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Pathways of the Research Innovator

> *Scientists must have the courage to attack the great unsolved problems of their time.*
>
> Otto Warburg (1964)[1]

In recent decades, there has been remarkable progress in advancing life sciences. Discoveries are pouring out of laboratories and research universities all over the world. Science is bringing us closer to realizing the dream of understanding, treating, and preventing major diseases and opening up new, unprecedented economic development opportunities. We live in the exponential times of life sciences: not just the number of discoveries is growing, but also the benefits to people and society are multiplying.

In general terms, research has not done a great job in defining its end product. Better understanding how scientific ideas, life-changing practices, or technologies are generated should help to see the trends of success and learn from the inspiring stories. By choosing areas of interest, researchers make decisions that shape futures and change lives. Ultimately, research should become better targeted, more accomplished, and effective more rapidly.

Scientific research is known for leading to peer-reviewed, replicable, and generalizable knowledge. The dopamine neurotransmission model in the brain discovered many years ago will also work next year. It can be used to treat many patients with comparable effects anywhere in the world. The new model of physiologic function can be confirmed by other researchers. Peer review means disclosing methodology and findings to be evaluated by experts not affiliated with the study.

Eugene Wigner's (1960) article on the unreasonable effectiveness of mathematics in the natural sciences elegantly describes the essence of reproducibility

1 Warburg, O. (1964). Prefatory chapter. *Annual Review of Biochemistry*, 33 (1): 1–15.

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and generalizability in science. As Erwin Schrodinger (1932) noted earlier, certain regularities in the events could be discovered in spite of the perplexing complexity of the world. Wigner pointed out that the laws of nature are concerned with such regularities. There is also a "succession of layers of 'laws of nature', each layer containing more general and more encompassing laws than the previous one and its discovery represents a deeper penetration into the structure of the universe than the layers recognized before." Wigner also highlighted the generalizability of the laws of nature: "it is true not only in Pisa, and in Galileo's time, it is true everywhere on the Earth, was always true, and will always be true."

A better understanding of long-term outcomes should make research more streamlined and dissemination of discoveries more effective. When producing peer-reviewed, replicable, and generalizable results, researchers always make important disclosure decisions, either knowingly or not. Examining various choices and their practical implications should improve understanding of consequential scientific discoveries, support researchers striving to innovate, and facilitate the development of more useful research infrastructures. This chapter clarifies concepts, defines terminologies, and introduces a model framework for biomedical research innovation.

Diverse Outcomes of Science

Among the many possible outcomes, models of important relationships, laws of nature, represent a crucial stepping stone in the progress of science. Some of them are complex, while others are simple relationships. When widely published, greater understanding and new models can not only change the usual course of health care but also serve as launch pads for further successful research.

The research concepts of better understanding, new knowledge, and penetrating insight can often be captured by scientific models: verbal, graphic, physical, or mathematical representations of an important feature of the world. The double helix of the DNA, the causative role of *Helicobacter pylori* in gastric ulcer, and rituximab-mediated immune destruction of lymphomas are all examples of models abundantly validated by subsequent studies and patient experiences.

The creative process in academia is called research or scholarly activity. When productive, the creative process leads to results that have great theoretical significance and practical value. Innovative biomedical research has repeatedly proved its value by finding cures for major diseases, improving public health, and generating economic prosperity.

In most academic institutions, the *peer-reviewed* research article and competitive extramural research funding have become the gold standard in expectations and most common pathways of delivering scholarly productivity results (Anderson et al. 2013). Most academic institutions require a certain quantity and impact factor of peer-reviewed research articles. It is noteworthy that the health sciences area is unique in its singular focus on peer-reviewed articles (Anderson et al. 2013; Gelmon et al. 2013; Smesny et al. 2007).

With advances in applied life sciences over many decades, there have also been growing numbers of biomedical innovations – not only to improve human life but also contribute to economic development. Major categories of results generated by biomedical research innovation include (i) products, (ii) services, or (iii) practice recommendations (i.e. guidelines, processes, systems, and organizational structures).

