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Translation of Academic Discovery into Societal Benefit: Proposal for a Balanced Approach—Part 1

Traditionally, academic medical centers have represented an exciting interface between basic scientific discoveries and their application in clinical settings. The current translation of technology into societal benefit at academic medical centers, however, is hampered by tenuous interactions between academic and for-profit entities. Universities play a role at both ends of the development cycle: in laboratory research at the beginning and in clinical trials at the end. Connections between the basic and clinical arms within academic medical centers have become progressively distant. For patients to benefit, the increasingly well-funded basic-research enterprise must be linked with clinical services. A recent article (1) raised this issue and called for the development and reporting of programs to enhance the ability of academia and the medical-products industry to meet their missions through creative partnerships.

Simultaneously, society has never scrutinized conflict of interest more intensely, leading to reports and recommendations that add layers of oversight, inhibitions, and prohibitions (2,3). We present an approach that we believe would allow academic medical centers to reinvigorate translational research by linking their capability for basic discovery to their growing expertise in clinical investigation. This approach also provides for transparent oversight to protect patients and investigators from inappropriate decisions motivated by conflicts arising during the development of discoveries. This environment could support a community of scholars whose basic discoveries could be linked to clinical investigators through financial and administrative mechanisms. Systems could be designed to assist an institution's scholars—its greatest resource—in managing their conflicts and sustaining their careers as academic investigators. The goal of the proposed approach is to motivate development of diagnostic technologies and therapies likely to be of the greatest benefit, while using faculty interaction to stimulate innovative clinical research and to carefully manage the release of discoveries to the private sector at the best possible time.

BASIC PREMISE–A NEED TO MODIFY THE COURSE

Our society greatly values the application of scientific discovery to benefit the human condition, as evidenced by the recent dramatic increase in funding by the National Institutes of Health (NIH) (4–6). As the principal recipients of such public investment in biomedical science, universities have an obligation to support the translation of knowledge into human benefit. Discovery is one important gauge of academic success, and a great discovery is judged by the breadth of its impact. Medical research, however, is charged with improving human health, and diagnostic and therapeutic applications also must be considered in assessing the impact and worthiness of academic pursuits. Translating discoveries into applications requires many expensive, highly regulated steps, which have not been a focus of academic institutions.

The traditional model of the academic medical center, which values individual intellectual creativity and measures societal benefit as the sum of its parts, is not ideal for translating discovery into therapeutic gain. First, connecting basic and applied research has not been a priority. Second, translating discoveries carries the potential for conflicts of interest and financial gains, leading academic institutions to eschew it out of concern about jeopardizing their other missions. Recent examples of suspected impropriety in dealing with milestones considered more financial than academic have stimulated further concerns (7). Third, the issue of protecting intellectual property has been inadequately addressed. Although academic institutions recognize that patent protection is essential to human application of a scientific discovery, they often fail to protect an idea or to fund the steps needed to determine its clinical relevance.

The academic world is increasingly discovering valuable technology, which is developed for societal benefit through a tenuous interaction between universities and for-profit entities. The university's role is limited mainly to patent protection and licensing. This passive role often results in a disconnect between the discovery and the de-

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velopment cycle. Because many discoveries at universities stem completely or partly from public support, we believe that investigators and universities should create a system that will enable discoveries to evolve into products that can benefit humanity. Recognition of this flaw has been increasing, just as the growing shortage of "translational" researchers has become a concern. Despite great difficulty even in defining translational research (8), the NIH has begun a major training initiative comprising more than 60 institutional training grants and individual career-development awards (6). This focus on the translational clinical researcher symbolizes the need to develop a translational clinical research system, requiring reorganization of existing and developing resources within academic medical centers. This system is needed because the cost of developing a drug has increased from the enormous estimate of more than $400 million in 1995 (9). The problem has been defined extensively by the recently convened Clinical Research Roundtable of the Institute of Medicine (10).

Because of these issues, more university involvement is required. Patent protection and product development not only are valued commodities but also must be carefully planned to allow academic centers to fulfill their missions. The investment of academic medical centers should not stop at patent protection, however. What is needed is a better system of translational research that will allow advances to be translated more quickly and that will encourage those making discoveries to continue to participate in academic communities by translating their discoveries into human benefit.

