

UPDATES ON HUMAN-RELEVANT METHODS IN PHARMACEUTICAL MEDICINE AND THE LEGISLATIVE PROCESS

CENTER FOR CONTEMPORARY SCIENCES DISCOVERY FORUM SERIES

December 2022

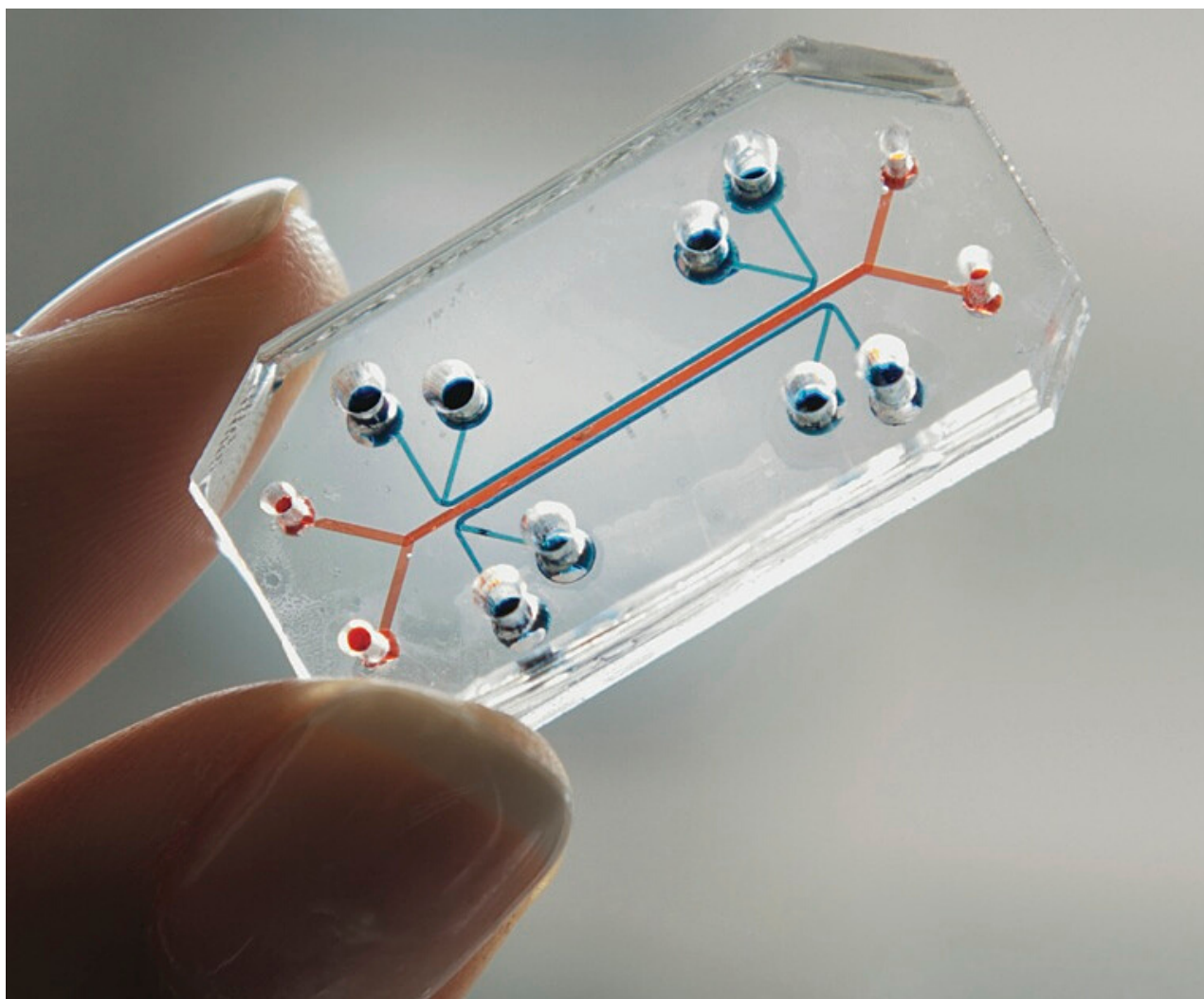


TABLE OF CONTENTS.

