# The Future of the Biopharmaceutical Industry

June 2020

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# Introduction

## It's time to take a look at the biopharmaceutical industry from outside the box. How will it change for the future?

The field of biotherapeutics is constantly growing and evolving, seeing advancements in technology and standardization, topped with shifting international focuses influenced by the recent COVID-19 pandemic.

Over the following pages, we'll explore what could be in store for the industry over the next decade, including technologies, strategies and challenges yet to be overcome.

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## 5. Can the Biotech Industry Lead Diversity in STEM?

As part of this year's Biotech Week Boston, stakeholders from across biopharma and biotech gathered for An Evening of Diversity and Inclusion. Industry thought leaders took part in a panel discussion centering on the importance of Diversity and Inclusion (D&I) initiatives in the biotech industry and addressing the challenges of changing perspectives.


# DON'T WAIT FOR THE NEXT PANDEMIC

## Ensure that the speed of science outpaces the spread of disease

The BioXp™ 3200 system is a fully automated benchtop gene synthesis platform that can build gene fragments, clones, and variant libraries — including SARS-CoV-2 genome parts — in an overnight run, helping develop diagnostics, vaccines, and therapeutics. COVID-19 research grants are available.

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# Looking to 2030: Survey Report

How will the biotherapeutics industry change in the next decade?

# How will the biotherapeutics industry look in 2030?

In March 2020, we surveyed a huge set of life sciences professionals representing every aspect of the global industry about the changes they expect to see over the next decade. With 432 responses, the results reveal unique insights into where those most central to the industry think the biggest opportunities and challenges lie in global pharma and biotech, and how they expect it to look in 2030.

Here we have filtered out the overall results to look at the 206 responses from those working in biologics.

**Click on any of the graphics in this report to explore the data further.**

# Demographics

## Insights

The majority of respondents are based in Europe (57%) or North America (23%).

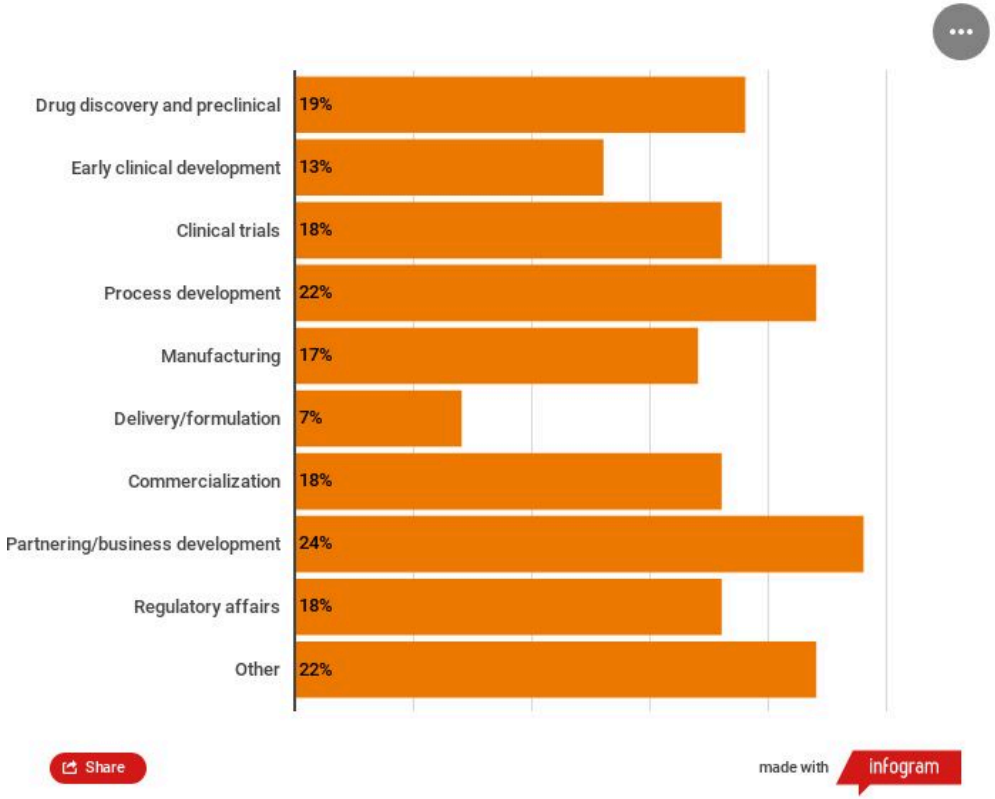
22% of respondents work for a consultancy or medical device company, followed by 18% at a pharmaceutical company.

Larger companies are best represented, with 52% of respondents representing organizations of 100 or more employees.

A majority of respondents work with medical devices (73%).

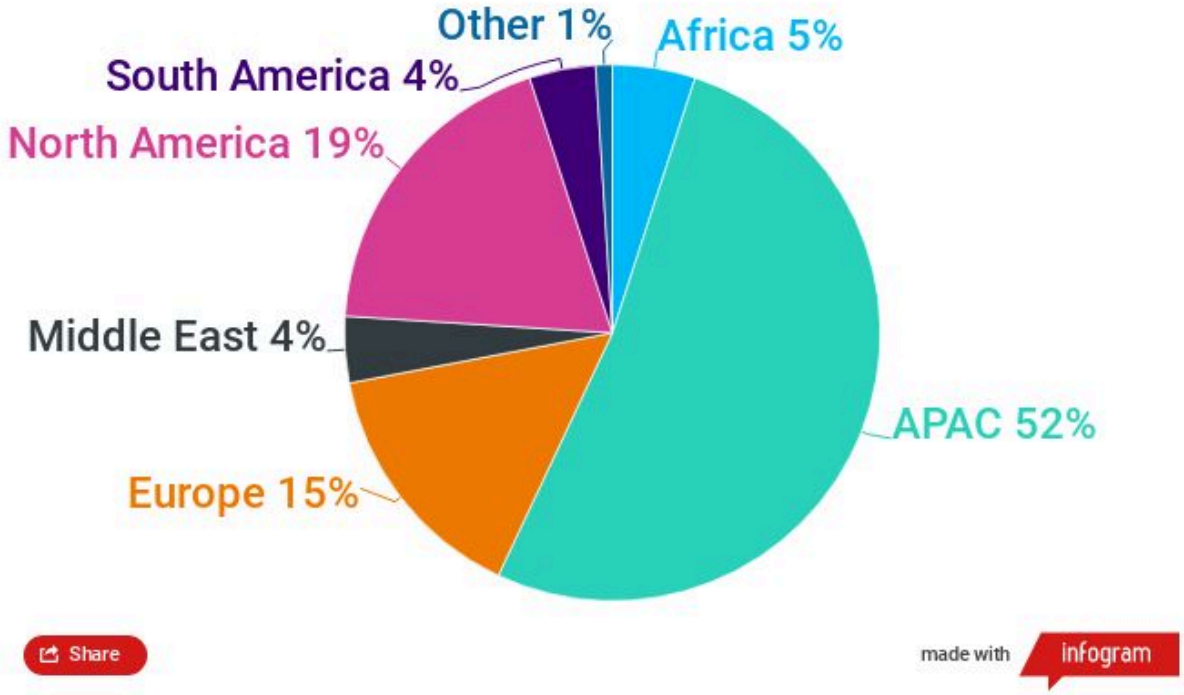
## Which department(s) do you work in?

Of all 432 respondents surveyed, 24% work in partnering/business development, followed by 19% in drug discovery and preclinical, followed by 18% in clinical trials, commercialization, and regulatory affairs.

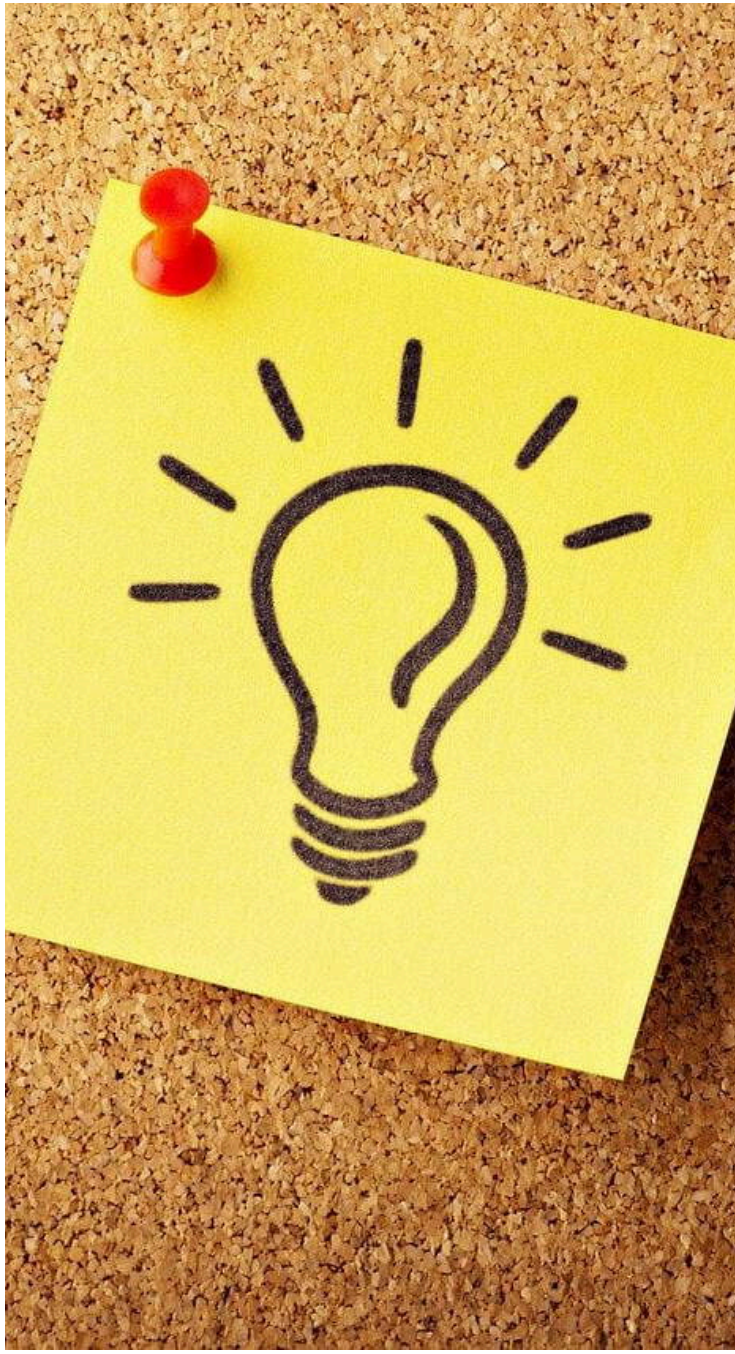


# Opportunities and Challenges

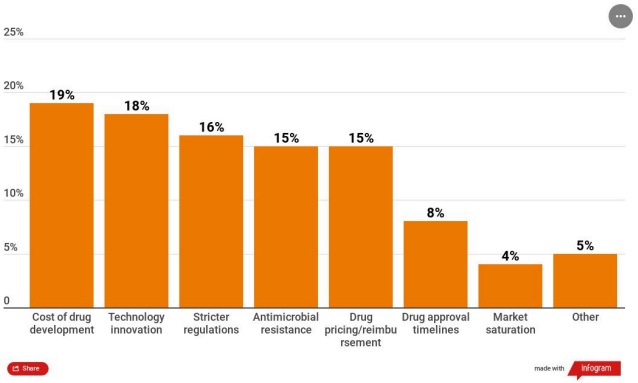
**Over half of all respondents predict Asia-Pacific will see the fastest growth in the life sciences industry in the next 10 years.**




"Which geographical area do you think will see the fastest growth in the life sciences industry in the next 10 years?"

