APRIL 2015 # 07

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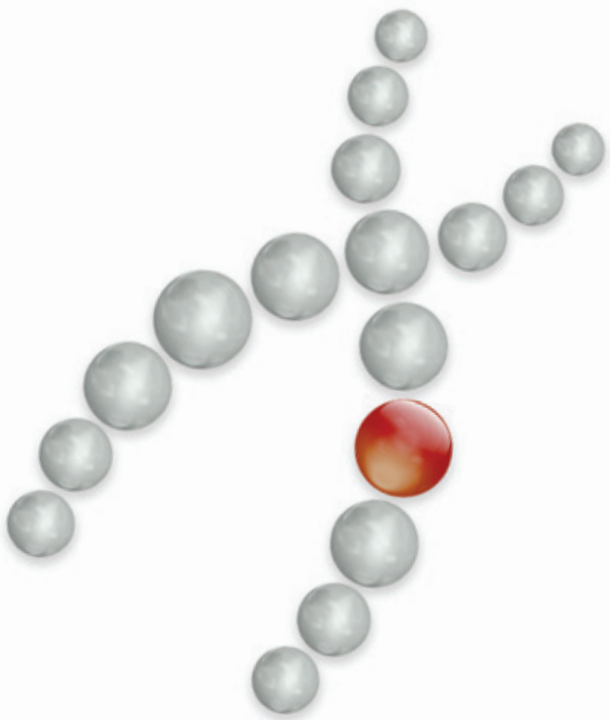

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Who's Who on the Cover? In no particular order. Turn to page 23 for The Power List 2015

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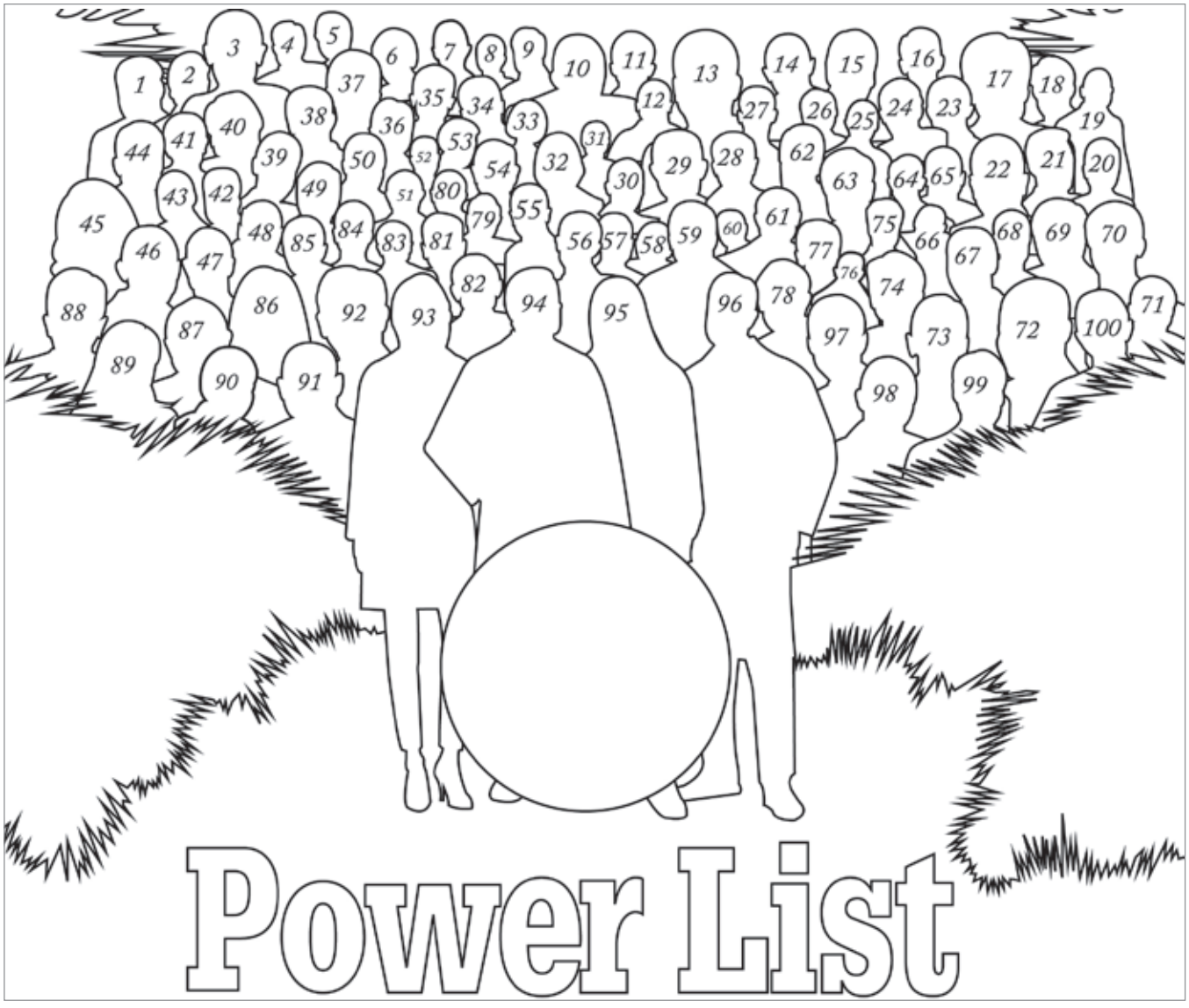

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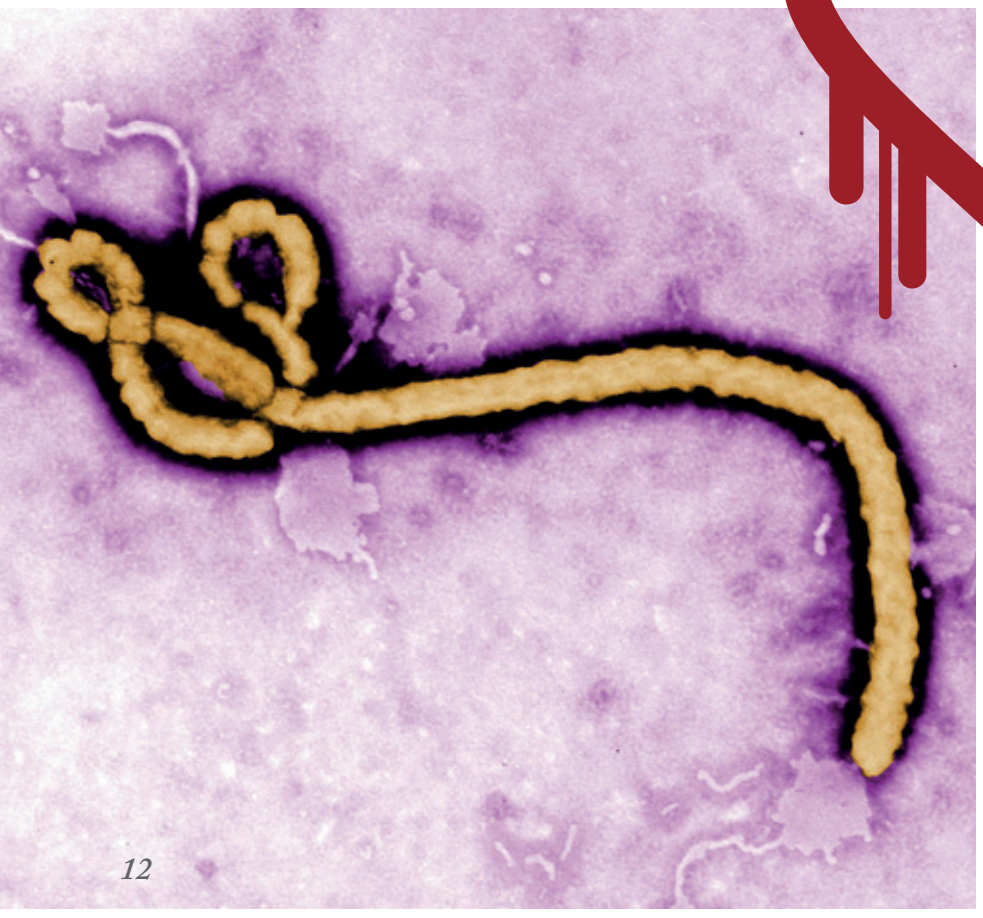

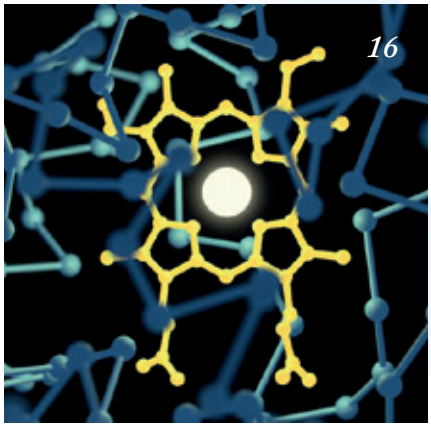

Upfront

In My View

On The Cover

Power List pastiche of Sir Peter Blake's "Sgt. Pepper's Lonely Hearts Club Band" album cover (1967).

the Medicine Maker

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TOSOH BIOSCIENCE

The Power of the List

Celebrating medicine makers of all stripes in our Top 100

The nominations are in, the votes have been counted. After considerable debate, detailed analysis, and some inspiration from The Beatles, we present The Medicine Maker Power List 2015 – our index of the 100 most influential people in the field – on page 23.

The list was developed in three stages. In stage one, we invited readers to nominate those who they thought deserved recognition. In stage two, a jury of four noted medicine makers (who prefer to remain anonymous) selected their top 100 from the slate of nominees: the results were consolidated into a list of 100 names. In the final stage, the jury ranked the list, and the average rankings were combined to provide the final Power List.

We make no claims that this is a definitive list – there really can be no such thing. We don't expect that all of our 20,000 print and 60,000 online readers will agree with who's on the list, let alone the order of the Top 20. So why make a list at all? In the immortal words of Kool and the Gang, it's a celebration. We want to recognize the achievements of the field's big hitters and unsung heroes alike – please do let us know of any glaring omissions you'd like to see recognized on the next list. I hope we can all agree on one thing: that celebrating the achievements of peers and colleagues is good for the industry.

There were some disappointments, with only eight women on this year's list, and a lack of cultural diversity. We hope to see those statistics change over the years, and we would welcome your feedback on how we can better serve under-represented groups.

That said, we were pleasantly surprised by the huge range of sectors and job roles encompassed in your nominations. We asked you to cast your net wide, and you obliged, putting forward everyone from Nobel Prize-winning scientists to leaders of global corporations, not forgetting payers, philanthropists and entrepreneurs. They may not all be traditional medicine makers, working in pharmaceutical development or manufacturing, but they all contribute to bringing medicines to patients. And after all, that is what this industry, and The Medicine Maker, is all about.

To all those who participated, our thanks. To those who feel aggrieved, let us know. And to those who made it into the Top 100, congratulations! Finally, please enjoy The Power List!

Charlotte Barker
Editor

Contributors:

Jon Platt

Armed with an MA from Oxford University in the UK, Jon forged a successful career in the advertising industry where he was creative director for three major multinational advertising agencies in the UK and Australia. After 20 years of writing commercials for everything from banks to AIDS awareness, Jon decided it was time to apply his creative skills to more strategic upstream problems, an impulse that led him to join ?What If!, where he went on to found the Manchester office and pioneer the company's move into the pharmaceutical sector.

Jon talks about the changing face of innovation on page 47.

Dennis Åsberg

Dennis Åsberg is a PhD student in the Swedish Separation Science research group at the department of Engineering and Chemical Sciences at Karlstad University, led by Torgny Fornstedt and Jörgen Samuelsson. "I started out studying chemical engineering and never planned on becoming a PhD student, but doing my master thesis with Torgny's group got me interested in separation science. After working as a research assistant for a short while, I became a full-time PhD student and am now halfway to the finishing line."

On page 19, Dennis describes a project to continuously improve quality control procedures.

Robert Bragg

Robert Bragg's main research interest is on the control of bacterial and viral diseases in avian species. He is particularly interested in disease control in a post-antibiotic era. Projects in this area focus on bacteriophages, improved vaccine development and improved biosecurity. After working at the Onderstepoort Veterinary Institute and Faculty of Veterinary Science at the University of Pretoria, he moved to the University of the Free State in 1998.

Robert discusses whether bacteriophages could be the saviour of the human race on page 18.

Seth Lederman

Seth Lederman is co-founder, CEO and chairman of Tonix Pharmaceuticals Holding Corp., a clinical-stage pharmaceutical company dedicated to the development of novel medicines for disorders of the central nervous system, including fibromyalgia, post-traumatic stress disorder (PTSD), and episodic tension-type headache.

Seth gives his tips for moving from academia to industry on page 20.

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Upfront

Reporting on research, personalities, policies and partnerships that are shaping pharmaceutical development and manufacture.

We welcome information on any developments in the industry that have really caught your eye, in a good or bad way.

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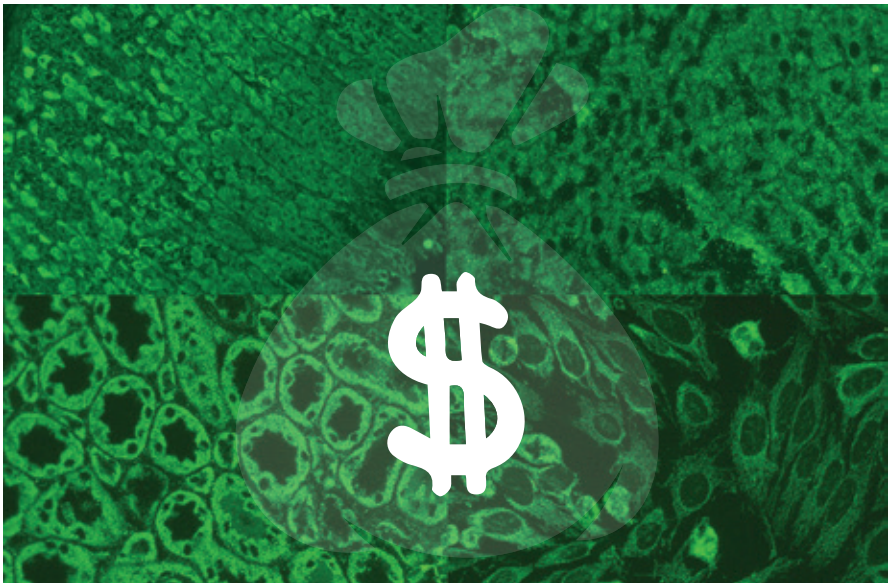

Cutting the Cost of Antibodies

By eliminating protein A, researchers aim to deliver continuous processing at a fraction of the cost of conventional techniques

Looking to reduce the costs of biopharmaceutical production, researchers from the Austrian Center of Industrial Biotechnology and the University of Natural Resources and Life Sciences, Vienna, have developed a continuous purification method for recombinant antibodies from clarified CHO cultures (1). The team converted a two-stage batch precipitation-based antibody capture step to continuous mode using continuous tubular reactors. There is no protein A capture step; instead, the precipitation process uses calcium chloride and ethanol, which are inexpensive.

"In essence it is a continuous precipitation," says Alois Jungbauer, one of the authors of the study, "but it is also very adaptable and could be a platform process. For instance, you could use it to replace certain steps in existing processes or go for a fully continuous sequence, and it can be applied to different antibodies. Recently, we've started a new project where we'll be working with pharmaceutical companies to test it at full scale."