01 EVENT SUMMARY

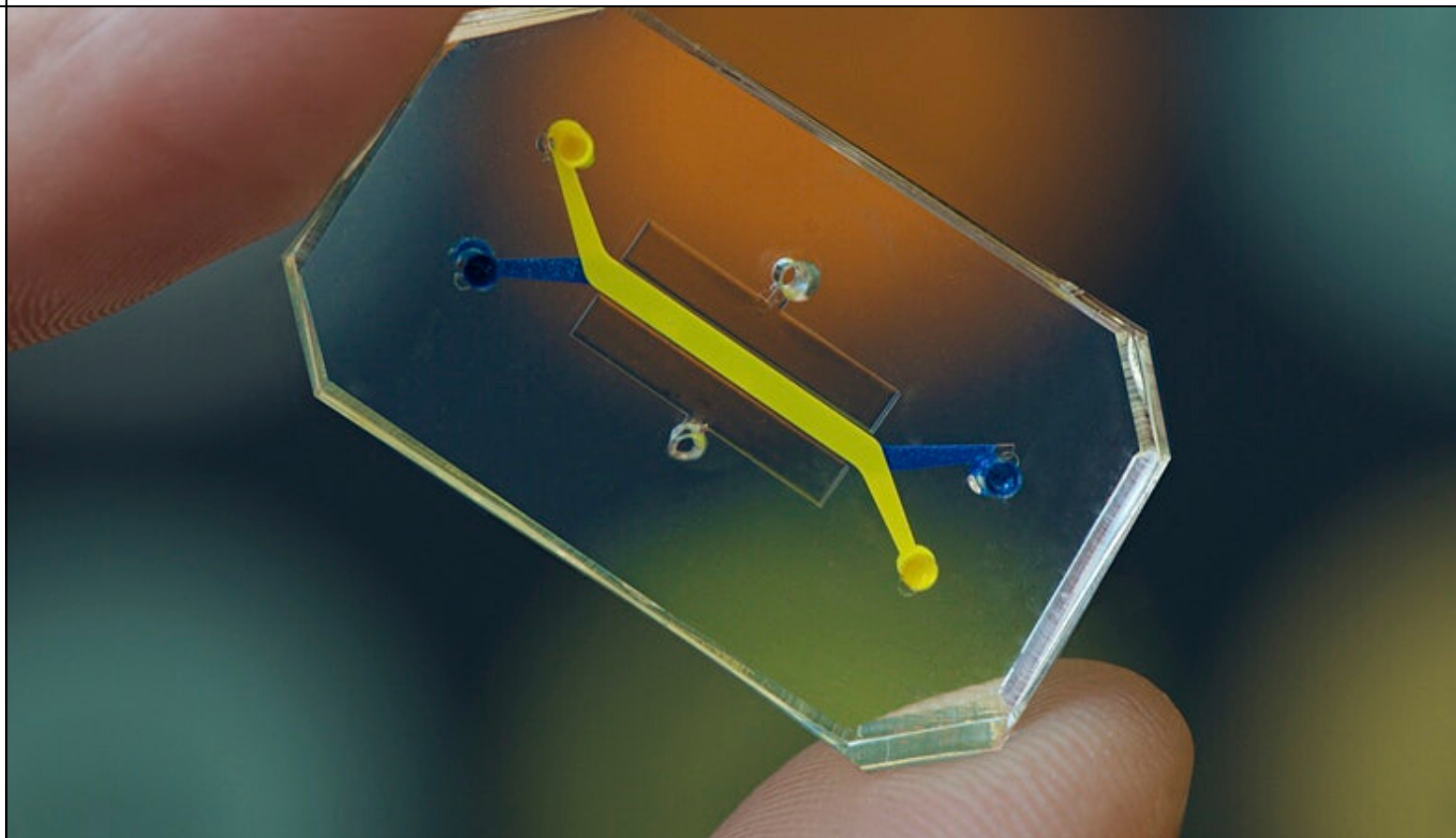
02 KEY TAKEAWAYS AND RECAP

03 SPEAKERS

04 FORUM PRESENTATIONS

05 QUESTION & ANSWER SEGMENT

06 MOVING FORWARD



DISCOVERY FORUM SUMMARY

On December 1st, 2022, the Center for Contemporary Sciences (CCS) hosted a Discovery Forum entitled "Updates on Human-Relevant Methods in Pharmaceutical Medicine and the Legislative Process" and featured leading experts from across the life sciences, biotech, academia, and nonprofits. Emphasis was placed on inventions enabled through regenerative medicine, electrical engineering, biophysics, and materials science. This includes platforms like Organ-on-a-Chip, 3D-bioprinting, and machine learning, all poised to transform biomedical research and the healthcare industry. The latest on implementing advanced technologies and enacting policies towards improving the drug development process, reducing the cost of medicine, streamlining biomedical research, and improving safety and toxicity testing was evaluated. The global agenda needed for the wider dissemination of Human-Relevant Methods was also analyzed, alongside the existing thresholds and barriers

DISCOVERY FORUM

KEY TAKEAWAYS

- Legislative advancements, such as the FDA (Food and Drug Administration) Modernization Act 2.0, are beneficial and crucial for the good of human health, our economy, and research.
- 3D bioprinted models are instrumental in modeling human diseases and human mechanisms in superior ways with better predictability than standard, ineffective, non-translational animal models.
- By working together, collaborating both nationally and internationally, and sharing knowledge and technologies, there is a greater chance of normalizing and optimizing human-relevant methods. Not only do individual researchers, labs, manufacturers, and testing facilities need to work together, but the support of government agencies as well is crucial.
- Key challenges include a reluctance from regulatory agencies, medical doctors, clinicians, and the pharmaceutical industry to replace animal models with human-relevant methods, a lack of industry guidelines, and validation of new models against the outdated, yet gold standard, which is the animal model.
- Forums like this one, that include multidisciplinary experts, are critical to bring fresh perspectives, refine existing ideas, spread much-needed awareness, and help design policies to promote disruptive technologies and their applications.

RECAP

This two-hour long Discovery Forum served as an opportunity to evaluate the progress underlying the most transformative innovations in human-relevant methods. The Forum featured short presentations by the panelists followed by an interactive group discussion. Panelists engaged in wide-ranging discussions focused on the technologies replacing animal testing and transforming the healthcare industry. Participants also addressed questions received from the audience. All panelists emphasized that collaboration and information sharing, including events like the Forum, are critical to unlock new potentials, gain fresh perspectives, spread awareness, and maximize the benefits of the emerging human-relevant technologies and their applications.