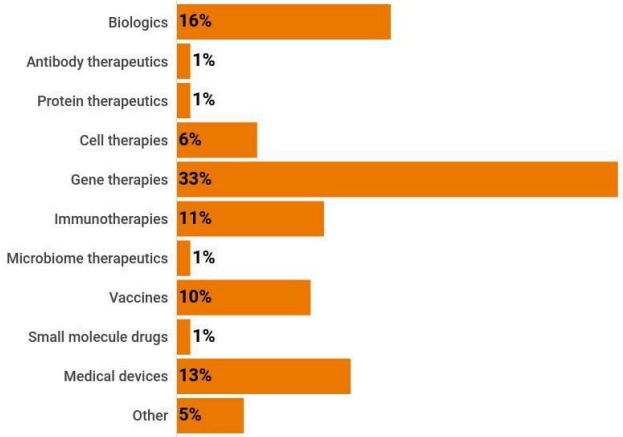


## The cost of drug development (19% of respondents) and technology innovation (18% of respondents) are seen as the biggest challenges facing life sciences in the next 10 years.




"Which therapeutic area do you think will see the fastest growth in the next 10 years?"

## Most respondents predict that gene therapies are the therapeutic area that will see the fastest growth in the next 10 years.




What do you think is the biggest challenge facing life sciences in the next 10 years?

**Click on a graphs to explore the data.**

**"In your opinion what has been the biggest breakthrough in life sciences in the last 10 years?" Selected responses.**

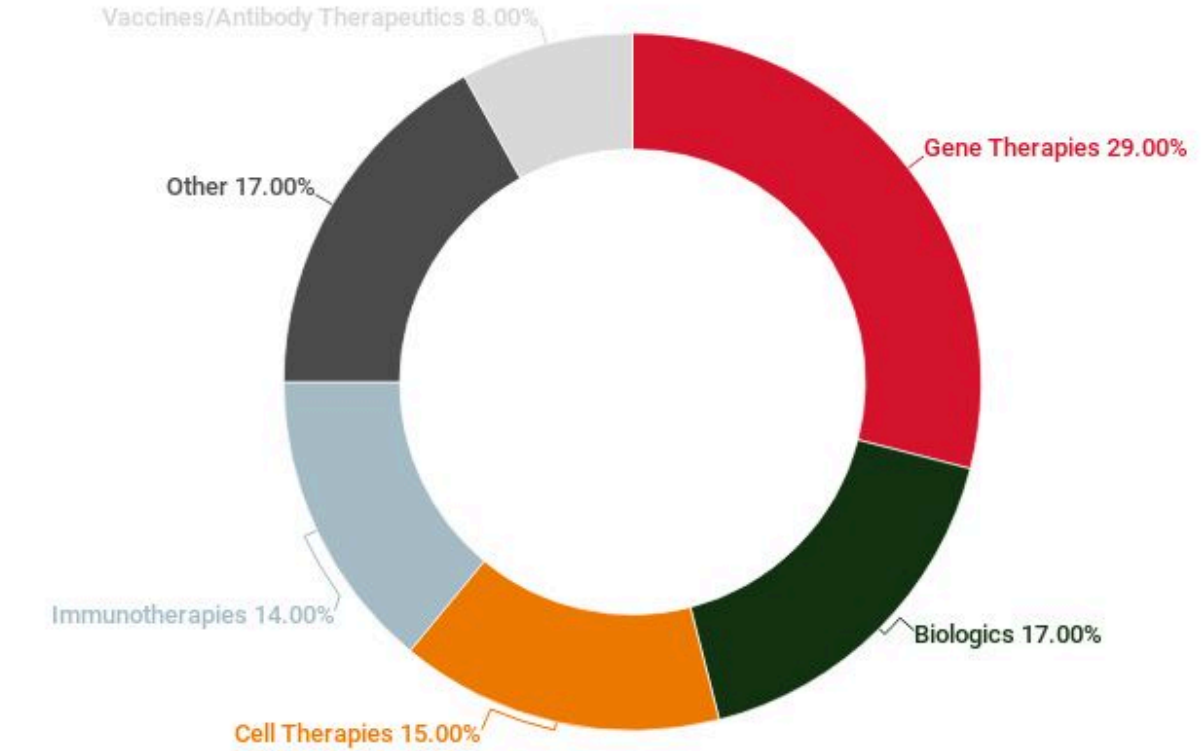
- Artificial intelligence
- Gene therapy
- Crispr
- Advances in immuno-therapy
- Affordability of treatments
- AI
- Biologics
- Biosimilars
- Biotechnology
- Cancer therapies
- Communication channels
- Digitalisation
- Drug-Device combination products
- Genome/Gene sequencing
- Globalization
- Immuno-oncology
- Oncology treatments
- Patient involvement
- Personalised medicines and medical devices
- RNA therapeutics
- Robotics and machine learning
- Stem cell research
- Targeted drug therapy

# Areas of Growth

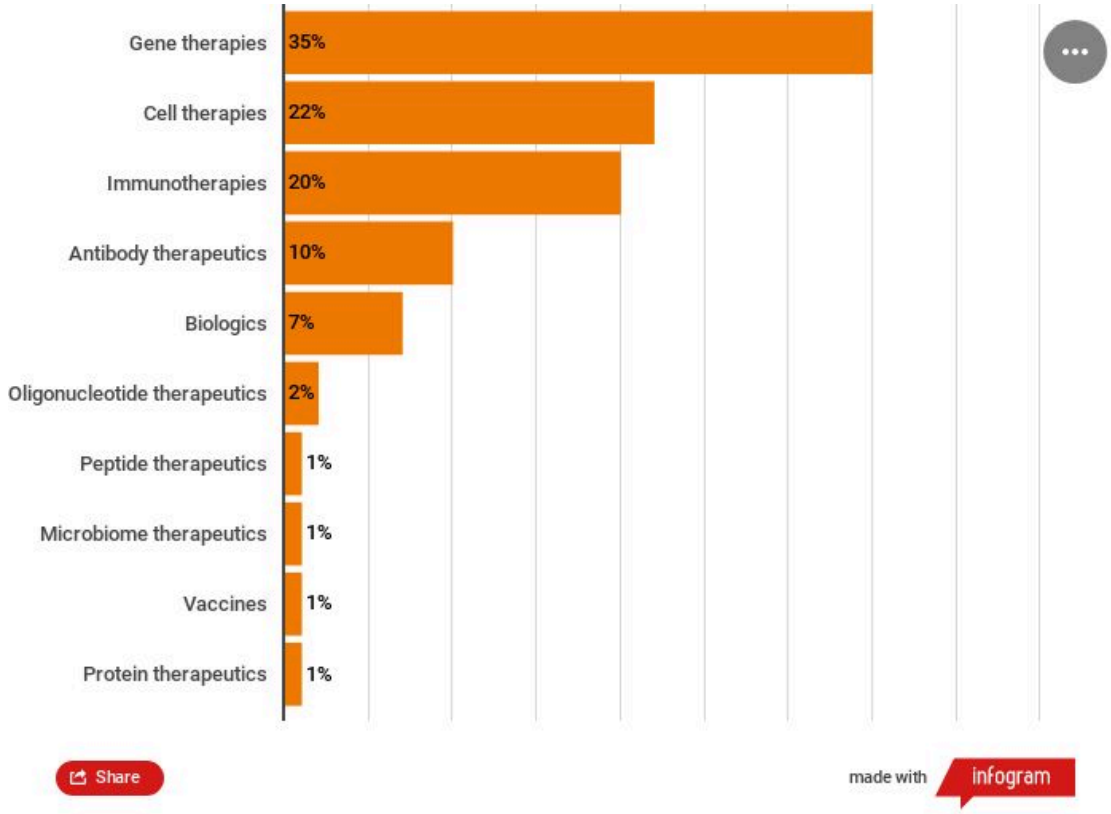
**29% of respondents think gene therapies will see the fastest growth in the next decade, followed by biologics, cell therapies, immunotherapies, vaccines and antibodies.**

Click on the graph to explore the data

"Which area do you think will see the fastest growth in the next 10 years?"



## 51% of respondents predict that oncology will improve the most over the next 10 years.



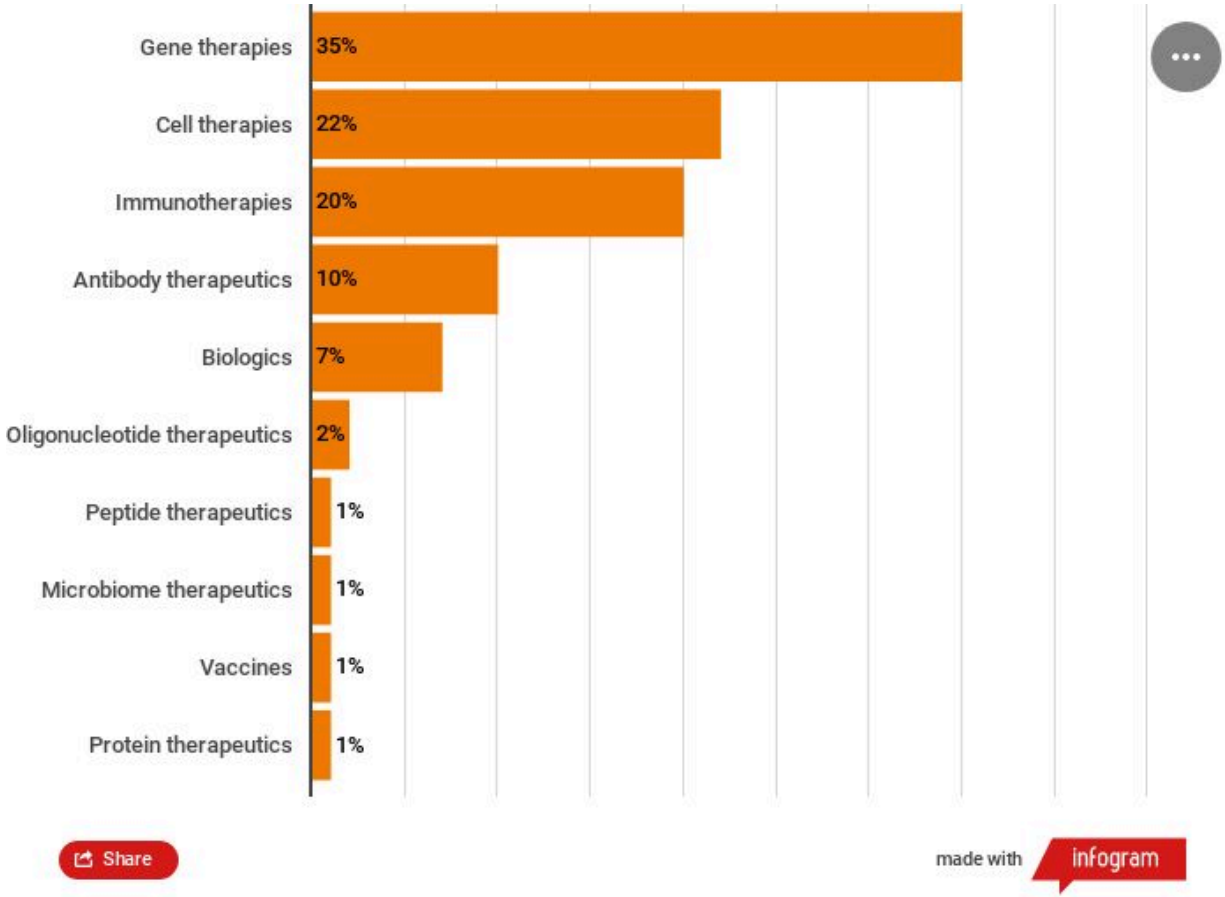

"In which of the following therapeutic areas do you think treatment will most improve in the next 10 years?"

