** In addition to using capital letters for the surname, please also include the organisation for each co-author if he/she belongs to a different organisation than the main author. If there is more than a co-author, please feel free to list additional co-authors after the coversheet.

Executive Summary:

Translation requires the development of teams consisting of translational and clinical (T-C) investigators who collaborate to overcome the obstacles that limit the execution of a human experiment.

The barriers that limit the success of T-C investigators remain largely unchanged. It is more and more difficult to recruit, mentor, and retain a critical mass of T-C scientists. Proper training and mentoring of scientists capable of conducting truly innovative patient-oriented research require dedicated time away from the escalating pressures of clinical-service demands. At the same time, the increasingly complex resources needed to conduct modern clinical and translational research are either missing or scattered. PTS Granada is an ideal resource for investment in research to improve the tools used by T-C scientists. Bioinformatics, bench-to-bedside laboratories, and statistical cores could be integrated in a manner that promotes, for example, both outstanding research and innovation in study design leading to a more efficient end result.

1. Introduction:

While impressive progress has been made in basic research science in recent years, real-world technologies based on these discoveries have often failed to materialize in the marketplace. This has highlighted flaws in the traditional system responsible for translating basic research into practical health and economics benefits (figure 1).

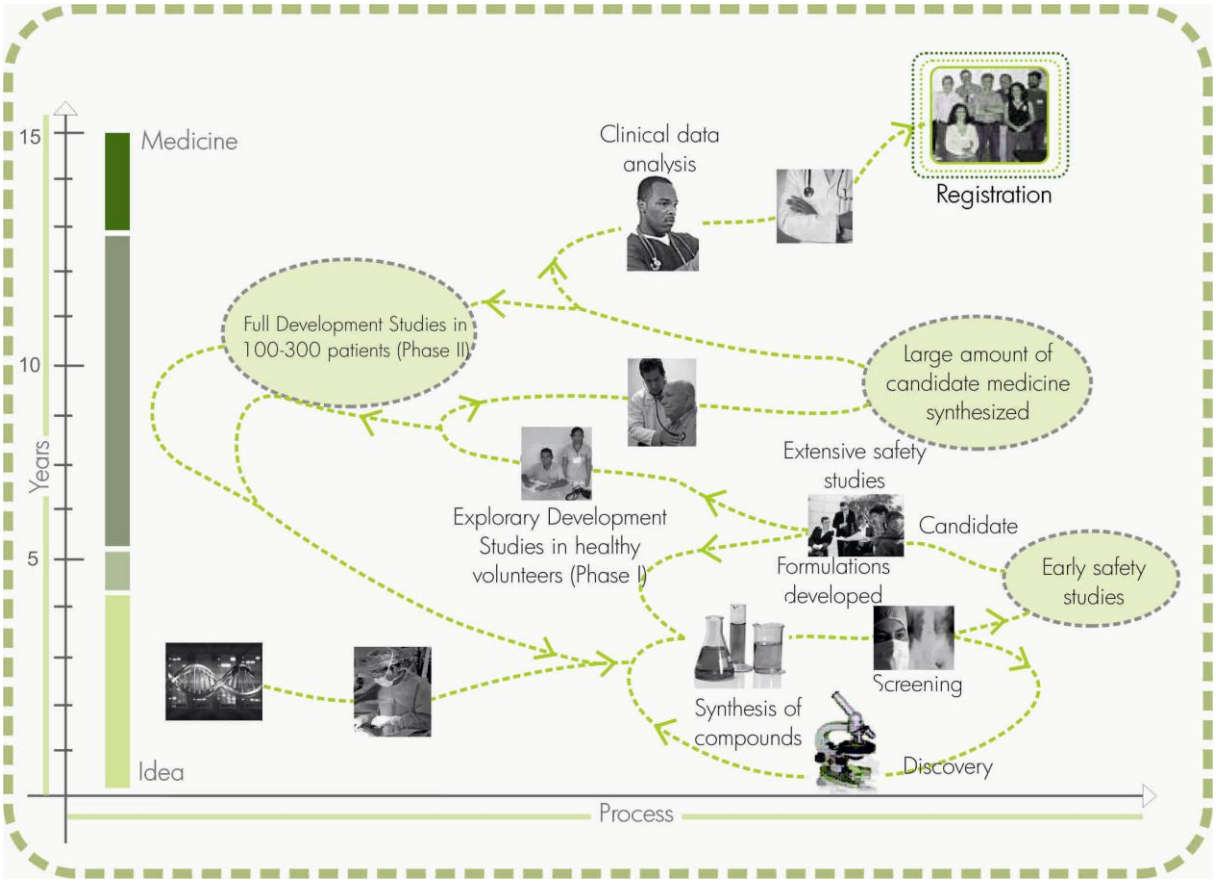

Fig. 1: Developing medicines is a long, risky and expensive endeavor

According to an analysis of the rate of translation of promising basic research findings to clinical applications shows the difficulty in converting progress in basic research into new treatment and cures. A study evaluating 25,290 articles published from 1979 to 1983 in six basic science journals found that 101 original articles clearly stated the implications of their research for human clinical applications and made a promise for a major clinical application of their findings[1]. Ten years later, only five of those promises were in licensed clinical use, and only one of them had a major impact on current medical practice[2]. Figure 2 shows the main bottlenecks in medical research.