FORUM SPEAKERS



PAUL LOCKE, DRPH, MPH, JD

JOHNS HOPKINS SCHOOL OF PUBLIC HEALTH

Dr. Locke is an environmental health scientist, attorney, and Associate Professor at Johns Hopkins School of Public Health. He leads a team of lawyers and scientists who advocate for policy change, including how on how to improve the drug development process.



YAAKOV NAHMIAS, PHD, ISRAEL

TISSUE DYNAMICS

Professor Yaakov Nahmias is the founder of Tissue Dynamics and Future Meat Technologies. He is a bioengineer and innovator whose breakthroughs include the first commercial human-on-chip technology



ALEX ARMENTO, MS, USA

MATTEK LIFE SCIENCES

Alex Armento is the President and CEO of MatTek Life Sciences. He is the youngest president in the history of the company and has used his scientific and business acumen to help MatTek become an industry leader in tissue engineering.



DANNY LEVNER, PHD, USA

EMULATE

Daniel Levner is the Co-Founder and Chief Technology Officer of Emulate, a leading company in the development of microphysiocal systems. Dr. Levner is a technology pioneer with extensive experience in biological and engineering technology development and commercialization.



ITEDALE NAMRO REDWAN, PHD, SWEDEN

CELLINK

Dr. Itedale Namro Redwan is the Chief Scientific Officer of Cellink. She is an expert in 3d Bioprinting and medicinal chemistry, as well as the former lead of the Cellink Bioink and Tissue Engineering Research and Development team before being promoted to CSO.



FORUM PRESENTATIONS

CCS welcomed the group to the Discovery Forum and delivered opening remarks summarizing the latest human-relevant technologies and their applications. CCS shared perspectives and data on the scientific, economic, and policy developments in the space, and highlighted the multidisciplinary nature of these disruptive 21st century technologies and outlined the learning objectives of the Forum: (1) to gain an appreciation of the cutting-edge technologies shaping drug development and transforming healthcare, (2) to be able to size up the key legislative progress in the biomedical innovation space/human-relevant methods, and (3) to join the movement demanding human relevancy across scientific research in the interest of advancing the public good. It was also emphasized that there are major challenges in the drug development process, including those related to efficiency, efficacy, and safety, and prefaced that the panelists would discuss several solutions to address these challenges. In addition, there was also provided baseline information about “human-relevant methods” and noted that this phrase is often synonymous with “alternative methods,” “in vitro complex systems,” and “in silico complex systems.”

In the presentation, it was noted that in the last ten years especially, these human-relevant methods, otherwise considered devices, systems, and research tools, have gained sophistications and continue to evolve and offer opportunities to model human diseases in ways we could not before with standard packages and animal models that are notoriously poor predictors of efficacy and safety—particularly in the drug development process. The growing interest in human-relevant methods, like 3D bioprinting an organ-on-a-chip is reflected by the increase in publications and investment in the field. In one such paper recently published in *Frontiers in Medical Technology*, CCS' chronicles twelve reasons why these technologies are better at modeling human diseases in general and references a study produced by Emulate Inc. conducted on liver toxicity showing that these human-relevant devices and innovations can predict up to 87% of sensitivity.

In addition to increased scientific output and market interest, there has also been an increase in legislative efforts aimed at bolstering human-relevant methods including the HEARTS Act, the Humane Cosmetics Act, and the FDA Modernization Act (the Act was recently passed by Congress as part of the Omnibus Bill and has been signed into law by President Biden).

The presentation was concluded by stating that developing relevant models has been the quest of scientists throughout history but that this is easier said than done because of the many factors to consider in developing and utilizing these models. As can be seen from the work of the panelists, momentum is building for development and adoption of technologies that can model and mimic human conditions and allow society to have quicker access to safer, cheaper, and more effective drugs.

YAAKOV NAHMIA, PHD, ISRAEL – Founder of Tissue Dynamics Ltd. and Future Meat Technologies introduced the groundbreaking technologies that are developed at the company using data and examples from recent studies including 3D human tissue models for the human liver, kidney, heart, and brain, that all offer validated human-specific response. These tissue models have human genetics and human metabolism in a microfluidic environment that mimics human physiology. Normally, with small animal models, these genetic, physiological, and metabolic differences cause 70% of the compounds that show animal activity to fail in clinical studies. Dr. Nahmias underscored the utility of the human-relevant methods in drug discovery and in understanding biological functions.

Dr. Nahmias elaborated on Tissue Dynamics' high throughput kinetic screening platform that utilizes groundbreaking sensor-integrated organ-on-a-chip technology to monitor changes in metabolic function in real time to better understand mechanisms of action and to develop new drugs. This technology, which is the first of its kind, has already been awarded the European Seal of Excellence and was used to discover the idiopathic mechanism of acetaminophen back in 2015 and to show a metabolic shift that nobody else had detected, indicating the drug was causing stress to patients and leading to idiosyncratic toxicity. Additional studies have been done with Cisplatin, a cancer therapeutic, to show lipotoxicity in humans that had not been seen in rodent models. This finding, which showed how human-relevant mechanisms critically differed from rodent models, was featured on the cover of Science Translational Medicine last year and was also featured in Nature Review and Nephrology due to the breakthrough discovery of seeing human arrhythmia on a chip. Using Dynamics models, the group has also discovered oscillations in mitochondrial activity in their heart-on-a-chip model that also previously hadn't been discovered. These are examples that illustrate how innovative technologies are enabling discoveries about disease conditions in humans that have been impossible to identify using experiments with animals. Tissue Dynamics currently uses a robotic platform that can run 19,000 human micro tissues at the same time. The goal is to have an autonomous drug development process where the robot makes its own decisions and can develop drugs for at least the early stages of discovery.