# Oncology

**35% of respondents predict that the biggest advances in oncology will be in gene therapies, followed by cell therapies, immunotherapies, antibody therapeutics and biologics.**

Click on the graph to explore the data

"Where do you think we will see the biggest advances in oncology in the next 10 years?"

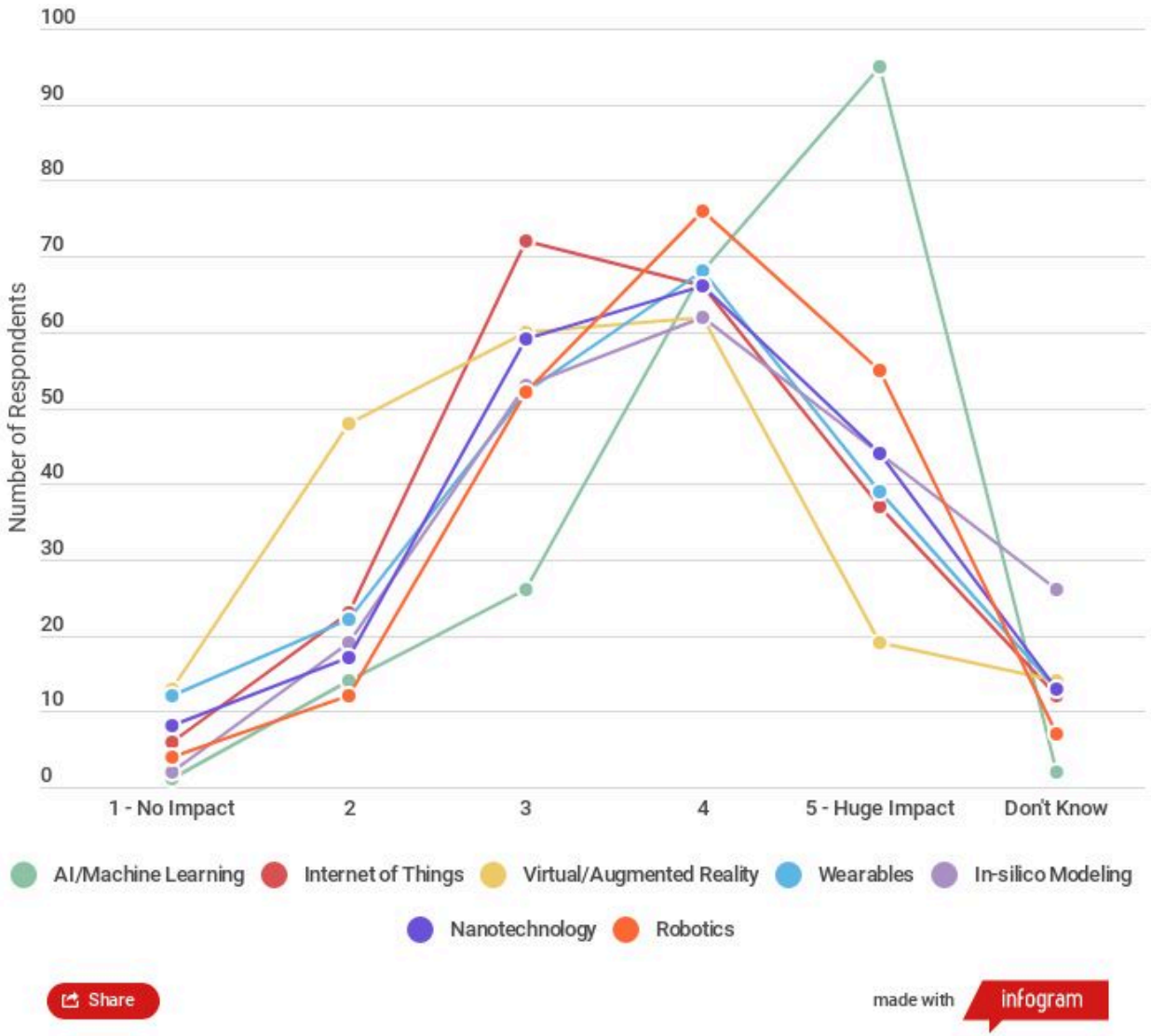


# Technology

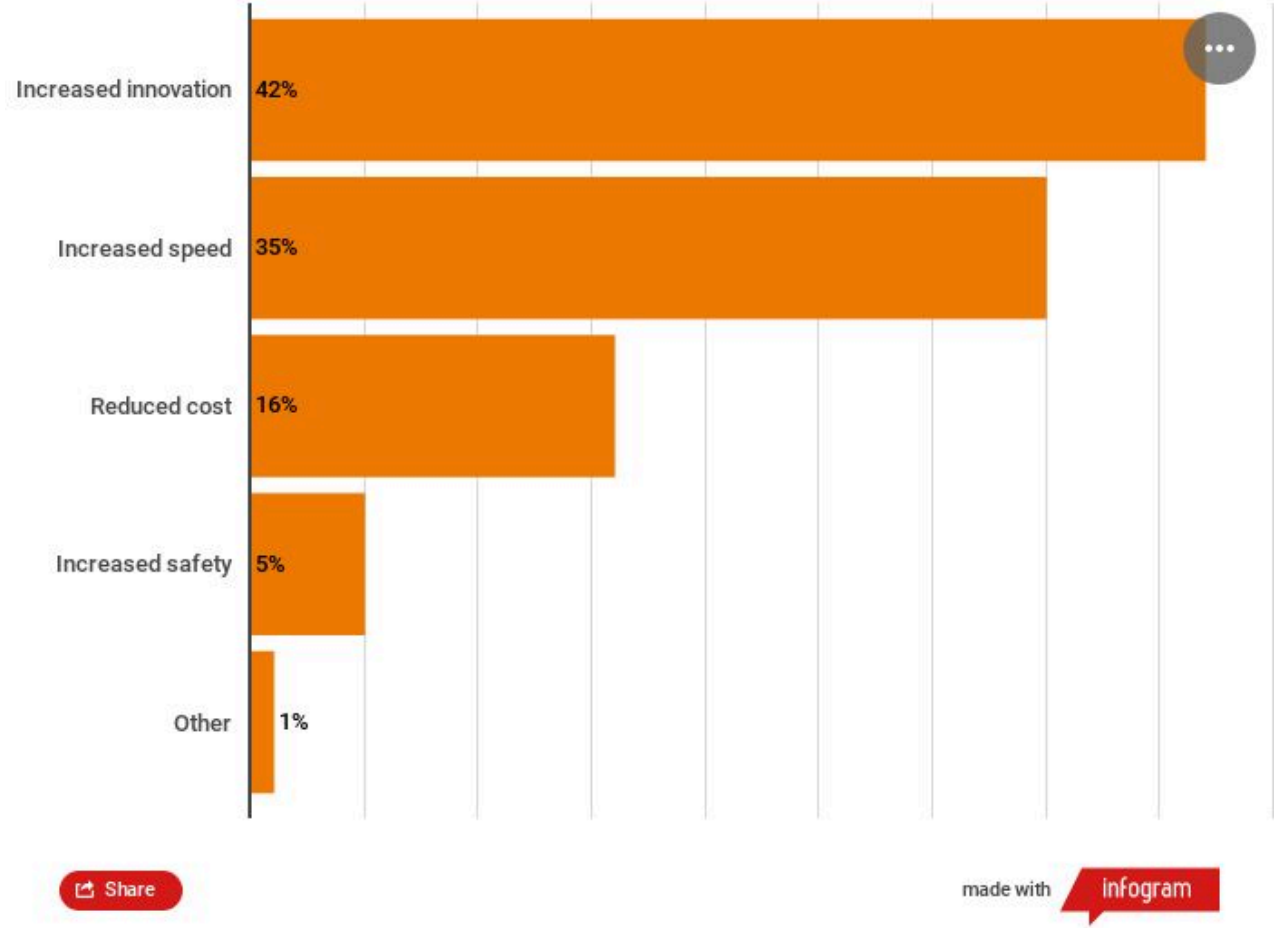
"What impact do you think each of the following technologies will have on your field in the next 10 years?"

**Respondents think AI/machine learning is the technology that will have the biggest impact on biologics in the next decade, with an average of 4.19 when asked to rank its impact from 1 to 5. Versus an average of 3.08 for virtual/ augmented reality.**

Click on the graph to explore the data



## Increased innovation (42%) and speed (35%) are seen as the biggest benefits that emerging technologies will offer in the next 10 years.

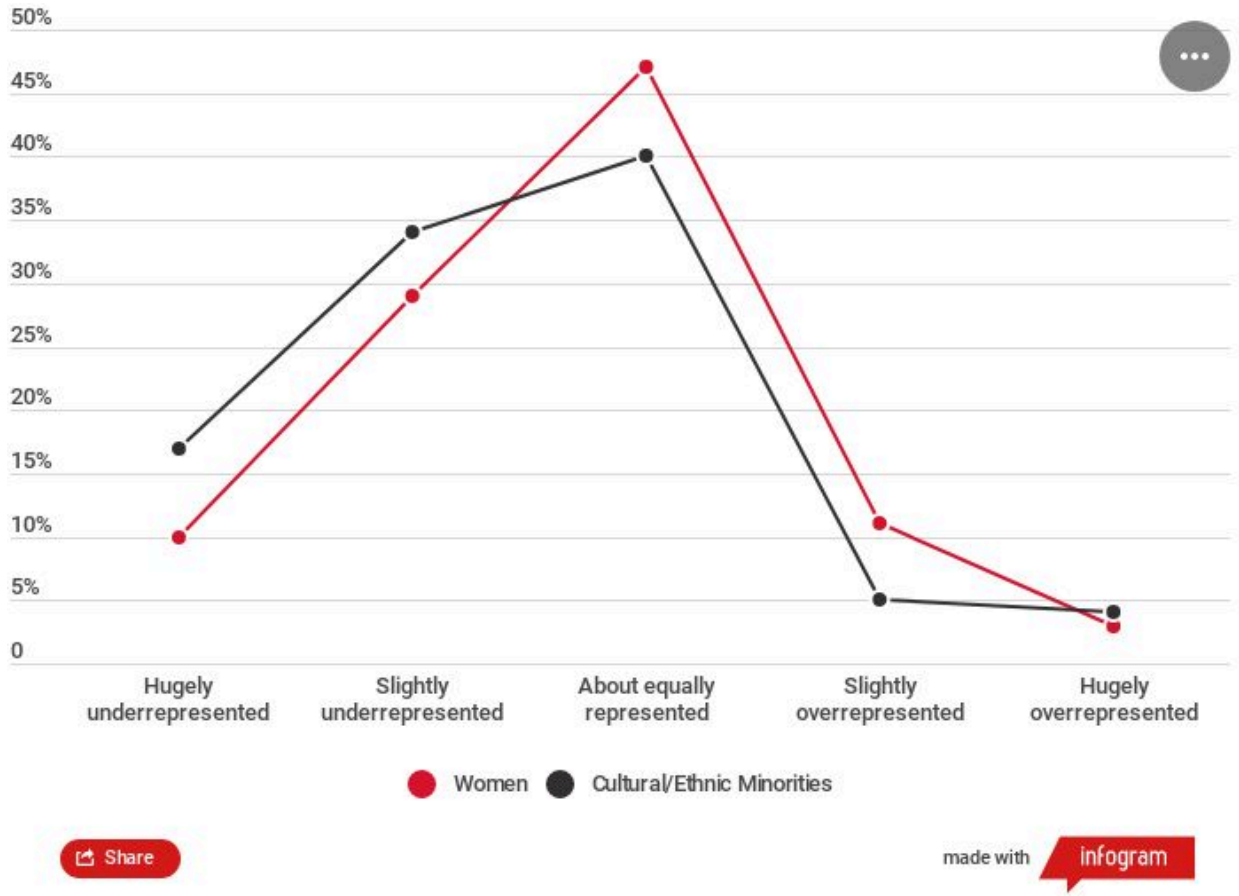



"What is the biggest benefit you think emerging technologies will have on the industry in the next 10 years?"