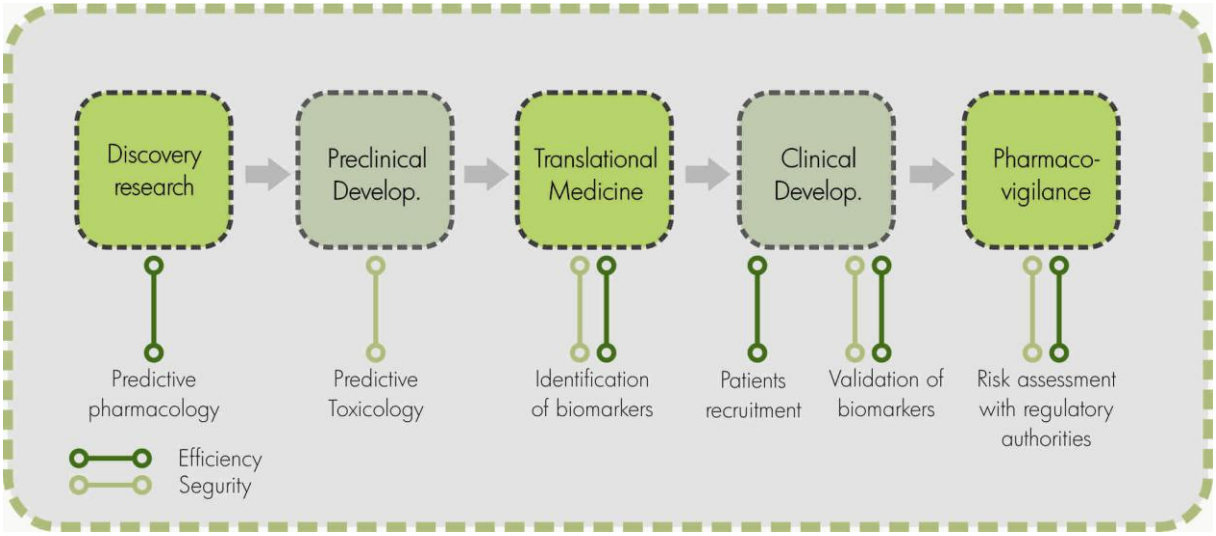

Figure 2. The bottlenecks: focus on pre-competitive research

The Health Science Technology Park (PTS) Granada is an ideal resource for the creation, implementation and expansion of institutes and companies, which converts knowledge into economic and social development, especially in the Pharmaceutical, Health Sciences, Healthcare and Food industries, making it the first park specialized in healthcare in Spain and one of very few throughout the world. The University Hospital helps Translational Research. PTS is backed by the 475-year history of Granada University.

Although we have made great strides in bringing novel diagnostics and treatments to our patients, we all agree that we can do much better. Over the past decade, we have recruited and trained increasing numbers of world-class basic investigators who are unraveling the differences between pathogenic and normal cells. These investigators all have the potential, desire, and commitment to translate their fundamental discoveries whenever their laboratory experiments generate a hypothesis that can only be tested in a human experiment. Translation requires the development of teams consisting of translational and clinical investigators who collaborate to overcome the obstacles that limit the execution of a human experiment. PTS, like all other academic health care institutions, has struggled to facilitate translation.

Academic investigators rarely conduct translational experiments using project management teams. Rather they attempt to implement translation using the identical methodologies that they have used to conduct their laboratory experiments. For this reason, translation at academic health care centers is usually undertaken by small numbers of highly motivated individuals with limited prior experience. Not surprisingly, each translational experiment turns out to be a new learning experience for the investigator and "their" teams. Moreover, translational investigators rapidly discover that academic health care centers are not equipped to support their efforts. Lacking are human and core resources that are critical to the success of the experiment. For example, T-C investigators struggle to: a) acquire, process, store, and retrieve human specimens, b) develop and conduct biologic surrogate endpoint analyses, c) develop and conduct novel imaging endpoints, d) write and manage INDs, e) write and manage complex translational clinical protocols, and f)

[1] Contopoulos-Ioannidis DG, Ntzani E, Ioannidis JP. Translation of highly promising basic science research into clinical applications. *Am J Med*. 2003
[2] Ioannidis JP. Materializing research promises: opportunities, priorities and conflicts in translational medicine. *J Transl Med*. 2004.

acquire, manage, and interpret complex clinical and biologic data. Even when they attempt to build a project management team, individuals skilled in trial design, regulatory affairs, industrial interactions, imaging, and molecular pathology are not readily available. All to often, translation proceeds much too slowly and, unfortunately, frequently fails.

Figure 3. Industry- Academia Comparison: Translational Capabilities

2. Purpose

T-C faculty have trouble finding a real HOME for their aspirations. Our challenge at PTS is to precisely define the roles and responsibilities as well as career pathways of translational and clinical investigators. In this paper we will focus on four important areas including: 1) Components of an Academic HOME, 2) Institutional Culture and Commitment, 3) Education, Training, Mentorship and Career Development, and 4) Establishment of a collaborative community (Intra-and Inter-Institutional Collaboration).

3. Methods

We reviewed the literature to identify noted challenges and solutions to T-C research. Search queries using combinations of the following key words were performed on PubMed: barriers, solutions, challenges, translational, clinical, research, interdisciplinary, collaboration, career pathway, education, promotion, next generations, training, mentorship, investigator, work environment, career experiences, innovation. In addition, we reviewed relevant publications referenced by these sources. We focused on publications that were the result of firsthand experience or empirical research and on publications that identified challenges and solutions through the use of organized interview and survey methodology.

Through an analysis of the literature, we categorized T-C definitions into three categories (translation, translational investigator and clinical investigator). We then studied the conduct of translation at other academic health care centers (with special focus on Spain, Europe and the United States) searching for an importable solution, trying to take advantages of the T-C Investigator Capabilities at the PTS.

