

Pharma and Academia: What We Have Here Is a Failure to Communicate

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In recent years, there has been substantial interest in the potential value of collaboration between academia and the pharmaceutical industry. In this Crosstalk, I discuss obstacles to these relationships being optimally productive.

The single biggest problem with communication is the illusion that it has taken place.—attributed to George Bernard Shaw

The Value of Pharmaceutical-Academic Collaborations

Let's start with something on which everyone agrees: the best hope for the development of novel therapeutics is through effective collaboration between the academic and private sectors, the latter including the biotechnology and pharmaceutical industries (Melese et al., 2009). Given the near universal agreement on this principle, the frequency at which such relationships are non-productive, if not frankly dysfunctional, is surprising. Most drugs on the market today are the result of academia delivering advances in basic biology and technology and the pharmaceutical sector then building on this knowledge base to create effective therapeutics (Kneller, 2010; Stevens et al., 2011). In general, the academic labs report data in the public domain and companies use the information as the starting point for drug discovery, which consumes substantial scientific and financial resources, but in most cases lacks direct interactions with the originating investigators. Undoubtedly, there is much successful collaboration between the pharmaceutical and academic sectors, and recently these have been further enabled by the formation within companies of specialized divisions that actively seek out such relationships (Dorsch et al., 2015; Ratner, 2011). Nonetheless, it is still rare that the drug development process is catalyzed by true collaborative activities of the sort common among academic laboratories and across disparate disciplines in the corporate

setting. In the pharmaceutical environment, effective collaboration between biology and such expert groups as medicinal chemistry, pharmacology, and drug safety are commonplace. Though issues hampering working relationships between academia and the private sector have been discussed in print a number of times, this Crosstalk article represents a personal view of the obstacles facing such collaboration, based on a 27 year career directing an academic laboratory followed by several years in the pharmaceutical industry.

Obstacles to Effective Collaboration

It seems obvious that many of the obstacles to effective academic-pharmaceutical partnerships result from a fundamental lack of understanding by each party of the other's motivations and career pressures. Though, at least in principle, hypothesis generation and testing drive the research in both environments, the culture, goals, and guiding principles of the two sectors are fundamentally different. Investigators who have spent their careers in one ecosystem are generally unaware of the values and beliefs of their collaborators across the public-private divide. Unfortunately, academic scientists are also often blind to the constraints dictated by the need to fund and publish their own work, having lived with them so long that they are no longer noticeable. Perhaps the root of most of the differences in culture can be traced to the fundamental disparity in the commodity serving as the main internal and external measure of achievement. In the academic world, the immediate unit of success is the publication, whereas in preclinical research in the pharmaceutical

sector it is a new chemical or biological entity that can be advanced safely into human trials to treat disease. There is little doubt that differences between academia and the private world in organizational structure, funding, governance, social structure, and career development contribute to the clash of cultures. But, nonetheless, I would submit that the greatest contributor to the mutual lack of understanding is that the principal goal, i.e., papers versus drug candidates, that defines success to both oneself and colleagues is so fundamentally different in the two sectors.

Setting up the Collaboration

It is not uncommon for large pharmaceutical companies to send small groups of emissaries to prestigious academic institutions with the express purpose of finding novel targets. The very nature of this enterprise, which is almost invariably a pointless "dog and pony show," demonstrates the lack of understanding by the industry of the process of academic research. While many principal investigators position their work as leading to cures for disease for the purpose of attracting grant funding, university researchers are largely devoid of expertise in the recognition of drug targets, having never been trained in this discipline and not motivated by that objective. Academic science is focused principally on the discovery of novel molecules or pathways, on the elucidation of a previously unknown biological mechanism, or often on the application of this knowledge to the understanding of human biology or pathophysiology. By contrast, pharmaceutical companies are focused on pinpointing sites, e.g., enzymes or receptors, for specific and safe intervention in pathways

that will lead to quantitatively predictable therapeutic responses. Certainly academics identify and utilize experimental probes that interact with biological targets to perturb a system as a means to understand its workings. However, the necessary attributes for such tools differ so greatly from the types of molecules needed to deliver drug candidates that the two endeavors cannot be considered equivalent. When representatives from drug companies approach academic scientists in the hope of working together, they should be asking for new science, not targets. The most productive outcome of these visits would be a conversation about how novel basic discoveries in academia can be turned into identification of potential therapeutic targets through collaborative work by the two interested parties, each utilizing his or her own expertise. Of course, this presupposes an open, honest level of communication between the two factions, which is often very challenging. However, the basic point remains that “drug hunters” should not be looking for drug targets in the academic community, but rather for exciting, new discoveries that can be transformed into new targets by capitalizing on the unique, complementary skills of scientists in the public and private domains.