Of the top 10 Achievements in Public Health from 2001 to 2010 identified by the CDC, a decline in vaccine preventable diseases was among the most spectacular scientific achievements (Centers for Disease Control and Prevention 2011). Two vaccine products, in particular, were singled out: the pneumococcal conjugate vaccine and the rotavirus vaccine. An estimated 211 000 serious pneumococcal infections and 13 000 deaths were prevented during 2000–2008 after the pneumococcal conjugate vaccine was introduced (Pilishvili et al. 2010). Similarly, vaccinations for the rotavirus now prevent an estimated 40 000–60 000 hospitalizations each year according to 2011 statistics (Centers for Disease Control and Prevention 2009; Tate and Parashar 2011; Yen et al. 2011). Rotavirus and pneumococcal vaccines also resulted in practice recommendations by the CDC to include these products in the regular schedule of vaccinations for infants and children.

The top 10 Achievements in Public Health also include successful breast, cervical, and colorectal cancer screening services. Particularly, colorectal cancer death rates decreased from 25.6 per 100 000 population to 20.0 for men and from 18.0 per 100 000 to 14.2 for women between 1998 and 2007 (Kohler et al. 2011).

Working in Switzerland, Andreas Grüntzig developed the first balloon angioplasty and successfully used it in patient care in 1977. This product and practice recommendation have saved numerous lives and made them more comfortable. Further refinement included the addition of a heart stent product, left behind after the procedure. The resulting nonsurgical service is used in multiple ways, allowing for devices and drugs to be utilized directly (Gruentzig 1982; Holmes et al. 1984).

According to the classic definition, innovation is the design, invention, development, and implementation of new or altered products, services, processes, systems, or organizational models to create new value for customers and financial returns (Schramm et al. 2008). Removing barriers to the development of innovative biomedical research has the potential to affect millions of people by finding solutions to major global public health concerns.

Successful biomedical research innovation cannot be equated with business success. Many new initiatives highlight the need for much more innovation in areas where business success is limited or nonexistent. For example, there is a great need for innovation in the treatment of rare and esoteric diseases as highlighted by the NIH Office of Rare Diseases Research Bench-to-Bedside (B2B) Awards and the FDA Office of Orphan Products Development. These programs seek to advance the evaluation and development of products for the diagnosis and treatment of often overlooked rare diseases. Increasingly, public–private partnerships are recommended for the development of noncommercial innovations (Nwaka and Ridley 2003).

There have been many commercial successes that later turned out to be health outcome failures. For example, a major maker of pomegranate juice made sweeping claims, citing university studies and researchers, that its juice reduced the rate of heart disease, prostate cancer, and erectile dysfunction. In 2012, the company received a cease-and-desist order after FTC determination that there was insufficient evidence to support claims. This order will remain in effect for 20 years unless they present at least two well-controlled randomized clinical trials substantiating their claims.

Best of Both Worlds: Scientific and Innovative

Innovation is often defined by the common criteria of being novel, non-obvious, and useful. Unlike naturally occurring DNA, practically valuable synthesized sequences can meet innovation criteria and can be protected as intellectual property accordingly (Golden and Sage 2013).

There is an apparent synergism between biomedical research and beneficial innovation. Society has no apparent benefit from research results that are not novel, not obvious, or useless by failing to benefit further research or the practice of health care. The criteria for innovation represent a more subjective or judgmental assessment. Nevertheless, they capture what is needed to benefit society.

The best discoveries of applied sciences are not only *reproducible* and *generalizable* but also *novel*, *non-obvious*, and *useful*. Scientific research leads to replicable and generalizable knowledge, but it is also expected to be novel, non-obvious, and useful.

In other words, the best applied scientific results not only meet but also significantly exceed innovation requirements by offering broadly usable and trustworthy solutions for a new product or service design (Balas and Elkin 2013). In the infrequent case of commercialization, a third set of sustainability considerations is added, including market demand, business model, and environmental impact.

Meanwhile, research interest in reviews of patented innovations has also increased in the scientific community. There are a growing number of articles that review new

technologies based on published patents, among other sources (Freschi et al. 2012; Horstkotte and Odoerfer 2012; Talevi et al. 2014; Telang et al. 2012). Patent reviews assist researchers interested in innovation because they identify available and unexplored technologies and highlight opportunities for new directions.