# Diversity, Inclusion & Sustainability

"How well represented do you think women and cultural/ethnic minorities are in your organization up to the most senior positions?"

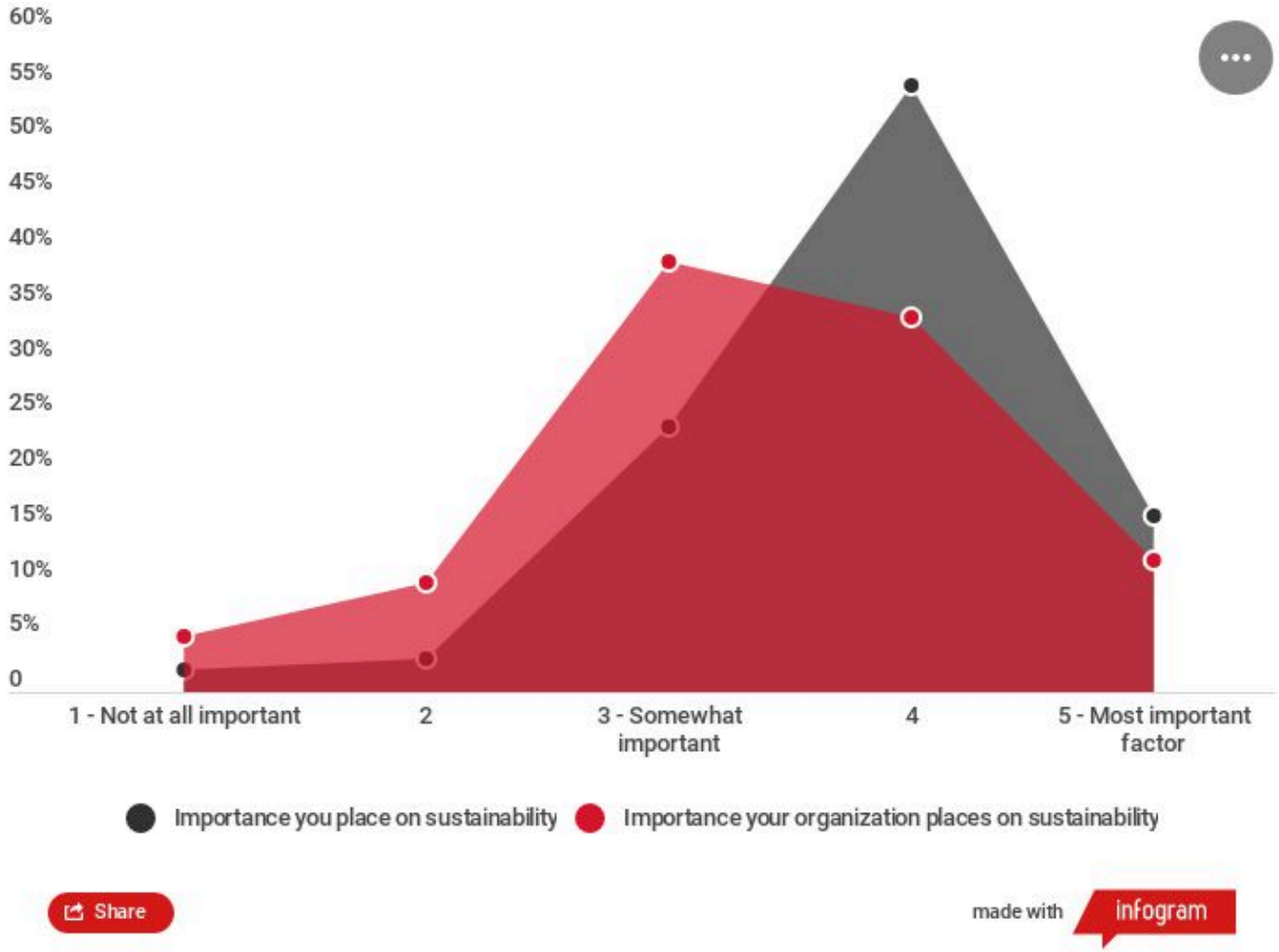
Responses around representation within organizations are hopeful, as many respondents believe that both women and cultural/ethnic minorities are about equally represented in their company. However, 39% still think women are under-represented and 48% see cultural/ethnic minorities as under-represented. Whether these views are reflected in the true data is another issue entirely.



Respondents were asked to give a rating from 1 - 5 for 'How important do you think sustainability should be when making decisions on the future direction of your company?' and 'What importance does your organization currently place on sustainability when making decisions on the future direction of the company?'.

It is clear that both individuals and companies place a fairly high importance on sustainability when making decisions, yet there is still a gap between the two. The average response rating for individuals is 3.8 / 5 - close to 'very important', whilst they see their company rating sustainability as 3.38 / 5 - closer to 'somewhat important'.

The importance put on sustainability when you and your organization are making decisions on the future direction of the company.



## "In general, what are the biggest changes you expect to see in the life sciences industry in the next 10 years? How will it look in 2030?"

"Automation and general adoption of mechanistic models. In-silico experimentation and process development. Continuous manufacturing as a standard. Widespread adoption of Process Analytical Technologies."

"I expect to see an increase in digitalization and of the use of modeling techniques to enable faster time to market in addition to improved optimization of drug candidates and processes. There will be an ever-increasing emphasis on modeling and automation to increase throughput and data acquisition.

"Industrial revolution 4.0 is what some are calling it. We will create the next generation of digital factories that are highly efficient and automated with operators able to do their jobs remotely via advanced process control and analytics as well as robotics and augmented/virtual reality."

"Big data analysis and personalized medicine."

"Development of new biologics and stem cell research will increase life expectancy."

"Nanotechnology development as well as other ways to provide precision medicine."

"Markets will continue to consolidate. Bigger players will continue to acquire smaller players. Gene and cell therapy approaches will be developing and will become more affordable."

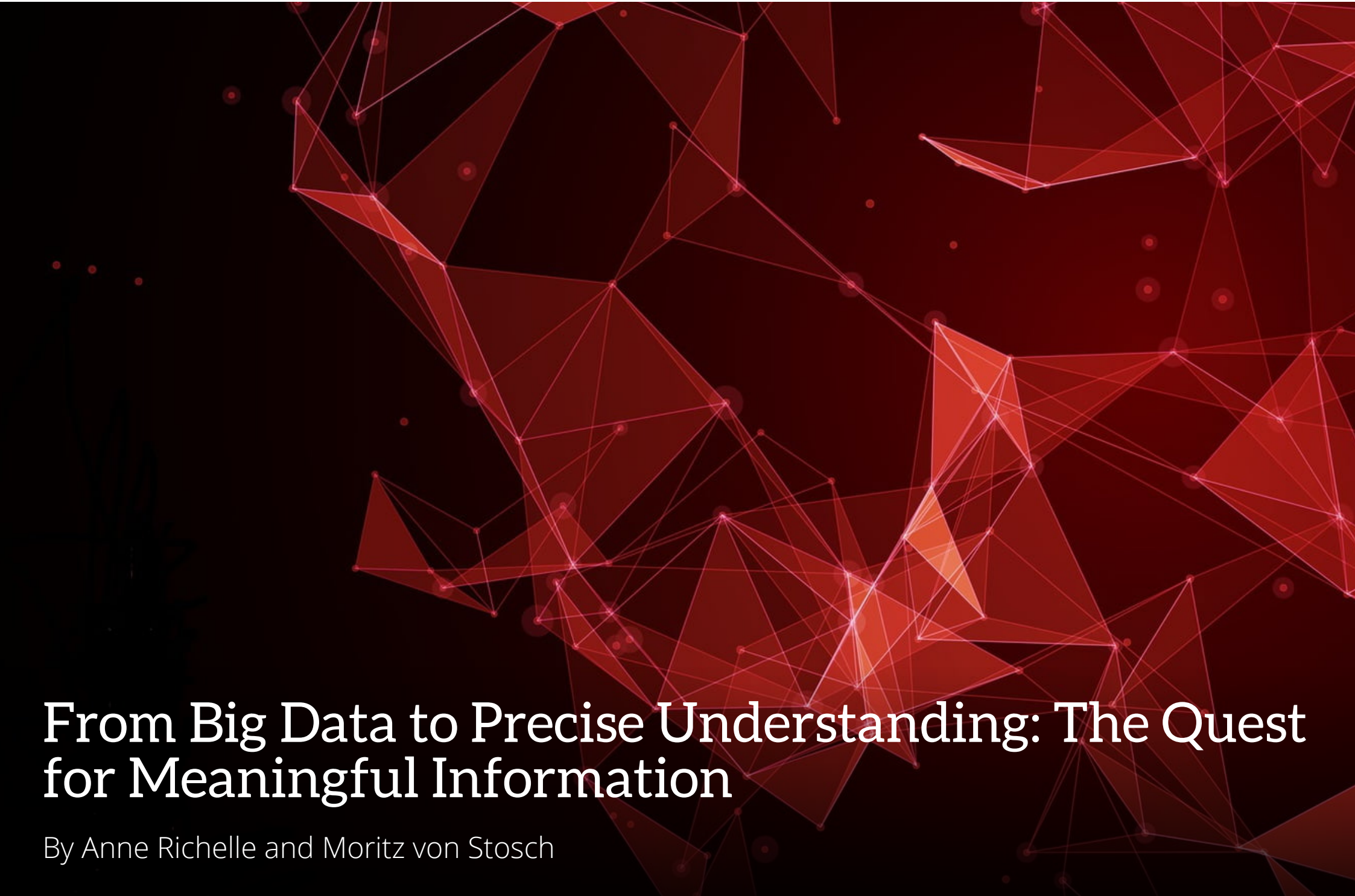
"With the emergence of cell and gene therapies, there is an opportunity of curing instead of treating diseases. But they are not technically mature, and there is likely to be setbacks (e.g. fatal side effects) that have to be encountered, understood, and overcome.

"Unfortunately the growth of the larger companies swallowing up smaller innovative companies is stifling innovation. A more relaxed regulatory overview with companies having to take on more risk analysis and self regulation. A move away from centralized manufacturing to more versatile point of use capabilities."

"Increased application of AI to proteomics will improve our understanding of the interactions between uncharacterized proteins, and will Icreate a huge list of potential drug targets and their implications in various diseases. Because of machine learning, we will know more about more, and will be able to do more to help.

