Open innovation networks between academia and industry: an imperative for breakthrough therapies

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The demand to bring transformative therapeutics to patients and the escalating costs of doing so are driving the life science industry to seek collaborations with academia to stimulate innovation. Despite the opportunities afforded by working together, companies and universities lack a systematic approach for capturing the full potential of such relationships. Detailed here are a few suggested strategies to help these collaborations succeed.

The term 'open innovation' was coined by Henry Chesbrough to describe "how useful knowledge and technology was becoming increasingly widespread," such that newly developing technologies and products benefited from integrating knowledge and expertise from multiple sources[1]. He also made the case that the economics of innovation is a key driver for companies to open their innovation process[1,2]. Pharmaceutical and large biotechnology companies, as an example, increased their research and development (R&D) spending by 147% from 1993 to 2004 to fuel their drug pipelines, yet the number of new drug applications submitted to the US Food and Drug Administration rose by just 38% (ref. 3). With little to show for all the money they had invested in research innovation, compounded with drug failures and patent expirations set to erode a substantial amount of their revenues, many companies realized that they needed to look beyond their own walls for innovation (**Fig. 1**)[1]. The idea that the next new approach might not come from internal research has led many companies to shift their R&D expenditures externally through collaborations with small biotechnology companies, other companies and academia.

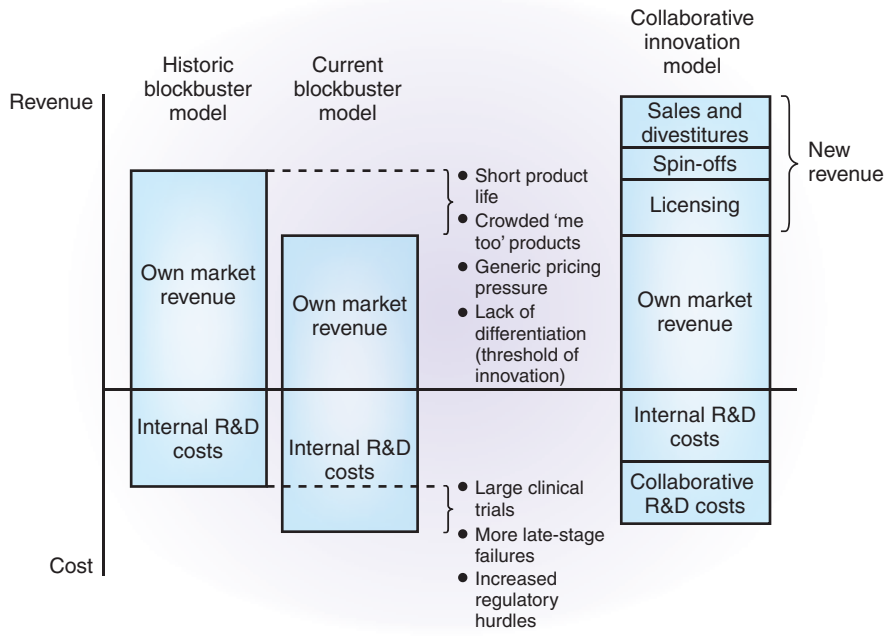

Figure 1 The current model for producing biopharmaceutical innovation is economically unsustainable. In the historic blockbuster model, the cost of internal innovation was exceeded by product revenues. In the current blockbuster model, the cost of internal innovation has increased with little impact on revenues generated. In the collaborative innovation model, companies look outside their boundaries for ideas and intellectual property, leading to new revenues generated through licensing, spin-offs or sales and divestitures. By this model, the cost of developing innovation internally is reduced if the companies can bring in new technologies through collaborations.

