these studies is to determine what care actually works (e.g., clinical efficacy research) and will answer questions like, “An academic medical center research lab has discovered a new treatment. Will this new treatment work in a small number of patients in the same medical center?” T1 Research can:

- Lead to the transfer of disease mechanisms identified in the laboratory into the development of new methods for diagnosis, therapy, and prevention in humans
- Facilitate defining health outcome and intended use
- Evaluate gene/environment/disease associations
- Describe biological mechanisms that link genes with disease processes
- Inform the design of clinical trials
- Establish analytic and clinical validity.

**T2 Research** is the second phase of the translation process and builds on the clinical efficacy work conducted in the first phase of the translation process (T1). It translates results from early clinical studies to controlled observation studies and phase 3 clinical trials for bedside patient care and health decision making and can answer the question, “Will the new treatment tested in a small number of patients in the medical center work in a large number of patients in the same medical center as well as other academic medical centers and clinic sites?” Also, T2 addresses the questions of who benefits from new treatment (e.g., outcomes, comparative effectiveness, and health services research). T2 Research can:

- Establish clinical efficacy
- Identify knowledge gaps (e.g., benefits, costs, safety)
- Be used in evidence-based processes

**T3 Research** is the third phase of the translation process and builds on the clinical efficacy work conducted in the second phase of the translation process (T2). It translates results from T2 research into clinical practice. It is the ‘how’ of health care delivery so that treatments and interventions studied in T2 are reliable in all patient care settings and do improve health of patients overall. T3 Research relies on the distribution and implementation of the results found in T2 and will answer questions such as:

- How widely is the treatment being used? If not, why not?
- Has the increased use raised:
  - New clinical questions?
New barriers?
Gaps in care
In this practice-oriented translation phase, the following can be measured and provide a basis for on-going research:
- Health care policy, quality, and cost
- Implementation of interventions and health care system redesign
- Scaling and spread of effective interventions.

**T4 Research** is the fourth phase of the translation process and builds on the results of third phase of the translation process (T3). T4 Research will help identify the best approach to reach clinicians and patients nationwide so that they not only understand the new treatment but will start to use it. Also, it includes:
- Defining outcomes of interest
- Identifying and developing appropriate metrics
- Implementing surveillance to determine benefits and harm
- Re-evaluation of guidelines and policies to identify needed changes
- Community education on the relationship between research and health, the process of research, and the distinction between research and medical care.

References:
- [http://icts.uiowa.edu/content/glossary-terms](http://icts.uiowa.edu/content/glossary-terms)
- NIH RFA-RM-07-007 CTSA RFA
- JAMA article, *Practice-Based Research – “Blue Highways” on the NIH Roadmap* January 24/31 2007, Vol 297, No 4, 403
- Based on Khoury et al Genet Med 2007