"I think that treatment of diseases will take a more tailored approach to each specific patient rather than a more general approach. Each person is different and their bodies react differently to things. I think that is the wave of the future with respect to how we will find more effective treatments and have more successful outcomes. I also think that some are taking a more holistic approach to their health and so integrating some of those types of treatments will be more prevalent. More therapies that work with your bodies unique makeup and disease state.

"More complicated API/cell therapies designed predominantly by AI and developed using fully automated workflows."



# From Big Data to Precise Understanding: The Quest for Meaningful Information

By Anne Richelle and Moritz von Stosch

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High-throughput technologies have transformed the biotechnology industry. The amount of data they generate is at least a hundred times higher now than it was two decades ago, primarily because of the rise of "-omic" technologies. As in many other industries, the biopharmaceutical sector entered the era of big data the day that high-throughput analytics were routinely implemented in experimental research.

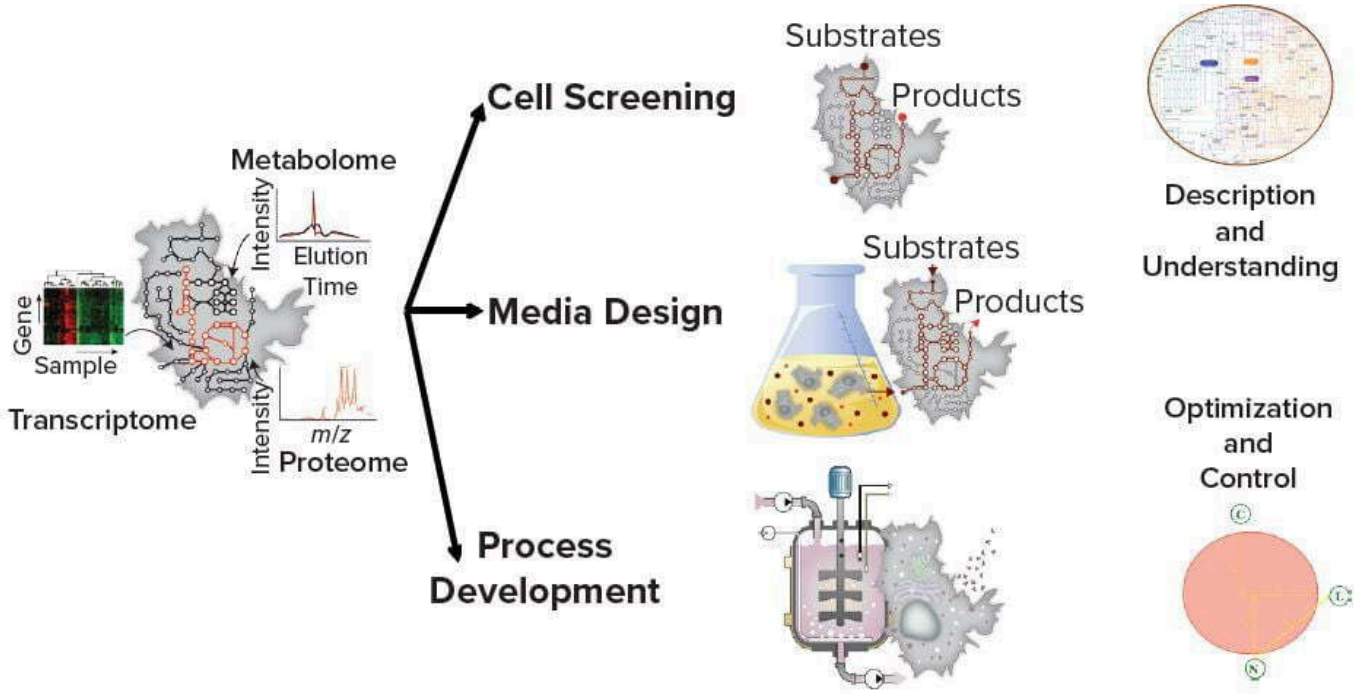



**Figure 1: Systems biology tools can facilitate upstream research activities** (bioreactor imagery: https://commons.wikimedia.org/wiki/User:Rocket000/SVGs/Chemistry#/media/File:Bioreactor_principle.svg)

**Big data refers to "datasets with sizes beyond the ability of commonly used software tools to capture, curate, manage, and process data within a tolerable elapsed time" (1).**

Big data refers to "datasets with sizes beyond the ability of commonly used software tools to capture, curate, manage, and process data within a tolerable elapsed time" (1). Technically, scientists from the field agree that big data is defined by specific attributes, the so-called 4V model: volume (scale of data), variety (different forms of data), velocity (analysis of streaming data), and veracity (uncertainty of data) (2). Considering these definitions, is the size of the datasets that biopharmaceutical researchers handle truly the problem?

Compared with other research sectors, the biopharmaceutical industry generates low amounts of data. That is mainly because of the costs associated with experimental procedures for producing good-quality data, but also because the industry's conservative mindset restricts dataset use to proprietary generators. Thus, experiments established in the context of a biopharmaceutical project rarely are big data. The size of datasets might begin to be a problem if data across projects or across the industry were considered together. However, even if the intellectual propriety burden of sharing bioprocessing data is assuaged, such databases are not easily accessible in machine-readable format. Furthermore, the lack of standardization among such databases makes them difficult to exploit systematically without extensive processing. Unfortunately, that statement is many times also valid for data generated by different research teams within one company because their data can be corrupted by the heterogenous environment (3) and potential hidden factors (4).

Although data have been generated for decades in the biopharmaceutical sector, the precarity of data management solutions in many companies renders exploitation of those data almost impossible. This consideration of historical bioprocess data also raises the question of data "longevity." Indeed, data support and experimental techniques are evolving continuously, making it difficult to extract data from obsolete storage supports (e.g., floppy disks) and to compare data generated using different generations of experimental technologies — such as serial analysis of gene expression (SAGE) compared with RNA sequencing (RNAseq). Thus, the main problem with biopharmaceutical datasets is not related to their size but more likely to the time researchers require to handle those data, including integration of diverse data sources and extraction of meaningful information from such integrated datasets.

### Machine Learning As a Discovery Driver for Large Datasets

Machine learning (ML) is a powerful tool that helps researchers extract information from data (5). ML is expected to be a significant tool

in the bioprocess industry (6). Over the past few years, biomanufacturers have invested greatly in the development of such data-driven methods and in data capturing and management solutions.

Increasing attention to those approaches has led to researchers questioning the ability of large datasets to "speak for themselves" (7). Many researchers have demonstrated that "big structure" is full of spurious correlations because of noncausal coincidences, hidden factors, and the nature of "big randomness." With a deluge of new ML tools, some researchers point to the complexity of algorithms developed, making it impossible to inspect all parameters or to reason fully about how inputs have been manipulated (8).

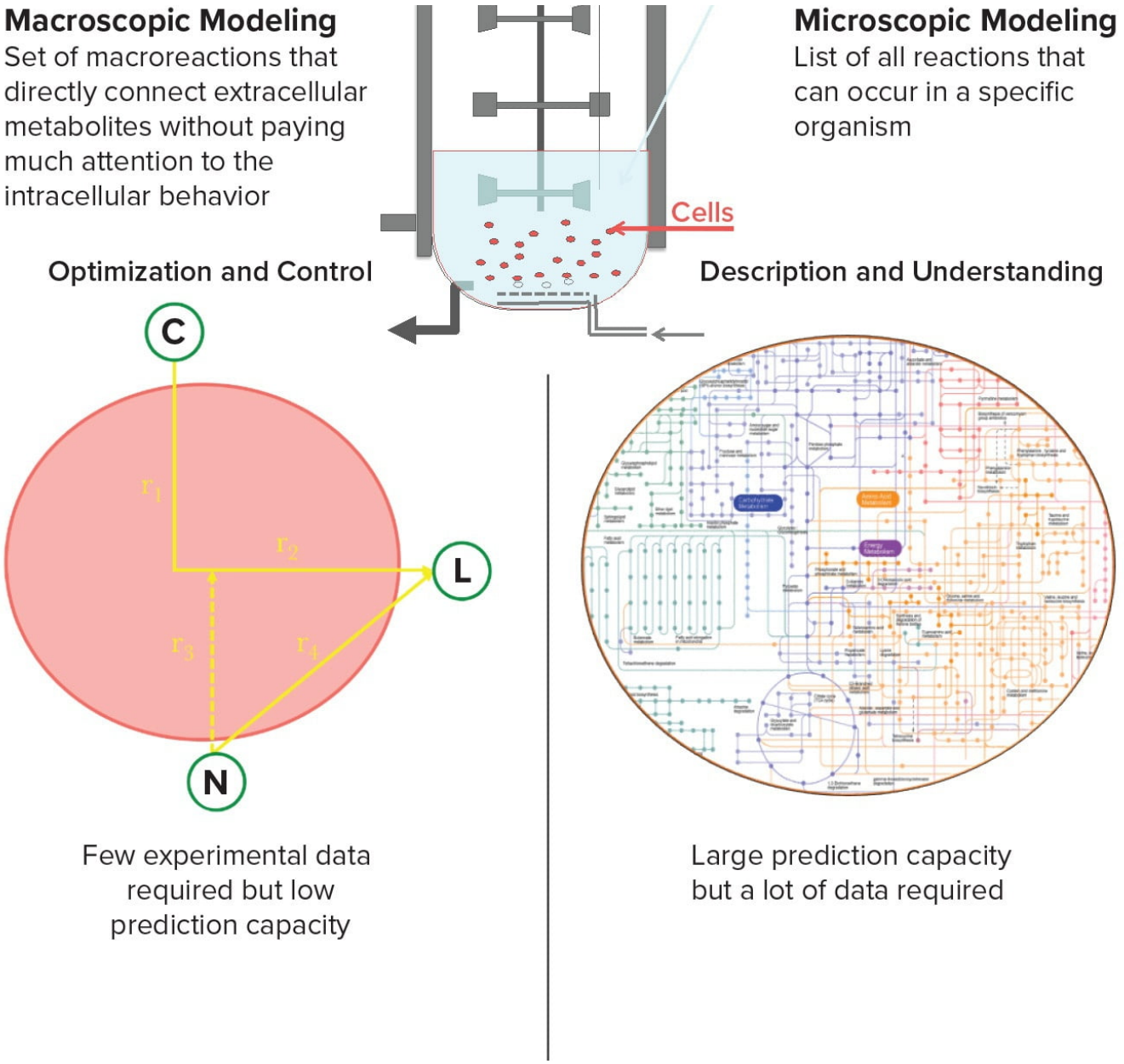
Although we can highlight only the invaluable potential impact of such techniques, it is important to keep in mind that ML tools also can turn out to be "fool's gold." Specifically in biotechnology, black-box approaches will support rapid development of powerful predictive models if a problem is concise and well structured. But their ability to provide biologically relevant explanations of predicted results from a given dataset might be somewhat compromised. To prevent such pitfalls, the empirical knowledge that has been accumulated over decades of biological research should be integrated as a baseline to guide such data-driven methods.

**Systems Biology Tools: Beyond Drug Discovery and Cell Design**

Systems biology tools are model-based approaches used for the description of complex biological systems. They enable the coherent organization of large datasets into biological networks, and they provide insights on biological systems that in vivo experiments alone cannot (9). In the context of metabolic processes, genome-scale metabolic network models (GEMs) are used as platforms for -omics data integration and interpretation by linking the genotype of an organism and the phenotypes it can exhibit during an experiment. Such networks can be used as libraries for developing cell- and tissue-specific models. Because some enzymes are active only in specific environments, context-specific extraction methods can be used for tailoring genome-scale models based on -omic data integration. Several algorithms have been developed to recapitulate the metabolism of specific cell and tissue types, providing useful insights into their metabolism under such specific conditions (10). Biological networks then can be used as frameworks to integrate diverse data sources and subsequently extract meaningful information. So a GEM can be described as not only a network of reactions, but also as an interconnected map of cellular functions.

