Challenging Assumptions

The freedom to pursue scientific research yields surprising results

By Amy Brown-Bowers

In science, as in love, music and mathematics, sometimes the unexpected or unplanned outcomes are the most beautiful and the most significant. But unlike the often accepted meanderings of artistic discovery, much of scientific research has become restricted to that which guarantees a quick pay-off.

“Science is not plannable but an unexpected thing,” says Dr. Heiko Heerklotz, Associate Professor and Canada Research Chair in Lipid Science and Technology at the Leslie Dan Faculty of Pharmacy, University of Toronto.

Heerklotz’s most successful research publication, ‘Triton induces domain formation in lipid raft mixtures’, was based upon such unexpected and seemingly paradoxical data.

Lipid rafts are putative, lipid-based domains in cell membranes that co-sequester specific proteins and, thus, have a major effect on signaling and many other functions. In the 1990s, rafts became a hot topic when some groups hypothesized that they could be detected and characterized by a certain detergent-based isolation technique which would dissolve the membrane except for the detergent-resistant raft domains.

Despite the failure of enormous efforts to detect these rafts by detergent-free assays, vast numbers of well-funded projects took the hypothesis for granted in the early 2000s. Heerklotz wonders whether it was the shared “(over)enthusiasm” of applicants and review panels or direction from leading agencies that led to this parallel and mistaken work. Meanwhile, Heerklotz and a sole Ph.D. student intuitively worked at better understanding the basics of lipid-detergent interactions in a laboratory in Switzerland.

“What I saw in my simple synthetic lipid mixtures was surprising: rafts could be created rather than isolated by the detergent,” Heerklotz says, adding, “My innocent thermodynamic data … challenged the mere existence of rafts or at least the traditional view of them.”

Heerklotz’s “heretic” paper, which was confirmed later by alternative methods, presents a strong argument against what he calls “too much parallel work on a few fashionable topics,” adding, “I believe part of the problem is the tendency to focus research on only a few fashionable key words, be it ‘rafs’ or ‘nano’ or whatever.”

One might expect industry-funded research to be most guilty of chasing such fads, committed purely to direct profit. However, the California-based company AgraQuest Inc. is funding Heerklotz’ current research “without a detailed work plan, with the freedom to publish in scientific literature, without constraining or directing [his] studies, and without [him] promising to obtain new intellectual property” he says.

His work is aimed at a basic understanding of the activity of a series of lipopeptides produced by the bacteria in the company’s “green” fungicide Serenade™ which is used for crop protection.

Such freedom to pursue pure scientific research “provides a basis for understanding and optimizing applied research” and, as the company seems to believe, might turn out to be actually more profitable than a project aiming primarily at improving active compounds or formulations.

“Indeed, pure science can stimulate ideas for applications later as well. Too much routine and planning is not productive and one should be open for exciting surprises and able to change the plan,” Heerklotz says.

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A Time for Change
Global responsibility in the pharmaceutical world

By Gina Vaccaro

A time for change. This phrase is immediately associated with the 44th President of the United States, Barack Obama. And while this expression gained notoriety through the campaigning hopeful, the sentiment behind it seems to echo a growing awareness that change must indeed come. But this statement begs the question – what needs to change?

Assistant Professor Jillian Clare Köhler addresses this broad question through the lens of global drug access each day in her work at the Leslie Dan Faculty of Pharmacy. There, Köhler teaches Health Systems in Society and The Power and Politics of Global Pharmaceutical Policy.

The answers that emerge are ones she and her students try to analyze and combat: the inequitable allocation of pharmaceutilicals, government pricing policies, corruption in pharmaceutical systems, and ethical issues related to pharmaceutical supply and public health needs.

“The problem is that the drug market is filled with information asymmetries,” notes Köhler. “It requires careful government oversight which doesn’t always happen in lots of countries, particularly those who are resource poor.”

This is a clear example of a system in need of change. As Köhler asks – “why are we relying on the private sector for drug development? Perhaps we need to have more public involvement in the research and development of medicines.”

Globally, Köhler is sensing a shift towards a greater reliance on the role of government for social welfare. Students who enter her classes each day are interested in getting involved in public service in some capacity.

“I’ve seen a dramatic increase in the number of students who want to do good, and who appreciate that they need to be active in making a difference,” notes Köhler.

The rich will always have the access they need, but those without financial means are left lacking with severe consequences. For example, according to UNICEF, nine million children under five years of age die each year without having had access to life-saving drugs. That means that 1,000 children under the age of five die every hour.

More than half of these cases are for diseases that could be treated with safe, essential medicines.