Opportunities That Are Not Just Timely But Also Timeless

The usual assumption that biomedical research accidentally bumps into meaningful discovery or disclosable IP may be intermittently true but is probably more often misinforming. Particularly, the enormous publication and patenting productivity of serial innovators challenge this usual assumption. Well-planned studies have always been viewed as best chances of good results. Therefore, a researcher needs to recognize not only when to start a scientific investigation in a particular area but also when to stop it and switch to a more promising field.

In recent decades, the complex and often controversial relationship between university research and innovation has been gradually highlighted. Better and earlier understanding of the kind of health sciences research that leads to impactful evolution in future research and public health is essential for effective research innovation. It is well known that the overwhelming majority of patents are nonperforming, never licensed, or utilized (Ledford 2013). Therefore, it is a vital interest to identify factors that lead to well-performing IP.

Like any other organized human endeavor, research needs to set targets to guide activities. Target selection is typically influenced by results from other diverse scientific areas. Traditionally, the targets are expressed as research objectives, hypotheses, and questions. It is reasonable to assume that the outcomes and products of research are going to play an increasingly important role in targeting research.

Target selection often starts with the development of a model based on already available data. For example, the discovery of the role of papillomavirus in cervical cancer by Harald zur Hausen was largely triggered by the epidemiologic studies showing the relationship between viral infections and cancers. In his declaration of war on cervical cancer, he wrote that "The condyloma (genital wart) agent has been entirely neglected thus far in all epidemiological and serological studies relating not only to cervical and penile, but also to vulvar and perianal carcinoma. This is particularly unusual in view of the localization of genital warts, their mode of venereal transmission, the number of reports on malignant transition, and the presence of an agent belonging to a well characterized group of oncogenic DNA viruses" (zur Hausen 1976). In other words, the hypothetical model of infectious origin became the target locator and ultimately the Nobel Prize-winning result of his research.

Concepts of forceful *research targeting* harmoniously coexist with accidental discoveries. The most frequently cited accidental classic is the dirty dish with staphylococci in Alexander Fleming's laboratory that led to the discovery of penicillin. "I certainly didn't plan to revolutionize all medicine by discovering the world's first antibiotic" – he stated later. The most newsworthy, contemporary example of serendipity is Pfizer's failed angina drug study that led to the discovery of Viagra.

One of the most practical discoveries in injury prevention also did not come from problem-oriented bioengineering research based on targeted technical specifications of the societal need, but from an accidental discovery. While working as a research associate for DuPont in 1964, Stephanie Kwolek was looking for a lightweight but also strong fiber to be used in tires. The original target was never fully achieved, but during the research, she instead discovered Kevlar, which is five times stronger than steel by weight. Today, Kevlar is widely used in combat helmets, ballistic vests, protective gloves, tennis rackets, racing boats, and many other areas.

The innumerable lessons of targeted and accidental discoveries tell us that we need to develop a better understanding of selecting and deselecting research targets based on good models and the chances of successful innovation benefiting society. When accidental discoveries come up, as they often do, the primary responsibility of researchers is recognizing them and fully developing their potential.

Balancing Research and Innovation

Most appropriately, discussions about scientific innovation should refer to the full range of scholarly creativity, including new models, research methodologies, peer-reviewed publications, IP disclosures, and tech transfer products. Congruently, the terms productivity, efficiency, and quality improvement should consider the full range of scientific innovation without overemphasizing one particular line of activity. The prevalent single-line evaluations, for example, counting only publications or patents, tend to misguide scholarly creativity and appear to be negligibly useful in promoting actual scientific progress.

The NIH Roadmap for Medical Research was launched in September 2004 to address basic steps of translation: basic science research translated to humans (T1 translation) and secondarily translated into clinical practice (T2 translation). The Clinical and Translational Science Awards (CTSA) program was designed to support diverse research teams working in collaboration toward a common goal (Blumberg et al. 2012). However, a review by the Institute of Medicine concluded that the lack of transparency in reporting and also lack of high-level common metrics are significant barriers to overall program accountability (Leshner et al. 2013).

For obvious reasons, the actual progress of science cannot be measured by the number of peer-reviewed research publications or successfully filed patents in any particular field. For example, there were 26 273 human subject studies on low back pain indexed in the PubMed database according to recent searches (February 2015); among them 2779 human subject publication type randomized clinical trials mention low back pain; there were 990 studies found for low back pain in http://clinicaltrials.gov; and there were 2480 patents in the USPTO US Patent Collection Database (www.uspto.gov). In spite of this vast amount of research and development, the treatment of low back pain is far from being fully resolved and continues to need creative prevention and new interventions.