Systems biology tools have proven to be invaluable at the level of preclinical research such as for designing new drugs by informing upon target selection (11) or for engineering cells by rewiring their metabolism toward the production of a product (12). But such approaches can be used for much more. For example, they could be applied at the industrial level in the field of upstream activities, including process design, monitoring and control, lowering experimental effort, and increasing process robustness and intensity (Figure 1).

Such efforts are expected to facilitate greatly the implementation of the quality by design (QbD) paradigm and process analytical technology (PAT) initiatives. Based on the potential predictive power of such mechanistic approaches, you might be surprised that improved bioprocess performance still is achieved mainly by semiempirical media and bioprocess optimization techniques (e.g., media screening and statistical design of experiments, DoE).



Current restricted applications of such systems-biology tools are caused by the lack of a systemic workflow to generate predictive models for upstream activities from biological networks. The complexity and structure of predictive mechanistic models mainly are defined by their final purposes (13) (Figure 2). A model with the objective of describing as accurately as possible the mechanisms underlying a process operation certainly will have a greater structural complexity than a model developed for optimization of that process.

It is important to note that the dynamics related to a process operation can vary in complexity themselves. Obviously, it is much easier to model the operation of a draining sink than to model the operation of a combustion engine, for example. So one part of a model's structural complexity also will mirror the complexity of the system being studied.

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# How Academia and Biotechs Can Work Better Together

An Interview with Knud Jensen, Ph.D., Department of Chemistry, University of Copenhagen

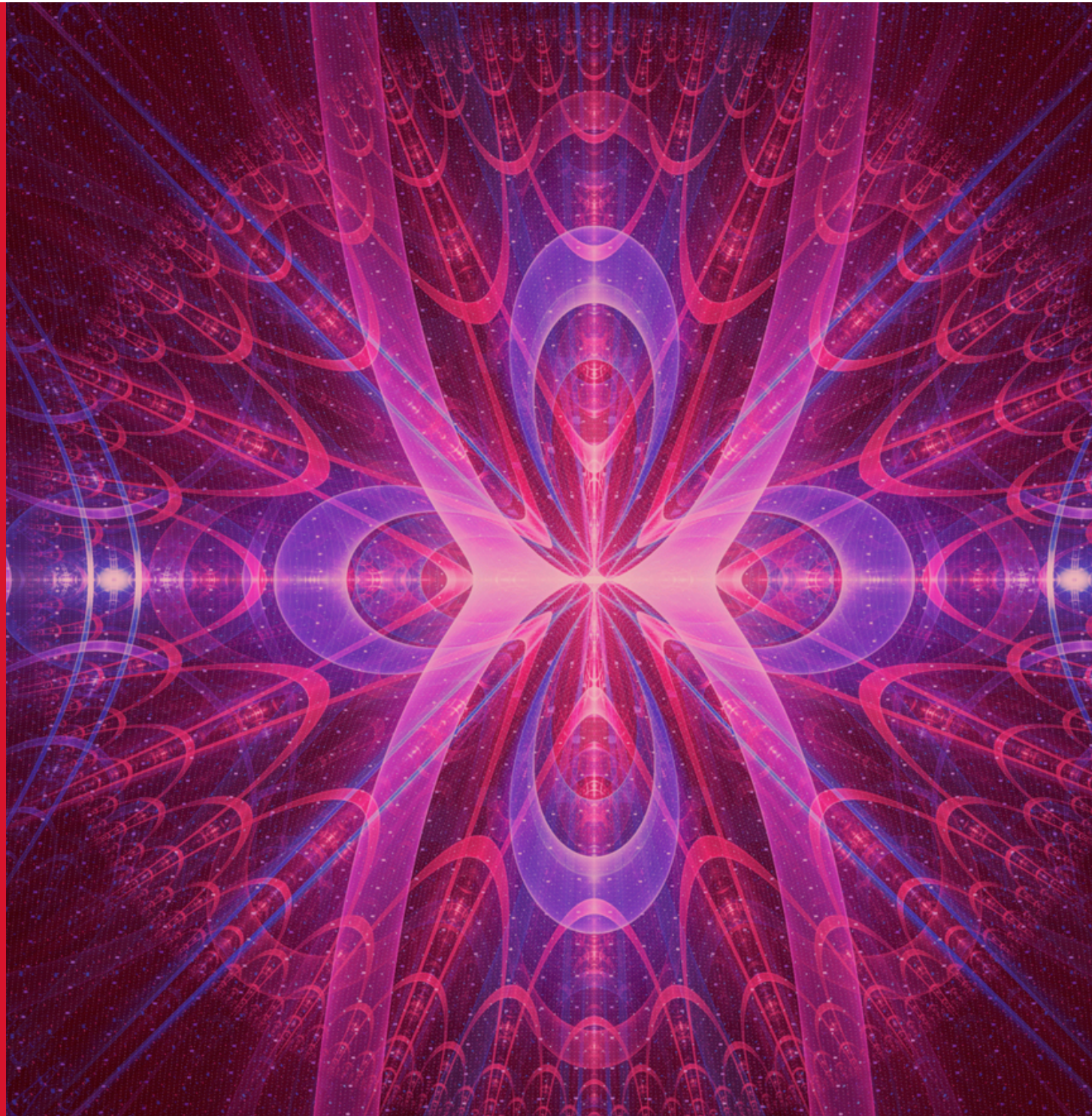
BioProcess International

**How Academia and Biotechs Can Work Better Together - An Interview with Professor Knud Jensen, Ph.D., University of Copenhagen**

Knud Jensen, Ph.D., a Professor in the Department of Chemistry at the University of Copenhagen, delves into how academia and industry can work better together to help propel the industry forward. What are the most important elements in building long-term dynamic relationships? How can each side benefit from developing such relationships?

# Future Trends in Proteins To Fight COVID-19

By David Orchard-Webb



# Future Trends in Proteins to Fight COVID-19

## Introduction

The global scientific community's attention has turned to COVID-19, a pandemic that has swept across the world causing over 276,863 deaths (May 08, 2020) since emerging in China in late December 2019. The future is now. The causative agent of COVID-19, the coronavirus SARS-CoV-2, has no vaccine, and no biologics or small molecules have yet been approved to treat it. There is a big opportunity for protein engineering to make an impact on this disease without a cure. In order to do so the industry will need to develop engineered proteins rapidly from preclinical to clinical studies, in many cases implementing next generation protein engineering techniques, to obtain regulatory approval. Virus containment measures have ground the world's economy to a halt. Protein engineering is one of the best strategies to turn the tide against the virus and bring the global economy back from the brink of disaster.

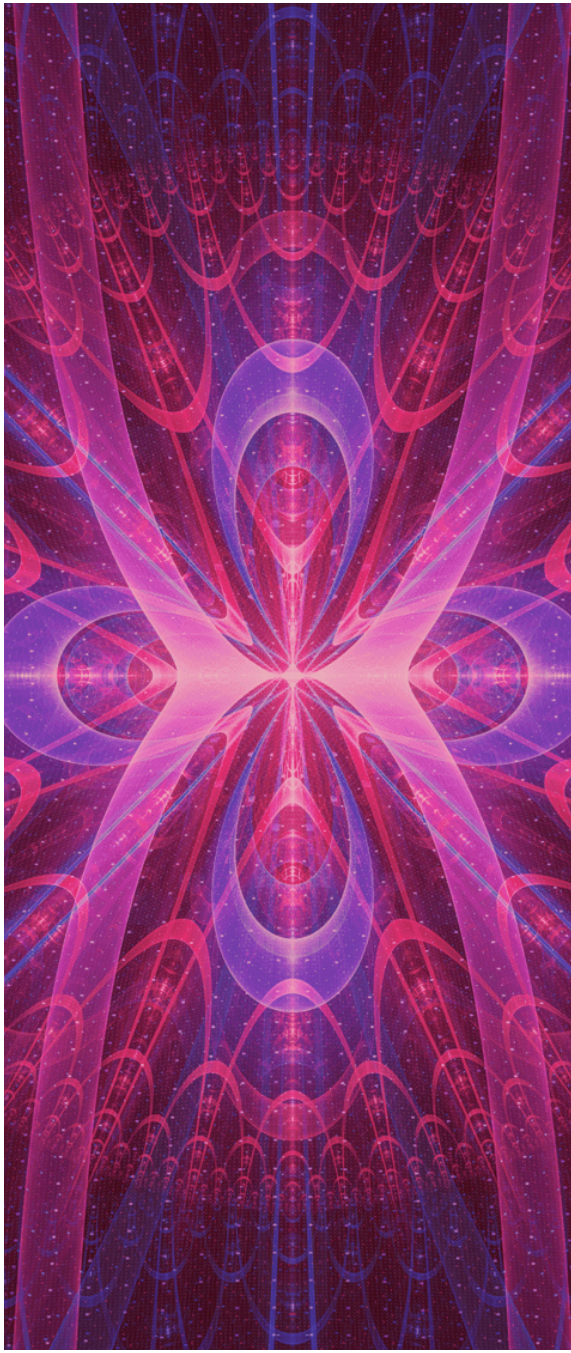
## Challenges in preclinical development

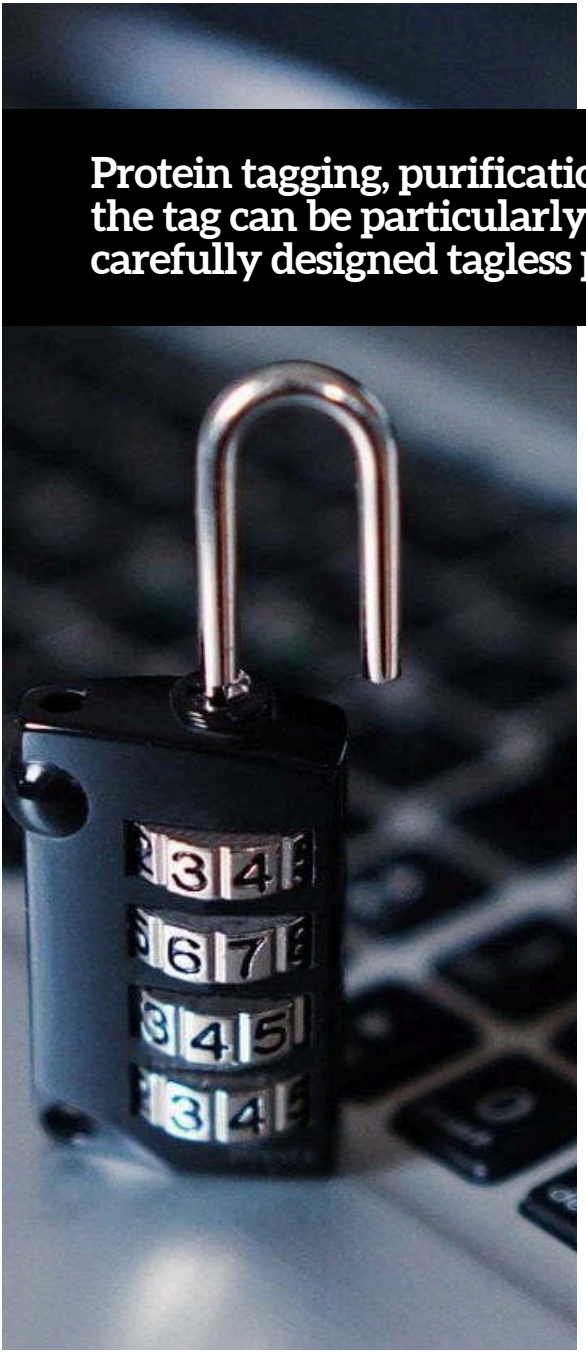
The challenges of protein engineering for therapeutic applications in preclinical development depend on the application. Protein engineering generally faces the following universal challenges:

- Separation and purification
- Solubility and bioavailability in physiological solutions
- Glyco-engineering
- Maximising half-life
- Avoiding protein aggregation
- Avoiding protease attack
- Production cell line selection
- Formulation for delivery

## Separation and Purification

Traditionally, the molecular weight and charge properties of the recombinant protein is known and can be used to separate it from impurities by size exclusion gel-filtration chromatography and ion exchange chromatography, amongst other chromatographic methods. Protein tagging,





**Protein tagging, purification and then cleavage of the tag can be particularly useful, however carefully designed tagless purification is possible.**

purification and then cleavage of the tag can be particularly useful, however carefully designed tagless purification is possible.