Jungbauer explains that the inspiration for this method grew over 10 or 15 years: "It was clear to me that a fully continuous process would be optimum for manufacturing, for both biopharma and other pharmaceutical molecules. We've applied the principles to antibody purification, but it could also be extended to other products such as recombinant proteins or viruses."

However, getting the biopharma industry to embrace continuous manufacturing has been a challenge. It's only in the past four years that attitudes have begun to change. When Jungbauer and his team first started investigating continuous processing, they hit a dead end. "The field was not ready for continuous manufacturing and all of my colleagues from the pharma industry told me that this technology will not be used in industry and that

it is not relevant. But now things are changing," he adds.

The researchers believe that their continuous principles can compete with conventional protein A capture steps in terms of yield and speed, and they've now done studies with several antibodies using feedstock from pharmaceutical companies. "Protein A is still the workhorse in the biopharma industry for antibody manufacturing," says Jungbauer. "It works very well and it is a complete, mature technology. It is the benchmark that any new technology has to beat. But at the end of the day, the question is: can you use Protein A to produce antibodies at an extremely low price? In 10 or 15 years, antibodies may become a large-scale commodity. At the moment, only a small number of patients can benefit from these medicines."

Continuous processes will never be suitable for some products, such as those where only 1 to 10 kg are produced per year. Jungbauer envisions his work being applied for products produced on a larger scale. Currently, the team are working with pharma companies and testing different options to fine-tune the process, with the aim of bringing production costs down to less than $10 per gram of antibody. *SS*

Reference

1. *N. Hammerschmidt et al., "Continuous Precipitation of IgG from CHO Cell Culture Supernatant in a Tubular Reactor," Biotechnology Journal, DOI: 10.1002/biot.201400608 (2015).*

Generic Love Triangle

It's the timeless story: Teva wants Mylan, Mylan wants Perrigo, and Perrigo wants none of it

The media have been speculating on a potential bid from Teva for Mylan for some time, and although Mylan dismissed the idea earlier in April as being "without sound industrial logic or cultural fit" (1), Teva has decided to make its move anyway; on April 21, the company made an offer of $82 per Mylan share in a 50 percent cash/50 percent stock proposal, which values Mylan at around $40 billion.

Mylan has harshly rejected the offer, claiming that it undervalues the company and adding that there is a significant overlap in the companies' businesses and that the deal is unlikely to obtain anti-trust regulatory clearances anyway.

In addition, Mylan is busy pursuing its desired acquisition. At the start of April, Mylan made a proposal of $205 per share to acquire Perrigo, an Irish manufacturer of generic medicines and other health-related products. In a letter to Perrigo's president, CEO and chairman, Joseph Papa, Mylan's Robert Coury said, "As you and I have discussed on a number of occasions over the past few years, a combination of Mylan and Perrigo offers clear and compelling strategic and financial benefits, has sound industrial logic, and would create a global leader with a unique and one-of-a-kind profile." He also offered Papa the opportunity to serve as co-chairman and member of the Mylan Board. But the same day that Teva made a bid for Mylan, Perrigo's board of directors unanimously rejected Mylan's proposal, claiming that it undervalued the company (2). Mylan has now taken its offer directly to Perrigo's shareholders.

Meanwhile, Teva seems confident it is the better suitor for Mylan (3). "We firmly believe that a combination of Teva and Mylan is a much more attractive and value-creating alternative for Mylan and its stockholders than Mylan's proposed acquisition of Perrigo," said a Teva statement. Although the company added that it was a little sore to have been rejected before its offer was officially made. "We were disappointed that you prematurely addressed a potential combination in your press release issued on April 17, 2015."

Which deal will be done? Only time will tell, but Mylan has already prepared its defenses against hostile takeovers with a Dutch "poison pill" plan. Perhaps, as in so many love triangles, it will all end in tears. *SS*

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1. *Mylan "Mylan Proposes To Acquire Perrigo For $205 Per Share" (April, 2015). www.mylan.com*
2. *Perrigo, "Perrigo Board Unanimously Rejects Unsolicited Proposal From Mylan" (April, 2015). www.perrigo.com*
3. *Teva, "Teva Proposes to Acquire Mylan for $82.00 Per Share in Cash and Stock" (April, 2015). www.tevapharma.com*

Ebola's Genomic Drift

Media attention on Ebola has largely abated, but the outbreak is not over yet. What impact will genetic changes have on new medicines currently in development?

A group of scientists from the Center for Genome Sciences at the US Army Medical Research Institute of Infectious Diseases (USAMRIID) say they have identified several mutations in the genetic makeup of Ebola that could shine a light on drug development. Their work describes the "genomic drift" of the virus and how this may affect therapies that target the virus's genetic sequence (1). We spoke with Army Captain Jeffrey R. Kugelman, a viral geneticist at the USAMRIID in Fort Detrick, MD, US. Kugelmn works with Gustavo F. Palacios, who directs the Center, and Army Captain Suzanne E. Mate, who worked alongside Kugelman at the Liberian Institute for Biomedical Research (LIBR).

What lessons have been learnt from your research?

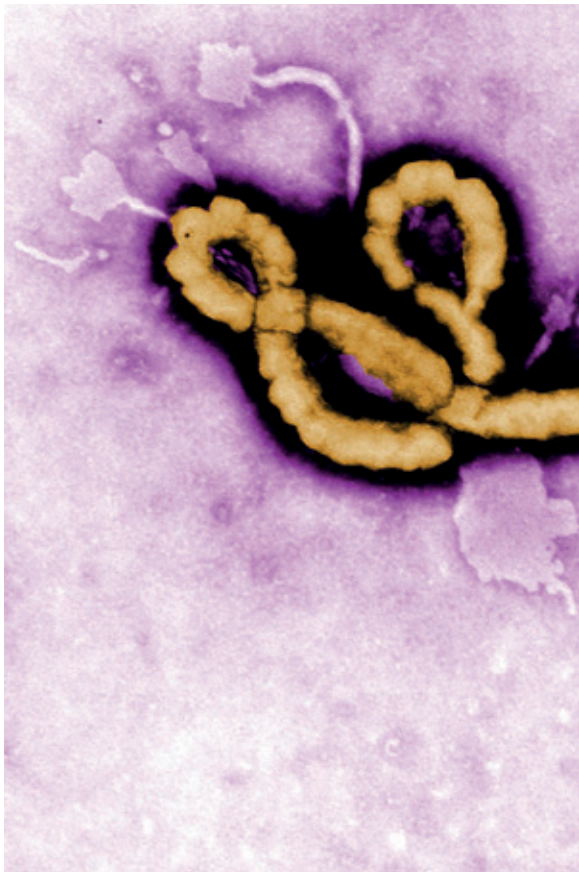
The first conclusion that we drew was that the description of the viral changes needed to keep pace with the outbreak, which highlighted the need for ongoing genomic characterization. This would inform treatment facilities about the effectiveness of their diagnostics (which are the basis for quarantine decisions), and inform pharmaceutical companies and regulatory agencies about the effectiveness of therapeutics. The second point, and one that will be a challenge to overcome in the future (if we move forward with these types of interventions) is that we need a more flexible regulatory approach to approval for human use. Targeted therapeutics, while having desirable traits in efficaciousness and for potentially limiting off-target effects, will also need to be continually monitored and possibly redesigned in the midst of an outbreak. This raises questions as to how much safety and efficacy testing, and regulatory review, would be required to use the redesigned therapeutic. If it follows the normal course, the outbreak would likely be over before the process can be completed.

What can pharma companies do to keep pace with genomic drift?

Questions of resistance development – also known as target erosion – are at the forefront of target therapeutic review for viral pathogens. Make plans early to study these effects to protect the efficacy of your investment, or trigger a move to another platform if there are questions of rapid resistance development.

Can you tell us about the genomic differences that you've identified?

Each of the therapeutics and diagnostics for Ebola virus disease has differing fidelity requirements when analyzing binding target erosion. Target erosion, very simply, is the accumulation of mutations that can lead to a loss of efficacy. Some therapeutics are nucleotide-targeted and tolerate very little change, so developers try to choose sites that have high conservation. These sites are protected by the biology of the virus, in that mutations would not be beneficial to the virus and are selected against in a normal setting. Introducing limiting factors, like therapeutics and environmental stressors, can increase the selection rates and lead to drug resistance, which is a primary study focus of our center. Other protein-based targets can tolerate far more change, as redundancy in amino acid encodings can result in a nucleotide change with no effect on the protein sequence. Our research shows that PMO sites have remained static, largely due to their location at the conserved translational start sites of the genes they target. The sites targeted by antibody-based therapeutics appear to have the most changes but also the greatest ability to tolerate those changes. Finally, siRNA targets have also seen changes. Based on these findings, which were disseminated immediately to pharma companies working on Ebola drugs, Tekmira indicates that the sequences of the company's TKM-Ebola therapeutic have been updated (2).



Studying Ebola must present certain challenges...

Viral RNA isolation from a priority pathogen with no approved vaccine or treatment requires high-level containment and raises difficulties in logistics for any sequencing effort. So the primary challenge is actually the transport and agreements to move samples back to containment labs supporting sequencing studies. This process took months and, while necessary, reduced the timeliness of the reporting. Most of the diagnostic work to date has been with quantitative PCR, which shares the same starting material needed for sequencing. Thus, a natural evolution of this report was to forward deploy a sequencing center to provide near real-time updates to the report, providing information on target signal erosion as it was happening. We addressed this issue by setting up a sequencing center at the LIBR in Charlesville (3).

What is the main technology deployed?

The lab is directed by Fatorma Bolay, and uses Illumina MiSeq chemistry to assay viral genomes. The capacity currently stands at 20 samples per week, or approximately 20–24 GB of sequence data. Analysis assets were deployed alongside the sequencer and a sample can go from isolation to sequence in approximately 5–7 days depending on ongoing runs. The aim is to provide near real-time data during the outbreak to analyze sequences for target erosion of diagnostics and therapeutics. The assay is not specific to Ebola virus, so this LIBR sequencing center will be a part of several surveillance studies to determine the prevalence of pathogens found in insects and small mammals in Liberia, as well as supporting public health for determining the causative agents of unknown febrile illness. It is hoped this capacity will be an asset to West Africa in determining what diagnostics, therapeutics and public health education will be needed to reduce the severity of future outbreaks of disease.

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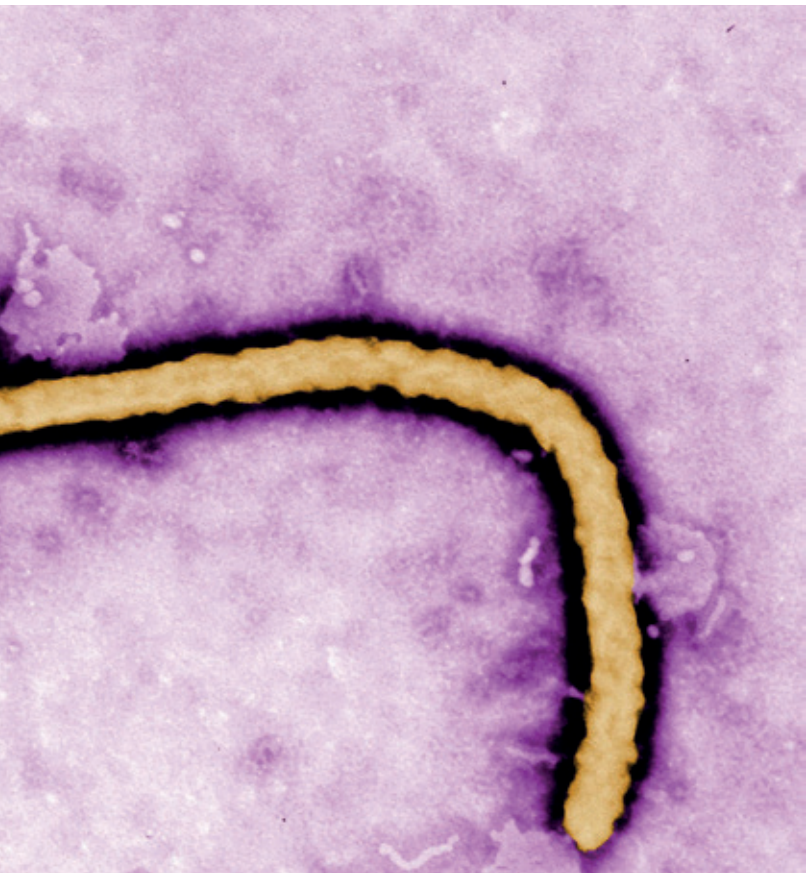

To Err is Human

But can pharma manufacturers do more to help prevent medication errors?

Medication errors are the most common preventable cause of adverse events, and the European Medicines Agency (EMA) is keen to tackle the root causes; the agency is inviting stakeholders to comment on two draft good practice guides that aim to help regulatory authorities and the pharma industry tackle the problem – and ensure proper reporting.

The first guide focuses on prevention of medication errors and outlines the key principles of risk management planning in relation to design, presentation, labeling, naming, and packaging (1). "Individual studies have reported inpatient medication error rates of 4.8 to 5.3 percent and in another study, prescribing errors for inpatients occurred 12.3 times per 1000 patient admissions," states the EMA guide. "In most cases medication errors are preventable, provided that the potential risks of medication errors have been considered during the product development and early marketing phases (when most medication errors will occur), appropriate measures put in place and reactive measures taken in response to documented reports of medication error."

Some of the elements discussed in the guide include the importance of product design and product differentiation. For example, the guide says that consideration should be given to already-available therapies and "whether there is the potential for confusion or mix-ups between products with the same indications due to similarities in posology, appearance, method of administration, strength or packaging." We discussed the power of product design in preventing medication errors in a previous issue (tmm.txp.to/0215/color).

And it's not just limited to marketed drugs – errors in clinical trial programs are also discussed, such as those resulting from poorly formatted or absent product information. The guide states that applicants should provide an appropriate risk analysis for errors that arise during the clinical trial program and use them as the basis for "refinement".

Recording, coding, reporting and assessing medication errors are covered in the second guide (2). Some of the recommendations in the guide include advice for dealing with medication errors brought to the attention of marketing authorization holders that are not associated with adverse reactions. "One of the objectives of this guidance is the establishment of good practice for sharing information on medication errors associated with adverse reaction(s) between national competent authorities responsible for pharmacovigilance of medicinal products and authorities, bodies, organizations and/or institutions responsible for patient safety reporting and learning systems in EU Member States," states the guide.

Both documents stem from a joint action plan on medication errors, which was produced in 2013. The closing date for comments is June 14, 2015. *SS*

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1. *EMA, Draft Guide, "Good Practice Guide on Risk minimization and Prevention of Medication Errors" (April, 2015), www.ema.europa.eu*
2. *EMA, Draft Guide, "Good Practice Guide on Recording, Coding, Reporting and Assessment of Medication Errors" (April, 2015), www.ema.europa.eu*

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Enzyme Evolution

By mimicking natural evolution of enzymes, researchers are creating biocatalysts for reactions unheard of in nature

We have covered the power of metabolic engineering – designing enzymes to build chemicals – previously in The Medicine Maker (tmm.txp.tp/0115/rebirth). Now, the latest research from scientists at Caltech demonstrates that by using nature's driving force – evolution – it is possible to induce existing enzymes to take on entirely new jobs (1).

The group started with the observation that nature often creates new enzymes by a process of gradual evolution from an existing enzyme. They reasoned that recapitulating this process in a test tube would likely have more success than trying to engineer a new enzyme from scratch.