Nevertheless, the number of peer-reviewed scientific publications does give some level of information about the scientific productivity of academic institutions. In the biomedical field, counting PubMed indexed publications may be a reasonable approximation if applied in a much larger set of indicators. Citations of research publications may provide further insight and indeed are used in the evaluation of individual researchers.

National statistics also highlight that innovation success is not a simple correlate of research expenditures: greater spending on research does not equal greater innovative results. The Association of University Technology Managers (AUTM) data suggest that at some universities $20 million research spending leads to a new startup company while at other universities it may take $200 million of research funding to launch a startup company (The Science Coalition 2013). Defining and harnessing the differences between these efforts is of great importance to funders and institutions alike.

The Carnegie Foundation for the Advancement of Teaching classified 207 universities as "very high research activity" or as "high research activity" in the United States (Carnegie Foundation for the Advancement of Teaching 2010). Out of this group, 187 institutions respond to the Association of University Technology Managers Licensing Activity Survey.

According to the AUTM survey, about half of all cumulative active licenses come from 18 universities (Balas and Elkin, 2013). Each of these universities produced an average of 1007 active licenses, creating a "Monument Valley" of high-performing institutions towering over less productive efforts. The remaining 134 universities produce an average of 140 cumulative active licenses (15 universities did not provide data).

An analysis of the 2013 AUTM Licensing Survey, a review of World of Science indexed publications from 2013, and the Integrated Postsecondary Education Data System (IPEDS) 2012–2013 report found that per institution averages (±SEM) were as follows: instructional and research faculty, 2099 ± 164; research expenditure, $362M ± $45M; publications, 3239 ± 368; IP disclosures, 133.2 ± 14; patent applications, 83.3 ± 10.6; patent awards, 33.5 ± 3.9; startup companies initiated, 4.8 ± 0.5; licenses 29.4 ± 3.1; and gross income, from

licenses $13M ± $27M. The top 10% institutions averaged were as follows: research expenditure, $848M; publications, 7882; IP disclosures, 33; patent applications, 176; patent awards, 80; startup companies initiated, 11; total licenses, 83; and gross licensing income, $34M.

A recently published review of university innovation successes further underscored the particular challenges of the biomedical research (The Science Coalition 2013). The vast majority of revenue-producing early successes of university startup companies come from the information technology field, while biomedical startup companies tend to be cash burners for a prolonged period.

The experience of an institution's technology transfer office may also affect their innovation productivity. Years of technology transfer office program existence significantly correlates with greater research expenditures, more licenses and options, greater number of startups, greater adjusted gross income, and greater royalty income in 2013 (all $P < 0.05$). For an individual researcher, the experience and length of existence of an institution's technology transfer office may be a significant factor in the success of promoting one's research discoveries.

An insightful analysis of the licensing results of six universities found that 56% of successful licensing contacts came from faculty inventors, 19% from marketing by TTO staff, 10% from the company (licensee), 7% from the research sponsor, and the rest from miscellaneous unknown sources (Jansen and Dillon 2000). Frequently, professors not just produce great innovations but also build valuable personal networks in the industrial sector (e.g. business card received at conferences, graduate students who have taken positions in industry, companies seeking expertise in academia, and others).

The number of patents, licensing revenues, and job creation of university startup companies are often used as innovation indicators of economic significance. A study of the Massachusetts Institute of Technology (MIT) research concluded that 25 800 active companies founded by MIT alumni employ nearly 3.3 million people and generate annual world sales of $2 trillion (Roberts 2009).

Essential Concepts of Research Innovation

A practical, useful model of innovation needs to integrate terminology to improve the visibility of common challenges and also consequences of variations, in both regulatory and institutional policies. It should support evaluation of public health and economic impact, assess the role of organizational culture and inventor recognition, highlight opportunities for better functioning policies, and show ways to increase biomedical innovation that benefits society and improves public health.

Innovation is the creation of new wealth-producing resources or endowing existing resources with enhanced potential for creating wealth, according to Peter Drucker (1985). In focusing on life sciences research, three-dimensional or triple innovation can be defined as the creation of new knowledge, health, and wealth resources (e.g. new scientific models, improvements in public health, and economic development).