The Nature of the Relationship

An additional aspect of research that is standard fare at drug companies but generally anathema to academics is timelines governed by milestones. For many scientists at universities and institutes, the course of research cannot be divided into discrete, predictable segments but rather follows a fluid, changeable course that adapts to new data as they are generated. In academia and industry, scientists struggle against the uncertainties of research to maintain timelines important to professional advancement and job security, and to be fair, there are many instances when collaboration can be framed in terms of concrete deliverables that serve as decision points for renewal of the relationship. But more often than not, the most productive partnerships are based on a common testable hypothesis for which rethinking and adaptation emerge from even the most seemingly linear experimental plan. The critical factor for success in such circumstances is that both parties are equally compelled

toward the same endpoint with a shared sense of urgency. To ensure high return on investment, pharmaceutical scientists should select their prospective collaborators not on the basis of prestige or pure technological expertise, but on common interest and mutual goals. Companies have to be prepared to write contracts that allow for the inability to describe research plans in detail a priori, but instead accommodate the changing course of investigation. While this can be readily accomplished by amendments, it is beneficial to recognize proactively the inherent unpredictability of scientific inquiry and construct collaborative or sponsored research agreements accordingly. The value of such collaborations to companies goes beyond the results of the proximal series of experiments, as they also provide a line of communication to the world of unpublished research, which is often difficult to access for pharmaceutical scientists. When both parties are consumed by answering the same scientific question and completely open in sharing data and ideas, the likelihood for success is high.

Agreeing on the Value of Contributions to a Research Program

In recent years, academic institutions have increasingly endeavored to obtain licensing income to support the growing cost of research (Edwards et al., 2003). This attractive source of funds has led to the establishment of large university offices devoted to protecting intellectual property and negotiating agreements with the private sector (Huggett, 2014). Now university faculty are repeatedly reminded of the potential monetary value of their work and warned not to disclose data prior to conversations with the technology transfer office. The problem arises when an academic applies his or her perspective of “value” to commercial matters. The most precious assets in the academic world are new ideas, naturally occurring molecules, or unique observations, all of which rarely have monetary worth and can almost never be legally protected. The perception of value in all data, together with uncertainty about what can be patented, leads to a culture in which many university scientists are hesitant to reveal *anything* to colleagues in industry. An ironic consequence of

this behavior is that by being uncommunicative, the academic scientist deprives him- or herself the opportunity to obtain significant research support from a commercial source. From the viewpoint of the pharmaceutical company, it is often-times preferable to fund a knowledgeable academic to perform research in an area where the company lacks expertise rather than building an in-house effort. Compared to academia, industry researchers have the luxury of being focused on getting the answers to important questions with less concern about who carries out and receives credit for the experiments. Principal investigators who work with industry deserve to have their collaborative research funded by private sources; in a time of scarcity of public funds, the pharmaceutical sector should serve as an important source of research support. However, companies are most comfortable working with contract research organizations (CROs), for which a list of experiments and deliverables is agreed upon and the plan rarely revisited and then only with serious discussion. On the other hand, academics often proceed under the principle that once grant funding is received, there is considerable flexibility in what studies are performed, as long as the principal investigator can demonstrate the merit of the experiments at the time of renewal or final report. It is readily apparent that these two approaches are incompatible and will breed discord. Sponsored research agreements work best when the university scientist limits collaborations to topics of great intrinsic interest rather than yielding to the temptation to accept money to work on a tangential project, and companies are well advised to approach those potential collaborators who have strong preexisting interests in the questions under study.

As noted above, it is a reasonable expectation that academic scientists and their institutions benefit proportionally to their contributions to the drug development program. Even in a time of inadequate funding, successful academic scientists often value novel reagents or knowledge more than pecuniary support. This is particularly true when the non-monetary resources are difficult or impossible to obtain elsewhere, as is often the case. Examples of such assets include chemical biology, small-molecule

libraries, tool compounds and biologics, and the capacity to analyze large datasets. However, it is also reasonable for academic partners to share in the financial reward of a successful drug. This is often best achieved by predetermined milestone payments, as this allows universities to receive compensation prior to registration of the drug and avoids the open-ended nature of royalties, which are often disquieting to drug companies. Academic institutions have to be realistic about expectations for financial reward when the pharmaceutical company incurs almost all of the risk and expense, which frequently can exceed hundreds of millions of dollars. Undeniably, there are times when unfounded expectations by the academic institution impede the investigator receiving meaningful support.

The Exchange of Information

A particularly perplexing phenomenon is the disproportionate aversion of many academics to revealing results to scientists in the private sector compared to academic colleagues and competitors, from whom the principal investigator has considerably more to fear. The private sector is seldom motivated primarily by publication; hence, the academic scientist should have little concern for being “scooped.” Moreover, scientists in the private domain are entirely accustomed to dealing with confidential information, being cognizant of the potentially cata-

strophic financial consequences of being inattentive to privileged communications. The individual faculty member should seek out opportunities to tell his or her industry colleagues about exciting new findings, under confidentiality if there is cause for concern. By avoiding prospective corporate collaborators, the academic persists in a disservice to medical science while at the same time potentially failing to accelerate his or her own research. Similarly, the pharmaceutical scientist should realize that in most cases, with the exception of structures, there is little danger in sharing data and insights with his or her academic collaborator. Open communication is not only required for an effective collaboration, but can generally be accomplished without undue risk to either party.

Academic-Pharmaceutical Collaborations Can Work

For the public-private collaboration to be successful, there must be a free and open interchange of information and alignment on common goals. There must exist trust between the parties conducive to sharing ideas as well as data and reagents. The two research teams need to meet frequently to exchange data and trade viewpoints; the academic lab cannot be given a research plan and simply generate reports every 6 months. When this private-public collaboration does work, success is facilitated by the distinct but complementary goals of the

two parties: publication for the academic and a potential therapeutic molecule for the drug hunter. Both parties' interests can be readily protected and still work productively together in the advance of science toward new therapies.

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