THE BRIDGE FROM DISCOVERY TO APPLICATION

There is little connection between discovery and therapeutic application in today's academic environment. In many cases, the best researchers at academic medical centers are unknown to clinicians and clinical trainees at the same center. Instead of a collegial transfer of discovery from laboratories to clinics, the private sector often forms the bridge between discoveries at the bench and application by clinical investigators. The path could differ greatly if the substantial resources of the academic medical center brought to bear, with benefit to society, the academic mission, and the researchers.

Society would benefit from easier development of new diagnostic and therapeutic products and a greater chance of capturing opportunities otherwise lost or delayed in the current system. The increased effect of university research would enhance the academic mission. Individual researchers would benefit from greater interactions with colleagues across a spectrum of intellectual disciplines, reductions in risk imposed from inevitable conflicts of interest, and enhanced ability to remain focused on discovery research or clinical research.

THE CHANGING FACE OF MEDICAL RESEARCH

The Interdisciplinary Nature of Discovery and Development

The evolution from the concept of a biological pathway to potential human therapy is being dramatically shortened. The NIH's investment in basic biomedical research has produced an explosion of potential therapeutic targets. Combinatorial chemistry, receptor biology, genomics, proteomics, and biomedical engineering all provide exciting possibilities. Characterizing the structure and function of molecules and devices is becoming easier. This line of discovery carries the burden of "knowing what to do with it."

This situation is similar to that faced by large pharmaceutical companies with major basic-research divisions—only the motivation differs. In both cases, discoveries occur in laboratories, and developing a path from the laboratory to the bedside is complex. In industry, basic research is guided by corporate decisions about areas of interest that might lead to marketable products. Basic academic research, however, is influenced by peer-review and direction from the NIH.

Industry organizes its opportunities and makes decisions about investing in the resources needed to move discoveries into the clinic. In contrast, the academic community often has viewed central organization as a diversion from the primary focus on academic freedom and discovery of new ideas. Although we believe that the discovery process should remain different between industry and academia, reducing hurdles to translation should be a goal common to both.

Even when a new technology does not emanate from academia, the pharmaceutical and biotechnology communities eventually turn to academic investigators. Understanding how to develop a useful product evolves through focus groups and scientific advisory boards, most of which have academic leaders. These advisory groups are needed because of their insight and multidisciplinary expertise, which is not easily duplicated outside of academia.

An example of the interdisciplinary potential of discovery illustrates this point. Both fungal infections and cancer involve pathological proliferation of cells, for example, but seeing the link between fungal infection and restenosis or prostatic hypertrophy requires higher-level integration among investigators. Some of the complexities and opportunities may be lost on a researcher making a discovery, but they often are known within the aca-

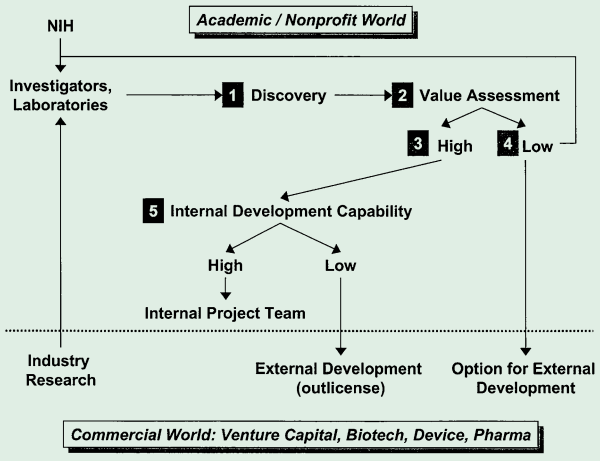

Figure. Translation of basic-science discoveries into possible diagnostic or therapeutic applications within academic medical centers. Investigators and laboratories in academic medical centers are primarily funded by government organizations and secondarily by industry. When investigators discover possibly valuable technologies (1), institutions should help determine their potential value (2) and devise a development plan while also assisting investigators in managing conflicts of interest. If the institution considers the discovery of high value (3) and can advance the concept itself (5), the technology can be further developed both inside and outside the academic medical center. If the discovery is deemed of low value (4), the investigator could take it outside for development. Assembling development teams (5) can enhance cross-functional interchanges among faculty members. At the appropriate time, each discovery is moved to the commercial world, depending on its value, the institution's capabilities, and assessment of the conflicts.

demic medical center at large. It is lack of coordination that prevents the needed connection between the two.

