Next generation partnerships in translational science and medicine

Partnerships between academics, big pharma, biotech firms, philanthropists and patients look set to change the way science advances

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During graduation season, it is not uncommon for senior scientists to dispense wisdom from stages, lecterns, bus stops or bar stools. Nearly 50 years ago, in a memorable line from the 1967 movie, The Graduate, a single word of career advice is bestowed upon the film’s protagonist: plastics. For the biomedical graduate in 2015, another “p” word might be more appropriate: partnerships. Partnerships between academia, pharmaceutical companies, biotech firms, foundations, patients, and their families are inexorably changing the nature of biomedical research and will inevitably impact on how science is funded, organized, and conducted. They will also, one hopes, unlock the enormous potential of translational science for finding new treatments, cures, prevention, and diagnostics against a wide range of complex and/or rare diseases.

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Since the Enlightenment, science has been a global enterprise, and universities, academies, and research institutions have always collaborated both nationally and globally in many formal and informal ways. Our own university, Karolinska Institutet (KI) in Sweden, is no exception and has always had many academic and educational partnerships. In recent years, however, new partnerships have begun to evolve with industry, private foundations, philanthropists, and patient organizations. These partnerships clearly present new challenges in terms of legal obligations, funding, intellectual property, and confidentiality, but they also offer new opportunities to tackle challenges in biomedical research that academia cannot easily manage on its own. In particular, new research collaborations beyond traditional government-funded schemes are likely to benefit translational research to test and develop new therapies. With these new kinds of partnerships in mind, the meeting Days of Molecular Medicine 2015 was held at KI to discuss how such collaborations are beginning to change human healthcare research.

Karolinska Institutet is one example of how an array of diverse partnerships can influence academia. For example, KI’s scientists are involved in projects sponsored by the Gates Foundation, and the university hosts one of the branches of the Ludwig Cancer Research institutes—an international community of scientists. KI also recently formed a research partnership with the German Max Planck Society to explore the genetics of inborn errors in metabolism, while Oxford University (UK), Copenhagen University (Denmark), and KI are discussing novel research interactions focused on immunometabolism that involve the Novo Nordisk Foundation—an independent Danish foundation with both corporate interests and scientific and humanitarian goals.

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These interactions represent, in part, new ways of thinking at research-oriented foundations—which have historically largely offered open competition-based grants to support students or projects—that see them becoming more active in fostering strategic, large-scale partnerships. One of the pioneers in this area is the Bill and Melinda Gates Foundation and its focus on and support of research groups seeking cures or vaccines for, for example, malaria and HIV. Since the Gates Foundation began following this model, others have followed in its wake. During the past decade, philanthropic support has also come to play an increasingly large role in catalyzing a multitude of high-risk research projects. By way of example, the family of Lau Ming-wai, a prominent Chinese business magnate, recently donated US$50 million to KI to help establish a regenerative medicine research platform based in both Stockholm and Hong Kong, with a larger vision toward catalyzing translational research between Hong Kong and mainland China.
For many years, pharmaceutical companies have also cooperated with academic scientists at the interface between basic research and drug development, albeit with a clear understanding that basic research would be publicly funded. This has been important to drive specific projects forward, but has also posed limitations in some respects. It has not, per se, generated new projects or ideas. Now, companies are drastically increasing their engagement and forging large research collaborations that circumvent both public funding and venture capital investment to include all steps from fundamental research to drug development. AstraZeneca recently invested US$100 million to establish a joint research laboratory at KI, known as the KI/AZ Integrated Cardiometabolic Center (ICMC), where industry and academic scientists work side-by-side on projects of common interest and benefit, thereby overcoming traditional boundaries between academic research and drug discovery. One purpose of the agreement is to clarify conflicts of interests, ownership, intellectual property, publication rights, and so on in order to facilitate multiple subprojects that can focus on the science without getting stuck in legal or administrative limbo. The ICMC is now fully set up, staff has been hired, groups established, and several new projects are up and running.

Industry is also sponsoring educational grants, which until now were not supported by pharmaceutical companies unless they were completely untethered from concrete research goals. Novo Nordisk recently created postdoctoral programmes for both research and education around diabetes research (http://ki.se/en/srp-diabetes/novo-nordisk-fellowships), and Janssen Pharmaceuticals (http://www.janssenpharmaceuticalsinc.com) is doing the same for evidence-based applied medical research (http://ki.se/en/news/karolinska-institutet-launches-new-collaborations-for-innovation-and-research). These programmes support research that is of interest to the companies, but which is not dictated by the companies. Instead, the companies seek to benefit either directly or indirectly from the knowledge generated and from establishing contacts with scientists. While insuring the academic values of intellectually independent and scientifically driven research projects, this support from “big pharma” differs from conventional publically funded grants by fostering more translational research that bridges fundamental and clinical science, and also research in the fields of real-world evidence and “outcome.”

Large pharmaceutical and smaller biotech companies are clearly establishing a more open and integrated model for translational science and medicine that goes beyond the conventional contract-type research projects of the past. According to Mene Pangalos, Executive VP of Innovative Medicines & Early Development at AstraZeneca, who spoke at the meeting, 70% of the compounds the company has in development come with a dedicated diagnostic marker. This underscores the need for cooperation with academic partners who have a good understanding of the biology of specific diseases. As a consequence, AstraZeneca decided to move its research infrastructure to Cambridge, UK, with the explicit goal of reaching out to the academic community. The new AZ center is currently under construction and will be located right next to the new Addenbrooke’s Hospital on site, to facilitate collaboration in real time between physicians and scientists at both sites. This is a general trend among pharmaceutical companies, many of which offer academic researchers free access to their compound libraries and knowledge base so they can directly test these for alternative uses.