Starting with a bacterial cytochrome P450, the team induced mutations in the active site of the molecule and selected for the variants with most activity in aziridination of olefins, a reaction of interest to the pharmaceutical industry, but not usually found in nature. By this process of directed evolution, the group succeeded in producing the first example of enzyme-catalyzed olefin aziridination. The authors write, "These results demonstrate the critical role of protein engineering in optimizing non-natural reactivity and suggest that the well-known plasticity of the P450 active site can be leveraged to target progressively more challenging non-natural reactions."

In contrast to rational protein design, directed evolution does not require an in-depth understanding of how protein structure impacts on function, instead relying on the same principles as selective breeding. Previous work by the Caltech group, led by bioengineering pioneer Frances Arnold, has generated enzymes able to withstand high temperatures and produce massively increased yields, useful for industrial synthesis pf pharmaceuticals, biofuels and more.

The authors of the current study believe that there are likely to be many more enzymes capable of taking on entirely new functions, concluding "This new aziridination biocatalyst is likely just one of many new catalysts that will be discovered when researchers start systematically exploring the new functions that existing enzymes can take on. Exploiting the catalytic promiscuity of natural enzymes combined with evolutionary optimization will enable us to greatly expand the reaction space of genetically encoded biocatalysts." *CB*

Reference

1. *C.C. Farwell et al., "Enantioselective Enzyme-Catalyzed Aziridination Enabled by Active-Site Evolution of a Cytochrome P450", ACS Cent. Sci., DOI: 10.1021/acscentsci.5b00056 (2015).*

'Fingerprinting' Drug Labels to Fight Fraud

Using tiny imperfections in the printing process to track individual products through the supply chain

Scientists at the anti-counterfeiting company Systech have spent years developing their e-fingerprinting technology, and they predict it's going to be a big hit in pharma and beyond. We caught up with president and CEO Bob DeJean at INTERPHEX 2015 in New York to find out more.

What is e-fingerprinting?

We already take a photo of each label to verify serialization at many stages during the manufacturing and packaging process – our patented e-fingerprinting technology analyses the printing imperfections of the label and other characteristics to give a unique signature. The system uses unique noise from the time each label was printed – it is as unique as a fingerprint or snowflake, there's only one – it can't be predicted or replicated, and so cannot be counterfeited. You can't reverse-engineer the random vibration of a production line or the humidity in the factory on a specific day. We have been trying to get rid of the 'noise' on our labels for decades – now we're using it to our advantage!

What's the benefit over serialization?

Imagine if two identical serial numbers come up on your system, or are found in the field by an inspector – how do you know which is the genuine product? When duplicates are identified in the supply chain, a simple smart phone photo taken via our app can be cross-referenced with our database to confirm whether it is an authentic product. You don't have to add anything to the packaging, like RFID tags or holograms, and no hardware is required.

How else could the technology be applied?

One of the biggest potential benefits is in creating point-to-point connections with the consumer. We're currently running pilot studies where manufacturers encourage consumers to use a branded application to take a photo of the label themselves as part of engagement/loyalty programs, providing both on-the-spot authentication and valuable marketing information.

July 20-21, 2015 Gaithersburg Marriott Hotel, Gaithersburg, MD

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In My View

In this opinion section, experts from across the world share a single strongly held view or key idea.

Submissions are welcome. Articles should be short, focused, personal and passionate, and may deal with any aspect of pharmaceutical development or manufacture. They can be up to 600 words in length and written in the first person.

Contact the editors at edit@texerepublishing.com

The Post-Antibiotic Phage

Will bacteriophages be the savior of the human race in the post-antibiotic era or is it just pie in the sky?

By Rob Bragg, Veterinary Biotechnology Research Group, University of the Free State, South Africa.

It is a well-known fact that we are rapidly running out of antibiotics, in both human and veterinary medicine. The time for the "blame game" is over; we need to start seriously looking for alternative methods to control bacterial diseases in a post-antibiotic era. Fortunately, there are a few options open to us, including discovery of novel antimicrobials, improved vaccine development, improved biosecurity and the use of bacteriophages. All of these options have their place, but here I will focus on bacteriophages.

The concept is sound: make use of viruses that specifically target bacteria to treat bacterial infections. The idea is actually not new – bacteriophages were first discovered in 1917, well before the first human use of antibiotics in 1935. With the discovery of antibiotics, most research into bacteriophages as antimicrobial therapy stopped, but as the problem of antibiotic resistance grows, bacteriophages may be ready for a renaissance.

The potential advantages of bacteriophages include the fact that they are very host specific. Phage therapy can therefore be designed to target specific pathogenic bacteria and leave the normal, non-pathogenic microbiota untouched. Another potential advantage is that the phages are self-replicating, so even small doses could provide effective treatment. There are already a large number of known bacteriophages for most pathogenic bacteria. Plus, there is a huge untapped pool of bacteriophages in the environment, giving us an almost limitless supply of novel phages should resistance develop.

Unfortunately, the main advantage of phage therapy is also its main disadvantage – high specificity. In itself this is not a bad thing, but when it comes to large-scale phage therapy, it is a huge problem. We are highly unlikely to find a single phage that will target all strains of a potential pathogen, for example, E. coli. There are two possible solutions. One is to make use of a cocktail of phages, which pushes up the price of treatment. Moreover, such indiscriminate use of bacteriophages will rapidly lead to resistance. The other option is to select the correct phage for the pathogen. Therefore, the successful use of phage therapy will be highly dependent on substantially improved laboratory-based diagnostic services to classify pathotypes or other molecular markers.

The technology to produce bacteriophages on a commercial scale is not problematic. There is a growing number of commercial companies that are starting to produce bacteriophages and the FDA approval of bacteriophages for the control of Listeria species on poultry products highlights the viability of producing and marketing bacteriophages.

Bacteria are not just sitting ducks waiting to be killed by any passing bacteriophage. They also have protective mechanisms. The restriction enzymes that have become everyday tools in the molecular biology lab are actually bacterial defense enzymes, used to attack infecting bacteriophages. Another potential problem with phage therapy is the possibility of the host developing

resistance (immunity) to the phages over time – an important aspect to consider in long-lived humans.

Another more sinister problem with phage therapy also needs very serious consideration. With the advent of full genome sequencing, the scientific community are only now starting to understand the complex relationship between bacteria and bacteriophages. There is an ever-increasing volume of work showing that many deadly bacterial toxins are actually phage-encoded. Phages have the ability to move genetic material from one bacterium to the next, which has resulted in the "creation" of deadly bacterial pathogens. The indiscriminate use of bacteriophages to treat bacterial infections could result in the development of a new deadly "superbug"...

Phage therapy has great potential, but it must be approached with care. We don't want replace our problem with a potentially more serious one.

Making Room for Improvement

To make way for more flexible approved analytical methods in pharma, we need a better understanding of the underlying scientific principles.

By Dennis Åsberg, PhD student, Department of Engineering and Chemical Sciences, Karlstad University, Sweden.

An article in a recent issue of The Analytical Scientist – "Breaking Out of the Black Box" (1) – highlights the problem of users not understanding the underlying science in analytical techniques, blindly generating data without the appropriate context and interpretation. The article by Wolfgang Lindner – a pioneer in chiral analysis – caught my attention because black box thinking is one of the problems I've been working on for more than a year. I am looking for more flexibility in developing regulatory-approved analytical methods for the pharmaceutical industry. Approved methods are locked and don't require much scientific knowledge – the user must follow them rigidly and there is little opportunity for improvement.

The core of this project, therefore (which was part of a larger study on molecular interactions) was to shift the focus to a more science-based approach that requires an understanding of the analytical methods, thereby enabling continuous improvements.

Anders Karlsson (AstraZeneca R&D in Mölndal, Sweden) came up with the idea that launched the project. He wanted to continuously improve his quality control procedures after the original methods had been approved by regulatory agencies. Actually, this is already possible to a certain extent, but only if the analytical method is filed according to the European Medicines Agency's (EMA) Quality-by-Design guidelines. That is to say, the guidelines do allow post-approval changes if – and only if – the changes are inside the original design space, which can be limiting.

For example, a pharmaceutical company that had developed and filed a high-performance liquid chromatography (HPLC)-based quality control method a few years before the commercialization of ultra-HPLC (UHPLC) would find it difficult, if not impossible, to upgrade its quality process simply because it would not have been able to include UHPLC conditions in the original design space. Done correctly, switching from HPLC to UHPLC is a minor modification because the essential difference lies in column dimensions and particle size – and yet it would offer significant improvements on analytical performance. However, according to the regulations, the changeover is not possible without resubmitting the method to the EMA

Working with Karlsson and Mikael Nilsson, Cambrex Karlskoga, and my supervisors, Jörgen Samuelsson and Torgny Fornstedt, I launched a project with the goal of finding a way to develop analytical methods that allow minor post-approval changes – even if they are outside of the original design space.

We modified an original quality control method for esomeprazole magnesium (Nexium), by switching from HPLC to UHPLC. Our first and most important step was to investigate the differences between HPLC and UHPLC in depth, which allowed us to explain the differences scientifically, making method transfer easier.

I strongly agree with Lindner that we should strive to understand the underlying principles behind the analytical methods we use every day in drug development and manufacturing. Greater understanding is often the solution to creating smart and efficient analytical methods. On a personal note, the project has also taught me that you can't be an expert on everything and that cooperation is needed to produce good and robust analytical methods. I believe that one of the reasons behind the success of the project was the diversity in backgrounds, perspectives and skills of the people involved.

Reference

1. *https://theanalyticalscientist.com/issues/0314/breaking-out-of-the-black-box/*

The Big Leap from Academic to Entrepreneur

If you want to launch a new drug company, you'll need experience, drive and excellent science... not to mention a great deal of perseverance.

By Seth Lederman, co-founder, CEO and chairman, Tonix Pharmaceuticals, New York, NY, USA.

I've always wanted to develop new medicines. I grew up in New York City and studied at Princeton University, both hubs for the pharmaceutical industry, so drug discovery and development is something I have always revered as a profession and life mission. I have been fortunate to have a diverse and successful career, both in academia and as a drug developer in start-ups. A lot has changed since I started, and I've learned valuable lessons along the way. Here, I'll give my view on some of the key factors for success for those looking to make the leap from academia to industry.

It's very important that you do not underestimate the difference between the academic and industry approach. It takes years to understand how to create and develop drugs. To that end, my first piece of advice is not to start your own company right away, but to get involved in some other capacity and learn about how the creative and development processes work. In my academic career, I worked with scientists at Biogen to develop a therapeutic monoclonal antibody, 5c8, that I had generated and characterized at Columbia University as part of discovering the CD40 ligand. Being involved in drug development (on someone else's nickel) helped me when I came to set up my first company (which became Vela Pharmaceuticals).

One of the big differences between academia and industry is that much of academia is about criticism, not discovery. That distinction isn't restricted to the sciences – it also applies to the humanities like literature and art. Creative people, like writers and artists, have traditionally been outside of the Ivory Tower, while the academics on the inside write about them and their work. In discovery, there's much more accountability – you have to make real progress, not just commentary that proves you are smart, erudite, witty or cruel. Of course, some academics make significant progress on problems, but in industry progress is a requirement and non-productive people cannot survive. For me, that is what makes working in a company so exciting.

When Donald Landry (a colleague) and I decided to start a company in 1996, the first question was, what should we work on? Don answered with another question: "What are the most important problems?" That question really crystallized what we both believe should be the cornerstone of our industry. Pursuing the most important problems has been the key driver for me in all of my endeavors, including my time in academia. In the 1980s and 1990s, I worked on AIDS, and later on autoimmunity and transplantation. I always wanted to tackle problems that lead to the greatest amount of human suffering, because I believe the satisfaction of ameliorating or solving problems is proportional to the need. I have carried that principle right through to the current work Tonix Pharmaceuticals is doing, for example, our new study in post-traumatic stress disorder (PTSD) patients. The "AtEase" study is recruiting subjects who are suffering from military-related PTSD. PTSD takes a huge toll on returning soldiers and their families and I believe that we are probably the world-leading firm in developing a therapeutic for PTSD at this point. We are very excited about the study, because of the potential to help people who have made so much personal sacrifice for our country

Being ahead of your time is not always a positive. At Vela, one of our programs involved using very low-dose cyclobenzaprine as a bedtime treatment for fibromyalgia. At that time, a lot of doctors were skeptical that fibromyalgia was even a real condition. Despite very promising data, Vela dropped the program. Fifteen years later I'm still working on the same active ingredient and the same therapeutic concept in fibromyalgia. If something is important it's usually very difficult. Important problems take a long time to solve.

And that brings me to my final piece of advice: be persistent! I was blocked from working on cyclobenzaprine for fibromyalgia after I left Vela because they were reluctant to relinquish the rights. The project languished for five years with no progress. It was a frustrating period because I remained passionate about moving the science forward and making new drugs available. But as you have probably guessed, persistence pays – the rights were eventually transferred back to Don and I, which led to us founding Tonix.

Now, at Tonix Pharmaceuticals, we are carrying out clinical trials for our new sublingual formulation of cyclobenzaprine for fibromyalgia and for PTSD, as well as developing what we hope will be the first new drug for tension-type headaches in 50 years. I believe these therapies will change people's lives, and that makes all the effort worthwhile.

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Royal Society of Chemistry Symposium
Right on Target: Sector Specific Formulation
This two day international symposium organised by the Speciality Chemicals and the Formulation Science and Technology Groups of the RSC in association with The Knowledge Transfer Network will be held in conjunction with the 2015 Chemspec Europe and Chemsource Exhibitions organised by Quartz Chemicals. It will explore approaches to the control and targeting of chemical delivery to optimise the effectiveness of speciality chemicals in agrochem, biocide, performance chemical, personal care and pharma applications.

Pharma Outsourcing Panel Discussion
The session will discuss approaches to developing global outsourcing strategies, identifying outsourcing partners, identifying approaches to mitigate risks, and addressing challenges associated with outsourcing and how to effectively manage partnerships. Chaired by Dr. Magid Abou-Gharbia, Associate Dean for Research, Professor of Medicinal Chemistry and Director of the Moulder Center for Drug Discovery Research (MCDDR) at the School of Pharmacy, Temple University, Philadelphia this debate features a world-class panel of speakers.

Agrochemical intermediates conference - in association with Agrow magazine
Returning as part of the Chemspec Europe Conference Programme after its successful launch last year, this 2 day conference will review the latest trends and developments in the agrochemical intermediates business worldwide.

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Returning for its 8th consecutive year the Regulatory Services Zone offers free-to-attend conference sessions to keep you up-to-date on requirements concerning REACH and other regulatory legislation affecting Europe's fine, custom and speciality chemicals industry. The exhibition zone will also give you access to the services they need for compliance. Organised in association with REACHReady.

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the Medicine Maker *Power List* 2015

Who are the most influential medicine makers? That's the question we posed to ourselves – and then to you – over two months ago, ahead of open nominations and a painstaking judging process. Here, without further ado, we celebrate the answer.