Improvement in upstream yield means that next generation, chromatography-free, purification techniques are becoming viable, such as aggregating tags including elastin-like polypeptide (ELP), repeat-in-toxin (RTX) domain, and ELK16. Aggregation can be triggered by temperature, salt or calcium.

Ideally, purification tags are self-cleaving as proteases don't always make a "clean" cut and need an additional purification step for removal. Self-cleaving tags can be generated by integrating an intein (internal protein) splicing domain. A commonly used intein is derived from the vacuolar ATPase subunit (VMA) of Saccharomyces cerevisiae, which is triggered to excise by thiol reagent. A drawback of intein systems is that although they function well in prokaryotic cells, they can cleave prematurely in eukaryotic cells, however more reliable inteins have been engineered for Chinese hamster ovary (CHO) cells.

Inteins can also be used in the reverse direction, to increase the solubility of an otherwise insoluble protein. Surface resident Ebola virus glycoprotein (EbolaGP) is responsible for membrane binding and virus entry, and is a target for vaccine development. Production of EbolaGP is hampered by its insoluble aggregation. A C-terminal intein-based tag greatly enhances the solubility of EbolaGP and allows one-step chromatographic purification of the untagged EbolaGP through thiol-catalyzed self-cleavage. The purified untagged EbolaGP was highly immunogenic in a mouse model. Similar strategies could of course be applied to SARS-CoV-2 vaccine development using virus derived soluble proteins.

**Solubility, bioavailability & immunogenicity**

Engineering proteins to dimerize can be helpful for purification as their increased size makes it simpler to separate them from smaller molecular weight impurities such as albumin. Dimerization can also improve solubility, bioavailability, half-life, and reduce aggregation. For example, larger sized proteins experience less renal

clearance, increasing half-life. The generation of fusion proteins with an Fc domain from antibodies can also increase half-life and bioavailability.

Fc domain fusion proteins are composed of an immunoglobulin Fc that is directly coded into the therapeutic protein. They first came to the fore in the late 1980s as a means to block HIV entry into cells (CD4-Fc). Therapeutic proteins in the blood are constantly internalized by endothelial cells and degraded by the lysozyme, however the Fc domain can interact with the salvage neonatal Fc-receptor (FcRn) inside the endothelial cell and return the Fc fusion protein back to the blood. In this way the Fc domain endows the fusion protein with a half-life similar to, but generally shorter than, that of the long-lived IgG and serum albumin, which use the same mechanism.

Through engineering of the Fc it may be possible to further improve the half-life.

Fc fusions that form multivalent protein complexes can also be envisioned. Such complexes could possibly clear viral particles more efficiently, although this has yet to be demonstrated.

SARS-CoV-2 can provoke a cytokine storm in some patients, thus further stimulation of the immune system in severe COVID-19 is not ideal, on the other hand immune stimulation at the early stages of the disease before progression to acute inflammation could rapidly clear the infection before it becomes severe, provided it does not in itself trigger cytokine storm. Such scenarios would need to be tested preclinically. Indeed consensus is yet to be reached regarding the most appropriate preclinical representations of COVID-19.

The choice of Fc domain can either stimulate or evade the immune system (IgG1 vs IgG2/4 Fc). The Fc domain is also subject to glycation which is required for effector function, therefore Fc immune properties can be modulated by the cell line used for production.

**Glyco Engineering**

Protein glycosylation can be necessary for therapeutic function. It also influences yield, pharmacokinetics, and immunogenicity of recombinant therapeutic proteins. Correct human type glycosylation of recombinant proteins poses a challenge for industry as the four main cell types used for production are not human; Escherichia coli, Saccharomyces cerevisiae, Pichia

pastoris, and CHO cells. Various plant and insect cells are also used successfully. There are at least six human cell lines used for recombinant protein production including HEK293 and PER.C6, but more than half of all recombinant proteins are produced in CHO.

Correct glycosylation in non-human cell lines requires glyco-engineering strategies. Non-human cell lines often produce glycans that are not present in humans and may be attached to the recombinant proteins, rendering them immunogenic or reducing their efficacy. One such example is aberrant fucosylation, which has been successfully mitigated in CHO cells. Glyco-engineered CHO fucosylation knockout cell lines can produce human IgG1 Fc domain with increased affinity for natural killer cells.

## Next Gen Biologics and Production Systems

### Photosynthetic Cell Lines for Bioproduction

Not all human proteins are heavily glycosylated including interferon alpha (IFN-α), an innate antiviral protein under clinical investigation for the treatment of COVID-19, simplifying production requirements.

**Low-cost biopharmaceutical proteins can be generated by recombinant DNA technologies in microalgae and plants by a direct photosynthetic production process, which can potentially dramatically reduce the energy input required compared to other cell types.**

Low-cost biopharmaceutical proteins can be generated by recombinant DNA technologies in microalgae and plants by a direct photosynthetic production process, which can potentially dramatically reduce the energy input required compared to other cell types.

Eukaryotic fusion proteins can be produced in photosynthetic cyanobacteria at up to ~20% of the total protein, provided they have a high expression leader sequence. This leader sequence could contain a self-cleaving intein.

Human interferon production in microalgae Synechocystis sp. PCC 6803 has been demonstrated, however the leader sequence was not removed. The activity of the interferon was lower than wild-type due to the presence of this leader. The proof of principle has been demonstrated, but refinement is needed. Bioactive human interferon-γ (IFN-γ) has also been produced in tobacco plants.

## Next Gen Protein Treatments for Coronavirus and Diabetes

### ACE2 - Angiotensin-Converting Enzyme 2

Safety monitoring is moving beyond traditional approaches to use sophisticated AI algorithms that identify safety signals arising from rare adverse events. Furthermore, these signals could be captured from a variety of sources like Websites and search engines. Other sources can include electronic medical records, and

consumer-generated media, which can be identified in real-time to identify early signals regarding safety issues of pharmaceutical products. A prompt and timely response on the part of the pharmaceutical manufacturer to physician and patient concerns could prevent regulatory and public-relations backlashes.

**CD26 / DPP4 - Dipeptidyl Peptidase-4**

CD26, a type II transmembrane glycoprotein and serine protease, is expressed ubiquitously in many tissues, including lung and immune cells and may potentially act as a secondary cellular receptor for SARS-CoV-2 as suggested by in silico data, but not supported by a small amount of 293T in vitro data produced thus far. In silico molecular docking suggests a possible tight interaction between the SARS-CoV-2 S1 spike domain loops and CD26.

**Signals can be captured from a wide variety of sources, including electronic medical records and consumer-generated media, which can be identified in real-time to detect early signals regarding safety issues of pharma products.**

Cellular context can be important due to glycosylation-based heterogeneity among other membrane factors, as is the nature of the putative binding site for CD26 on the viral spike protein. There is not enough experimental data to draw any firm conclusions with regard to SARS-CoV-2 binding of CD26, however co-purification with the related MERS-CoV S1 domain demonstrates that CD26 can bind to at least some pathogenic coronaviruses. A patented soluble fusion protein consisting of a modified CD26 consensus binding sequence for the MERS CoV S1 spike glycoprotein and an antibody Fc domain has been developed. The Fc domain would be expected to improve half-life of CD26 in the bloodstream. This receptor decoy fusion protein, called DPP4-Fc, may prevent MERS-CoV from infecting human lung cells in vitro. Development was never completed due to lack of funding.

DPP4-Fc is produced in glyco-engineered tobacco plants. It has been tested preclinically, but it is not known whether the construct would need further modification to act as a receptor decoy for the SARS-CoV-2 spike protein. Further preclinical development and testing is needed.

Monoclonal antibodies against CD26 may also be effective inhibitors of viral binding and or CD26 protein function.

**Diagnostic Bispecific Antibodies Targeting Coronavirus Spike Protein**

For diagnostic purposes bispecific monoclonal antibodies that bind the 2003 SARS-CoV-1 spike protein have been developed. One arm binds the spike protein while the other binds horse radish peroxidase for single step detection in an ELISA, detection limit of 0.019 g/ml.

A similar bispecific antibody for

sensitive detection of 2019 SARS-CoV-2 could be developed. Currently most ELISA assays attempt to detect antibodies against SARS-CoV-2 but not the virus itself. Detecting virus by ELISA could confirm PCR and potentially detect virus earlier than assays that detect immunoglobulins.

A bispecific antibody approach for ELISA has two obvious advantages 1) the total absence of background and 2) higher sensitivity, compared to traditional sandwich ELISAs.

Such bispecific antibodies could potentially also be used for one-step immunohistochemistry to determine the tissue distribution of 2019 SARS-CoV-2.

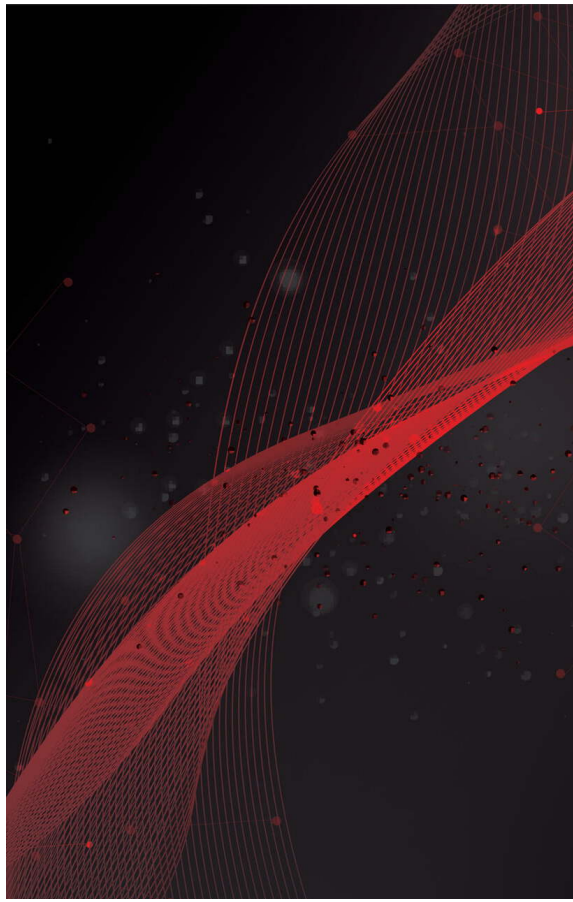
**Targeting COVID-19 Inflammation and Diabetes**

Severe COVID-19 is characterized by an inflammatory profile that is not unlike cytokine release syndrome. Corticosteroids, IL-6 inhibitors and other modulators of inflammation are under clinical investigation for severe COVID-19. Those with preexisting inflammatory conditions such as metabolic syndrome may be vulnerable to COVID-19, however further research is needed to understand the risks.