Dr. Nahmias mentioned major problems of drug development include a timeline of taking 12-14 years and \$2.6 billion, only to still be met with more than 88% of clinical trials failing and industry costs of over \$10 billion a year. Additionally, 10% of drugs are still withdrawn after approval, and this cost equals approximately \$2 billion a year. Dr. Nahmias indicated that these failures still exist because of the unknowns. For example, when a person participates in a clinical study, not only is there a lack of predictive ability to say whether something works or not, there is also a failure to understand exactly how things work. We do not completely understand the mechanisms of



action of a drug and that leads to surprises and major expenses, and this is happening because we are still relying on small animal models—which have different physiology, genetics, and metabolism from humans and these components all have different mechanisms of action.

ALEX ARMENTO, MS, USA – President and Chief Executive Officer at MatTek Corporation, a BICO company, delivered remarks addressing the future of preclinical testing and outlined the process of drug development, examining the challenges confronting the industry as well progress made to date. He noted that BICO is a leader in merging biology and technology with laboratory automation and robotics to optimize workflows and reduce the time and the cost of pharmaceutical drug development. MatTek also has the largest portfolio of proprietary 3D human tissue and disease models in the world. MatTek's tissue models are all produced from primary human cells using innovative tissue engineering technologies, which provides a microphysiological platform that models highly relevant and more predictive human biology. Mr. Armento shared MatTek's experience in product launch and standardization, including international standard development and certifications per the ISO (International Organization for Standardization) guidelines. Some of these products and test methods have already been formally validated and recognized by U.S., European, or international regulatory agencies as standalone replacements for animal-based tests.

The latest innovations from the growing MatTek portfolio of solutions, including available discovery and testing products in toxicology, cosmetics, immunology, and drug delivery, were also summarized in Mr. Armento's remarks. Mr. Armento underscored the value provided by new models like 3D technologies and organ-chip to accelerate the discovery process and increase productivity in the pharmaceutical industry. Mr. Armento also emphasized the importance of understanding of how different industries are using MatTek's different tissue models and by appreciating a customers' pain points and their existing testing processes, MatTek can shift internal product and asset development to meet the future demands of the customers, as being customer-centric is of great importance to the company.

Mr. Armento also mentioned another driver of market growth and focus on human-relevant methods, is by considering both ethical and scientific perspectives. He used the cosmetics industry as an example and how consumers have pressured industry to shift away from animal testing. Such efforts have been successful as animal testing is now banned in several countries, and has received pushback in the U.S., due to legislative wins. In terms of the scientific perspective, reliance on animal models has led to years of lost time and money, and the legislative push for the FDA Modernization Act to become law has further emphasized the growing interest, and need, for microfluidic platforms and human-relevant models. Ultimately, being able to interconnect the tissue models of various organ systems, continue to increase assay throughput, and improve customer interfacing are goals of MatTek.

DANNY LEVNER, PHD, USA – Co-Founder & Chief Technology Officer of Emulate, Inc. gave an overview of the industry today and focused on a landmark study from Emulate and collaborators that was published on December 6, 2022, in Nature Communications Medicine. Dr. Levner explained the key findings of the study validating organ-on-a-chip technology for predictive

toxicology in preclinical development. He shared data demonstrating how the Emulate Liver-Chip was able to correctly identify 87% of drugs that caused drug-induced liver injury to patients despite passing through animal testing and animal models. This finding is significant because according to Dr. Levner, 100% of those drugs would have gone to clinic and made it into humans, even though around 9 out of 10 drugs evaluated would have been toxic in people. He summarized this model can be used to potentially reduce the number of liver-toxic drugs by almost a factor of 10. Dr. Levner reiterated that with drugs, the issue is not necessarily in the approval process itself, but what happens ahead of drugs in the clinic. He explained that it is because the wrong candidates are going into clinics, in part because it is challenging to predict whether the drug is going to be safe or efficacious for humans ahead of giving it to humans.

Dr. Levner also shed light on the economic evaluation conducted in the study showing that routine use of just liver-chips could generate \$3 billion per year to small-molecule drug development by driving an increase in research and development productivity. The economic value model that Dr. Levner referenced will be made available to the public. This economic model framework will track a hypothetical model through testing and allow users to create estimates of how a particular model with sensitivity specificity can impact the economics of drug development.