Since the beginning of 2008 alone, Merck, GlaxoSmithKline, AstraZeneca and Pfizer have all established multimillion-dollar, multiyear collaborations with academic institutes across a number of therapeutic areas[4,5]. Although some of these relationships are built on long-standing collaborations with academic institutions, the recent increase in the number of these collaborative relationships is part of a major change in strategic direction. These partnerships come at a crucial time for both industry and universities and have the potential to profoundly alter the means by which healthcare is delivered. An important aim for both types of organizations is to close the gap between basic and clinical research, thereby allowing for a more evidence- and outcomes-based approach

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Table 1 Principal models for industry-academic partnerships

Model	Definition	Advantages	Innovation disadvantages
One company–one investigator	A company forms a relationship with an investigator by providing funding for research	Provides a starting point for establishing a productive relationship	Does not explicitly encourage and often restricts communication with other investigators or companies that might bring value to the research; dilution of research effort
One company–one university	A company develops a master agreement with a university and provides resources for a number of research projects with a single university	Better leverage of an existing relationship; master agreements streamline process of initiating new collaborations	Might be limited to capabilities and expertise of a single university; working with one company might limit the scope of the research; university is seen as extension of the company
One company supports a university consortium	A company builds a consortium of several universities that focus on a specific topic	Universities share and leverage their joint knowledge and the company funds a broader scope of research	Limited interaction with a single company will not address industry-wide obstacles
One company supports a university institute	One or more companies give a large donation to fund an existing institute or to establish a new institute at a university	The company has access to network of investigators and university receives funding to support its research in a specific area	Researchers are often asked to keep resources and information around a project proprietary
Industry consortium (pre- or noncompetitive)	These consortia could be structured to include many companies with one AMC, or conceivably many companies with multiple AMCs	Ability to effectively resource and address important but noncompetitive innovation challenges (for example, biomarkers)	Agenda might be dominated by individual company contributors and could erode perception of meritocracy; companies and AMCs will need to find ways to profit from their activities to sustain participation
Competition	A company invests in multiple investigators to research the same topic; the team to achieve the goal first receives funds for the next phase	The company engages multiple parties to focus on its problems	Researchers cannot share resources or information with other universities; the team that finishes first might not be best one to continue the project
Venture capital investment	A company provides several experts with seed money to start a company; milestones are established	May foster more rapid commercialization	Researchers sever their academic ties, thereby forfeiting a major source of information and ideas
Fee-for-service	The university provides a unique service to the company	Investigator can apply technology to real-world problems and receive funding; company has access to commercially unavailable technology	The researchers feel like "hired help" rather than partners; defining the challenge limits the value the university can provide

This table refers to sponsored research agreements and not philanthropic gifts, which are not subject to restrictions on their use. AMC; academic medical center.

to therapeutic development that provides real healthcare value to patients. This requires the development of new testing technologies to clearly identify who will benefit most from each therapeutic treatment and determine the conditions under which the benefit will be achieved[6,7]. Despite the commitment of organizations to foster healthcare innovation along these lines, most companies and universities still lack a systematic and coordinated approach to entering into these relationships or capturing the most value from them.

Interviews with companies and universities indicate that most research collaborations between them occur on an *ad hoc* or opportunistic basis. As these collaborative activities are often based on personal relationships between individuals in each organization, the opportunity to build on these relationships and extend them to others within each organization is often not understood or pursued. As a result, it is not uncommon for the company and the university to lose important opportunities to leverage existing research relationships and broaden the scientific focus. A more systematic and less individualistic approach to understanding the current scope of research activities would allow universities and companies to capitalize on such *ad hoc* opportunities and derive the greatest value from the synergies with collaborators across therapeutic and clinical areas for both internal and external research relationships.

Although a more orderly process for defining and expanding research collaborations will benefit all parties, other measures will also be essential if we are to overcome some of the industry-wide obstacles to developing a new generation of safer and more effective treatments. One such measure is more effective classification of different kinds of information, so that industry executives know what they can freely share with academic research partners and what must remain confidential. Another is the creation of nonexclusive consortia in precompetitive areas of research, that is, research that seeks to advance industry-wide healthcare initiatives as opposed to those of an individual company. Two examples would be developing new technologies such as RNA interference (RNAi) and identifying biomarkers to aid in predicting patient benefit and adverse response to specific classes of drugs. Productive partnerships of this sort will also address some of the concerns expressed by industry, academia and the public about the value of such collaborations.