In other words, *research innovation* is the production of replicable, generalizable scientific discoveries that lead to new models, products, services, or practices benefiting research, people, and society. Again, according to Peter Drucker, innovation is the change that creates a new dimension of performance (Drucker 1985).

The person responsible for the creative result is often called *researcher, author*, inventor, discoverer, scientist, scholar, designer, creator, assignee, investigator, or analyst. Research laboratories are identified as teams of researchers focusing on a significant area of scientific investigations and having specialized methodological capacities and competencies.

The process of research reaches a conclusion when *disclosure* is made (i.e. decision to disseminate the results). Synonyms for results include discovery, practice recommendation, invention, prototype, source program, information system, and others.

Nondisclosure remains a frequently exercised but undesirable research outcome. While exercising such option is currently entirely at author/researcher discretion, it is a major and growing concern of research integrity. Based on self-reported clinical trial outcomes, over 25% of trial reports never published, mainly due to "negative" results and lack of interest (Dickersin et al. 1992). An estimated 50% of innovations with commercial potential are never disclosed, and the negative impact on public health is potentially huge (Thursby et al. 2009).

When applied research results are disclosed, they are supposed to lead to valuable outcomes. In biomedical research, the major outcome categories include further productive research, public health impact, and economic impact:

- *Scientific results* are systematic descriptions of difficult-to-observe objects or phenomena to explain and predict behavior under varying circumstances. The scientific model can be material, graphical, narrative, mathematical, or computational approximation of a real system that leaves out all but the most essential variables. By referencing to existing and commonly accepted knowledge, scientific models are used in the construction and demonstration of scientific theories.
- *Public health outcome*, in the context of the public's health, refers to the general health of a population and the desired distribution of health. Public health includes prevention of diseases, promotion of health, cure of diseases,

prolonged life expectancy, and conditions in which people can be healthy. It can be concerned with the population as a whole or geographic populations such as nations or groups like employees, ethnic groups, disabled persons, prisoners, or others.

- *Economic outcome* is a general improvement of living standards and economic health of a specific locality. Economic development involves advancement of human capital, improvement of infrastructure, improvement of health and safety, and other advances of the general welfare of citizens. Economic development outcomes of innovation can be realized through institutional revenue generated, startup company initiation and success, commercialization of new products, cost savings, and jobs created.

Research Innovation Pathways to Effects

The origins of innovation recognition are simple, clear, and compelling in Article One of the US Constitution: "Congress shall have Power…To promote the Progress of Science and useful Arts, by securing for limited Times to Authors and Inventors the exclusive Right to their respective Writings and Discoveries" (Art. I, Section 8, cl. 8.).

Today, there are numerous complex, divergent categories of writings and discoveries that lead to different practical implications, levels of legal protection, and rewards to authors and inventors. A myriad of laws, regulations, and business expectations has emerged that contribute to making the innovation field much broader but difficult for academic researchers to access successfully. This variety of terminology also provides a pretext to variations in processing and recognition of innovation.

To highlight connections between biomedical research and discovery outcomes, the Research Innovation Pathways to Effects (*RIPE*) *model* conceptualizes the transfer of innovative ideas to future research, public health practice, and the general economy (Figure 1.1). Five research disclosure pathways have the greatest significance to biomedical innovation. They are governed by dissimilar laws, offer variable rewards to inventors, and produce divergent practical results. When research discoveries are made, the results can be made available to the public (general or limited) on one of the following pathways of disclosure:

1) *Direct (PRP) disclosure*. Most frequently, *peer-reviewed publication (PRP)* is the chosen or default pathway for dissemination. It also indicates that the work was reviewed and deemed acceptable by other scientists with relevant expertise in the field. Through this line of disclosure, knowledge becomes reliably, publicly, and essentially freely or for a nominal fee available to anyone who might be interested. On the other hand, limited readership and practical