Dr. Levner emphasized that animal biology is different from human biology (and these differences are especially the case when looking at smaller animals). When talking about conducting human-relevant research and testing, Dr. Levner noted that once a human cell is out of the body and put in a Petri dish or other construct, these cells will start behaving differently than they do in the body and will likely lead to wrong results. Emulate was created to address this discrepancy and was at the forefront of developing organ-chip technology that gave cells “a ‘home away from home’ by controlling the cellular microenvironment” and allowing them to experience the environmental elements they would within the body, such as “the right protein and chemical environment, fluid flow interaction, multiple cell types, and mechanical forces that are carefully configured for each model.” Regarding validation, Dr. Levner stressed that validation must be specific to a particular model in a particular application.

Dr. Levner also mentioned that a large component of economic impact is regulatory change, such as the impact of the passage of the FDA Modernization Act, which will allow researchers to use the best human-relevant tools available and remove animal testing mandates. He also cited a European Parliament Resolution in which the European Commission voted to establish “an EU-wide Action Plan for the active phase out of the use of animals in experiments to incentivize progress in the replacement of animals with non-animal, human-relevant methods.” The focus must be on the human impact and patient safety requires modernization.

ITEDALE NAMRO REDWAN, PHD, SWEDEN – Chief Scientific Officer at CELLINK, a BICO company, introduced the growing field of bioprinting from various angles, focusing on its applications in tissue engineering, pharmaceutical sciences, and the cosmetic industry. Dr. Namro Redwan also summarized the bioprinted human tissue models for pharmaceutical and cosmetic product testing at CELLINK. She explained the mission of CELLINK in advancing tissue engineering and gave an overview of the suite of new products launched, all of which serve to

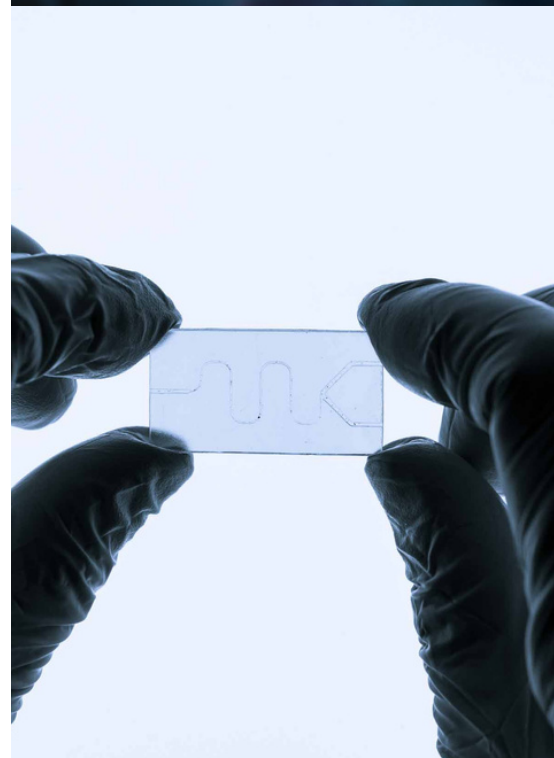
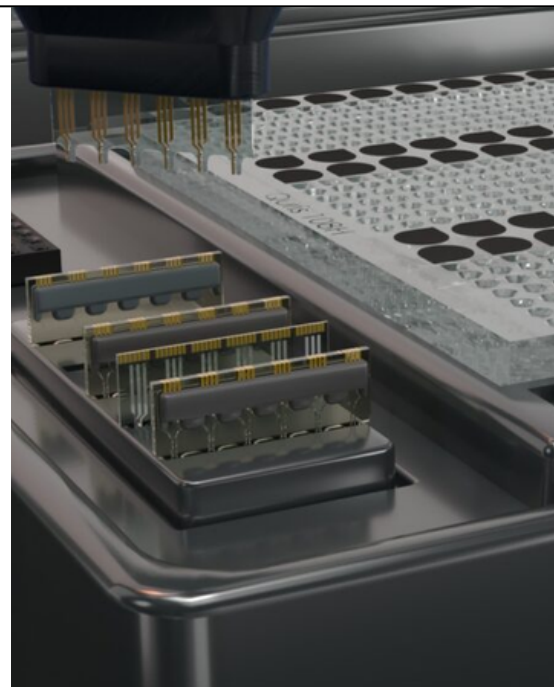
facilitate human-relevant discovery and testing methods. Dr. Namro Redwan updated the audience on the latest innovations in bioprinting designs, including bioprinters and biomaterials like bioinks– materials (typically cells) used to produce engineered live tissue using 3D printing.

Dr. Namro Redwan reiterated that the development of new treatments takes too long (10 years), costs too much (\$2 billion), and targets symptoms rather than the disease. She also indicated that on average, 16 lives are lost every day (by those waiting in the transplantation queue) due to the lack of organs for transplantation. She cited that 9 out of 10 drugs fail in clinical stages due to poor models for testing and due to the lack of representative models for human mechanisms.

By creating 3D bioprinting technologies, products, and services, to master biology, Dr. Namro Redwan hopes that CELLINK can be a catalyst for enabling the development of life-saving treatments in the future, noting specifically using biofabrication methods to create structures that can be used for regenerative medicine and further development of disease modeling for drug development using organ-on-a-chip. She emphasized that because none of our organs grow flat, it is essential to be able to use 3D architecture to support tissue models of interest with nutrients and to be able to remove waste.