Cultivating innovation in structuring collaborations

Many large life-science companies are looking further upstream than biotechnology companies for innovation, one such source being academia[8]. Traditionally, pharmaceutical companies funded academic research as a means of getting access to interesting science. Such funding was probably appealing because of the ability to leverage corporate funding with resources from the federal government and to build good will with investigators at leading universities at the same time. Research funds were often provided with little or no

expectation of a return on their investment. However, as the industry started to invest more strategically in academic research, the deal structures changed[4,5]. **Table 1** presents relationship models based on interviews with some of the leading life-science companies and the academic researchers with whom they work.

Despite the plethora of collaboration models, many of the most successful models do not provide open access to data or resource sharing. This protective approach to data management limits innovation. Although sharing data is part of the mission and culture of universities, it does not fit within the traditional competitive business models practiced by most companies. However, there are emerging examples of new open business models that support open innovation[2]. The continued development of such open business models will be as crucial, if not more crucial, than technology development to sustain highly innovative collaborative structures between industry and academia. It is the hope that such open research collaborations will lead to the development of new paradigms to approach disease treatment, yielding high-value therapies and testing technologies that better define those patients who will benefit from a given therapy and therefore provide true value based on healthcare outcomes.

Of conflicts, cultures and funding

Although concerns about potential conflicts of interest arise when members of the academic community interact with industry as consultants, as scientific advisors or in other capacities, these concerns should not undercut the development of mutually beneficial collaborative relationships that advance healthcare[9–11]. Still, industry and academic institutions will need to prospectively identify potential sources of conflict and ensure that they are addressed as part of the groundwork for setting collaboration agreements in place[12].

An analysis conducted by IBM Global Business Services and the University of California–San Francisco identified two other major areas that affect industry-academia collaborations in terms of strategy and operations: organizational and cultural issues and funding challenges. These constraints often have an even more substantial influence on the negotiations and set the tone for how the parties will deal with each other, sometimes undermining the primary purpose for the collaborative relationship. As the value of these collaborations or alliances has become more apparent, the thinking around negotiating tactics is also changing. Companies are being advised to focus less on forcing their collaborators to adopt restrictive terms that will adversely affect the collaboration and more on terms that will allow all parties to achieve their goals[13]. By working together to define mutually acceptable objectives and expectations early in the negotiations, companies and academic researchers can help to ensure that the process and the end product better meet the expectations of both parties.

The traditional conflicts between public and corporate collaborations are confidentiality, publishing and intellectual property rights and ownership. With respect to confidentiality and publishing, most universities routinely file confidentiality agreements before discussions with companies to protect proprietary information for both parties, and they also grant reasonable publication delays to allow companies time for patent filing.

Intellectual property rights, however, continue to pose a challenge for cultivating collaborative environments that support innovation. More thought needs to be given to how to structure contractual agreements that promote innovation while continuing to respect the intellectual property rights of the collaborators. It will be important to find terms that promote continued innovation and to clearly define what knowledge requires protection and what knowledge, if shared, can result in an innovation stream that creates new avenues of research and development. If the intellectual property protection terms are too broad, it will be difficult for academic researchers to collaborate. If intellectual property protection reaches too far into the future to include research that might be performed after the collaboration ends, the result will be to restrict research with other collaborators. This serves to unnecessarily limit or tie all inventions exclusively to one partner and will therefore be a major barrier to innovation.

Companies should be willing to take a certain amount of risk in the collaboration if they wish to promote innovation. Negotiations will need to make sure that the value process is equitable, that all parties receive a return on their investment and that the collaborators receive equity on the basis of their contributions. In general, companies need to understand that many universities are limited by federal and state laws with respect to ownership rights of the intellectual property generated by their faculty. These constraints can be addressed if they are acknowledged and if all parties are willing to negotiate terms of mutual benefit.

There are substantial differences between the academic and industry cultures, values and norms. A company typically defines the goals, objectives and timelines for their researchers, whereas, in academia, researchers have the freedom to define their own goals, objectives and timelines. So, it is crucial to understand these differences and develop relationships that provide opportunities for investigators and companies to pursue research interests and goals that naturally overlap.