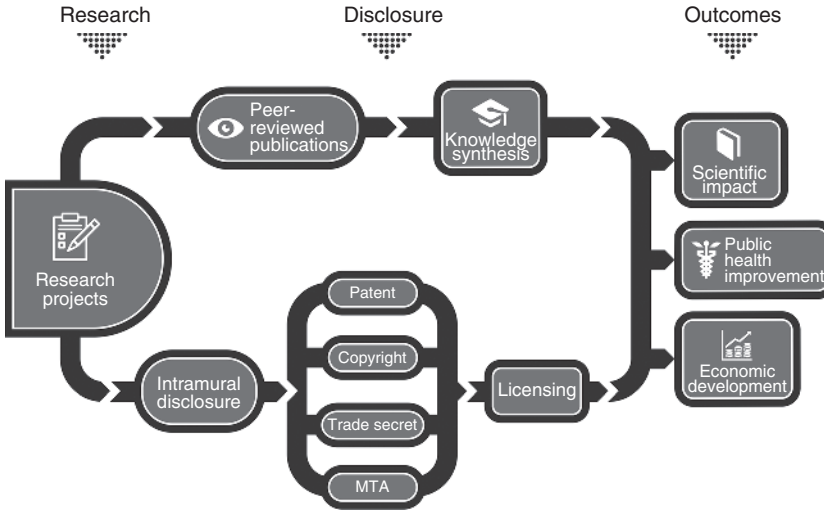

Figure 1.1 The Research Innovation Pathways to Effect (RIPE) model of research discovery disclosure.

impact are frequent concerns due to the large volume and variable quality of scientific articles. Recently, Jeremy Grimshaw and others suggested that most PRP reported research becomes actionable through scientific reviews that synthesize knowledge for practical implementation (Grimshaw et al. 2012).

2) *Staged (IP) disclosure* leads through *intellectual property (IP)* protection of results that appear to be not only novel, useful, and non-obvious but also have commercial potential. It occurs in three subsequent steps: intramural disclosure, legal protection, and extramural disclosure. Typically, the process starts with confidential intramural disclosure to the technology transfer office of the research institute to assess the potential for IP protection and commercialization. Based on the type of legal protection, four IP disclosure pathways are particularly relevant to biomedical research innovation (Figure 1.1):
   a) A *patent* creates intellectual property right granted by the government to an inventor to exclude others from making, offering for sale, selling, using, or importing the invention for a limited time, usually for a period that begins when the patent issues and ends 20 years after the date that the application for the patent was filed.
   b) *Copyright* is an exclusive right to the use and distribution granted to the author of an original work. Copyright protects the expressive aspect of the innovation. The default time a copyright is enforceable is the life of the author plus 70 years in most countries.

c) A *trade secret* has three parts: information, reasonable measures taken to protect the information, and the economic value it derives from not being publicly known. It is essentially limited extramural disclosure only to those who are intended users. It is protected at the state level so that requirements may vary from state to state.
d) *Material transfer agreement* (MTA) is a contract regarding the transfer of research materials to a recipient that intends to use it for research purposes (e.g. chemical compounds, biological material, reagents, cell lines, plasmids, vectors, and software). Typically, MTAs cover rights to resulting intellectual property, rights to data and use of results generated by the work, publication rights, indemnification and liability, jurisdiction for legal disputes, and governing law for legal disputes.

Frequently, the practically useful innovative results fit multiple intertwining categories. Many innovations can be communicated through any of the listed pathways. For example, medical natural language processing software can be disclosed through any of the above pathways (i.e. peer-reviewed publication, patent, copyrighted documents, trade secret, or material transfer agreement).

While the technicalities of the disclosure may suggest otherwise, researchers and their employing institutions have a large degree of freedom in choosing the disclosure pathway. Obviously, different pathways represent different positioning for practical impact and author rewards. For example, disclosing a new medication through peer-reviewed publication without IP protection would undermine commercialization, manufacturing, and ultimately broad public access. Patenting is the well-functioning disclosure pathway for new drugs.

An additional special type of intellectual property, the use of trademarks also has great potential in scientific communications. Of course, trademarks cannot be viewed as substantial channels of communicating the details of scientific discoveries. On the other hand, they can be very helpful in making discoveries better recognized and easier to remember. When commercialization is at stake, registering a trademark can provide the much-needed stronger protection of the brand by identifying and distinguishing the original researcher/creator from others and indicating the genuine source.