Dr. Namro Redwan also mentioned her team has been working on developing advanced skin models. She also mentioned that stem cell development relies on, and benefits from, 3D architecture. Using their bioprinted constructs and bioinks, CELLINK can build the desired tissue architecture and allows researchers to take the cell or cells of interest and mix them. In fact, CELLINK developed an ink based off specific skin cell components (including nanocellulose) and was able to select the different cell types of the skin and bioprint a skin construct.

Advancing the use of human-relevant methods in research is a collaborative effort. Dr. Namro Redwan noted that CELLINK's goal is to do the proof of concepts for the industry and then have customers and collaborators help to advance the technology further.



QUESTION AND ANSWER

KEY HIGHLIGHTS FROM THE Q&A SESSION. TOPICS HAVE BEEN COMPILED INTO THEMATIC GROUPS FOR BREVITY.

LEGISLATION:

(Note: At the time of this forum, the FDA Modernization Act had not yet passed in the House, but it has since passed and has been signed into law by President Biden as part of the FY2023 Omnibus Bill.)

Introduction to the question, from Dr. Paul Locke, Associate Professor, Johns Hopkins BSPH: At least one of you mentioned the FDA Modernization Act which is close to being enacted into law and that would remove a section of the Federal Food, Drug and Cosmetic Act that requires animal testing and replace it with the term “nonclinical tests,” which would expand the idea of what you could use, and you would not have to use animal tests. You could still use animal tests if they were the best, but you could use non-animal tests. Additionally, there is a bill that would create a National Institute centered around alternatives, a new agency funded at \$1 billion, the ARPA-H (Advanced Research Projects Agency for Health), that Dr. Akhtar and I wrote an opinion piece about.

Q: In terms of federal legislation, what would you like to see? What do you need from legislative regulatory folks to help things run more effectively (especially thinking about how those could be used to advance the great technologies and the work that your organizations and other organizations like you are doing)?

A: All panelists agreed that legislation, the FDA Modernization Act specifically, will be extremely beneficial as it removes an outdated requirement to use animals in testing and it is this legislation they all have been following closely. All experts agreed that animal models mis-predict, and current processes are costly and ineffective. They unanimously supported the importance of actively investing, and highlighting, where alternative technologies can reduce risk to people. Dr. Levner expressed it is not only crucial to acknowledge that animals are inferior to other alternatives (you get the door open), but you need to put some fire behind it (you need to be able to walk through!). But in addition to needing federal legislation, Mr. Armento emphasized that industry must make guidelines. If you try to do this at the state level, you might get 50 different rule sets.

Introduction to the question, from Dr. Locke: I think for many reasons, at least in the United States, state legislation is probably not going to be a particularly good option because you really need the federal engine to move things since that is where the regulations really are.

Q: But what about state legislation? Does anyone have any information to share about their relationship with their state and any innovative approaches to get support there?



A: Most of the panelists mentioned the importance and focus on the FDA Modernization Act and that passing in both the House and the Senate, which would mean bipartisan consensus was reached, would be a major challenge to overcome. The experts also recommended that members of the public could write to their congressperson and state representatives stating their support for the FDA Modernization Act and shift to modern models (and one of the experts noted that their organization had done that).

VALIDATION AND REGULATORY ACCEPTANCE:

Q: When we think about validation and regulatory acceptance, what are your experiences in other jurisdictions? Are they good? Bad? What can we learn as an international community?

A: All experts agreed that it is essential to work with partners to help move these innovative technologies forward. Dr. Locke indicated that there are useful models being used in the EU and perhaps the U.S. should look to other jurisdictions to develop base practices to implement in the U.S. Dr. Levner mentioned that Emulate has some experience outside of the U.S. and noted that whether it is here or abroad, these new innovative systems need to be pushed with some urgency because peoples' lives are on the line. Mr. Armento reiterated that the acceptance timeline is lengthy, and perhaps there can be some mechanism to more quickly accept work that is outside validation systems. He further emphasized it is crucial to work together to drive the validation process forward to gain widespread adoption. He also mentioned that having an agency at the forefront of validation would be especially helpful. MatTek has lots of experience validating models and assays through the ISO (International Organization for Standardization) and these are very rigorous validations. He noted several existing OECD (Organisation for Economic Co-operation and Development) validations took 10 years from start to finish and \$1 million dollars each. If we knew the criteria and level of rigor that is acceptable by an accepting agency, like the FDA, could we work to bring facilities together to streamline the process? When we work together with industry partners, we can accomplish more, quicker.

Q: Considering the differences in markets (China vs the U.S. or European Union) how were your experiences in terms of regulation, standardization, and common data elements for your products?

A: Mr. Armento noted that most validation is through OECD and this validation has been accepted by multiple countries. But he also mentioned that each individual country can accept the OECD test guidelines or not. Europe and U.S. are well aligned. But China, for example, has a very different approach from the U.S. and Europe when it comes to cosmetics testing. Although the U.S. has guidelines that are validated and approved, China still says testing must occur on animals in their country for it to be accepted (this requirement has relaxed in certain situations, but not all). Data will not be accepted from outside their country. But OECD does a great job being an umbrella organization that provides guidance to anyone who wants it.

Q: What is the scientific value of validating in an animal model IF already proven effective in human-models?