Shinya Yamanaka

Director and Professor, Center for iPS Cell Research and Application (CiRA), Kyoto University, Japan

Shinya successfully reprogrammed adult mouse (2006) and human (2007) somatic cells into what are now called induced pluripotent stem (iPS) cells, an alternative to embryonic stem cells with huge therapeutic potential. For the achievement, he won the Nobel Prize in Physiology or Medicine 2012.

www.cira.kyoto-u.ac.jp

Vikramaditya G. Yadav

Assistant Professor, Department of Chemical and Biological Engineering, The University of British Columbia, Canada

'Biosynthonics' – a novel paradigm for discovering and synthesizing potent bioactive molecules – is a focus of Vikramaditya's research group. The group also focuses on formulation and assembly of drugs and their translation to certain pathological conditions. They recently embarked on the development of a brain-on-chip device for preclinical testing of anti-neurodegeneration drugs.

www.ubc.ca

Keith Williams

Founder and Managing Director, GXPi and Formpipe

At the age of 27, Keith became Managing Director of a pharmaceutical validation company, which was later sold to Invensys. He adds, "I'm also proud of my lecturing on GxP principles at Loughborough and Entrepreneurship at Nottingham and Sheffield Universities to budding engineers and entrepreneurs , which allows me to give something back."

www.formpipe.com

J. Michael Wallace

Director, Global Standards & Serialization, Abbott Laboratories, USA

Mike's role is to implement GS1 global product and customer identification standards as well as an enterprise approach to serialization. He also represents Abbott on the GS1 Global Healthcare Leadership Team and is currently serving as a tri-chair. He has consulted with a cross section of groups across Abbott and the supply chain to implement these emerging standards and technologies.

www.abbott.com

Jens H. Vogel

Global Head, CMC Strategy & TRA, Boehringer Ingelheim Biopharmaceuticals, Germany

For Jens, building a high-performance development organization at Boehringer Ingelheim Fremont, California, was an immensely satisfying achievement. "We succeeded in tripling our output, established a new flexible drug substance manufacturing capability in record time and kick-started potentially disruptive innovation that may significantly impact the way protein drugs are made."

www.boehringer-ingelheim.com

J. Craig Venter

Founder, Chairman, and CEO of the J. Craig Venter Institute (JCVI), USA

John Craig Venter has made significant contributions to genomic research and his team has sequenced hundreds of genomes. He's authored more than 280 research papers, including areas such as environmental genomics, the first complete diploid human genome, and the creation of the first self-replicating bacterial cell constructed entirely with synthetic DNA.

www.jcvi.org

Harold Varmus

Lewis Thomas University Professor at Weill Cornell Medical College, USA

On April 1, 2015, Harold Varmus took up his role at the Weill Cornell Medical College faculty, where he will be conducting cancer research. Harold is previously the director of the National Cancer Institute, and co-winner of a 1989 Nobel Prize for the discovery of the cellular origin of retroviral oncogenes.

Judge's comment: "Harold Varmus is a pioneer in recognizing the existence of oncogenes: a concept that changed our thoughts on cancer. He was a leader of the NIH for many years and

until recently led the National Cancer Institute. At 75, he is returning to New York, still active in his field."

http://weill.cornell.edu

Catherine Tuleu

Director, Centre for Pediatric Pharmacy Research, UCL School of Pharmacy, UK

Since 2003 Catherine's patient-centric research has been aimed at facilitating the development of better pediatric formulations. "My research is very applied and translational which is ever so gratifying," she says. "Plus, by working in a very responsive field, I can witness the impact of efforts individually and collectively made and how this has enthused younger researchers and colleagues. What a privilege!"

http://iris.ucl.ac.uk/iris

Bernhardt Trout

Raymond F. Baddour, ScD, (1949) Professor of Chemical Engineering, MIT and Director, Novartis-MIT Center for Continuous Manufacturing, USA

Bernhardt says, "The achievements I'm most proud of? Working with students, staff, and colleagues from MIT and worldwide, to successfully develop pharmaceutical development and manufacturing technology and to raise public awareness of the benefits of that technology to patients, and to get them medicines in a more streamlined and less expensive way."
https://novartis-mit.mit.edu

Nigel Theobald

Founder and CEO, N4 Pharma, UK

"As a serial entrepreneur and passionate developer of new products, I'm now in the position of owning my own drug reformulation company with an incredibly experienced and respected board and two world class technology platforms," says Nigel. "This shows what can be achieved if you stick to a focused business model!"
www.n4pharma.co.uk

Marco Taglietti

CEO, Scynexis, USA

Marco previously served as Executive Vice President, Research and Development and Chief Medical Officer of Forest Laboratories and President of the Forest Research Institute until the company was acquired by Actavis, plc. A nominator described him as an "energetic, enthusiastic, knowledgeable, and passionate leader within the industry."
www.scynexis.com

Abbe Steel

Founder and CEO, HealthiVibe

Abbe created HealthiVibe, after 25 years in the life sciences industry, to help pharma sponsors gain insight into their patients' needs. "As a result, I've helped companies create more patient-centered trials and worked to advance a culture where the patient comes first."
http://healthivibe.com

Indresh K. Srivastava

Vice President, Product Realization, Protein Sciences

With a strong background in vaccine development, particularly immunogen design, purification, analytical and formulation development, Indresh has published extensively in these areas. He served on the NIH special emphasis study section focused on vaccine development for 10 years and spent more than 12 years at Chiron Corporation/Novartis Vaccines and Diagnostics.
www.proteinsciences.com

Lars Rebien Sørensen

Chief Executive Officer, Novo Nordisk A/S
Revenue: DKK 88.8 billion ($12.9 billion) (2014)
Employees: circa 41,500

Lars Rebien Sørensen joined Novo Nordisk's Enzymes Marketing in 1982 and in May 1994 he was appointed a member of Corporate Management. He was appointed president and CEO in November 2000.
www.novonordisk.com

Manish Soman

President and CEO, Sciformix

In just three years, Manish helped Sciformix to evolve from a niche area into a leading global scientific process organization for the biopharmaceutical, generic pharmaceutical, consumer product, medical device and contract research industries.
www.sciformix.com

Andy Skibo

Head of Global Biologics Operations and Global Engineering at AstraZeneca/MedImmune

Andy is the current Chair of the International Society for Pharmaceutical Engineering. He considers his greatest achievement to be "developing our AZ/MedImmune Biologics team and network into a reliable, highly productive operation…involving everything from the development of a strong team… to complex physical plant upgrades across a five site network in locations around the globe."
www.medimmune.com

Joseph Schlessinger

William H. Prusoff Professor of Pharmacology and Chair of the Pharmacology section, Yale School of Medicine; Director, Yale Cancer Biology Institute

Joseph is an internationally recognized expert in personalized treatment for cancer and sits on the editorial boards of several leading scientific journals. He is a member of the National Academy of Sciences, the American Academy of Arts and Sciences, the Institute of Medicine, and the European Molecular Biology Organization.
http://schlessinger.yalemedicine.org

Andreas Seidel-Morgenstern

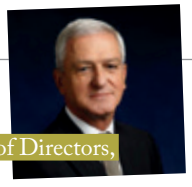
Director, Department of Physical and Chemical Foundation of Process Engineering, Max Planck Institute for Dynamics of Complex Technical Systems, Germany

Andreas' research interests include heterogeneous catalysis, new reactor concepts, and preparative chromatography and he has published almost 400 research papers. He is a member of the Berlin-Brandenburg Academy of Sciences and Humanities and the German National Academy of Science and Engineering (Acatech).
www.mpi-magdeburg.mpg.de

Charles L. Sawyers

Memorial Sloan-Kettering Cancer Center; investigator at Howard Hughes Medical Center, USA

Charles is President of the American Association for Cancer Research and was recently appointed by President Obama to the National Cancer Advisory Board. He serves on the National Cancer Institute's Board of Scientific Counselors and his research focuses on the signaling pathways that drive the growth of cancer cells.
www.mskcc.org



Joerg Reinhardt

Chairman of the Board of Directors, Novartis AG

Joerg also serves as Chairman of the Research and Development Committee. He previously served as Chairman of the Board of Management and the Executive Committee of Bayer HealthCare, Germany. Prior to that, he served as Chief Operating Officer of Novartis from 2008 to 2010, and as Head of the Vaccines and Diagnostics Division of Novartis from 2006 to 2008.
www.novartis.com

George A. Scangos

Chief Executive Officer, Biogen Idec
Revenue: $9.7 billion (2014)
Employees: circa 7550

Before joining Biogen Idec, George served as the President and CEO of Exelixis, where he continues to serve on the board. He is also Treasurer of the Board of Directors of PhRMA, and a member of the Boards of Trustees of the Boston Museum of Science and the Biomedical Science Careers Program.
www.biogen.com

Tomasz Sablinski

Co-founder & CEO, Transparency Life Sciences

Tomasz's most satisfying achievement to date is the ongoing experience of building a clinical-stage drug development company based on a vision of patient-centric clinical trials that use crowdsourcing and 21st century technologies; with goals that include increasing the availability, affordability and utility of new medicines.
http://transparencyls.com

Ian C. Read

Chairman of the Board and Chief Executive Officer, Pfizer
Revenue: $49.6 billion (2014)
Employees: circa 78,000

In 2000, Ian became Executive Vice President, Europe, and was then named a Corporate Vice President in 2001. He came to assume responsibility for Canada, as well as Europe, and later for operations in both the Africa/Middle East region and Latin America. He is Chairman of the Board of PhRMA.
www.pfizer.com

David E.I. Pyott

Former Chairman and CEO, Allergan

During his 17 -year tenure, David transformed Allergan from a small eye care business with about $1 billion in sales to a global specialty pharmaceutical and medical device company, with sales over $7 billion in 2014, with most of the increase stemming from organic growth.

www.allergan.com

Alain Pralong

VP New Product Introduction & Technical Life Cycle Management, GSK

"Initiating and driving maturation of ways of working within biopharmaceutical product development and maintenance by applying lean-six sigma principles has given me significant satisfaction," says Alain. He found that developing sophisticated end-to-end processes with appropriate levels of granularity permitted effective management of various activities across the future and current portfolio.

www.gsk.com

Ulo Palm

Senior Vice President Branded Drug Development Operations, Actavis Pharmaceuticals

Ulo's personal vision is to expedite drug development by linking top medical science to performance excellence and 21st century technology. He is a member of the TransCelerate BioPharma Operations Committee, co-chair of the ASQ FD&C Research Committee and on the Board of Directors of ANAB, the ANSI-ASQ National Accreditation Board.

www.actavis.com

Brian Overstreet

Co-Founder and President, AdverseEvents

Brian has more than fifteen years of experience building and managing companies in the data, research and investment industries. Nominator comment: "He has changed the way FAERS data is viewed, from a mess of untamed, unmanageable data to a treasure trove of information that helps determine the true safety profiles of FDA approved prescription drugs."

www.adverseevents.com

Stephen Ostroff

Acting Commissioner of Food and Drugs, FDA

Stephen joined the FDA in 2013 as chief medical officer in the Center for Food Safety and Applied Nutrition and senior public health advisor to the FDA's Office of Foods and Veterinary Medicine. Before being named acting commissioner in February 2015, he served as the FDA's chief scientist.

www.fda.gov

Julie O'Neill

Executive Vice President, Global Operations, Alexion, Ireland

Julie studied pharmacy at Trinity College Dublin and has spent much of her time since then working in the pharma industry. She is currently responsible for Alexion's global manufacturing operations and the company's supply chain and quality operations. Prior to Alexion, she worked for Gilead Sciences where she established the company's Irish subsidiary and plant operations.

www.alxn.com

Mark Offerhaus

Founder and CEO, Micreos, The Netherlands

Mark is proud of the technologies at Micreos. "I really think that the introduction of Staphefekt, the first endolysin for human use…represents a real game changer. Nothing makes me happier than reading all the authentic user reviews of the product online." Nominator comment: "Mark's enthusiasm and drive has guided Micreos in their journey as a very small biotech company taking on big pharma to tackle the global issue of antibiotic resistance."

www.micreos.com

George Nakayama

Representative Director; President and Chief Executive Officer, Daiichi Sankyo Co., Japan

George has served as President and Chief Executive Officer of Daiichi Sankyo Co., Ltd. since June 2010. He joined the former Daiichi group as President of Daiichi Suntory Pharma Co., Ltd. upon the spin-off of the Pharmaceutical Division of Suntory Co., Ltd. in 2002. He earned a Master of Science degree from Osaka University in 1976 and an MBA from Northwestern University in 1979.

www.daiichisankyo.com

Kent Clemenco

Kary Mullis

Distinguished Researcher, Children's Hospital and Research Institute, Oakland, USA

Kary received a Nobel Prize in chemistry in 1993 for his invention of the polymerase chain reaction (PCR). Today, he serves on the board of scientific advisors of several companies, provides expert advice in legal matters involving DNA, and lectures at college campuses, corporations and academic meetings around the world.

www.karymullis.com

John C. Lechleiter

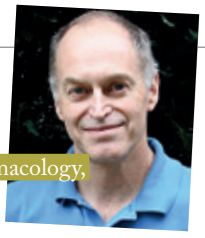
Chairman, President and Chief Executive Officer, Eli Lilly and Company
Revenue: $19.6 billion (2014)
Employees: circa 41,000

John joined Lilly in 1979 as a senior organic chemist in process research and development and became head of that department in 1982. He has served as president and CEO since April 2008 and became chairman of the board of directors in January 2009.
www.lilly.com

Tarit Mukhopadhyay

Lecturer, Vaccine Bioprocess Development, University College London, UK

Tarit is a biochemical engineer who has been active in vaccine development for over 10 years. He creates scale-down models to accurately mimic the production environment. "With this, I can employ high-throughput techniques to quickly attain the optimum manufacturing process," he explains. "This methodology has been successfully applied to bacterial and virus vaccines."
www.ucl.ac.uk



Randy Mrsny

Professor, Department of Pharmacy and Pharmacology, University of Bath, UK

Before taking up a Professors' post in Cardiff University (UK) and now the University of Bath, Randy led research groups in two companies: ALZA and Genentech. He has also been involved in starting two new biotech companies through venture capital funding. Currently, the Mrsny Laboratory focuses on a variety of aspects of epithelial cell structure/function in health and disease.
www.bath.ac.uk

Julian Morris

Emeritus Professor of Process Control, Newcastle University, UK and Technical Director, Centre for Process Analytics and Control Technology (CPACT)

"My most satisfying achievement has been the privilege to collaborate with, mentor and support the development of PhD students and postdoctoral researchers who have gone on to successful careers in engineering science and higher education," says Julian.
www.cpact.com

Louis Monti

Executive Vice-President and Secretary, Pherin Pharmaceuticals

Before Pherin, Louis held various professorial positions at the University of Utah and the University of Uruguay. He holds an M.D. degree from the School of Medicine, University of the Republic, Uruguay, and a Ph.D. degree from the School of Medicine, University of Utah. He has published over 100 scientific articles and holds several patents.
www.pherin.com

Anthony S. Lubiniecki

Senior Scientific Director & Fellow, Chemistry, Manufacturing & Controls (CMC) Strategy, Pharmaceutical Development & Manufacturing Sciences, Janssen R&D

During his 40 years in industry, Anthony worked on the development of 40 recombinant derived investigational products using both microbial and eukaryotic expression systems, of which ten have become marketed products. He serves as CMC strategist on a number of large molecule projects and several cell therapy projects, and also chairs the Large Molecule CMC Council.
www.janssenrnd.com

Archie Lovatt

Scientific Operations Director, SGS Life Sciences

Between 1996 and 2007, Archie was Scientific Director of Q-One Biotech-BioReliance-Invitrogen. He pioneered the development and implementation of quantitative PCR and PERT services for the testing of cell substrates and viral vectors/vaccines. In early 2007, Archie co-founded Vitrology, which was acquired by SGS in 2012.
www.sgs.com

Claus-Michael Lehr

Professor, Helmholtz-Institute for Pharmaceutical Research Saarland (HIPS); Helmholtz Center for Infection Research (HZI); Saarland University, Germany