Since translational research has become such an important buzzword at academic healthcare centers, everyone, basic scientists and clinicians alike, all think that they are “translational investigators.” Clarity of definition is one of the major reasons that we are facing an “international crisis” in clinical investigation. For this reason, unlike our definition of translation, which was, cast very broadly, the definitions of a translational investigator and a clinical investigator will be highly restricted.

Translation must include:

1) bringing novel experiments from the laboratory to the clinic
2) bringing important clinical problems to the laboratory

3) partnering with industry at an early enough stage so that we are active collaborators in the conception and development of a new diagnostic and/or treatment

Any basic scientist can become translational investigator and therefore the pool of potential translational investigators is extremely large. Medical training is not necessary to become a translational investigator. **A translational investigator is a basic scientist whose laboratory based research culminates in a hypothesis that can only be answered by conducting a human clinical experiment.** Translational investigators do not simply study human specimens but rather conduct pre-clinical experiments that form the basis of a clinical protocol. The translational investigator must be intimately involved in the objectives and endpoints of a clinical trial but need not write nor conduct the human clinical experiment.

A clinical investigator conducts a first into human or early phase "proof of concept" clinical experiment. Such trials, for example, study a new diagnostic test, surgical devise, imaging technique, therapeutic or prevention strategy. Clinical investigators, not only conceive and conduct the human clinical experiment, but also develop, execute, and interpret biologic surrogate or imaging endpoints. Although clinical investigators need access to a laboratory to conduct pre-clinical studies and/or endpoint analyses, they spend the majority of their time conducting the clinical experiment (i.e. the clinic is their primary laboratory). A clinical investigator frequently partners with a translational investigator and together they have the skills and resources to go "from bench to bedside." In addition to conducting bench to bedside clinical experiments, clinical investigators make bedside observations that give rise to a hypothesis that can only be studied in a laboratory. Here, the paradigm is reversed and the experiment goes from the "bedside to the bench."

A clinical trialist is an individual who conducts later stage human clinical trials that address efficacy, FDA approval, and changing the standard of diagnosis, treatment, and prevention. Clinical investigators, unlike clinical trialists, are intimately involved in: a) pre-clinical development; b) assessment of pharmacokinetics, pharmacogenomics and pharmacodynamics; and c) development of biologic assays or imaging techniques that will be used as endpoints of the trial. The clinical trialist does not focus on the development, validation, and interpretation of biologic endpoints but rather examines more conventional clinical endpoints. A clinical trialist spends significantly more time caring for patients than does the clinical investigator.

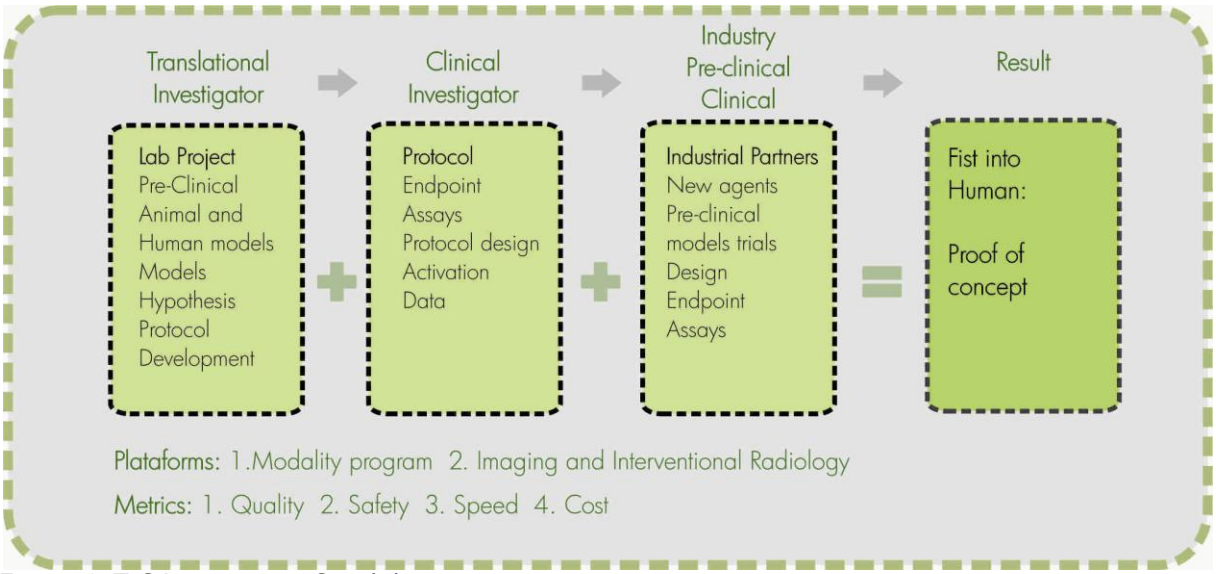

Figure 4. T-C Investigator Capabilities

It must be emphasized that our faculty model and career pathways are not static. Basic investigators who become translational investigators can return to basic investigation. Translational investigators who become clinical investigators can return to careers as translational investigators. Clinical investigators who become clinical trialists can again become clinical investigators. Therefore, PTS must be very clear that our definitions apply to an individual's efforts at a particular time. Since individuals change their career focus, PTS must be dedicated to facilitating career

transitions. Without a culture that is fluid and supportive of teamwork, PTS will never be able to meet our patient's and supporters expectations.