A: Dr. Namro Redwan mentioned that animal models provide the whole system, whole body, and it is the first resort before using humans. The animal model has been where we have had a living organism, full body, all organs, the blood system, being tested. But as noted, there are entire mechanisms/pathways that do not exist in animals, but they exist in humans. A mouse is not a human. So, are infecting rats with COVID a real model? It is artificial. Dr. Levner also weighed in that we do not typically have a "head-to-head" comparison of a human chip versus a rat model because they are different models. When asked to make animal versions of the chips it is important to realize they are different cells, different protocols.

To try and develop a human diagnostic and use it in the veterinary market—it is redevelopment. It is not the same product. Mr. Armento further commented that when validating a new method, we must consider what we are validating against. Typically, the comparison is to a gold standard. And in most cases, this validates a human model against an animal model and obviously that will be different. We are not trying to mimic animal responses with these models. For example, one of MatTek's validated assays (for skin hazard assessment) were not 100% predictive according to the gold standard (which was the rabbit Draize test) but if you look at some of these materials through human patch testing, our data was correct. Mr. Armento also indicated that in conversations he has had, a point of view has been "if your animal in vitro method matches the animal in vivo, then we'll have more confidence that your human in vitro methods should match humans in vivo." According to Mr. Armento, the best way to move this technology forward is "to validate a human assay against retrospective analysis of actual human data. This data is limited. But there is enough for us to get some substance out of it."

PATH/TIME TO PROGRESS:

Q: Have you received pushback from any sector?

A: Dr. Namro Redwan noted that medical doctors want traditional methods, and there is a hurdle to make these new models or new ways of doing drug identification acceptable. Especially for disease modeling, it takes time for medical doctors to adopt new technologies. Notably, the pharmaceutical industry has been quicker at picking up these new technologies because the industry knows it is important to have more advanced and representative models of human physiology, in addition to having the courage, and the funding, to support campaigns for models that lead to better results. She also noted that biostructures, specifically, have been a huge challenge for acceptance because government bodies are using old assays and some of the tests performed do not assess the true thing or mimic the bioprinting process. She further indicated that it is a challenge to get bioprinting approved with current processes. Because of this, she and her colleagues are trying to involve governmental bodies early on so they can work together to show them we need to change how we assess biocompatibility (especially with regenerative medicine applications). CELLINK hopes to optimize current methods and at least propose alternative methods that can be used for FDA testing and approval later. Luckily, recruitment within these agencies for biomaterial and tissue engineers working with bioprinting has increased. This is an important step forward because these individuals can provide specialized knowledge while working within governmental bodies. The way we treat disease has changed and will continue to change. Alternative methods are representative of what we want to measure.

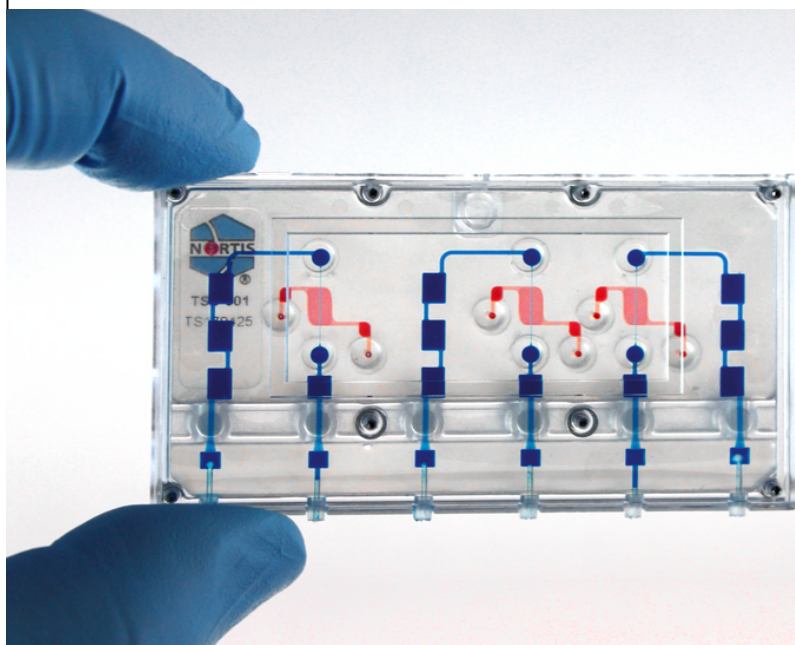
Q: What are potential fear points that have come up? With industry? With regulators?

A: Mr. Armento reiterated that even with growing interest in these new methods, there is still a lack of trust with them because they are so new. And this is where rigorous validation must come in. He noted that if a researcher can prove that their assay is 95% sensitive, overall accuracy is known with a large set of compounds, and a model can be tested thoroughly, then confidence and trust can be built. Customers have asked questions such as "we have this data from a rat and another data set from primates—which one is right?" His answer? These are opposing datasets. Dr. Levner indicated there is a lot of focus on regulators as major gatekeepers. But he also expressed the importance of the role of the pharmaceutical industry in accepting new methods, since pharma can already use some of this technology without regulatory approval to make better selections of what will go in their work up. However, there has also been a roadblock with pharma, as one concern that is often expressed is that while the data from alternative methods may be convincing, there is fear about using such methods in the event there is a finding not in line

with animals. What happens then? There is potentially an obligation to report this to the FDA, which can be intimidating. There are industries that have produced some type of “safe haven regulation” where experimenting with this technology is encouraged without the fear of certain repercussions. Dr. Levner posited, to what extent can legislation reduce some of these fear points for industry? Of course, nobody will complain about one more data point that shows something valuable. But the value here is in catching things that the animal models miss. He explained that you can trust that if you see something with the chips, this should raise an alarm bell and further investigation should take place. But because it is new technology, pharma will want to double and triple check the data because it could mean “killing” a particular candidate or whole program. So, it is not a decision to take lightly. And if an investigation is done using new methods and the results are still not believable, for whatever reason, pharma may still have an obligation to report to the FDA. Other groups worth mentioning here are toxicology groups. If technology is offered that allows them to prevent bad drugs from entering a clinic, they might be penalized for taking fewer drugs into the clinic. There is a disconnect between the company and patient-based incentives.