"In our research on non-invasive drug delivery across the body's major epithelial barriers (gut, skin and lung), often based on nanotechnology, we could make some significant progress with human cell- and tissue-based in vitro models." Claus-Michael believes that such models could be "instrumental" for translating new medicines into clinics.
www.uni-saarland.de

Patricia Wolf

Wim Leereveld

Founder and CEO, Access to Medicine Foundation

Wim says, "Publishing the first Access to Medicine Index in 2008 brought me great satisfaction, which grew as so many big pharmaceutical companies responded to successive Index iterations. I am still more encouraged by the cooperation I see today between all stakeholders, including institutional investors, aimed at seriously addressing the issue of access to medicine for the very poorest."

www.accesstomedicineindex.org

Daniel S. Kohane

Professor of Anaesthesia, Harvard Medical School, USA

Daniel's research covers broad areas in biomaterials, drug delivery, and nanoscience. He directs the Laboratory for Biomaterials and Drug Delivery at Boston Children's Hospital at Harvard Medical School, with his clinical practice in pediatrics, anesthesiology and pediatric critical care medicine.

http://kohane.tch.harvard.edu

Andreas Koester

Vice President, Clinical Trial Innovation, Janssen R&D, Janssen Pharmaceutical Companies of Johnson & Johnson

"I'm passionate about pre-competitive cooperation between pharma companies for the benefit of patients and investigators," says Andreas. He is Operations committee member of Transcelerate Biopharma and co-creator of the Investigator Databank, launched in collaboration with Merck and Eli Lilly to reduce the administrative burden for investigators and to streamline the site selection and start up process.

www.janssenrnd.com

Joseph Kim

Senior Advisor in Clinical Innovation, Eli Lilly

Joseph focuses on developing and implementing innovative patient engagement solutions. He has spent over 16 years in the pharma industry utilizing an approach that integrates his experiences working for sponsors such as Shire and Merck, as well as CROs and technology vendors. He holds a BS in Molecular Biology from Lehigh University and an MBA from Villanova.

www.lilly.com

William G. Kaelin

Professor of Medicine, Dana-Farber Cancer Institute and Brigham and Women's Hospital, Harvard Medical School; Investigator, Howard Hughes Medical Institute; and Associate Director, Basic Science, Dana-Farber Cancer Institute/Harvard Cancer Center

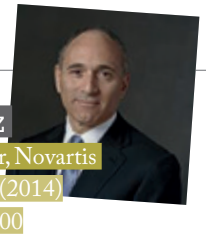
William's research seeks to understand how mutations affecting tumor-suppressor genes cause cancer. His laboratory is currently focused on studies of the VHL, RB-1, and p53 tumor suppressor genes. His long-term goal is to lay the foundation for new anticancer therapies based on the biochemical functions of such proteins.

http://kaelin.dfci.harvard.edu

Jeff Kasher

President, Patients Can't Wait, LLC

Jeff has a passion for improving outcomes, bringing patients and research sites into the development process and decreasing time to market. His experience includes novel product development from bench through market launch, research and clinical trial leadership, innovation center start up, and new industry paradigm creation.



Joseph Jimenez

Chief Executive Officer, Novartis
Revenue: $57.9 billion (2014)
Employees: circa 135,000

Joseph joined Novartis in April 2007 as Division Head, Novartis Consumer Health. Previously, he served as president and CEO of the North America business for the H.J. Heinz Co. and as president and CEO of Heinz in Europe from 2002 to 2006. Prior to joining Novartis, he was a nonexecutive director of AstraZeneca plc, from 2002 to 2007.

www.novartis.com

Dennis R. Jenke

Baxter Distinguished Scientist, Baxter Healthcare Corporation

Science and farming are related, according to Dennis. "You plant a seed (make an initial discovery), nurture the seed (build onto that discovery) and if the seed was strong it grows into a majestic tree (a discovery that makes a significant difference in the human condition). There is nothing quite as fulfilling as enjoying the shade of a tree that grew from a seed you planted."

www.baxter.com

Tyler Jacks

David H. Koch Professor; Director, Koch Institute for Integrative Cancer Research; Investigator, Howard Hughes Medical Institute, USA

Tyler has pioneered the use of gene targeting technology in the mouse to study cancer-associated genes and to construct mouse models of many human cancer types, including cancers of the lung, brain and ovary. His lab has made seminal contributions to the understanding of the effects of mutations of several common cancer-associated genes.

http://jacks-lab.mit.edu

Ajaz Hussain

Executive Director, The National Institute for Pharmaceutical Technology and Education, USA

Ajaz has previously worked for the FDA, where he became deputy director of its Office of Pharmaceutical Studies in 2000. He also held a Senior Biomedical Research Scientist position. He is widely recognized for his leadership of several FDA initiatives such as Process Analytical Technology and Pharmaceutical Quality for the 21st Century.

www.nipte.org

Robert J. Hugin

Chairman and Chief Executive Officer, Celgene

Robert has been CEO since June 2010 and Chairman since June 2011. He is immediate past Chairman of the Board of The Pharmaceutical Research and Manufacturers of America. In 2014, Celgene topped a Business Insider poll of America's Best Employers, which Robert attributed in part to the "aspirational objectives" of the company.

www.celgene.com

Jane Griffiths

Company Group Chairman, Janssen EMEA

Jane says, "It is a privilege to lead an amazing team at Janssen, providing medicines every day to millions of people, helping to extend and improve lives. It is an enduring source of pride for me to be part of that endeavor, and to have raised two great kids along the way!"

www.janssen-emea.com

Richard Heyman

Founder, Aragon and Seragon

A nominator comments: "Using selective nuclear hormone receptor modulators Dr. Heyman pioneered a very lean R&D strategy, which yielded the sale of Aragon to J&J for over $1billion in 2013 and Seragon to Roche for $1.7 billion in 2014...The class of drugs developed by Dr. Heyman was developed by rational drug design and to my knowledge are the first successful efforts to modulate these receptors in specific ways."

Yoshihiko Hatanaka

Chief Executive Officer and President, Astellas Pharma

Revenue: $11 billion (2014)

Employees: circa 17,500

Yoshihiko has been CEO and President of Astellas since 2011. He's served in a number of other roles within the company including Chief Financial Officer, Chief Strategy Officer and Senior Corporate Executive of Astellas Pharma, Inc. He has also served as CEO of Astellas Pharma US, Inc.

www.astellas.com

Craig Lipset

Head of Clinical Innovation, Worldwide Research & Development, Pfizer

Craig says, "Through transparency, collaboration, and nurturing a vast network, I am proud to have helped create a global community of individuals committed to improving the lives of patients by bringing innovative new approaches to the development of new medicines."

www.pfizer.com

Dalvir Gill

Chief Executive Officer and Member of the Board of Directors, TransCelerate BioPharma

With over 25 years in drug development, Dalvir says that his most satisfying career achievement is leading the charge as CEO for TransCelerate BioPharma. "It's an innovative collaboration across the global biopharmaceutical R&D community to identify and solve common R&D challenges, in order to deliver high-quality medicines to patients," he says.

www.transceleratebiopharmainc.com

Kenneth Getz

Director, Sponsored Research Programs and Associate Professor, CSDD, Tufts University School of Medicine; Founder and Board Chair, CISCRP

"Perhaps my most satisfying moment was the decision to leave the comfort of a management consulting position to start, and ultimately sell, two entrepreneurial ventures," says Ken. "I learned to rely on my intuition; to take risks and not fear failure; to treat disappointments as opportunities; to be unyielding with respect to quality and integrity."

http://medicine.tufts.edu

Parrish Galliher

Chief Technology Officer, Xcellerex, Life Sciences from GE Healthcare

Parrish Galliher is a well-known thought leader in bioprocessing, and is co-inventor on a number of patents in the field. Parrish says, "The achievement that gives me the most pleasure is bringing the vision of a truly modular manufacturing facility - our FlexFactory - to reality…ultimately helping the industry bring these live-saving medicines and vaccines to more people worldwide."

ww.gehealthcare.com

Chris Frampton

Professor of Structural Chemistry and Crystal Engineering, Wolfson Centre for Materials Processing, Brunel University, UK

Chris also holds the post of Research Associate of Girton College at University of Cambridge. He has acted as an expert witness in a number of high profile legal cases, involving the solid form of pharmaceutical drug substances, in both the US and the UK.

www.brunel.ac.uk

Mark C. Fishman

President, Novartis Institutes for Biomedical Research

The aim of Novartis Institutes for Biomedical Research is to identify and advance promising drug candidates. Before joining Novartis in 2002, Mark was Chief of Cardiology and Director of the Cardiovascular Research Center at Massachusetts General Hospital, and Professor of Medicine at Harvard Medical School.

www.novartis.com

Dennis Fenton

Retired

Dennis is a former Executive Vice President at Amgen and is now a board member of several bio/pharma companies.

Judge's comment: "He has an unfailing appreciation for the bottom-line reason we are in business, namely we develop and deliver breakthrough medicines serving critical needs in human health. In spite of many pressures, Dennis always maintained a focus upon the ultimate purpose of our business: delivering medicines. I use his motto to this day: 'Every Patient, Every Time'."

Joseph Famulare

Vice President, Global Quality Compliance and External Collaboration, Genentech

Before joining Genentech in 2009, Joseph spent more than 30 years at the FDA and is the former Deputy Director of FDA's CDER Office of Compliance. He has been a member of ISPE for over 15 years and is active in ISPE global activities as a speaker and panelist.

www.gene.com

John P. Farris

President and Chief Executive Officer, SafeBridge Consultants, USA

John has extensive expertise in executive management, industrial hygiene, laboratory safety, control of potent pharmaceutical compounds, environmental protection and environmental remediation. John says, "The founding of SafeBridge Consultants in 1997 from the former Environmental Health & Safety Division of Syntex (USA), Inc. marked the first time a 'big phama' health and safety department transitioned from a corporate entity to an independent consulting firm." *www.safebridge.com*

Marijn Dekkers

Chairman of the Board of Management, Bayer AG

Revenue: €42.2 billion ($45.4 billion) (2014)

Employees: circa 118,900

Marijn studied chemistry and chemical engineering, and began his professional career in 1985 as a scientist at the corporate research center of General Electric in the US. He spent 25 years of his career in various companies and positions in the US before joining Bayer in 2010.

www.bayer.com

Sir Andrew Dillon

Chief Executive of the National Institute for Health and Care Excellence (NICE), UK

A nominator says, "NICE guidance is influential beyond the borders of the UK and Europe for physicians, patients, nurses, carers, reimbursement decision makers, as well as for financial analysts. Sir Andrew joined NICE as its founding Chief Executive in 1999 and has held this position ever since."

www.nice.org.uk

Meindert Danhof

Professor of Pharmacology and former Scientific Director of the Leiden Academic Center for Drug Research (LACDR), Leiden University, the Netherlands

Meindert's research focuses on novel concepts of systems pharmacology, interfacing concepts from systems biology with quantitative pharmacology. He is (co)author of 420 publications and has mentored 58 PhD students and 16 post-doctoral research fellows. He is also President, European Federation of Pharmaceutical Sciences.

http://lacdr.nl

Charles Cooney

Robert T. Haslam (1911) Professor of Chemical Engineering Emeritus, Department of Chemical Engineering, Massachusetts Institute of Technology, USA

"I've helped to educate many of today's leaders in biotech and pharmaceutical manufacturing, and participated in the teams that designed and built the first biotech manufacturing plants for recombinant proteins at Genentech and Genzyme," says Charles. "I've also established the principles for end-to-end continuous manufacturing of pharmaceuticals."

http://web.mit.edu

Francis S. Collins

Director, US National Institutes of Health, USA

Francis is the Director of the US National Institutes of Health, the largest supporter of biomedical research in the world. He is a physician–geneticist noted for his landmark discoveries of disease genes and his leadership of the international Human Genome Project.

www.nih.gov

Marshall Crew

Global PDS Scientific Excellence, Patheon

Marshall was CEO and founder of Agere, a CDMO specializing in oral bioavailability of insoluble molecules that was acquired by Patheon in 2015. He has devoted his career to developing innovative technologies and approaches for the delivery of poorly soluble drugs. More than 28 patents and patent applications have been filed under his name.

www.patheon.com

William Chin

Executive Vice President, Scientific and Regulatory Affairs, Pharmaceutical Research and Manufacturers of America (PhRMA)

Bill says he is most proud that he has spent his entire life focusing on how to help patients through innovation. "From exploring the mysteries of how hormones work, to mentoring next-generation physician–scientists, to helping develop new medicines and foster collaborative partnerships, I've been blessed with the opportunity to make lives for patients a little better."

www.phrma.org

John Chiminski

President and Chief Executive Officer, Catalent

"I am proud to have led Catalent's transformation into the world's leading drug delivery technology, development and supply organization, culminating in last year's successful IPO," says John. "More importantly, I lead a company that is committed to bringing better, innovative treatments to market, in the shortest possible timeframe, ultimately improving patient outcomes."

www.catalent.com

Pierre Chambon

Professor of Molecular Genetics, Institute of Advanced Studies, Strasbourg University, France

Pierre's scientific achievements are numerous; the discovery of multiple RNA polymerases (1969); the discovery of animal split genes (1977); and a marked contribution to the discovery of the superfamily of nuclear receptors (1987). He is also Honorary Professor at the Collège de France (Paris); and Emeritus Professor at the Faculty of Medicine of the Strasbourg University.

www.usias.fr

Barry Buckland

Chief Executive Officer, BiologicB, USA

Barry previously worked at the Merck Research Laboratories where he built and led a world-class bioprocess R&D group. He was part of the development team whose work led to the licensure of many breakthrough vaccines, including vaccines against HPV, Shingles, Chicken Pox, Hepatitis A, Hepatitis B and Rotavirus.

http://biologicb.com

Olivier Brandicourt

Chief Executive Officer, Sanofi
Revenue: €33.8 billion ($36.3 billion) (2014)
Employees: circa 110,000

Olivier took up his new duties at Sanofi on April 2, 2015. He has 28 years of global experience in the pharmaceutical industry, most recently as Chairman of the Board of Management of Bayer HealthCare AG and member of the Executive Council of Bayer AG.

www.sanofi.com

John Aunins

Executive Vice President and Chief Technology Officer, Seres Health, USA

"During 2006, the team I was part of at Merck licensed four new vaccines addressing infectious diseases that pose significant public health threats and did not otherwise have a preventative strategy," says John. "I hope to leverage this experience at Seres to develop novel biologics to treat diseases by targeting dysbiosis of the microbiome."
http://sereshealth.com

Richard Bergström

Director General, European Federation of Pharmaceutical Industries and Associations (EFPIA)

Over the past 20 years, Richard has worked for Roche, Novartis and with the Swedish pharmaceutical industry association (LIF). A pharmacist by training, he received his MScPharm degree from the University of Uppsala, Sweden in 1988. Since 2006, he has been an advisor to the World Health Organization on Good Governance in Medicine.
www.efpia.eu

Stéphane Bancel

Chief Executive Officer, Moderna Therapeutics

Prior to Moderna, Stéphane was CEO of bioMérieux and he has also held leadership positions at Eli Lilly. He joined Moderna in 2011 and helped raise its financing, including the largest private biotech round in January 2015 at $500 million. Today, Moderna has 160 employees and agreements with AstraZeneca, Alexion and Merck.
http://modernatx.com

Alan Armstrong

Chairman & Group Chief Executive Officer, Almac Group

"Overseeing the achievement of year-on-year growth and the development of the global company – and knowing that Sir Allen McClay (Almac's Founder and original Chairman) would be proud of our achievement – is what has given me the most satisfaction," says Alan. He is also Chairman of the charity, the McClay Foundation.
www.almacgroup.com

Lisa Anson

President, AstraZeneca UK and Ireland

Previously, Lisa has held a number of Global Vice President level roles in AstraZeneca plc, including providing the lead commercial input to the company's R&D. She also led the cross functional Global Product Team for Mental Health, launching major products globally. She started her career in Strategy Consulting with KPMG.
www.astrazeneca.co.uk

Lamberto Andreotti

Chief Executive Officer, Bristol-Myers Squibb
Revenue: $15.9 billion (2014)
Employees: circa 24,000

Lamberto Andreotti joined Bristol-Myers Squibb in 1998, holding numerous roles of increasing responsibility until his election to the Board of Directors in 2009, and CEO in 2010. On May 5, 2015, Lamberto will retire from the role of CEO and become Chairman of the Board of BMS, while Giovanni Caforio takes over as CEO.
www.bms.com

18 David Baltimore

President Emeritus and Robert Andrews Millikan Professor of Biology, California Institute of Technology, USA

David says that his most satisfying achievement was his 1970 discovery of reverse transcriptase for which he received the 1975 Nobel Prize in Physiology or Medicine at the age of 37. "It culminated the first 10 years of my career in science, showing that information can flow from RNA to DNA and explaining the lifecycle of viruses that came to be known as retroviruses. The discovery strongly implied that cancer could be caused by genetic means, then a wide-open question. It provided a route to capturing genes and making them available for biotechnology. It also laid the groundwork for the discovery of HIV some 12 years later."