4. Results

Using the above definitions for translational and clinical investigators, the number of individuals that meet these stringent criteria are few. Very few of our basic scientists have been involved in the conception and conduct of a clinical experiment based upon work done in their own laboratory. Likewise, very few individuals conduct first into human and early phase clinical experiments and also analyze biologic endpoints. Although there are brilliant examples of translational and clinical research, the challenge is that we are not capitalizing on our scientific opportunities. If greater numbers of basic investigators were enabled to translate, there would considerably more opportunities for clinical investigators.

What are the barriers that limit the number of individuals who conduct translational and clinical investigation? As stated above, these barriers are considerable and frequently lead to avoidance. For the basic scientist to become a translational investigator, the major barriers include availability of human material, laboratory space, funding, and availability of clinical investigator partners as well as regulatory barriers and complex interactions with industry. For the clinical investigator, the major barriers include paucity of translational investigator partners, laboratory space to conduct pre-clinical studies and develop endpoint assays, funding, writing and holding INDs, complex interactions with industry, and information systems. For both translational and clinical investigators, the absence of mentors as well as critical core and facilitative functions that will help them overcome these barriers presents a very significant obstacle. Finally, the pharmaceutical industry does not consider us as the "go to place" for early human experiments because of the paucity of T-C investigators as well as the absence of infrastructure and human resources that ensure their success.

The goal of a Center for T-C Research (Figure 5) is to attack and overcome each of these obstacles. PTS's intention is to become the "lens" to focus on translational enablement. Enablement will consist of helping to develop, coordinate, and integrate project management teams as well as to provide human, core, and fiscal resources to ensure success of each translational project.

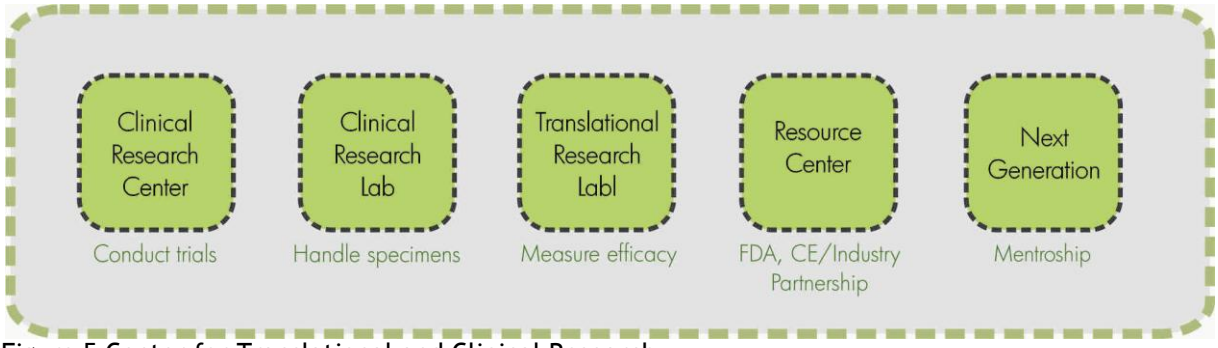

Figure 5 Center for Translational and Clinical Research

The components of a Center for T-C Research will support the training, promotion, and retention of T-C Investigators as follows:

a. Resource Center

The Resource Center will be the functional unit to facilitate the work of both T-C investigators. It will have four major functions: 1) developing and supporting translational project management teams, 2) facilitating the interaction of T-C investigators with operational units (e.g. Integrative Centers, non-academic departments, Core Labs, Clinical Trials Processes, Technology Transfer, etc.) 3) pre-clinical and clinical investigational industrial liaison with biotechnology and the Pharmaceutical industry, and 4) developing, writing, and holding INDs and regulatory compliance.

When a basic scientist believes that they are ready to embark on a translational experiment, they will approach the Resource Center. An analysis of the needs of the project will be made and

a project management team will be charged composed of individuals with diverse expertise. The project management team will help the translational investigator and their clinical investigator partner to determine what resources are necessary and will facilitate project management to lessen the complexities and burdens that the translational and clinical investigators must face.

b. Translational Research Lab

This laboratory focuses on bedside to bench hypothesis driven experiments. Once a hypothesis has been articulated, the leadership and staff of the translational research laboratory will meet with the clinical investigator and whenever possible their translational investigative partner(s). The Translational Research Lab will determine whether existing technology can address the question or whether technology needs to be developed and/or imported. One of its major functions of will be to stay current with regard to novel biologic surrogate endpoint technologies. If a promising technology exists but is not commercially available to import, the Translational Research Lab will attempt to partner with the company gaining access to the technology with the objective of importing it. If no technology is identified that can address the bedside to bench hypothesis, it will collaborate with basic scientists, translational investigators, and clinical investigators to develop a technology. The Translational Research Laboratory not only will develop technologies to assess biologic endpoints but will also collaborate with clinical investigators to execute pre-clinical experiments. The clinical investigator will always be the first author of these studies. Such publications will be essential for promotion and obtaining grants for clinical investigators.

c. Clinical Research Center

The Clinical Research Center is a freestanding specialty clinic that conducts complex first into human and early phase clinical experiments. It should be staffed by highly skilled world-class nurses and pharmacists.

d. Clinical Research Lab

It receives, processes, stores, and retrieves specimens from human clinical trials. Professionals will ensure that patient samples are handled and stored according to good laboratory practice.

The Center for T-C Research will provide two major functions for the next generations of T-C investigators (Figure 6).The first will be training, mentorship, and establishment of a collaborative community. The second will be ensuring that the necessary infrastructure and human resources are available to support their success.