Budgeting and staffing problems in research collaborations are often overlooked but can be the source of considerable tension. Most academic researchers seek and obtain multiple sources of funding to pursue different aspects of their research interests. The level of funding to generate any real innovation must be sufficient to support staffing to allow for mid- to long-term projects. At the same time, companies typically need to balance support with short-term commitments to meet quarter-to-quarter business demands and constraints. In some cases, companies are looking to investigators to create a budget for a project on the basis of defined modules of activity that provide decision points for continuation of the project, as opposed to personnel costs. The academic community needs to be prepared to think of new ways to scope, frame or describe proposed projects to align with the corporate budgeting expectations and process. As part of framing the budget, academic researchers often overlook the expertise a company can provide with respect to access to technology resources and staff (especially biostatisticians and experts in bioinformatics) who can advance projects and can be factored into the budget.

Compounding budget and staffing challenges is the way companies manage their budgeting processes. Most companies go through a rigorous annual budgeting process where projects are justified to the senior management. Specific program budgets often have limited resources, and project leaders must decide whether to use the money internally, where they have oversight, or to spend it on a bright university investigator over whom they have less oversight. Many collaborative agreements now include the establishment of governance structures such as joint steering committees that promote two-way scientific knowledge exchange and co-development of research plans that include specific milestones[4,5].

Academic medical centers as innovation partners

Academic medical centers (AMCs), including both health science schools and health systems, are well positioned to be partners in developing innovative approaches to fuel the next generation of breakthrough therapies for complex diseases. Such advances will require gaining a considerable understanding of the mechanisms underlying disease, the individual susceptibil-

ity to disease and the individual response to treatment. In addition, AMCs train future generations of physicians, pharmacists, nurses and other professionals who will integrate mechanism-based approaches into their practice, question current practices and define new approaches to optimize outcomes and human safety. As a result, these clinicians can be strong partners with basic scientists and industry in developing innovative therapies. Importantly, to collaborate with industry, AMCs will need to develop an integrated internal administrative process to develop, manage and implement such alliances[14].

Both public and private funding agencies also recognize the need to foster research programs that can be translated into improvements in clinical care and maximized overall benefit. In 2006–2007, the US National Institutes of Health Clinical and Translational Science Awards (CTSA) funded a national consortium of AMCs to transform the way medical education and clinical and translational research is conducted[15]. Through the CTSA program, and as a result of this effort, AMCs are attempting to train more clinician-scientists and to improve the research infrastructure to foster innovations in clinical care[16]. The CTSA initiative has also emphasized the importance of collaboration between AMCs and community providers. It recognizes that many of the advances in clinical care will require large numbers of patients and extensive clinical databases to better understand the populations at risk and the impact of innovative therapies in diverse populations. The hope is that crossdisciplinary and interinstitutional research will produce more innovative therapies. In recognition of the importance of collaborating with industry, a CTSA public-private steering committee was formed to address aggregation of intellectual property and resources, sponsored research agreements and entrepreneurial education and to consider specific joint initiatives with life science companies (http://www.ctsaweb.org/index.cfm?fuseaction=committee.viewCommittee&com_ID=25). It is too early in the process to know how successful the consortium will be, but individual campuses are realizing its potential value and are working toward building a national network of CTSA collaborators.

Areas of crucial importance in establishing collaborations are those that provide mutual benefit and those where knowledge, resources and expertise are complementary. Examples include building well defined patient cohorts (especially for rare diseases) and establishing biological specimen banks (healthy subjects and patients being tested with specific drugs) that can be subjected to molecular and pharmacogenomic analysis to identify genes essential for response, transport and metabolism of drugs. Obtaining molecular biomarkers with corresponding clinical outcomes from failed or successful drugs would offer the opportunity to gain a scientific understanding of an individual's response to treatment. Providing academic investigators with access to well characterized compounds might also help to elucidate disease mechanism by studying disease pathways in preclinical models, guide the strategy for the design of clinical trials and allow better early decision-making about which compounds to advance for development.