Judge's Comment: "David Baltimore can be considered one of the pioneers of modern medicine. His far reaching mind traversed the established boundaries, leading to new approaches to disease detection, mechanism and potential treatments. Reverse transcriptase and cloning are just two breakthroughs he has pioneered."

www.bbe.caltech.edu

20 Robert Langer

David H. Koch Institute Professor, Massachusetts Institute of Technology, USA

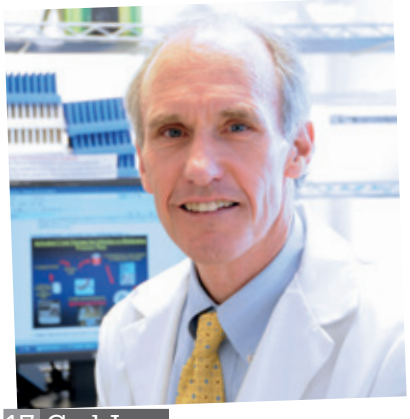
Considered one of the most prolific inventors in medicine, Robert has over 1080 issued and pending patents, which have been licensed or sublicensed to more 300 companies. Current research in his lab focuses on developing new ways to deliver drugs or engineer tissues using polymeric systems.

http://web.mit.edu/langerlab

19 Rino Rappuoli

Former Global Head of Research and Development for Novartis Vaccines

Rino was the Global Head of Research and Development for Novartis Vaccines before it was divested to GlaxoSmithKline in March 2015. He has authored over 600 research papers and has introduced a number of novel scientific concepts, with widespread impact on the vaccines industry, including genetic detoxification (1987), cellular microbiology (1996), reverse vaccinology (2000), and the pangenome (2005).



17 Carl June

Richard W. Vague Professor in Immunotherapy, Department of Pathology and Laboratory Medicine, University of Pennsylvania, USA

Carl is Director of the Center for Cellular Immunotherapies and an Investigator at the Abramson Family Cancer Research Institute, both located at the University of Pennsylvania. He maintains a research laboratory that studies various mechanisms of lymphocyte activation that relate to immune tolerance and adoptive immunotherapy for cancer and chronic infection. In 2011, his research team published findings which represented the first successful and sustained demonstration of the use of gene transfer therapy to treat cancer.

www.upenn.edu

16 Severin Schwan

Chief Executive Officer, Roche Group

Revenue: CHF 47.5 billion ($49.6 billion) (2014)

Employees: circa 88,500

After completing his studies at the University of Innsbruck in Austria, Severin joined the Roche Group in 1993 as a trainee in corporate finance. Thirteen years later, he was appointed CEO of Roche's Diagnostics Division and in 2008 he became CEO of the Roche Group.

www.roche.com

15 David Bentley

Vice President and Chief Scientist, Illumina

"It is a great pleasure and honor to reflect that, after graduating as a biochemist from Cambridge 35 years ago, I have spent the last 20 years back there, working on DNA," says David. "This echoes the tradition and history of Cambridge of course, with the work of Crick and Watson, Sanger and many other alumni that I have enjoyed meeting over the years. In 2015, my team has been working to sequence 100,000 genomes in partnership with Genomics England, the UK National Health Service."

www.illumina.com

14 Ruth McKernan

Chief Executive, Innovate UK

Ruth McKernan will begin her work at Innovate UK on May 1, 2015. Before this, she was Chief Scientific Officer of Pfizer's Neusentis Unit, which has funded groundbreaking work in regenerative medicine. Scientifically, Ruth is best known for her research in neuroscience on ligand-gated ion channels with over 130 publications and 15 patents. She has also won awards for science writing and her first book for non-scientists, Billy's Halo, was short-listed for the 2007 MIND awards.
https://www.gov.uk/government/organisations/innovate-uk

13 Kenneth C. Frazier

Chairman of the Board and Chief Executive Officer, Merck & Co.
Revenue: $42.2 billion (2013)
Employees: circa 76,000

Having joined Merck & Co. in 1992 as general counsel, Ken held a range of senior management positions before snagging the top spot in 2011. Despite his background as a lawyer, Ken is credited with prioritizing R&D at the company. He also sits on the boards of PhRMA, Weill Cornell Medical College and Graduate School of Medical Sciences, Exxon Mobil Corporation, The Pennsylvania State University and Cornerstone Christian Academy in Philadelphia.
www.merck.com

12 Carsten Brockmeyer

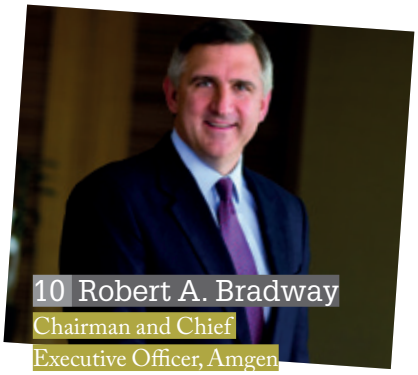
Chief Executive Officer, Formycon AG

"For me, my greatest achievement is the development of Binocrit (epoetin alfa), the world's first complex biosimilar anemia drug," says Carsten. "I designed the strategy and led the cross-functional team, which succeeded by applying quality-by-design principles for biosimilars from R&D to commercialization. It resulted in the highly successful launch of Binocrit and I think it's a major game changer in global access to quality medicines."
www.formycon.com

11 John Talley

Chief Scientific Officer, Euclises Pharmaceuticals

John is a co-inventor of eight marketed drugs, with several more still in development. He is a named inventor on more than 200 issued US drug patents and has been honored with the prestigious PhRMA Discoverers Award. "The thing that has given me the greatest satisfaction is seeing medications I've discovered helping patients with arthritic diseases and HIV/AIDS," he says.
www.euclises.com



10 Robert A. Bradway

Chairman and Chief Executive Officer, Amgen
Revenue: $20.1 billion (2014)
Employees: circa 18,000

In 2006, Robert joined Amgen as Vice President, Operations Strategy. He was appointed to the Amgen Board of Directors in October 2011, and became Chairman in January 2013 and CEO in May 2012. Before Amgen, he was a managing director at Morgan Stanley in London where he held responsibility for the firm's banking department and corporate finance activities in Europe.

www.amgen.com

9 Robin Robinson

Director of Biomedical Advanced Research and Development Authority; Deputy Assistant Secretary for Preparedness & Response, US Department of Health and Human Services

Robin was recruited from the vaccine industry in May 2004 to establish a Manhattan-like program to implement strategic plans and policies for medical countermeasures. During his time in the pharma industry, he developed patented platform vaccine technologies including virus-like particles and subunit protein vaccines for human pathogens.

www.phe.gov

8 Pascal Soriot

Executive Director and Chief Executive Officer, AstraZeneca
Revenue: $26.1 billion (2014)
Employees: circa 50,000

Judge's comment: "Pascal Soriot is an archetype of the transformative chief executive. Few such inarguable examples exist of a leader who moves into a struggling, large global firm and, in less than two years, produces such dramatic and positive change. Before Soriot's tenure, financial analysts considered AstraZeneca as one of the 'dogs' of the global pharmaceutical industry. Today, AstraZeneca's pipeline is rated as one of the top three in the industry and stock is up 65 percent. Soriot led the company in a successful defense against acquisition by Pfizer - no easy feat, and an unthinkable outcome before this transformation."

www.astrazeneca.com

7 Peter Seeberger

Director at the Max-Planck Institute for Colloids and Interfaces, and Professor, Free University of Berlin, Germany

Peter's research covers a broad range of topics from engineering to immunology, and has been documented in over 380 peer-reviewed journal articles, more than 35 patents, and more than 680 invited lectures. He says, "One of achievements I'm most proud of is the development of the automated glycan assembly platform. This is the basis for the creation of novel fully synthetic carbohydrate vaccines against malaria and bacterial infections, as well as diagnostics to rapidly and reliably detect infections, allergies and auto-immune diseases."

www.mpikg.mpg.de

6 Raman Singh

President, Mundipharma Asia Pacific, Latin America, Middle East and Africa

Raman oversees all aspects of the Mundipharma business – a leader in pain management – across his territories, which operate as a network of independent companies. Prior to this appointment, Raman was the Vice President of Commercial Operations for Emerging Markets at GlaxoSmithKline. A nominator commented that Raman is "putting patients at the center of healthcare business."

www.mundipharma.com

4 Arthur D. Levinson

Chief Executive Officer, Calico, USA

Arthur ('Art') Levinson got his start in the industry as a research scientist at Genentech in 1980, and moved up through the ranks to eventually become CEO in 1995, where he stayed until April 2009. Today, he heads up R&D biotech company Calico, which was established by Google in 2013, with an ambitious goal to "tackle aging" with "interventions that enable people to lead longer and healthier lives." He also serves as Chairman of the Board of Apple. He has authored or co-authored more than 80 scientific articles, holds 11 US patents and has received numerous awards, including the US National Medal of Technology and Innovation.

www.calicolabs.com

5 Heather Bresch

Chief Executive Officer, Mylan
Revenue: $7.7 billion (2014)
Employees: circa 30,000

Heather is responsible for a workforce of approximately 30,000, a manufacturing footprint comprising nearly 40 facilities, and a portfolio of roughly 1,400 products sold in about 145 countries and territories. She aims to lead the next chapter of Mylan's growth by transforming it from a pharmaceutical company into a healthcare company. She is also a leading advocate for global competitiveness and global quality standards — she was instrumental in the development of the US Generic Drug User Fee Act.

www.mylan.com

3 Sir Andrew Witty

Chief Executive Officer, GlaxoSmithKline, UK
Revenue: $34.4 billion (2014)
Employees: circa 100,000

Sir Andrew graduated from the University of Nottingham, UK, in 1985, with a BA in Economics, and joined GlaxoSmithKline the same year. Over the years, he worked in various roles in the UK, South Africa, the USA and Singapore, and in 2003, he was appointed President of GSK Europe and joined GSK's Corporate Executive Team, before beating several other industry heavyweights to the CEO spot in 2008.

He still maintains close ties with the University of Nottingham and in 2013 was installed as the seventh Chancellor of the university – something he has previously described as a "super honor" and "great privilege". He is also a Member of the UK Prime Minister's Business Advisory Group and Member of the Global Health Innovation Advisory Board, Imperial College London, and past President of the European Federation of Pharmaceutical Industries and Associations (EFPIA).

In 2003, he was awarded the Public Service Medal by the Government of Singapore and in August 2012 he was also awarded the Public Service Star. In the 2012 New Year Honors list, he was awarded a Knighthood for services to the economy and to the UK pharmaceutical industry.

www.gsk.com

2 Kiran Mazumdar-Shaw

Chairperson and Managing Director of Biocon, India

From a tiny start-up company launched in 1978 with seed funds of Rs 10,000, Kiran has grown Biocon into a leading biotechnology company

You started out as a Master Brewer; how did you end up a biopharma entrepreneur? I found that, as a woman, I wasn't very welcome in the brewing fraternity. When I was looking for a job people actually told me that it was high risk for them to hire a woman because it will be difficult for their all-male management to deal with me. I wanted to prove people wrong about the perceptions they had about hiring a woman. An opportunity arose in an entrepreneurial role to set up a biotechnology company in India, and the rest is history!

How have things changed for women in science today? Today, things are very different and there has been a huge acceptance of women all around – in the workplace, as professionals, as entrepreneurs, and as business leaders. For example, eight of the top ten banks in India are headed by women.

What excites you about your work? The kind of drugs we are developing are very exciting. For example, we have an oral insulin under development, which could be a huge game changer in diabetes management. I'm also really excited about our work with monoclonal antibodies, and the whole area of immunology. Depending on the success of our programs we could be a very, very different company in 5 years' time.

What have been your biggest impacts so far? Biocon has already made a huge difference to diabetics through its affordable insulin, not just in India but across the world because it is available in many countries. We also have a number of other biosimilars in the pipeline. Recently we introduced the world's most affordable trastuzumab, for breast cancer. We have already taken two novel biologics from lab to market, one for head and neck cancer and other for autoimmune condition, psoriasis. I am personally very excited to be able to develop these affordable therapies for chronic diseases like diabetes, cancer and autoimmune disease, that enable greater access to otherwise expensive treatments, thus impacting global healthcare.

www.biocon.com

Photo: NIAID/NIH

1 Anthony Fauci

Director, National Institute of Allergy and Infectious Diseases, USA

Role

Anthony has served as Director of NIAID for over 30 years and oversees an extensive portfolio of research to prevent, diagnose and treat infectious diseases, including HIV/AIDS and other sexually transmitted infections, influenza, tuberculosis, malaria and potential agents of bioterrorism. He is also the long-time chief of the NIAID Laboratory of Immunoregulation, and serves as one of the key advisors to the White House and Department of Health and Human Services on global AIDS issues, and on initiatives to bolster medical and public health preparedness against emerging infectious disease threats. He has been instrumental in US efforts to fight the ongoing Ebola outbreak in West Africa, and quell public panic over the handful of cases in the US. Still regularly treating patients despite his heavy workload, he recently helped treat a US healthcare worker who contracted Ebola in Sierra Leone.

Research

Anthony has made huge contributions to basic and clinical research on the pathogenesis and treatment of immune-mediated and infectious disease. Achievements:

- Helped pioneer the field of human immunoregulation by making important basic scientific observations that underpin the current understanding of the regulation of the human immune response.
- Developed effective therapies for formerly fatal inflammatory and immune-mediated diseases such as polyarteritis nodosa, granulomatosis with polyangiitis (formerly Wegener's granulomatosis), and lymphomatoid granulomatosis.
- Developed highly effective strategies for the therapy of patients living with HIV/AIDS.
- Continues to devote much of his research time to identifying the nature of the immunopathogenic mechanisms of HIV infection and the scope of the body's immune responses to HIV.

Selected Awards

- Presidential Medal of Freedom
- National Medal of Science
- George M. Kober Medal of the Association of American Physicians
- Mary Woodard Lasker Award for Public Service
- Albany Medical Center Prize in Medicine and Biomedical Research
- Robert Koch Gold Medal
- Prince Mahidol Award
- 38 honorary doctoral degrees from universities in the US and abroad.