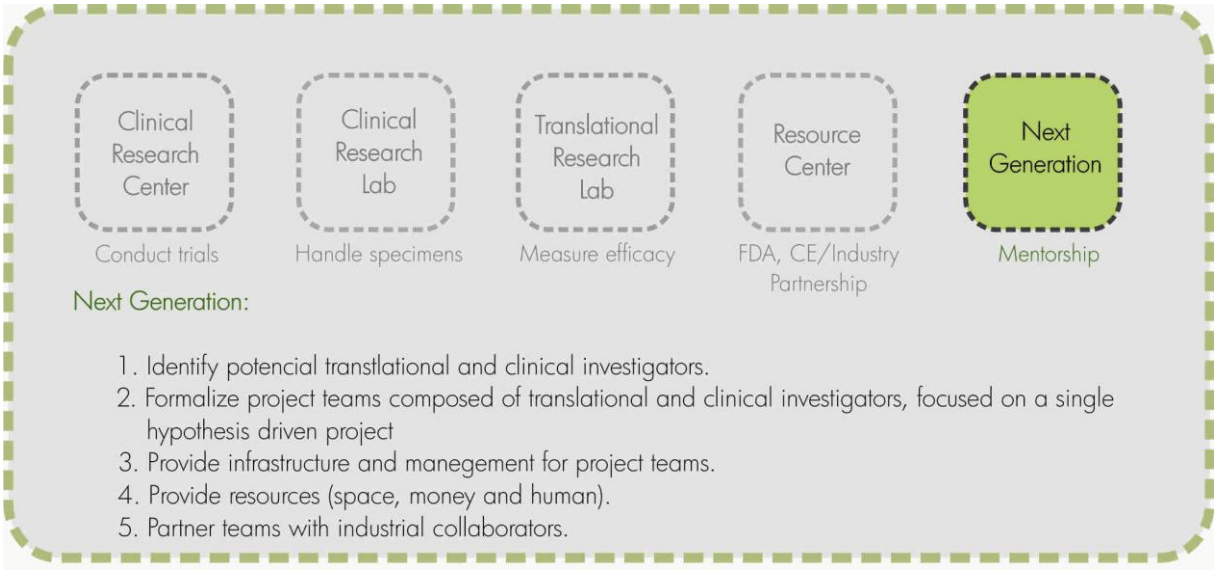

Figure 6. Next generations

a. Next Generation of Translational Investigators

As stated above, any basic scientist can become a translational investigator. Therefore, transition from basic investigation to translation is opportunity driven. However, certain individuals are more likely to translate. Such individuals focus their basic investigation on either the pathogenesis or pathophysiology of a specific disease or alternatively the study of a disease associated discipline (e.g. chemical biology, immunology, angiogenesis, metastasis, or death pathways). These basic investigators are constantly identifying unique properties of illnesses that might lead to a new diagnostic. Alternatively, they might identify a novel target that might be amenable to intervention.

One of the major functions of the Center will be to collaborate with Department Chairs, Division Chiefs, and Disease Center Leaders to identify specific opportunities for translation. When need is identified and consensus established, the Department may elect to recruit a new investigator. Alternatively, Departments may elect to invest in established basic investigators to support their translational experiments. At this stage in translation, the Center will have limited impact and will only attempt to facilitate crossing Departmental barriers thus bringing individuals together to address a specific project. The Center will also attempt to bring other Center Leaders to these discussions. One of the most important functions of the Center will be to integrate across Institutional structures to improve teamwork, quality, and speed.

In addition to the services that the Center will provide to the individual translational investigator, the Center is committed to building a community of translational investigators. Since most translational investigators presently reside within or are associated with Disease Centers, cross fertilization across Disease Centers and Departments is less than optimal. The Center for Translational and Clinical Research collaborating with other Integrative Centers plans to develop a "home" where inter-Disease Center and inter-Departmental translation will be facilitated. This home will not only provide the services stated above but also attempt to provide opportunity for investigators to present ongoing experiments, identify and recruit trainees to the translational investigators laboratory, create an environment of mentorship, and identify opportunities to formally collaborate. There is great enthusiasm among basic investigators committed to translation to create this environment.

b. Next Generations of Clinical Investigators

One of the major functions of the Center for Translational and Clinical Research will be to train, mentor, and provide both human and core services to ensure the success of the next generations of clinical investigators. Unlike the large pool of potential translational investigators, there is a severe shortage of potential clinical investigators as well as senior clinical investigators to mentor them. The reasons underlying this shortage are well established and have been analyzed and articulated by multiple committees during the past decade.

The barriers that limit the success of clinical investigators remain largely unchanged. Very few clinical fellows embark upon this career pathway because of the length and complexity of the training period and their impressions that this pathway is too difficult and not rewarded. Paucity of mentors, lack of start-up resources, and difficulty in obtaining ongoing funding combined with the very long list of those who have tried and failed, or simply elected to leave their hospitals for more supportive environments, serve as the most serious deterrents. Academic promotion for clinical investigators is based upon the identical criteria applied to all other basic investigators. Since early phase human trials take several years to initiate, conduct, analyze, and publish, promotion is considerably slower and much more risky than more traditional laboratory based career pathway. Grants that appropriately fund clinical investigators are difficult to obtain, much more difficult to renew, and frequently do not support the critical needs. The conduct of early phase human experimentation is fraught with burdensome regulatory obstacles, reporting requirements, and ever increasing complicated interactions with industry. Lastly, and perhaps most importantly, academic health centers, do not provide an institutional environment supportive of the training and development of clinical investigators. The Center for T-C Research is committed to creating a more supportive environment. If successful, we hope that the number and quality of clinical investigators will increase and that we will become the go to place to train, grow, and retain clinical investigators.