Traditionally, pharmaceutical companies have relied on clinical research organizations to manage clinical studies and have shied away from AMCs for some of this support. For early-phase studies and assessment of the methodology and effectiveness of clinical trials, however, understanding the science is essential and is best achieved by also collaborating with AMCs. Many AMCs have interdisciplinary research institutes or programs that are focused on specific diseases that mirror the small, therapeutic area–focused R&D units now found in pharmaceutical companies. By working together collaboratively, these groups of scientists can more efficiently and effectively identify and seek solutions for rate-limiting innovation gaps in the discovery of breakthrough therapies and develop new approaches for advancing their clinical research programs.

The path forward

To maximize the impact of biomedical research done at universities and the therapeutic value of products developed at pharmaceutical and biotechnology companies, innovative research networks are becoming a necessity. Such networks are being successfully built in the semiconductor and device industry (for example, by IBM, Intel and GE Healthcare), and it is reasonable to expect that some of the same principles that apply to them will apply to networks in the biomedical space.

Such an approach will allow collaborative teams to work together to identify what the innovation gaps are in the development of new therapies, what needs to be accomplished and who is best positioned to contribute value. Moving forward, there are several steps that collaborators should follow to ensure that the potential of such relationships can be fully realized: (i) recognize the value proposition of the collaboration; (ii) manage the industry-academic collaborations as they would an investment portfolio; (iii) adopt a new attitude about sharing of information; and (iv) create new innovative models. An approach to each of these steps is detailed below.

Recognize the value proposition of the collaboration. As noted, R&D costs are rising, whereas the ability of companies to sustain a return on those investments is diminishing. At the same time, it is well recognized that patients, insurance companies and government sponsors are no longer willing to pay high costs for incremental therapies and, in many cases, for investigational interventions[17]. To identify breakthrough strategies for new therapies that will not result in costly failures late in development, there is a need to fill several knowledge gaps—to understand more about the molecular underpinnings of disease and the individual response of patients to treatment.

Both industry and academic researchers recognize that the field is at a tipping point that demands that we reach across our organizations for the complementary knowledge and resources required for tackling the problem effectively. A difficult issue that each collaborative partner will need to address is how they weigh the value of their assets (materials, data, knowledge and expertise) versus the value of their partner's assets and versus the potential creation of new value and allocation of the return on investment created through collaboration. It is impossible to know beforehand whether collaborations will be productive, although it is possible, as discussed here, to create infrastructures that optimize the potential for success. If potential collaborators are not flexible and equitable in their approach to valuation, they will not be able to establish such an infrastructure and will limit innovation and the probability of success.

It has been often said that whereas a company places the most value on a discovery or invention that can provide benefit when applied to real-world problems, an academic researcher values the discovery or invention that increases the depth of understanding in a specific area. It is important to realize that innovative solutions to real-world problems will best arise when there is an increase in the understanding and knowledge of the problem. Thus, the goals of both types of researcher are more aligned than is often acknowledged. It is precisely the lack of knowledge of the pathophysiology of complex diseases in humans that is at the root of the current problems in developing high-value therapies.

Manage the industry-academic collaborations as they would an investment portfolio. Most companies currently choose external collaborators for research projects within a therapeutic area by consensus and rely on individual knowledge of previous projects to avoid duplication. However, this becomes more difficult over time, as those involved in the decision

making are promoted or go to another organization. The traditional industry-academic relationship that is entirely dependent on personal collaborations further undermines effective management of the research agenda. It is therefore essential to document all collaborations properly, define the opportunities for more integrated approaches and ensure that they are visible to everyone within the company. Treating industry-academic collaborations like an investment portfolio can help accomplish this goal (**Fig. 2**). Any good portfolio manager has a 'sell' strategy. This means that academics will have to get used to a more rigorous evaluation of their work.