Connectivity

Large academic institutions do well with discovery, mostly because of opportunities provided by the NIH for investigator-driven research. However, they typically are poor at linking discoveries and therapeutic applications, partly because of the traditional academic model, in which success is identified with self-sufficiency and too often can be interpreted as isolationism. Independence of thought is essential for scientific independence, but independence of action to the exclusion of teamwork is antithetical to the development of new applications. These cultural factors make it difficult to apply collective resources to a problem; as a result, the investigator often is not connected to delivery of actual benefit, and applied clinical investigators have no opportunity to work on 'home-grown' discoveries. This lack of investment in a system of translational research detracts from the academic mission and increases the likelihood of distancing basic and clinical investigators within the institution.

The typical course taken by many academic centers is to move discoveries out of the institution. Publicity about inadequate academic systems for managing conflicts of interest has strengthened the desire of many academic institutions to eschew their own discoveries (3). The paradox in this position is that academic medical centers, particularly those with substantial clinical-research infrastructures, are well positioned to participate in drug and device development and in the promotion of basic discoveries. Removing discoveries from the institution thus denies opportunity to researchers and the university while it adds barriers to societal benefit. We believe that a new set of attitudes, processes, and support systems is needed to assist basic researchers in identifying the potential applications of their work, moving them forward efficiently into animal studies and definitive testing in humans. Central to this effort is the attitude toward managing conflicts of interest. Although we do not deny the existence of conflicts or the serious problems associated with them, we believe that avoidance may not be in the best public interest.

The Figure represents a schematic illustrating the relative roles of the academic and commercial worlds in the translation of basic-research discoveries into potential therapies, and the Table presents several variables that can be measured to guide or refine development of translational medicine programs.

Table. Measures of Institutional Commitment to Translational Medicine

- Faculty surveys
  - Support for translational medicine
  - Support for patent efforts
  - Importance of basic-clinical collaborations
- Number of patent applications and awards
- Formal TM mentoring policies in place
- Attendance at TM conferences
- Personnel dedicated to development and maintenance of Discoveries Database*
  - Completeness of database
- TM efforts formally recognized as a positive factor in promotions or tenure
- Number of TM researchers who leave the institution to pursue commercialization
- Dollar amounts that the institution dedicates to TM
- Number of sabbaticals granted to pursue "start-up" opportunities
- Formal TM career-track option present
- Compensation tied to TM efforts
- Activity of Conflict of Interest Committee
  - Evidence of active oversight for each project

For a more complete discussion of these measures, access http://www.dcri.org/appendix_stamler.pdf.
* Computerized record of all diagnostic and therapeutic technologies discovered at the institution.
TM = translational medicine.

Ultimately, private industry must perform the pivotal research to support applications to regulatory authorities, and the drug, biotechnology, or device company or venture-capital firm must invest. The timing of such investments should maximize the probability that the discovery will become a useful technology while striving to optimize the return for inventors and the institution, to support and reinforce the cycle of discovery and application.

By bringing discoveries to the appropriate stage of development before handing them off to industry, universities may entice talented researchers to stay in academia rather than leave to pursue their research further. Given that this migration to the private sector reduces productivity (in terms of basic discovery) and takes talented and inspirational teachers out of the environment where they most affect developing young scientists, there is much to be gained from keeping researchers connected to delivery of benefit within academia.

SUMMARY

Academic medical centers devote substantial resources to support basic research of possible diagnostic and therapeutic technologies, but we believe that they devote inadequate resources to translating these discoveries into beneficial products. The ability of academic medical centers to capitalize on basic discoveries while also meeting their academic missions could be enhanced through creative partnerships with the medical-products industry, but concerns about patient safety and conflicts of interest have hindered such collaborations. We find that the mindset of avoiding conflicts of interest at all costs is not in the best public or academic interest; rather, we favor careful oversight to assess and manage conflicts so that important discoveries can be translated into products.

In Part 2 of this series, appearing in the next issue of the *Journal*, we describe the structure and organization of a system we have designed in an effort to relieve investigators of direct conflicts during the commercial development of therapeutics and to prevent the institutional financial conflict from dominating the academic mission. Such a system could create an exciting academic environment that would result in development of therapies most likely to provide benefit to patients.

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