The Center for T-C Research will partner with the Disease Centers, Divisions, and Departments to fill the gaps. First and foremost, the Center will attempt to provide an environment where clinical investigators from multiple Disease Centers, Divisions, and Departments can create a community. This community will provide a platform to present their ideas, find collaborators, generate funding mechanisms, share resources, and leverage their combined needs to create infrastructure. Moreover this community environment, very much like a large laboratory, laboratory floor, or Division; will foster mentorship, recruitment, and training of young investigators. Creating an investigative environment composed of senior clinical investigators, mid level clinical investigators, and trainees will create that critical mass of clinical investigators that has been absent now.

In addition to fostering a community and culture of clinical investigation, the Center for T-C Research will provide cross cutting services that are beyond the resources and expertise of individual Disease Centers, Divisions, and Departments. The Center will not attempt to duplicate any resources that presently exist in academic or non-academic Departments. Rather the Center will develop a catalogue and roadmap of these resources. Here, the Center will "be on point" to understand what is available and it will work with the Park to optimize these resources. Alternatively, for those resources that do not presently exist or are not sufficiently developed, the Center leadership and staff will work with PTS to build these resources.

Central to development of the next generations of clinical investigators will be the recruitment, training, mentorship, and ongoing support of these individuals.

Over the past year, we have analyzed a plan to increase the number and success of clinical investigators. The initiatives described below summarize the elements of the plan and will require significant institutional consensus, support from the Department Chairs and Division Chiefs, and most importantly commitment from the highest levels of leadership.

1) **Recruitment of Clinical Investigators:**

   The elements of a clinical investigator recruitment package include:

   a) Competitive compensation comparable to new clinical trialists. Salary level will depend upon length of prior training. Start up will mirror basic science recruit package with five-year guaranteed salary support.
   b) Expectation that salary will ultimately be fully supported by grants, clinical trial efforts, and clinical effort.
   c) Clinical responsibilities will include no more than 25% required service patient care (2 clinic sessions per week, preferably one full day). Limited attending time. Clinical investigator will spend additional time accruing patients to protocols and caring for patients on their protocols. First into human studies require hands on clinical care between the protocol chair and the research patient. This should not increase the effort of the clinical investigator more than an additional 25%. Since care for these patients is reimbursed, these efforts should be supported by clinical funds. Clinical investigators, like basic investigators, need protected time. The remainder of their effort must be committed to identifying opportunities, conducting pre-clinical studies, interacting with translational investigators and the pharmaceutical industry, developing surrogate endpoint markers, addressing regulatory issues, attending meetings, and writing grants.
   d) Laboratory space will be available on a unit dedicated to clinical investigators shared with several basic/translational investigator anchor tenants. The Translational Research Laboratory will share the identical space or will be in close proximity.
   e) Individual dedicated laboratory space allocation will depend upon evidence of need but will be divided between designated clinical investigator laboratory space (at least one bay per investigator) and shared space within the Translational Research Laboratory.
   f) Office space, serving both clinical and laboratory effort, will depend upon preference and availability within Disease Center/Division. When appropriate

office space adjacent to their clinical investigators laboratory may be appropriate and even advantageous.

g) Clinical investigators will need access to research nurses and clinical research assistants who will be housed in clinical investigational space. Depending upon the needs of the individual investigator and the resources of the Disease Center, the clinical investigator will share the resources of the Disease Center or hire their own full time staff.

h) Start-up funds will include support for at least one staff scientist, one post-doctoral fellow, one laboratory technician, laboratory supplies for these individuals and the clinical investigator, one research nurse, and one clinical research assistant. The start-up funds, required to support each recruit for the first five years, will be offset by clinical effort, industrial trial support funds, and grants.

2) Mentorship, Critical Mass of Clinical Investigators, and Development of A Community

The issues of mentorship, community, and critical mass are our greatest challenge as well as our greatest opportunity. Since there just a handful of senior clinical investigators at PTS, there is consensus that we do not have sufficient clinical investigator mentors to train even our first cohort of recruits. Many argue strongly that if we could identify a senior world-class clinical investigator that could be recruited, we should do so immediately. It is essential that we identify our senior and mid-stage clinical investigators and request their commitment to training the next generations.

There is consensus that clinical investigators should have dual mentors. A basic/translational investigator should provide primary laboratory mentorship for a clinical investigator. A senior clinical investigator should provide primary clinical investigation mentorship. There has been a strong sentiment that junior clinical investigators also need mentorship from a clinical trialist.

Mentorship will be formalized with clearly defined yearly goals and benchmarks. Assessment of the success of a clinical investigator will be the responsibility of their Division Chief. Assessment of the success of the mentor will be the responsibility of the Division Chief and Department Chair. If the mentor is not a member of the clinical investigator's Department, the clinical investigators Department Chair will still be responsible for determining the success of the mentors. We must develop incentives and rewards for both primary and secondary mentors. Whether it is appropriate for mentors to be co-authors on manuscripts needs to be resolved and, if appropriate, cross-Departmental criteria for authorship must be established. Since successful mentorship will be time consuming, PTS must determine how it will compensate these mentors.

Finally, is the issue of development of community. If once per month about 10 individuals (senior fellows, instructors, and Assistant Professors) who are trying to become clinical investigators meet and present their ongoing experiments our conclusion is that the nidus of a community of clinical investigators has been established.