Managing multiple research projects as an investment portfolio enables a company to eliminate redundancies and capitalize on any synergies between research projects in different therapeutic areas; for example, nanotechnology has applications in both diabetes and oncology. This managment strategy also facilitates the development of a master agreement with a university to cover all of the collaborations into which the company enters with that university, regardless of the therapeutic area. Universities can also benefit from taking a similar approach to increase the awareness of existing collaborations across the campus, among departments and among both basic scientists and clinicians. A potential collaboration with a company can often provide resources to motivate internal university research groups to work together on a project that might not otherwise be possible.

For major and repeat collaborative partners, it makes sense to put master agreements in place. Master agreements streamline the process for establishing new collaborations and can serve to increase the level of collaboration between participating organizations. When properly crafted, they also provide a foundation for creating a secure interface between the participating organizations that enables researchers to share knowledge, data, materials and resources freely and to develop a culture that fosters innovation. The development of a good master agreement requires that the parties articulate a common vision not only between the researchers but also with the legal counsel, business development personnel and management, including those at the top of the organizations. Although master agreements lower the barrier for collaborations, the true test of longevity is the cultural and scientific fit between the partners.

Adopt a new attitude about sharing of information. Although developing better approaches to structuring industry-academic collaborations is an important step in cultivating innovation, it is not sufficient to produce the revolution that is required to develop safer, more effective and relevant treatments. Many companies, including pharmaceutical firms, currently rely on patents to protect the returns on their investment in R&D and tend to patent all information regardless of whether or not they know the value they will be able to derive from it[2]. Although this strategy is effective in blocking competitors, it has the tendency to hinder innovation and collaboration[18]. Researchers are often forced to spend time and money repeating research that has already been conducted. A better approach would be to classify information into two categories—proprietary and nonproprietary—and educate all parties as to the distinction between the two. This would enable companies to share nonproprietary information with academic research partners without fear of jeopardizing future revenue and thereby increase the potential for innovation.

Proprietary information could, in turn, be divided into two separate subgroups—information that should be safeguarded and information that can be disclosed without damage—using the sort of valuation processes that companies already use to determine the value of patented discoveries and inventions. Information that is not central to a company's business, such as data derived from toxicity assays, could then be sold to other companies or academic research institutions at market value[2]. Any company that fears giving its competitors an advantage could delay selling the data until it is entirely safe to do so, although it should bear in mind that the value of its research could depreciate over time.

Along these lines, it will be necessary to adopt new business strategies that promote value creation through open innovation research networks as opposed to traditional business strategies that promote the development of barriers to competition. A new approach called 'open strategy' has been described that "balances the tenets of traditional business strategy with the promise of open innovation"[19]. A challenge for these new business models will be value capture and sustainability. A new breed of companies, such as InnoCentive, act as intermediaries to help companies foster innovation and efficiency in the area of R&D. InnoCentive was launched through the e.Lilly division of Eli Lilly and seeks to connect companies to the worldwide scientific community, enabling them to collaborate to solve difficult R&D problems[20]. To address a lack of financial incentive associated with developing innovative therapies for rare and infectious diseases, realignment of the relationships among innovation, incentive and access by creating 'open-access drug companies' has been suggested[21]. Such open-access compa-