Branding of a new clinical intervention or research method helps to stand out, be remembered, and become the preferred choice. Successful examples include memorable names of landmark systems, studies, and methodologies (e.g. BLAST, Framingham study, zero defect data, radioimmunoassay). In the world of science, many more names and acronyms are created but seldom used by other than their creators. When the intervention or research method is more widely used, the brand becomes valuable and deserves protection. In academia, the strict deterrents of plagiarism alone provide sufficient protection for the brand in most cases. Interestingly, the usefulness of many identifiers is not limited by the fact that official registration and protection as a trademark is often not pursued by the researchers or their institution.

Preferentially choosing peer-reviewed publications for disclosure does not make the channels of intellectual property protection and subsequent commercialization irrelevant. Researchers striving to be in touch with reality need to learn about the societal need for their results, the full range of disclosure channels, and also basic tactics of negotiation with business interests (see Chapter 18).

Learning from Award-winning Scientists and Serial Innovators

Successes of serial research innovators suggest that scientific discovery and innovation cannot be considered just a matter of luck. More frequently good planning and hard work are in the background. The most accomplished researchers and their laboratories have a unique sense of innovation opportunities and also the skills to make them broadly successful and accessible. The successes of innovative researchers indicate skills that are likely to surpass one time or incidental inventors. Successful serial innovation requires meeting great challenges by applied and translational health research.

Historical exploration and reverse engineering of biomedical innovations with the greatest public health benefits could offer many lessons for future research projects. Beyond inspirational value, historical references are also helpful not only to illuminate the research and innovation culture but also to pinpoint the dichotomy of intellectual property protection and dissemination through scientific commons in transferring research results to practice.

Studying the performance of serial research innovators from academia offers unique insight. The list below summarizes the performance of several university researchers who have built a track record of a large number of peer-reviewed publications, numerous patents, notable commercialization successes, and major contributions to better health care:

- Tillman Gerngross, PhD, Dartmouth College (PRP: 23, IP: 24). Most notable achievements: Humanizing the glycosylation machinery in yeast to produce human therapeutic proteins, including antibodies, with fully human carbohydrate structures. Public health impact: Discovered novel and efficient ways to produce new drug proteins through yeast. Economic impact: Cofounded GlycoFi, which is sold to Merck for $400 million. Adimab, cofounder, biotech startup valued at $500 million, privately held. Venture partner with SV Life Sciences.
- Michael Merzenich, PhD, University of California, San Francisco (PRP: 200+, IP: 50+). Most notable achievements: Cochlear implant and sensory cortex mapping. Public health impact: Improved quality of life for the deaf. Understanding of brain function and training informs further brain research. Economic impact: Global hearing implants market is projected to exceed $2 billion in 2017.

- Andrew Schally, MD, Tulane University, Baylor College of Medicine (PRP: 2200+, IP: 29). Most notable achievements: Structure of LH-RH and Nobel Prize in Physiology, 1977. Public health impact: Luteinizing hormone-releasing hormone, which inhibits the growth of prostate cancer. Most widely used prostate cancer treatment.
- Mark Skolnick, PhD, University of Utah (PRP: 139, IP: 9). Most notable achievements: Skolnick directed the group that discovered the breast cancer susceptibility gene BRCA1; found the full-length sequence of BRCA2. His group developed restriction fragment length polymorphism (RFLP) method for genetic mapping. Public health impact: Women with harmful BRCA1 mutation or BRCA2 mutation have nearly 50% chance of developing breast cancer, and genetic testing provides early detection of the risk. Economic impact: He launched three companies, and among them is the biotechnology company Myriad Genetics, Inc., in Salt Lake City.
- Edward Taylor, PhD, Princeton University (PRP: 450, IP: 52). Most notable achievements: Alimta, cancer drug for mesothelioma. Public health impact: Most common drug in use for mesothelioma treatment. Economic impact: Princeton received $524 million from 2005 to 2012 in license income, mostly from Lilly. Alimta earned $1.2 billion in the United States and $2.7 billion globally in 2013.
- Elias Zerhouni, MD, PhD, Johns Hopkins University (PRP: 212, IP: 8). Most notable achievements: High-resolution CT development for heart and lung study and cancer diagnosis; computed tomographic densitometry for lung cancer detection. Economic impact: Founded five startup companies based on inventions and research from Johns Hopkins University.
- Jackie Yi-Ru Ying, PhD (PRP: 350, IP: 180), is a nanotechnology pioneer, former MIT professor, and currently director of the Institute of Bioengineering and Nanotechnology in Singapore. Most notable achievements: Nanomedicine applications, drug delivery, cell and tissue engineering, medical implants, and biosensors, among others. Economic impact: Her work has been instrumental in launching 11 spin-offs. Public health impact: One of her inventions led to the founding of SmartCells, Inc., a spin-off that developed a technology capable of autoregulating the release of insulin, depending on the blood glucose levels for diabetes management. It was acquired by pharmaceutical giant Merck for more than $500 million to further develop this technology for clinical trials.