Q: In terms of refinement and reduction, how do you see this change happening? Gradually?

A: CCS reiterated the importance of having forums like this one and meetings with industry experts and like-minded partners to come together just as we are doing for this webinar. We are the changemakers. He noted that we must depend on those spearheading these innovative technologies to keep pushing through. Or else we will always fall back on animals. He posed the question, “How do human-relevant models create solutions for the gaps we are currently seeing in this space?” We must show why and how these human-relevant models work. Dr. Namro Redwan agreed that the movement had started. It is by combining technologies and sharing knowledge that gives society the best chance for advancement and acceptance of this technology. She expressed that convincing arguments can be made as to why we should avoid and exclude animal models, but it will be hard to get there. Dr. Levner noted that there are others in industry who have made statements about eliminating animal testing but that might not be a realistic goal, at least for the near future. He said that co-existence of animals and alternative models was important because we can learn things from both. He suggested that with current requirements of the FDA to test on two animal species, perhaps the more expensive animal species can be dropped? Several of the experts indicated that another roadblock to a quicker adoption of these methods is that there are so many small players in this industry and so the industry can feel fragmented. For this reason, it may be beneficial to focus on the major players, the ones with the mature technology, and we can build from there. And in fact, Dr. Levner mentioned that customers and academic users he has spoken with have been overwhelmed by how many different options there are in this space (and it can be confusing knowing which companies offer services versus mature products that can be purchased for use in labs).



PERSONALIZED MEDICINE:

Q: Using technology today, and speaking about individualized/personalized medicine (specifically in reference to bioinks currently being developed), can bioinks be created on demand, on request? For example, are we able to build bespoke tumor drugs using patients' own bioprinted cells?

A: Speakers emphasized that we need to humanize the data. It is important to bring focus back to the individuals behind the numbers and that the data is not just numbers, but real futures and opportunities. Dr. Namro Redwan mentioned that CELLINK currently works with a collaborator out of the UK called Carcinotech, which is a company that takes cancer biopsies from hospitals and creates advanced cancer models specific for that patient. They then take the heterogeneous tumor (which is a minimum of five cell types) and they mix it with the appropriate biomaterial and print reproducible structures that can be used not only to identify which drug is active for that patient, but also at which dose. She asserted that now, what needs to be done, is validation together with the clinicians and compare it side-by-side with the methods used today to show that these newer methods are stronger or at least more representative of what we are trying to study. CELLINK is also working with a team in Italy that is using biostructures within clinical tests for patients who suffer from blood cancers. Personalized models are being used to help patients identify which drugs work the quickest for them so the patient can be put on the correct treatment as soon as possible. Dr. Namro Redwan also noted that there is still a challenge to convince the clinicians to enter bioprinting into their clinical practices, but there is a lot of amazing work going on within that industry.

ACADEMIA/CALL TO ACTION:

Q: Several speakers ended with a call to action. Are we doing enough on the academic side to train the future generation of scientists and researchers? If there is more we should be doing in academia, what should we be doing?

A: All experts expressed there is a growing interest from academia to connect with biotechnology groups and to learn more about the work that is being done in this space. This interest is dramatically higher than it was ten years ago. The speakers agreed on the importance of training future generations on these new technologies because science, and research, is changing. Mr. Armento mentioned that MatTek has been doing significant outreach, training, and hosting of workshops with academia in both the U.S. and Europe. Dr. Namro Redwan added that CELLINK has increased outreach efforts as well, and the group has been contacted by professors who want to send their students to their labs internationally. She expressed that the opportunity for students to work side-by-side with researchers, exploring their own scientific questions using CELLINK's technology, has been wonderful. CCS spoke of how academia, and training, has changed since he was in school and that this shift to more acceptance and use of human-relevant technologies is evident through the increased number of publications on the technology and overall recognition from industry that these innovations are valid. He also notes that the training piece for using this new chip technology is essential. You cannot just make available these new methods of testing and then not provide the proper training.

MOVING FORWARD

In the month following the Discovery Forum The FDA Modernization Act was included in the FY2023 omnibus appropriations bill, passed by congress, and signed into law by President Biden on December 29th. This is not only beneficial, but a crucial step for the good of human health, our economy, and research. Although this is a significant move towards acceptance of human-relevant models, other changes like increased funding for human-relevant technologies, updated guidelines, and faster validation of new models are necessary to depart from animal testing as the default standard. Moving forward, CCS will continue building relationships with researchers, academics, and legislators to help facilitate the paradigm shift away from animal models and bring biomedical research and safety testing into the 21st century.

THANK YOU TO OUR SPEAKERS



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