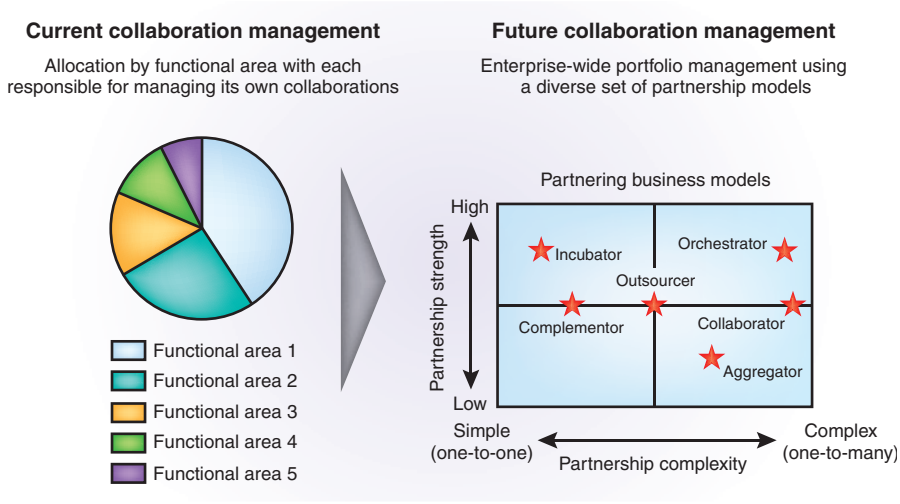

Figure 2 How to manage industry-academic partnerships as one would an investment portfolio. The current management strategy for collaborations (left) segregates by functional area. The portfolio approach suggested here is depicted on the right. The company as orchestrator manages a network of partners, each of which has a stake in the outcome. The company as outsourcer manages a network of providers, each of which performs activities that would otherwise have been performed in-house, with no stake in the outcome. The company as collaborator can enhance the value of its product within a network of noncompeting partners, each of which has a stake in the outcome. The company as complementor can enhance the value of its product by developing a new 'companion' or complementary product in collaboration with partners. An example is the bundling of diagnostics with therapeutics. The company as aggregator uses its access to the market to combine individual products in a package that might enhance the value over offering the individual products. Such a package would provide ease of use for patients taking multiple medicines for a single disease. The company as incubator provides funding and expertise for other companies so that they can bring new products to market.

nies are traditional pharmaceutical companies that agree to designate a sector of their R&D facility to permit collaborative partners from academia or industry to access their resources (for example, compound libraries, screening facilities, medicinal chemists or pharmacologists) on a fee-for-service basis.

Create new innovation models. Once companies are able to manage their information more effectively, they can also develop new models for generating innovation. For example, rather than working with one or more research institutes on specific projects, they could establish alliances in areas of precompetitive research. Such initiatives would advance knowledge or technology development of benefit to the entire healthcare community. This would overcome the drawbacks associated with many of the collaborative models that are currently used, which address the needs of a specific company but do not encourage the sort of information sharing that is needed to deliver the next wave of innovation.

For example, in the past five years, almost every major biotech and pharmaceutical company has implemented a proteomics program to study the role of proteins in disease pathways. Lack of standardization across the laboratories conducting proteomic research has made it very difficult to compare, let alone validate, the results of these studies. The overall field of functional proteomics has therefore progressed very slowly[22]. Establishing areas of precompetitive research, with open standards and protocols, would enable companies to pool their knowledge and resources to fill current technology gaps. A number of public-private consortia already work on this basis. One such instance is the RNAi Consortium, which is developing various RNAi technologies that will enable the scientific community to probe the functions of mouse and human genes[23]. Others include the Biomarkers Consortium[24], which aims to develop and validate biomarkers for detecting, diagnosing and treating diseases, and the Diabetes Genetic Initiative[25], which aims to identify the genetic connections between type 2 diabetes and other cardiovascular risk factors.

Conclusions

These are truly exciting times in healthcare. Our understanding of the mechanisms of disease is rapidly expanding, and the development of the tools that enable us to transform this knowledge into meaningful therapeutics is accelerating. The challenge now is to integrate this new knowledge to provide the most accurate picture of the individual, the disease and the community on which to base the development of new breakthrough therapies of higher value. As both the public and private sectors have key roles in bringing new therapies to patients, it is imperative that the value each sector creates is leveraged such that the collective brain power and expertise across the two sectors is focused on securing effective and safe therapies.

Industry-academic collaborations will continue to have an important role in developing better treatments, and any pharmaceutical company that wants to fully capitalize on such partnerships will need to adopt an approach that takes the interests of both parties into account. It will also need to treat its alliances with academic researchers as a portfolio, both to reduce the duplication of effort and to optimize the synergies across therapeutic areas.

But no matter how successful such alliances are, they will not be sufficient to generate the innovation that is required to make a great leap forward. It is only by identifying areas of precompetitive research and pooling their resources that pharmaceutical companies will ultimately be able to develop therapeutics and testing technologies that break completely new ground.

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