Judge's comment "Dr. Fauci's work with infectious diseases, both in the US and in the developing world, has saved millions of lives. His work demonstrates that all sectors of society are important, and that work with under-represented populations can have truly amazing outcomes."

www.niaid.nih.gov

Glyco-Pioneer

Mass spectrometry's ever-increasing resolution has placed it at the forefront of glycan analysis. In this second article of a two-part series, we call upon the expertise of Jasna Peter-Katalinić – a forerunner in the field based at the University of Rijeka in Croatia – to understand the challenges, assess the breakthroughs, and discuss the impact on the biopharma market.

How did you get started in glycobiology?

I have been active in the field for about 35 years. My first glycan-centric project investigated the role of breastmilk oligosaccharides in the immunity of newborns. At that time, very little was known about the glycosylation of proteins beyond a few well-known examples. But it soon became apparent that most proteins are glycosylated during their lifecycle, and this plays a very important role in numerous physiological processes. Indeed, there are a whole range of rare congenital diseases associated with disordered glycosylation, many with severe symptoms.

What do you find so fascinating about the area?

You certainly have to be passionate to stay in an area for so long! When we started, many years ago, we had no precise idea where we were going. We were led by scientific curiosity and the opportunities that we could see in our exploratory experimental work. We formed collaborations with virologists, clinicians and many other life scientists. That crosstalk was inspiring. When I first presented our data at conferences, there was a big gap between people who developed instruments, physicists, chemists and so on. Fortunately, the gap has now largely closed. I have no trouble transmitting my enthusiasm for the subject to my colleagues and students – there is so much potential for the future.

How does glycosylation affect protein therapeutics?

Glycosylation is crucial to the activity of therapeutic monoclonal antibodies (mAbs) and there has been a lot of effort over the past 20 years to identify how glycosylation in the Fc portion of the mAb can influence activity, improve pharmacological efficiency and decrease toxicity. The question now is whether it is possible to replace glycans with other chemical groups that can fulfill the same function but are less complex in their molecular structure, making bioprocessing easier.

The classical IgG molecule is made up of heavy and light chains, linked by disulfide bridges. The two subunits are both glycosylated at a single natural glycosylation site - asparagine 297 - but the glycan group can consist of longer or shorter chains. Researchers are looking at whether the shorter chains are sufficient to keep the conformation of the antibody in its active form and, if so, whether they can be replaced by engineered molecules. We also need to know what other aspects are crucial to maintain conformation – shape, charge, polarity, hydration, and so on.

Engineering of glycosylation sites appears to hold great promise...

Absolutely. The lifetime of a mAb in the body when administrated as a drug is also crucial. If we add more glycosylation sites by molecular engineering, we could increase lifetime, and the dosage could be reduced. Reducing dosage is always a positive in terms of potential side effects and pricing.

Engineering of new glycosylation sites means introducing a specific sequence of amino acids – a consensus sequence – for N-glycosylation, which is achieved by molecular engineering; essentially, we alter the genetic code that forms the blueprint for the protein. Accurate analytical techniques are extremely important for quality control of engineered glycoproteins to confirm both the glycosylation site and the structure of the attached glycan.

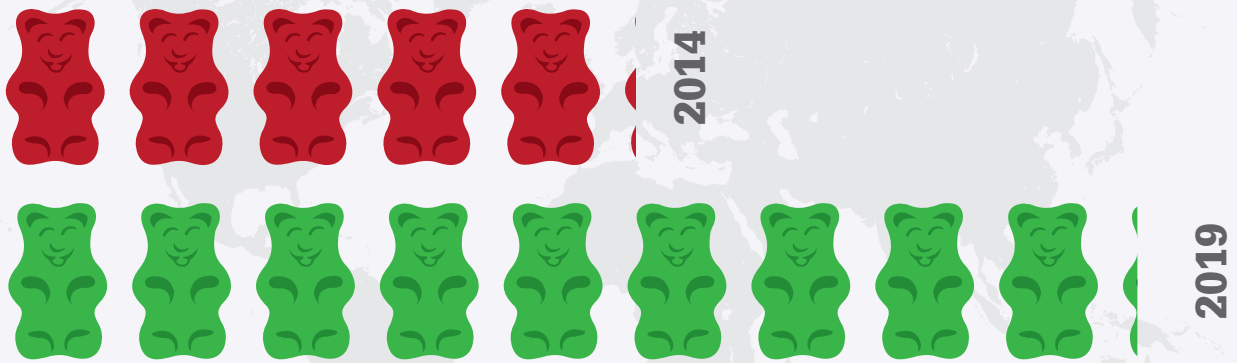
How have mass spectrometry techniques for glycan analysis evolved?

In my view, mass spectrometry is the crucial method for quality control of glycoproteins. There are several approaches - some focused on high throughput analysis for monitoring profiles and some that are trying to clarify all structural aspects of these complex molecules.

Mass spectrometry is now in very good shape to answer most of the questions we have about glycosylation. Resolution has increased dramatically over the years and, put simply, higher resolution means better results. For example, Orbitrap technology allows you to collect fragment ions from the non-reducing/sugar end of the molecule and also from the residual peptides, so you can reconstruct the complete structure in a short timeframe.

What challenges remain?

With such a high level of instrumentation, good glyco-scientists can solve most structural problems involving N-glycans. The question of O-glycosylation is much more complex. There are no general



The global glycomics market is expected to reach $928.11 million by 2019 from $512.38 million in 2014.

enzyme systems to cleave O-glycans from the protein, so glycobiology researchers developed strategies such as the SimpleCell method, in which cell lines are engineered to generate only the core/truncated version of the O-glycan. Such strategies allow discovery of all O-glycosylation sites of a protein (and there can be more than 100).

There is also an unmet need in analytical software. There is no software currently in use that can take the raw data from mass spectrometry and interpret de-novo data. Now that mAbs are such a big segment of the market, and software can be more easily adapted to different instruments, this looks likely to change in the near future.

What are your main career highlights?

Several times, I've been involved with the inception of an entirely new area of research. Early in my career, I remember experiments that led to the discovery of a new type of modification on an embryonic antigen, in collaboration with an eminent leader in glycobiology research – Professor Saul Roseman – which led to a host of new theories. Another highlight was discovering new types of sialyation found in starfish (sea stars) that totally changed the biochemical theories of that time – they literally had to re-write chapters of some biochemistry textbooks. Some of my most cited papers are those where, in collaboration with other groups, we defined some of the key sites for glycoengineering – O-mannosylation and O-fucosylation sites in large molecules. It was like finding a needle in a haystack, but it is a very satisfying to know that we were able to provide a solid molecular basis for functional studies.

However, I consider my greatest achievement to be the scientific and professional success of my graduate students, some of whom are now professors at their own universities or laboratory leaders in other institutions; many still work on topics they were introduced to in my lab.

What are you working on right now?

As well as N- and O-linked glycans, there are another type of sugars which intrigue me – glycosaminoglycans. They are major ingredients of the extracellular matrix and are involved in many human diseases, from rare inherited metabolic disorders like mucopolysaccharidosis to common diseases of old age like osteoarthritis. Researchers are now looking at potential drugs made up of sulfated oligosaccharides, which is a tough analytical challenge – if you are not careful, you can easily lose the sulfate during ionization or fragmentation. In addition, we do not know what size of oligosaccharides are functional. By combining capillary electrophoresis, chromatography and mass spectrometry, we hope to find the answers.

At the moment, the Department of Biotechnology at the University of Rijeka is in the process of implementing new equipment, so that is taking up a lot of my attention. I expect to establish several options for glycosylation analysis, including an ion mobility mass spectrometer and simpler machines for routine analysis. We hope eventually to add the highest resolution mass spectrometry machines – Orbitraps (Thermo Scientific™ Orbitrap™ based high resolution accurate mass spectrometers) and ion cyclotron resonance (ICR) systems – to maintain our position as the best-equipped laboratory for mass spectrometry in Croatia.

How can we push the field forward?

Large-scale collaboration is crucial for integrating our knowledge, from math and physics to biology and medicine. Our group is looking for collaborations in medicinal chemistry and drug development, so if any readers are interested, please get in touch!

Jasna Peter-Katalinić is a professor in the Department of Biotechnology at the University of Rijeka, Croatia.

New for 2015:
Pharma Logistics Zone (Hall N4)
Russian Pavilion (in Hall E1)

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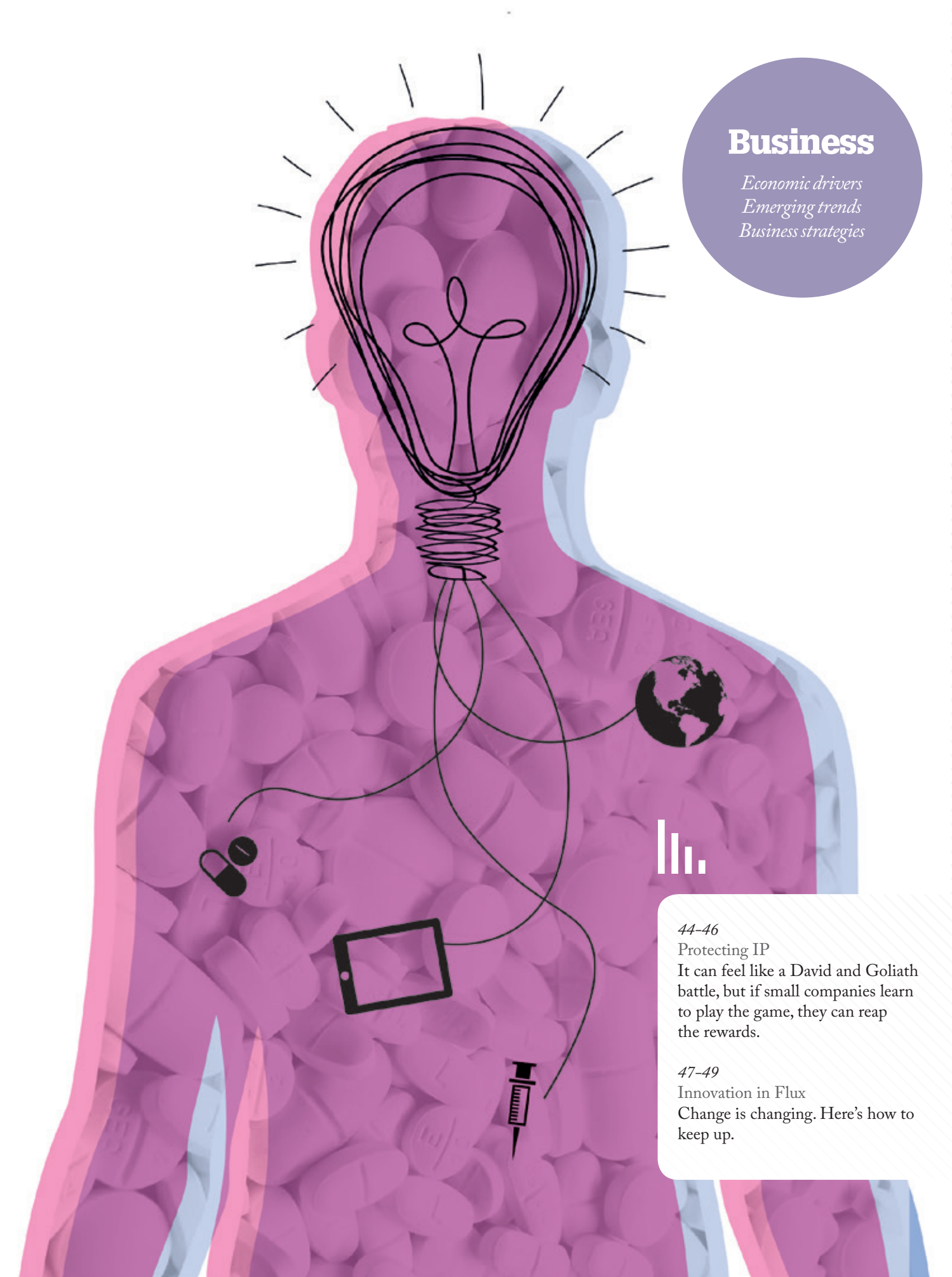


Business

Economic drivers
Emerging trends
Business strategies

Protecting Intellectual Property

When it comes to IP, large companies regularly trample over the rights of smaller firms. But by playing the game, it is possible for a small company to make IP a core revenue stream.

By Mark Bloomfield

Innovation is the lifeblood of our industry and of the patenting system. And yet in their day-to-day business, larger companies consistently adopt a very aggressive policy when dealing with intellectual property (IP) assets of smaller firms. This policy is not easy to detect or make public, because it generally consists of taking no action at all: simply ignoring the IP of smaller firms wherever possible.

This is bad for small companies in all sectors, but in life sciences, therapeutics and med-tech, it's also bad for the patient and public health. Disrespect for IP discourages further innovation; simply put, small companies do not reap what they have sown. By robbing or ignoring the IP of smaller firms, and so removing the incentives for the creation of these innovator companies, the large players stifle future creators and transformers of original and innovative research.

Might is right

How does this disregard for the IP positions of smaller firms typically manifest itself in practice? Imagine you are a small company that becomes aware of a larger firm using your patented technologies without any compensation or acknowledgement. You naturally

contact the big player and make your case. What happens next? Absolutely nothing – no comment... no response at all. While this is unlikely to be an explicit company policy, there seems to be an implicit understanding amongst all large companies that this is the first line of defense.

Assuming you don't give up, the executive you contacted will eventually pass your complaint on to the IP, legal or business development department., who will proceed to give you answers to questions that you never asked, dragging the process out even further. By now, the process may have already taken years.

When the big company decides that it can't ignore you any longer, they will usually set up a phone conference. Not surprisingly, the topics and arguments will nearly always be the same. The legal people from the big company will say:

- That they think that your IP position is weak.
- That you may have IP, but that it does not really apply to what they are doing.
- That your claims are not really valid and will be hard to enforce.
- In light of this, they see no reason to make a license agreement or to enter into a product supply agreement.

Of course, the small firm wouldn't be in this phone conference without thinking otherwise, and will argue that its IP position is strong and relevant to what the big firm is doing, and that an IP agreement is needed.

Everybody on the call is doing what she or he is paid for – the legal team rejecting all claims, the small firm insisting on its rights. But as the call progresses, when some of the technical and business details have finally been touched and it becomes obvious that the IP in question is at least partially relevant, will the big company move forward and propose to discuss a license agreement? In my experience, only in about one out of 50 cases.

In all other cases the legal department of the big firm will tell you that they continue to disagree with your position, but that it is your right to go to court. For many small start-ups, the cost and risk of having a multi-million Euro/Dollar lawsuit is prohibitive. So the small firm just walks away from the table and keeps silent. And that is what the big firms expect.

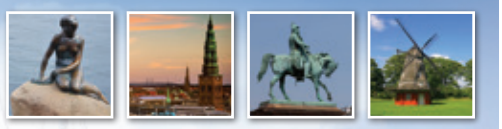
David and Goliath

Polyplus produces transfection reagents, which are used to bring nucleic acids and many other biomolecules into living cells. We are a very small company – just 25 people currently. Polyplus owns a number of patents and, in our core technology areas, we believe our IP position is very strong. Unusually for such a small company, Polyplus is very active in ensuring that our IP position leads to revenues, either in the form of license royalties or product purchases from Polyplus. We consider our IP position and respective revenues core areas of our business model. Accordingly, we put a lot of focus and as many resources as we can manage into this. We have one full-time employee dealing with IP, and the business development director and I spend a considerable part of our time on these issues. We also have two external lawyers working with us. All in all, we have the equivalent of about two and a half full-time people working on IP.