Regeneron Pharmaceuticals (http://www.regeneron.com) is setting up screening systems to identify naturally occurring gene knockouts in humans that provide resistance to extreme clinical phenotypes. They hope to be able to repeat their recent success with a similar screening approach that uncovered PCSK9 as a target for treating hypercholesterolemia and led to a new drug that has successfully finished phase 3 trials and is awaiting approval. Novartis is sponsoring studies of early-onset Alzheimer disease (AD) prevention in Colombia, and conducts screening in human stem cell models of rare neurodegenerative diseases with academic partners in the USA, Europe, South America, and elsewhere. These are just a few examples of how industry-financed initiatives move private and public research into a common space, with the ultimate goal of
speeding up research and creating a powerful alliance to fight human diseases.

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The ongoing collaboration between the Banner Alzheimer’s Institute (http://banner-alz.org), the US National Institutes of Health (http://www.nih.gov), Genentech (http://www.gene.com), and a large extended family in Colombia who suffer from very early-onset AD is now yielding benefits not only for the families involved, but also potentially for preventing AD. Advances in sequencing technology have enabled the researchers to identify carriers of a single autosomal dominant mutation in the presenilin 1 gene, allowing them to test whether it is possible to prevent the onset of AD using best-in-class compounds and monitoring with advanced biomarkers. This study may provide proof-of-concept for preventative treatment of AD and enable FDA-approval of biomarkers for prognostic use. This new type of clinical trial of preventive therapies was only made possible through the collaboration of NIH, philanthropists, and industry.

The NY Stem Cell Foundation (NYSCF) provides another striking example of how charitable organizations are building bridges between academia, biotechnology, and pharma. NYSCF has built a technology platform for automated high-throughput generation of human iPSC cell lines that has caught the attention of pharma, academia, and fellow nonprofit foundations such as the Stanley Foundation/Broad Institute and the Batten Disease Foundation. The NYSCF has also raised critical support for the next generation of young leaders in the field of stem cell research and regenerative medicine. These nonprofit foundations have the freedom to operate between academia and biotechnology to navigate the sometimes-complex terrain of translational science.

One of the most intriguing types of research partnership is that driven by patients and their families, who often do not have an extensive scientific or medical background. Hugh and Chris Hempel, the parents of twins, Addi and Cassi, who are affected by a rare version of Niemann–Pick disease, illustrate how this patient-driven research changes the face of research, in particular for rare diseases (http://www.youtube.com/watch? t=15&v=3N8QMeI2X2c). Niemann–Pick is a devastating lipid-storage condition that leads to the accumulation of sphingomyelin in the brain and other organs. The more severe forms are ultimately fatal during childhood after years of physical and mental decline. Faced with a diagnosis of severe Niemann–Pick disease for their twins, the Hempels conducted extensive research on the Internet in an effort to find new treatments. They started a foundation—the Addi and Cassi Fund—to raise money for research into Niemann–Pick disease; they also actively contacted scientists, doctors, the NIH, the FDA, and other affected families to encourage research. The Hempels’ efforts ultimately paid off, as a potential drug to treat the disease is now fast-tracked for phase I clinical trials. The Hempels started out as novices and will soon coauthor a publication in Nature.

Their case, though exceptional, highlights the power of partnerships that embrace the passion and curiosity of “citizen scientists.” Interestingly, support from another patient foundation has led to the discovery of a completely unsuspected connection between Niemann–Pick and Ebola. The receptor molecule that is mutated in the Hempel twins make cells highly resistant to Ebola infection. A patient cell bank and registry is now being created in the hopes that this knowledge and material collection might lead to new ways to fight the deadly virus.

Another example of the growing importance of family foundations is the Simons Family Foundation (https://www.simonsfoundation.org), which supports cutting-edge research in the genetics of autism via the screening of de novo mutations in hundreds of families using next-generation sequencing. Likewise, the success of a new first-in-class therapeutic to treat a subset of patients with cystic fibrosis (CF), Kalydeco, has shown how important patient advocacy groups, such as the CF Foundation (http://www.cff.org), have been in pushing forward novel therapies for orphan diseases. Initial support from private foundations has also led to new therapeutic strategies for treating spinal muscular atrophy via screening of patient-specific pluripotent stem cell models (The SMA Foundation, http://www.smafoundation.org) and new gene therapy approaches to treat retinal diseases (The Fight for Sight Foundation, https://www.fightforsight.org; and the Wellcome Trust, http://www.wellcome.ac.uk) and fostered a new wave of immunotherapies against tumor cells based on engineering patients’ own immune cells (Alliance for Cancer Gene Therapy, http://www.acgtfoundation.org).

Nowadays, a whole new ecosystem of funding, research and development is emerging; it is interdisciplinary, interconnected and clearly disruptive to conventional partnership paradigms.”
new treatments for human diseases. Interestingly, the focus of many of these partners is not so much to “translate” existing knowledge *per se* into medical progress, but more to foster “transcriptional medicine” by directly funding primary research and development at the early stages and by providing substantial resources to translate their own discoveries into cures for affected patient populations. For the current cadre of biomedical graduates, the real challenge may therefore not be choosing the right project, but choosing the right partners.

**Conflict of interest**

Kenneth R Chien currently serves as a Scientific Advisor to AstraZeneca.