Road to Meaningful Research Disclosure

According to recent reviews, science policies have developed a hypercompetitive culture where learning about grant writing and competing for grants appear to be more important than spotting health needs, recognizing scientific

opportunities, and choosing research targets (Alberts et al. 2014). More appropriately, researchers should look into what makes good sense in choosing biomedical research targets, as opposed to being completely driven by requests for proposals of various funding agencies.

The steps after disclosure are widely discussed and relatively well defined in the business and law literature. Usual university technology transfer discussions tend to center on commercialization and business development of intellectual property (IP) disclosures already made, without much emphasis on how you get to meaningful disclosures. Commercialization after disclosure has been the focus of many reviews and books. The fundamental research process leading to well-performing research disclosures has been largely neglected, but it is the focal point of this discussion.

Contrary to this trend, there is a need to study more intensely the fundamental research process that can produce meaningful invention disclosures. In spite of huge public interest in the process of innovation, there has not been enough research on the road leading to meaningful innovation disclosure. Comprehensive reviews have not focused on how individual researchers and research laboratories become better sources of discoveries. More should be known about how research can reliably lead to practically valuable disclosures.

In response to pressing societal need to increase the productivity of research innovation and in light of the above-described model of research innovation pathways, researchers should become better educated about pathways of research disclosure and the societal outcomes of research. Many students of biomedical PhD programs graduate, and many biomedical researchers spend years in the laboratory without good understanding of public health needs, without reading a patent or copyright registration, without knowing what happens with scientific discoveries after the research is completed, and without understanding technology transfer or commercialization.

There is an emerging need to increase awareness of the roads to practical impact and innovation. Researchers should be knowledgeable about public health needs, able to protect their ideas, and get a better chance to share the benefits of their research. To promote meaningful disclosures, students and practitioners of biomedical research need to learn about the ultimate outcomes of biomedical research; recognition of public health needs; process of choosing promising research targets; basic steps of research disclosure and technology transfer; experiences of innovative research laboratories and serial innovators; methods of successful collaboration with communities and industries; use of the IP literature on patents, copyrights, and case studies of trade secrets; legal and regulatory environment of intellectual property protection; basics of launching new products, services, and companies; and institutional environment and resources of supporting innovation.

There is particular need to learn from research on research and biomedical innovation. We need to understand consequential discoveries, support

researchers striving to innovate, and facilitate the development of more useful institutional policies and legislation. Defining and harnessing the differences between institutions in technology transfer is of great importance to sponsors and research institutions alike to ensure successful use of research funding.

Research leadership of institutions can do more in promoting the full range of scholarly creativity and should ultimately be judged based on their ability to do so. To assess performance and inform researchers, institutional effectiveness should measure the major impact of scholarly creativity including peer-reviewed publication, intellectual properties, and successes of practical application. Generation of new ideas is largely dependent on an organizational culture that promotes and protects research innovation, which is likely to have significant further research and public health impact. Academic institutions should bring innovation to the center of scholarly discussions.

Life sciences are at a remarkable moment of opportunity. Research is leading to understanding, treating, and preventing a growing number of diseases. Investment in biomedical research has done many wonders. To realize the exciting opportunities, life sciences research needs talented researchers who can build studies and also societal support, including government and private funding, to achieve ambitious goals for the future.

Beyond learning about pathways and creating institutional infrastructures, a variety of important measures are emerging to promote high-impact and innovative research. We call them boosters of research innovation and chapters of a major section provide further insight. After all, every difficulty, every unknown, and every crisis in health care is a need and opportunity for innovation. Academic institutions do not innovate, only creative individuals and laboratories do. At the epicenter of great discoveries is the talented, innovative, and well-prepared researcher working in the laboratory.

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