Now, let's assume there are three types of researchers using our technology without taking a license: (i) those who know about our technology and IP and use it nonetheless, (ii) those who know about our technology, but are not aware of our IP, and (iii) those who "invented" the technology themselves and know nothing about us. The third option is highly unlikely, as the technology is well

Rules of the Game

1. You need to make sure you have an attractive technology and a very solid IP position.
2. Put in place an IP strategy as early as possible – long before your product is even ready for marketing.
3. If your focus is science and technology, always consider finding others to commercialize it. You have to concentrate on what you are best at. Consider outsourcing everything else.
4. Aim for a minimum of two full-time employees working on IP issues, however small your headcount is.
5. It is very helpful to have senior level management with experience in big industry (but external consulting can fill the gap).
6. Always write a custom letter to a specific person in the organization, never use "one-size-fits-all", "to-whom-it-may-concern" standardized letters.
7. If you don't know where to start, go directly to the CEO or COO.
8. Make a realistic and flexible offer to potential customers, in line with your value proposition.
9. Always remain very polite, calm and professional – however churned up your inner emotions may get.



known to everybody in the field. Those who are unaware of our IP position may make up 10 to 20 percent, but the great majority of researchers use it knowingly, hoping that they are not held responsible.

Over the years we have established a routine but flexible process for handling IP issues. It all starts with looking at publications, patent applications and other documents in the public domain, and visiting conferences to see posters and listen to oral presentations. Why? To detect research results that may have used our patented technologies. The second step is to review these research projects in-house and evaluate whether the scientists have used our commercial products – which are supplied with an implied license for use in transfection applications – and decide whether to write to the researchers or company leadership, to ask what technology or potentially counterfeit product they may have used. If so, we develop a well researched, well-written and personal letter.

Polyplus started going after our IP and trying to reach license or supply agreements in 2009. Since then, we have signed about 20 license and 10 supply agreements, resulting in about $4 million paid license fees and $1 million in sales. A significant revenue stream for a small company, but only a small proportion of the maximum market potential, which is in the order of $17 million per year.

Playing the game

If you enter a poker game with $100 in your pocket and the other players come in with $1 million, you shouldn't complain about losing – whatever your cards may be. Or to put it another way, if you are a middleweight boxer stepping into the ring with a heavyweight, you should not be surprised to lose – painfully.

How can a small company negotiate with one of the big players about IP, without being KO'd? First, it is essential to be realistic about the value you can achieve or help create value for your potential licensee. As a general rule: never ask for royalties in the final marketed products, unless you have a very rare and strong IP position and value proposition. I would recommend to go first for a research license and only afterwards for a commercial license. In addition, it makes life much easier if you go for a one-time payment. An alternative would be to go for an upfront payment plus yearly royalties to be paid at the beginning of each year. Always remember that cash is king. Above all, be pragmatic, flexible and keep the process going all the time.

"Larger companies consistently adopt a very aggressive policy when dealing with IP assets of smaller firms..."

We are not children any more. We all know that the world is not divided into "the good guys" in the small companies against "the bad guys" in the big companies. Instead, we need to understand the structure of the game and learn to play to our advantage.

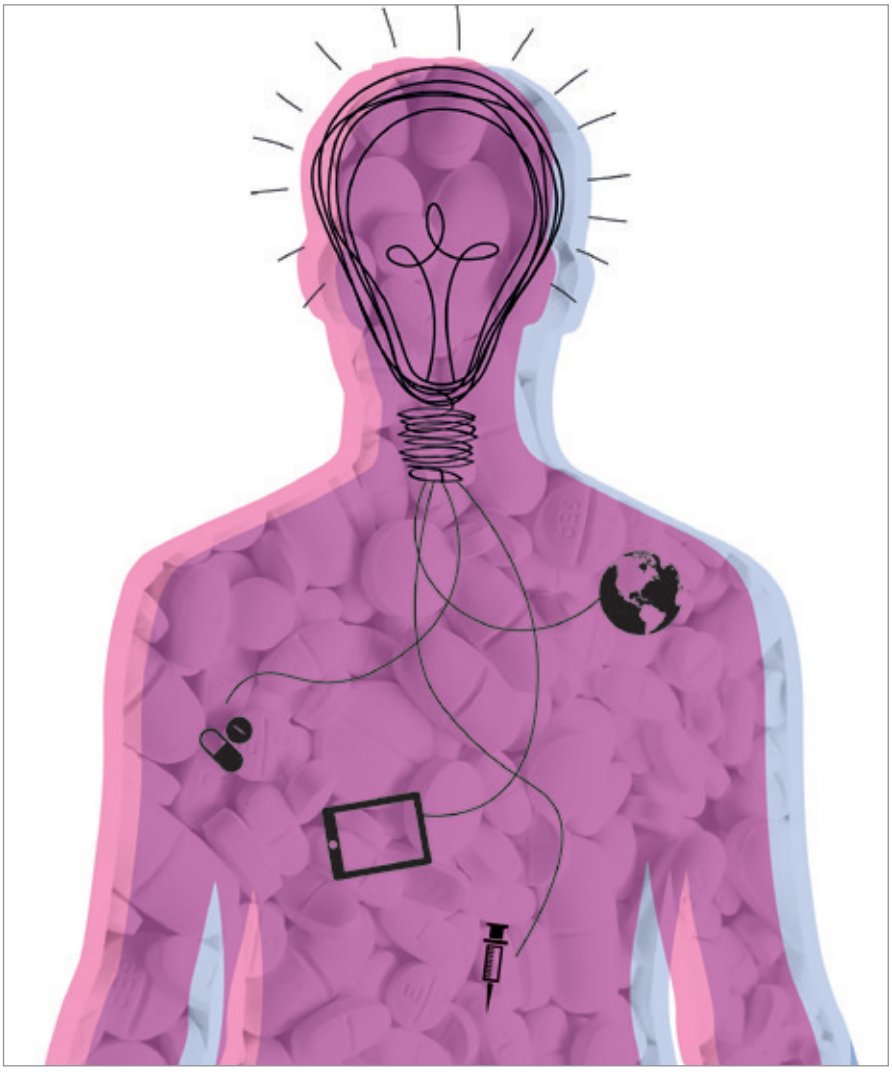
Mark Bloomfield is CEO of Polyplus-transfection SA, Illkirch, France.

Mark Bloomfield originally spoke with Marcus Lippold, Editor in Chief, Life-Sciences-Europe.com – to read the interview in full, visit tmm.txp.to/0415/IP

Innovation in Flux

Over 70 percent of pharma leaders admit their business relies heavily on fading revenue streams – but how can we promote much-needed innovation in the current climate of uncertainty?

By Jon Platt



The world used to be a predictable place. From the dawn of human history up until around 1980, it could be argued that the world – and technology specifically – changed at a more or less steady and easily anticipated rate. Occasionally accelerated by large-scale environmental or human events, or disruptive breakthroughs like steam power, electricity or atomic energy, businesses could, nonetheless, place strategic bets on what would happen next.

As the pharmaceutical industry became established, there arose a clear need for long-term strategic thinking and investment, but it was still acceptable to take 15 years to get a new drug to market, because the clinical need would likely still be there when it finally launched. Pre-1980s, innovation was (for the most part) about gradual evolution rather than taking a leap into something new.

Around 1980, we started to see the velocity of change increase exponentially, driven by accelerating globalization and digital technology. In the pharmaceutical industry this was the beginning of biotech-mania, during which many traditional big players were only able to keep up with smaller, entrepreneurial start-ups through a frenzy of expensive acquisitions. Smaller players in turn lacked the cash and global reach to conduct large-scale drug trials and carry out global marketing. At this time, there was an increasing proliferation of future-gazing, as the industry tried to make sense of where the world was heading.

Jumping ahead to the collapse of Lehmann Brothers and beyond, we find ourselves living in a new age; a world of chaotic change, with technology advancing by seemingly random leaps, innovation becoming increasingly discontinuous, and global stability under threat. It is an age when old certainties die, with knock-on effects on apparently unrelated industries and institutions.

No longer is it enough to just keep a wary eye on competitors in your own sector; change now comes from anywhere and at any time. For the CEO, rigorous analysis is no longer enough. Moving quickly won't help you when the goal posts keep shifting. More and more, leaders must possess skills of imagination, creativity and comfort with uncertainty.

What next?

How can we plan for the future? And how prepared is the pharmaceutical industry to adapt? Recent research by ?What If! revealed that 48 percent of pharma leaders say their assumed

"No longer is it enough to just keep a wary eye on competitors – change now comes from anywhere and at any time."

innovation pipeline has the greatest influence on the market's perception of their company's value. Despite this, only 38 percent are very satisfied with their current pipeline. More concerning still, almost three quarters (72 percent) believe their business model relies too heavily on fading revenue streams. And despite this clear need to innovate, almost two thirds of leaders (64 percent) say it's almost impossible to gain support to test new ideas.

So, what can pharma leaders do to embrace this age of chaotic change and future-proof their organizations? No one strategy can guarantee success, but four key tenets can help companies navigate times of uncertainty.

1. Have a heart

Rather than trying to guess what future technologies might emerge, make sure you anchor your development strategy to an enduring emotional customer need.

When exploring the human needs around advanced breast cancer for example, we hear again and again that being able to continue to 'feel like a woman and a mother' mattered more to patients than many of the clinical signifiers of disease. A smart company would explicitly build 'feel like a woman and a mother' into the goals of treatment alongside a more technical goal such as 'increase progression-free survival by X percent'.

2. Bet on the trend, and against it

Just a few years ago the mobile phone industry seemed to be on a certain and inevitable path towards ever-smaller devices. Who then would have predicted that Apple would this year announce its biggest ever iPhone alongside its most compact product to date; the Apple Watch. In other words, the trend continued but also took a dramatic U-turn as content streaming demanded bigger screens.

The lesson here is that when your industry or category seems to be on any sort of definite path, be sure to place a side bet on the opposite happening.

3. Form bonds

In an age of chaotic change, the innovation that will disrupt your business may already be here, just in a different area or another part of the world. Can you build new networks today with smart folks in other categories to help each other spot emerging disruptions outside your own business?

Find an issue you have in common, which will typically be wider than your own category concern. For example a question around 'what is the future of the home?' will draw in more collaborators from more fields than a narrower question such as 'what next for telemedicine?' Synthesizing possible futures from these conversations will allow you to place a number of large R&D bets on the future with confidence.

4. Hedge your bets

Humans are ingenious and our history suggests that if a problem matters enough, we will always find a solution. If your business is based on incremental improvements to existing solutions for a major problem, such as diabetes, be prepared for a major disruption that you can't see yet. Recent reports of a putative cure for type 1 diabetes in the press (1) suggest that this may in fact be quite close.

From a practical point of view, you must diversify away from a business model that has too many eggs in the same basket, embrace business model innovation, and be ready to accept the inevitable early, if a genuine disruption to your business appears.

Disruptive change is constantly threatening to sweep away the foundations on which many people have based their careers by introducing simpler, cheaper, faster solutions. And faced with a threat, the super-intelligent inhabitants of pharma companies can find myriad ways to form roadblocks, citing safety, regulation, lack of proof, their own deep expertise and so on, to create a thick layer of internal glue. A partial solution to this can be found in using organizational models of innovation that create a protected space for innovation where needed.

In pharma, more agile companies are increasingly moving towards creating specific innovation eco-systems with everything from people to funding to governance, at arm's length from the rest of the organization, particularly when attempting the business model innovation that will reshape their futures.

Change has changed. From travelling to the future along predictable straight lines to making breathtaking leaps to unimaginable new universes. If you are prepared for the journey, it could be the ride of your life!

Jon Platt is a Director at ?What If!, Europe.

Reference

1. *F.W. Pagliuca et al., "Generation of Functional Human Pancreatic β Cells In Vitro", Cell 159(2), 428–439 (2014).*

Pharma Leaders on Innovation

From a ?What If! survey of healthcare leaders in the UK.

Eye on the Prize

Sitting Down With... Dirk Sauer, Novartis' Global Head, Development Franchise Ophthalmics.

How did you get into the pharmaceutical industry?

I trained as a pharmacist and then did a PhD in pharmacology – specifically in neuroscience. Getting into the industry was largely by chance. I was hoping for a career in academia, but I saw that Ciba-Geigy was looking for a post doc researcher in the same area as my PhD – cerebellar ischemia – so I decided to apply.

And you ended up staying in the industry?

Yes. If you would have told me when I joined that I'd stay for more than 25 years and eventually end up in ophthalmology, I would not have believed you. My plan was to stay for two years and then go back to academia and become a professor. Clearly that didn't happen, but that's no bad thing! I very much enjoyed my time in research at Ciba-Geigy. We had very good people and excellent collaborations with academia. And we certainly had more funds than you have in academia; I was able to publish a lot. I stayed for nearly eight years in research and then moved into clinical.

What prompted that switch?

I had come to a point where I felt I wanted to do something different. I had been involved in clinical development programs and found it interesting. After all, that's why you join the pharmaceutical industry: to bring medication to patients for unserved medical needs.

What have you learnt about bringing drugs to market?

One thing you quickly learn is that it is great to have a good scientific hypothesis, but until you have proven it, you really have nothing! For example, back in the 1990s, we had a program directed at stroke. The theory was that the blocking of excitatory amino acid receptors could be a valid target. We were able to develop a compound that exactly matched the physiochemical properties, the receptor specificity, and the potency at the receptor. From a theoretical point of view it was ideal… but it didn't work.

I've also learnt that, if a drug fails, it's best that it fails early. You don't want to bring something all the way to Phase III trials, only to find out that it doesn't work.

How did you apply those early lessons?

The next clinical program I took on was focused on chronic neurodegenerative diseases - amyotrophic lateral sclerosis (ALS) was our lead indication because it is a very fast-progressing disease. Until we did this study, survival was the main outcome measure for ALS, but obviously survival is not a good measure for early-stage trials.

We came up with an idea of using a functional outcome scale instead, using each patient as his or her own control. We first recorded the functional scale over two or three months without treatment, and then started treatment and measured again. This gave us the power to do a study with fewer patients and a shorter duration. This is now a standard design for ALS trials, so although we didn't manage to release an ALS medication onto the market, it was a big achievement nevertheless.

At what point did you move to ophthalmology?

I went into ophthalmology in 2005. One of my colleagues moved within the company from neuroscience to the ophthalmology business unit and asked if I would like to join. It was a difficult decision because I didn't know much about ophthalmology, but I knew that person very well. I trusted him and knew I liked working with him. He offered me a position in project management that I couldn't resist.

"It is great to have a good scientific hypothesis, but until you have proven it, you really have nothing!"

What is your management style?

If you really want to know you should probably ask my direct reports! But I can tell you what I aim for: to give my people as much autonomy as possible, which is helped by the relatively flat decision structure that we have at Novartis. Of course, empowerment also comes with accountability. I try to personally select the key people whenever possible, so that I know I can trust them to run the show.

How do you motivate your team to gain success?

I think autonomy goes a long way. But giving as much positive feedback as possible is also vital. Recognize success, recognize good performance and recognize achievements. I can give a recent example: I have been working a lot over the past few years in Japan – the development team there has been working extra hard and has been very successful. So when I was at a conference in Tokyo, I took the whole development team out for dinner, thanked them in person for their work and gave them a little gift – not much, really, but such gestures can count for a lot. It's not only about giving people an extra bonus – although we do that as well – but also showing that you acknowledge good performance and success.

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