3) Designated Laboratory Space For Clinical Investigators, Availability of Space within the Translational Research Laboratory, and the Concept of Cohabitating with Basic/Translation Research Anchor Tenants

The most compelling space configuration would be the establishment of a designated clinical investigator unit that would co-localize three groups of individuals: (1) clinical investigators, (2) Basic/Translational investigator anchor tenants and (3) staff of the Translational Research Laboratory. This model would ensure those clinical investigators and their staff scientists, post-doctoral fellows, students, and technicians would work in an environment that would foster the highest quality of laboratory-based investigation. The advantage of this model

would be the development of a community of clinical investigators, high standards of research and mentorship fostered by the anchor tenant Basic/Translational investigators, and seamless interaction with staff scientists within the translational research laboratory.

Operationally, anchor tenants would serve as unit mentors and general floor operation leaders. The close proximity of anchor tenants would ensure that their talented post-doctoral fellows, students, and technicians could closely interact with the clinical investigators and their staff. The close proximity of the Translational Research Laboratory would achieve the identical objectives. Cross-fertilization of clinical investigators with the anchor tenants laboratories and the Translational Research Laboratory should assuage the concern of some that the quality of the science performed on the unit might not be optimal.

Our plan is that each clinical investigator would be designated a single bay on the unit. Additional space would follow opportunity, accomplishment, and funding. The unit would function as a laboratory without walls with clinical investigators, Translational Research Laboratory staff scientists, post-doctoral fellows, and technicians sharing infrastructure and collaborating on most projects. Anchor tenants would be allocated the traditional number of bays of designated laboratory and office space based upon academic rank and funding. These anchor tenants would be selected based on the quality of their science as well as their commitment to translation and mentorship. The unit would have laboratory meetings with presenters selected from the three component laboratories. Whenever possible, non-anchor tenant translational investigators, Disease Center Leaders, and Division Chiefs would participate in laboratory meeting and retreats by presenting their work and critiquing the work of the clinical investigators.

4) Clinical Research Support Staff and Space

One major outstanding issue is whether it will be possible for clinical investigators to co-localize their clinical investigation support staff and personal office space within the clinical investigator research unit. If clinical investigators could share research nurses and clinical research associates, PTS would benefit. It will be much more complicated if they attempt to share Disease Center research staff since most clinical trialists are conducting industry sponsored phase II and phase III trials and their staffs are already over committed.

5) Promotion and Funding

One of the major deterrents to pursuing a career as a clinical investigator is the difficulty and length of the promotional process. The central issue is that a human experiment frequently takes one year to plan, one to two years to conduct, and one year to analyze and publish. During this 4-year time interval, basic investigators can easily publish 10 basic scientific manuscripts to each 1 human clinical experiment published by a clinical investigator. This discordance is precisely why the Translational Research Laboratory was conceived. The Translational Research Laboratory will help clinical investigators develop and valid surrogate biologic endpoints assays. The clinical investigator in a time line comparable to basic scientific investigation can publish development and validation of these assays. Once developed the clinical investigator can collaborate with multiple other clinical investigators and trialists and become co-authors of their manuscript. By having laboratory space, clinical investigators can undertake pre-clinical experiments that will underlie their protocol and also publish these observations. Only through laboratory-based publications can we expect clinical investigators to be promoted in a timely fashion.

The second issue is sources of funding for clinical investigators. We expect clinical investigators to support their salaries by the end of the start-up package. Each clinical investigator will receive clinical support for their clinical service efforts and

for their clinical research efforts (i.e. accruing and caring for patients on their clinical trials). This will range from 25% to 50% of their effort. There was considerable concern among clinical investigators that they were under compensated for their clinical service effort and not compensated for the evaluating and caring for patients on their clinical trials. This will be formally addressed. The remainder of their salaries will come from grants and industrial support. Clinical investigators should be able to support at least 30% of their effort on grants. Finally, clinical investigators should allocate salary support from each of their clinical trials. The combination of clinical care euros, research grants, and clinical trial support should be sufficient to support their salaries. It is expected that this support will offset early start-up Park commitment and fully fund them by the end of five years.

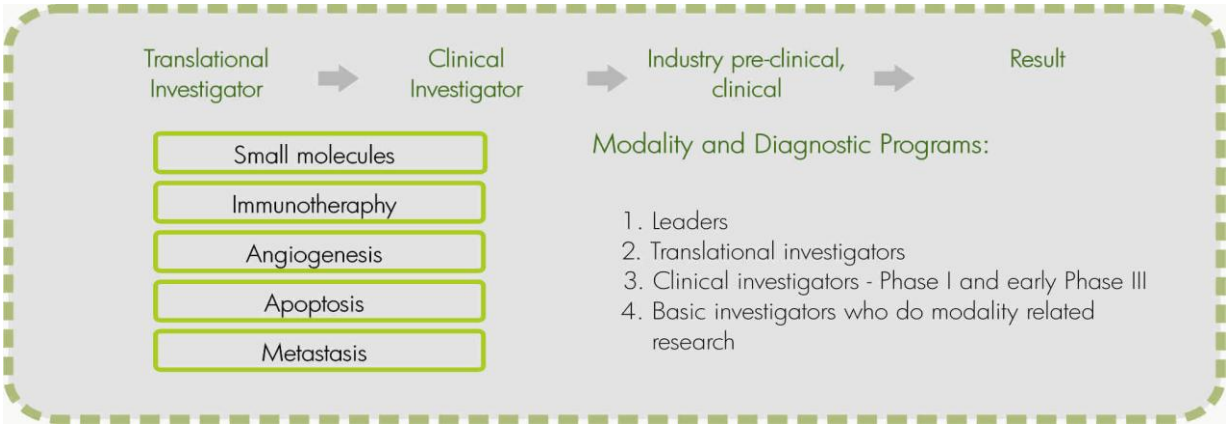

Figure 7. Example of Modality and Diagnostic Programs

The metrics to determine the success of the Center for T-C Research in creating the Next Generations of T-C Investigators are defined as follows:

a. **Institutional Measures**
   - Number of first into human and early phase trials led by PTS clinical investigator
   - Number of new validated surrogate biological markers discovered and validated at PTS
   - Number of new stand of care diagnostic tests developed by PTS investigators
   - How many of the above result in changes in the standard of cancer care
   - Institutional Branding as a "Model Disease Center"
   - Positive financial impact
   - Number of collaborations with other Integrative Centers
   - Increase in satisfaction by Department Chairs, Division Chiefs, and Disease Center Leaders
   - Increase in personal satisfaction by clinical and translational investigators
   - Increase in number of trainees and faculty who become clinical and translational investigators
   - Successful recruitment of clinical investigators
   - Retention of clinical investigators

b. **Academic Measures**
   - Academic Promotion
   - Manuscripts
   - Grants

c. **External Measures**
   - Progression toward clinical impact and change in standard of care

- Satisfaction by industry

5. Discussion

Table 1 summarizes the barriers Heller and de Melo-Martín[3] identified in the literature (2009). Most articles identified them as a result of firsthand experience in implementing organized T-C research programs[4], empirical research on interdisciplinary research centers or programs[5], evaluation of mentoring opportunities[6], or organized efforts to identify barriers using interviews, workshop discussions, and/or survey results[7].

The barriers were grouped into three areas: research workforce, research operations, and organizational silos (i.e., related to the departmental structure of most institutions).

Table 1: Barriers Identified in the Literature to Efficient Clinical and Translational Research

Barrier category	Specific barrier identified by the literature
Research workforce	Lack of qualified clinical and translational investigators [8]
	Lack of sufficient mentoring[9]
	Academic reward system and career disincentives[10]
Research operations	High research costs and lack of funding[11]
	Regulatory burden [12]
	Fragmented infrastructure [13]
	Lack of willing participants in clinical trials[14]lack of outreach to minorities[15]
	Incompatible databases between clinical practice and clinical research [16]

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Organizational silos	Lack of communication, coordination, and connection between basic scientist and clinical investigator [17]
	Lack of systematic implementation of interdisciplinary centers by universities [18]
	Department-based budgeting structure of universities [19]
	Different departmental policies and procedures [20]

First-listed set of barriers and solutions are **training and mentoring**. There is a need for institutions to develop graduate degree-granting and postgraduate educational and training programs in T-C science. It also strongly encourages institutions to train investigators from diverse disciplines as well as other key research personnel, such as study coordinators and project managers, and to include mentored career development components. Most institutions planned to offer Master of Science programs directed at students already enrolled in health professions training, doctoral programs in T-C research, and postdoctoral and junior faculty mentored training programs aimed at physicians. Most also planned to offer programs for study coordinators and project managers.

Second, two barriers to T-C efforts widely identified by the literature are the existence of a spotty and **fragmented infrastructure** to support clinical research **and the increasingly time-consuming task of complying with governmental regulation**s in clinical research. All of the programs described plans for a Web based portal as an entry to these services, and all also planned to have various types of supportive faculty and/or personnel to act as guides to access and/or learn how to use resources.

Third, **lack of clinical trials participants**. It is emphasized the need to create resources that promote interactions between clinical researchers and potential research participants, especially recruitment of research participants from the community, which would be expected to address the lack of clinical trial participants, particularly minority subjects.

Forth, **lack of systematic implementation of interdisciplinary centers**. Establishing an academic home integrated into the institution is central, and so all institutions responded in detail regarding the structure, governance, and integration efforts.

Fifth, **improving communication**. Most institutions mentioned inadequate communication between basic and clinical investigators as a barrier to T-C research. All planned to provide pilot grant funding to promote interdisciplinary translational studies, but there were no other solutions that provided incentives for basic scientists to participate in translational research.

Sixth, **high research costs and lack of funding**. All institutions have developed funding programs to support pilot studies and collaborative research. They also offered funding for the development of innovative research methodologies. A few institutions are planning more extensive strategies to address the high research costs and the need for funding, especially of early-stage applied projects. Others partnered with industry or government funded entities to bring in complementary funding.

6 Conclusion

The Center for Translational and Clinical Research has been given the responsibility to improve the capacity of PTS investigators to translate.

At PTS, our definition of translation will be intentionally broad. Translation must include bringing novel experiments from the laboratory to the clinic, bringing important clinical problems to the

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laboratory and partnering with industry at an early enough stage so that we are active collaborators in the conception and development of a new diagnostic and/or treatment. During the past decade, PTS has studied the conduct of translation at other academic health care centers searching for an importable solution. To date, we have been unable to find a successful model and therefore, we have concluded that we must build our own. It is our hope that we will eventually serve as the model for others.

The Center for T-C Research at PTS will partner with the Disease Centers, Divisions, and Departments to fill the gaps. First and foremost, the Center will attempt to provide an environment where T-C investigators from multiple Disease Centers, Divisions, and Departments can create a community. This community will provide a platform to present their ideas, find collaborators, generate funding mechanisms, share resources, and leverage their combined needs to create infrastructure. Moreover this community environment, very much like a large laboratory, laboratory floor, or Division; will foster mentorship, recruitment, and training of young investigators. Creating an investigative environment composed of senior T-C investigators, mid level T-C investigators, and trainees is creating that critical mass of T-C investigators that has been absent at PTS.