At the Leslie Dan Faculty of Pharmacy, this active student interest manifests itself in internships in developing countries, which are made possible through the support of the Student Experience Fund and students who finance their own placements.

At the same time, health care institutions and universities are also addressing these issues through initiatives driven from within by professionals passionate about the global good. Prime examples of this are Köhler’s Initiative for Drug Equity and Access (IDEA) and Universities Allied for Essential Medicines (UAEM). Both organizations will host a workshop in April that will discuss universities, innovation and global medicine.

Köhler herself embodies the passion she sees in her students. Brimming with excitement and intelligence in an office filled with multicultural art and an Elect Obama sign on her wall, perhaps the shift toward greater global responsibility that she foresees will come. It is, after all, a time for change.

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Technology and Tupperware®
Collaboration and accessibility come together to make health care truly universal

By Sam D’Alfonso

Once out of the Reagan “make-it-or-break-it” era, global health systems learned that cookie-cutter therapeutics have a limited ability to improve health. Yet the collaboration required to make health care more responsive to individual needs depends on health professionals in different locations accessing personal and central health data. At the moment, however, global health information technologies are as unified as the crowd around the Tower of Babel, with little ability to “speak” to each other.

“Information-sharing technology isn’t keeping up with the expanding patient-centred circle of care approach to dealing with and preventing chronic diseases,” explains Professor Peter Pennewer of the Leslie Dan Faculty of Pharmacy. “This has huge repercussions since chronic diseases account for 60% of the global disease burden.”

Still, within large, well-funded hospital systems in the developed world, the challenge isn’t as acute as for health care centres in the developing world lacking large complements of health professionals and expensive infrastructure. “Under-resourced communities have to reach out across hundreds of kilometres for the expertise needed to build a necessary team,” says Pennewer. “So the greatest need for sophisticated infomatics technology is in the developing world where they can least afford and support it.”

“Beyond accessibility to records we also need to bring the patient into the process of their own healing by utilizing narrative data,” Pennewer points out. “By narrative, we mean things like doctor's notes describing patient needs and hopes.” But posting notes from verbal communication is tricky. “We know conversations taken out of context can be problematic,” says Pennewer. “We need to maintain the contextual integrity of any narrative dialogue that’s recorded and used by other diagnostic collaborators.”

But where can you find technology that can capture biomedical data, cross format barriers throughout various
The Patent Problem

Patents and their role in encouraging (or discouraging) pharmaceutical research and development

By Amy Brown-Bowers

Drug patents seem to make sense – they encourage innovation by allowing companies to recoup costs and earn profit through a government-sanctioned temporary monopoly. But mounting evidence in the pharmaceutical industry suggests otherwise – that drug patents may in fact be an ineffective way of encouraging pharmaceutical research and development.

Dr. Paul Grootendorst, Associate Professor with the Leslie Dan Faculty of Pharmacy at the University of Toronto, is exploring the effects of patents on research and development in the pharmaceutical sector.

While teaching a course on the economics of health care, he “came across a number of issues that made the downsides of patents more obvious,” he says. Citing a study from the book Against Intellectual Monopoly in which investigators researched the effects of variation in patent terms across different time periods and societies, Grootendorst says no conclusive evidence has been found to support the belief that patents are a strong motivator for innovation in general. Rather, patents can actually become barriers to innovation.

Grootendorst says patents are problematic for three main reasons: they create deadweight losses, they waste potential profits and they increase the cost of innovation. Deadweight loss is an economic term referring to the loss to society that results from the high prices of patented products. The loss comes from the reduced use of the good owing to its high price. Consider, for instance, HIV/AIDS medications. They are relatively cheap to produce but are priced beyond the means of many HIV/AIDS sufferers in developing countries. Without the patent, the price would drop and more people would be able to afford these drugs.

As for wasted profits, the seeking and defending of patents causes something Grootendorst calls “rent seeking.”

“The idea is that if there’s a prize to be had – for instance if you’re giving away $1,000 – people will compete for that $1,000 until the last dollar they spend trying to get the money from you is equal to their expected gain,” he says. “So the value of the prize is essentially lost.”

The patent is a valuable asset and companies will spend considerable resources competing for a patent and once they get one, will need to spend resources to preserve its value.

“It all is essentially unproductive activity … It’s the death of 1,000 cuts … and it’s only there because of the patents,” he says.

While Grootendorst sees the benefit of patents for textbook, stand-alone inventions, he points out that drug innovation is increasingly sequential, “building on previous innovation,” which is typically covered by a patchwork quilt of patents. To get a new patent or develop a new technology that builds upon preexisting technology is increasingly expensive, Grootendorst says. And evidence suggests that the incentive to innovate in such cases can be more than offset by the increased difficulty and expense of doing so.