Diabetes may be a significant comorbidity of COVID-19. Data from Italy indicate that more than two-thirds of those who die from COVID-19 have diabetes. Notably SARS-CoV-1 (2003), which is reported to use ACE2 as a cellular receptor like SARS-CoV-2 (2019), can damage pancreatic islets and cause acute diabetes. Ambient hyperglycemia was reported to be an independent predictor for mortality and morbidity in SARS patients.

Although its functions are not fully understood, CD26 plays a major role in glucose and insulin metabolism. It is an inhibitor of glucagon-like peptide-1 (GLP-1) and other incretin peptides. Preventing CD26 mediated degradation of gut hormones such as GLP-1 potentiates islet hormone secretion and enhances metabolism, reducing hyperglycemia in patients with type 2 diabetes. CD26 is also expressed in the lungs, modulating the function of various proinflammatory cytokines, growth factors and vasoactive peptides in the deep respiratory tract.

It is believed that the use of a CD26 inhibitor in diabetics hospitalized for Covid-19 may reduce the inflammatory lung disease. Among the drugs that selectively block CD26, the one with the greatest affinity is the small molecule Sitagliptin, currently in a randomized controlled open label phase 3 intervention study of patients hospitalized for COVID-19 and affected by type 2 diabetes mellitus.



# Regulatory Approval - How Close Are We to Having These New Biologics Approved?

**GLP-1 Mimetics**

Downstream of CD26, GLP-1 may be of therapeutic benefit for diabetics with COVID-19 could therefore be a target for drug repurposing of FDA approved GLP-1 biologics. For example, GLP-1 agonists have been shown to protect against encephalomyocarditis virus (EMCV) induced diabetes in a mouse model. Table 1 lists two FDA approved GLP-1 mimetic proteins, peptides are excluded.

**Table 1: FDA approved protein (> 50aas) GLP-1 mimetics[1]**

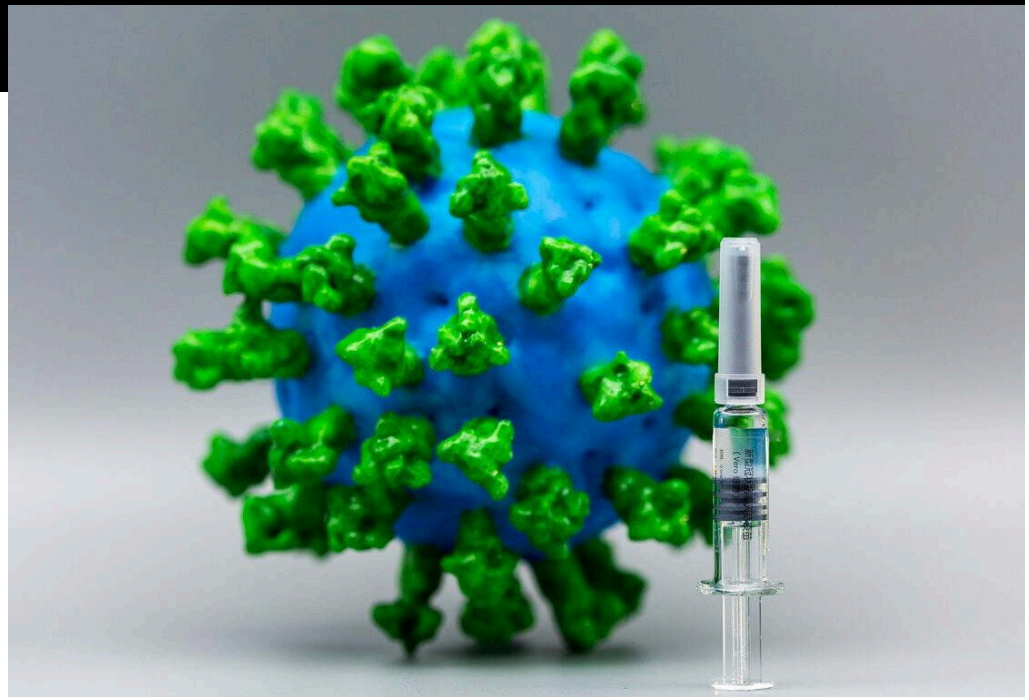
| Protein (Brand) | Description | Approval Status | US$ | Marketed By |
|---|---|---|---|---|
| **Albiglutide (Tanzeum/Eperzan)** | Albiglutide consists of 645 amino acids with 17 disulfide bridges. Amino acids 1–30 and 31–60 constitute two copies of modified human GLP-1, the alanine at position 2 having been exchanged for a glycine for better DPP4 resistance. The remaining sequence is human albumin. | 2014 FDA approved for type II diabetes. GlaxoSmithKline discontinued the manufacturing and sale of Tanzeum in July 2018 due to limited prescribing of the drug and declining sales. | N/A | GlaxoSmithKline |
| **Dulaglutide (Trulicity)** | GLP-1 receptor (GLP-1R) agonist consisting of GLP-1(7-37) covalently linked to an Fc fragment of human IgG4. | 2014 FDA approved for type II diabetes | 203.22/pen injector | Eli Lilly & Co |

### Spike Protein Nanoparticle Vaccine

Novavax is developing a SARS-CoV-2 recombinant spike protein nanoparticle vaccine, NVX-CoV2373 produced in Sf9 insect cells. High titres of spike protein-specific antibodies with ACE-2 human receptor binding domain blocking activity and SARS-CoV-2 wild-type virus neutralizing antibodies were observed after a single immunization. In addition, the already high microneutralization titers seen after one dose increased eightfold with a second dose. High titer microneutralizing antibodies are a positive signal of possible efficaciousness in people. A phase I clinical trial has been initiated with preliminary human data expected in July 2020.

## Conclusion

Good progress has been made in developing protein biologics for treating COVID-19. Upwards of 300 papers are published per day on the subject of COVID-19, some of which provide valuable clues as to the optimal treatment strategy. Research surrounding the coronavirus spike protein and its interaction with its putative receptors in different cell types is likely to uncover further information that can be used in biologic treatment strategies.



# Can the Biotech Industry Lead Diversity in STEM?

By Claudette Hodge

# Can the Biotech Industry Lead Diversity in STEM?

On September 11th, 2019, stakeholders from across biopharma and biotech gathered for An Evening of Diversity and Inclusion at Biotech Week Boston. Industry thought leaders took part in a panel discussion centering on the importance of Diversity and Inclusion (D&I) initiatives in the biotech industry and addressing the challenges of changing perspectives.

It emphasized that diversity is not simply something that is nice to have in an organization - it is crucial to sustaining the economy of life sciences and medicine. The talk was rich with personal experiences and practical ideas for driving change within organizations and partnerships.

## Representation in Biotech

Nadeem Sarwar, President at the Eisai Center for Genetics Guided Dementia Discovery (G2D2) started off with a personal anecdote on how representation in leadership can impact a person working in biotech from their first day. “When I was a kid at an internship of a large global pharma company, their parking lot was organized by hierarchy. So the more senior you were, the closer you parked to the entrance. As I walked into work on my first day, two things looked very obvious to me. The first was that the cars got fancier and fancier. The second was [that] the drivers got whiter, and maler, and balder as I approached the entranceway. Before I’d even entered the workplace, I had a very clear idea on what this company will look like.”

He then described his visit to a newly-designed site of another biopharma company which had glass offices for executive management

separated from the rest of the employees. “And of course you could see that inside these glass offices, the people inside were the same, aging, balding white men that I recognized from my [first] day of internship,” he added. “Despite this organization trying to strive for transparency, the literal window into their organization was emphasizing they hadn’t really done much to inspire their workforce.”

The focus then turned to the impact of representation on the patient. Edie Stringfellow, Director of Diversity and Inclusion at MassBio, shared that her brother is currently battling sickle cell anemia. “We’re also dealing with the mental aspect of what he deals with when he has to go to the hospitals,” she said. “We need more people from a diverse background in our clinical trials… in our hospitals. It also means we need to be more reflective to the patient in our biotech firms.”

Supporting this, Joanne Duncan, President of the Membership and Business Operations Division at Biotechnology Innovation Organization (BIO) said “our patients are diverse and we need to make sure we’re providing the support to that population. We can’t do it alone, we need to do it within partnerships. Together, we can make a difference.”

## Tracking D&I Success

As Duncan explained, BIO has launched a campaign, The Right Mix Matters, which provides online tools for accelerating diverse representation in biotech company boards, C-suites, and other leadership positions. As part of the campaign, it has partnered with Women in Bio to create the Bio Boardlist, a directory of diverse candidates for boards. The candidate profiles can be searched and endorsed on The Right Mix Matters website.

The campaign comes a result of BIO’s D&I initiatives for workplace development. As a Washington-based organization representing all biosciences on a national level, its goal is to drive the initiatives across all 50 states. “We’re putting a survey together that is part of this campaign… to continue to monitor and track our metrics,” said Duncan. “The beauty is when we get asked to come to Capitol Hill and sit down with the congressman or congresswoman, and they ask us, “what are you doing as an industry, you biotech people?”, we’re able to point to something [to show] what we’re doing.”

Stringfellow reflected on her role at MassBio in which she collaborates with member organizations in implementing their D&I initiatives. She detailed how regular success measurement of such initiatives can ensure real change in biotech organizations. “You will see D&I initiative success rates change overnight when you treat D&I as any other business item, [such as] sales or marketing. Human capital, human intelligence and human work should be treated just the same as any other R&D pipeline.”

## Leading a Change for the Future

The panel explored how they see biotech changing by the year 2050. Sarwar highlighted that D&I will be a key component in engaging future generations of biotech professionals. "Thirty years from now, the person who's going to cure cancer or prevent heart disease or eradicate diabetes is currently thinking [about] what they should study. Why should they study something relevant to drug discovery right now? How do we ensure we inspire the next generation of medicine makers to choose to be medicine makers and not politicians or lawyers?"

As an example, he explained that G2D2 run a selection of training courses targeting young scientists from as early as middle school. These include Girls Who Cure, a summer course for high school girls, and internships for underprivileged college students as part of Massachusetts-based Project ONRAMP. Duncan remarked at how biotech was a great place to start in driving D&I initiatives across STEM. "What an industry to take [The Right Mix Matters] through the country and around the globe! We need a global community to help continue to solve the problems that our industry is facing, the challenges and opportunities for cures," she said. "In 2050, [the biotech industry] will be a leader in changing diversity in all aspects, ahead of all the other techs, because we are innovators." Stringfellow passionately noted that in the heat of talent wars, staff retention and workforce sustainability are currently at stake in life sciences, particularly for Massachusetts. "People are not going to stay where they don't feel included, they don't feel as if they belong. They don't feel they have that opportunity to contribute, they don't have that opportunity to grow. It's no excuse for that to happen here," she said.

"If you look at the how much opportunity biotech provides an economy, with jobs in biotech, we can close some of those economic gaps, we can close some of those health gaps because you will have better health insurance. There's so many things we can do that affects other areas."

Thank you for reading

# Looking to 2030: Future of the Industry