Grootendorst is currently attempting to quantify the money being wasted through the patent process and is evaluating patent alternatives. While he doesn’t yet know what the optimal solution will look like, it certainly won’t involve “unproductive battles over potential profits.”

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Noteworthy

This fall, Assistant Professor Suzanne Cadarette joined the Faculty Dr. Cadarette’s research interests include improving pharmacoepidemiologic methods by developing new analytic strategies for studying the safety and effectiveness of drugs.

Assistant Professor Stephane Angers recently received an Early Researcher Award from the Ministry of Research and Innovation. Dr. Angers and his research team are working to understand enzymes called ubiquitin ligases, which control the recognition and destruction of proteins in cells. The inability of cells to destroy their protein has been linked to several diseases, including cancer. Dr. Angers is optimistic that this research will lead to the design of better treatments for disease, and improved quality of life in Ontario.

Assistant Professor Olavo Fernandes led a team of researchers that recently received a Commitment to Care & Service Award for Hospital Pharmacy Initiative from Pharmacy Practice. Their efforts to address the problem of medication discrepancies among pharmacists, physicians, nurses and other professionals partner with patients to develop, implement and sustain organization-wide medication reconciliation practices from admission to discharge, improving the accuracy and safety of medication information transfer processes as patients move from one health care setting to another.

At the Annual Meeting of the American Association for Pharmaceutical Scientists (AAPS), Professor K. Sandy Pang received the Pharmacokinetics, Pharmadynamics and Drug Disposition Section Service Award. Dr. Pang has served on the association’s executive committee in a number of roles, been involved in fundraising efforts, planned conferences and student mentoring programs, and organized numerous workshops, symposia, and roundtables.

Peter Pennefather (right) and West Suhanic with a collection of fluorescence microscopes, a point-and-shoot camera, and an inexpensive homemade computer system equipped with a low cost Intercase system useful in the cytometric diagnosis of malaria, T.uberculosis and HIV/AIDS.
Voices from the Future
When graduate students learn, so does the faculty

By Sam D’Alfonso

Graduate students at the Leslie Dan Faculty of Pharmacy are engaged in changing the world. The original research they perform each day supports the work of their supervisors, rendering the title ‘students’ a bit of a misnomer. The dialogue between what they learn at the Faculty and what we learn from them teaches us to envision the future – a future that they are already in the process of creating.

“This is such a new and emerging field that when I started my Doctoral thesis, there wasn’t another program like it in Canada,” says Kinsley Wilson of her research in technology transfer and manufacture of antiretrovirals (ARVs) in Sub-Saharan Africa.

“She was the first student at the Leslie Dan Faculty to do research on ARVs. It’s a very new field and there’s not a lot of work on it,” Wilson explains. “She was the only one of our students who was interested.”

“G Protein-Coupled Receptors are known for their signaling function in brain cells, but a role in neurogenesis? We’re only beginning to understand that potential,” Jordan Antflick observes about his research on a barely understood group of proteins (GPCRs) which are already the target of 25 to 50 percent of all drugs currently on the market.

“As you start to do your research other questions open up,” says Luca Pisterzi. He’s also doing research on those infamous GPCRs, concentrating on their structure. In the process Pisterzi has learned to use tools such as Green Fluorescent Proteins (GFPs) and Fluorescence Resonance Energy Transfer (FRET). “Once you’re comfortable with the lab setting, experiments and literature, you begin to think more creatively about future experiments. That’s the progression you make, that’s the Graduate experience.”

Central question that drives all our research in drug discovery and development is ‘what does the population need?’” Bendayan points out. “This question is explored in all aspects ranging from the molecular to clinical practice and socio-economics.”

Interestingly, maintaining our traditional focus reveals new ways of looking at old structures. Jennifer Beales’ work on the Interprofessional culture of Family Health Teams, another field of immense importance on which the literature is still scant, makes the following observation: “Despite the focus on Interprofessional Education, if curriculums are still focused on developing the orientations or ‘world views’ of various health professionals, with a silent/unspoken hierarchy that preserves physicians on the top, doesn’t this contradict the concept of an egalitarian health system? This is the challenge we’re trying to meet and I think we’re getting there.”

Ten years ago, the Graduate Department of Pharmaceutical Sciences was home to 50 students. Today that number has grown to 150. This large complement of graduate students at the Faculty continue to hone their research skills by asking original questions about our world and challenging the day’s accepted notions, and do so already speaking the language of a world that is to be.