CASE STUDY REPORT

Paving the Way For Animal Free Models by Leveraging 3D Cell Culture, Organoids & Organ Modelling

A Concise Report Featuring Insights From The Prominent Thought Leaders Of 3D Cell Culture & Organ Modelling 2024

Introduction

This market report aims to explore the industry's latest cutting-edge technologies, where breakthroughs in 3D cell culture, organ modelling and microphysiological systems are shaping the future of therapeutic developments.

From regenerative medicine to cancer research, the application of 3D cell culture spans a broad spectrum. Unlike traditional 2D cell cultures, 3D cell culture provides a more physiologically accurate platform for studying cellular behaviour, interactions, and responses to various stimuli. We gain insights into how 3D cell culture predicts drug efficacy, toxicity, and pharmacokinetics more accurately than traditional methods, reducing the attrition rate of drug candidates in later stage clinical trials.

As a result researchers gain a deeper understanding of biological processes and drug responses, thus improving drug discovery and development processes.

At the centre of report there are three key themes, each representing a cornerstone in the ongoing evolution of 3D cell culture:

Innovative disease modelling techniques:

This market report offers insights into novel modelling techniques. The expert speakers covered a wide range of modelling methods including organoids, organ-on-a-chip systems and other microphysiological systems.

Expert opinions in this market report show how this 3D cell technology provides an effective platform for drug testing and disease modelling. It helps simulate complex organ systems in vitro allowing for more accurate prediction of drug responses and disease mechanisms.

Patient-specific and personalised medicine approaches

Tailoring treatments and models to individual patients or specific disease states can enhance therapeutic outcomes. Several case studies span a wide range of personalised approaches, from using iPSC-derived follicular organoids for hair restoration to using brain organoids to model neurological disorders, these methods provide better targeted treatments.

Collaboration and inter-disciplinary research efforts

Collaboration efforts between different institutions and disciplines foster knowledge exchange and advances research. This market report shows how collaborations have led to important advances in developing 3D models.

As we explore the 3D cell culture landscape, we draw on the wealth of expertise present at our recent 3D Cell Culture & Organ Modelling 2024 event, a gathering of over 200 industry professionals dedicated to pushing the boundaries of 3D cell culture. Through a comprehensive analysis of presentations, data and expert perspectives, this report aims to provide a nuanced understanding of the current landscape, strategic challenges, and emerging opportunities in the field of organ modelling and 3D cell culture.

Lucia Simmen
Digital Content Assistant, Oxford Global

Contents

Key Speakers Include

MARCELO RIBEIRO,
CSO,
River Biomedics

SABRINA MAISEL,
Principal Scientist ,
Stemson Therapeutics

TAMARA ZIETEK,
CSO, Doctors Against Animal Experiments

Key Speakers Include

BRUNO FONTINHA,
Principal Scientist,
a:head Bio

STEFAN PLATZ,
Senior Vice President
Clinical Pharmacology
Safety Sciences,
AstraZeneca

MOLLY TREGIDGO,
Associate Senior
Scientist, Cell and
Gene Therapy Catapult

Innovative Disease Modelling Techniques

According to Precedence Research, the 3D cell market size was valued at $1.42 billion USD in 2022. By 2032 it is estimated to be valued at $5.29 billion USD by 2032. There is an increasing demand for more physiologically relevant models in drug discovery. Furthermore, developments in technology have facilitated complex tissue engineering and the growing prevalence of chronic diseases necessitates more accurate preclinical testing.

Source: BioSpace

Why is 3D Cell Culture Important?

Unlike 2D cell culture, 3D cell culture more accurately mimic in vivo-like cell interactions, cell division and morphology. 3D cell culture is a method of cultivating cells in an extracellular matrix that mimics the in vivo microenvironment and allows cell-to-cell interaction.

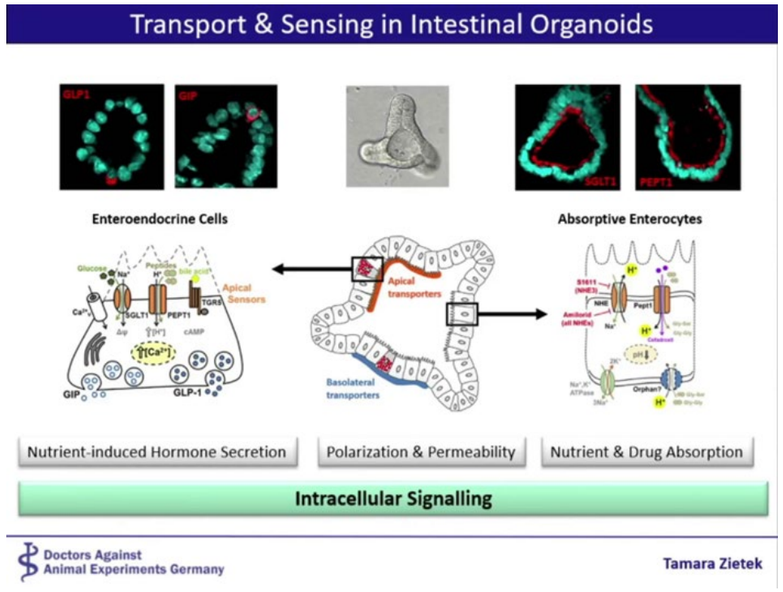
Animal models sometimes fail to identify toxicity signs caused by a drug in humans. Leveraging organoids is a powerful approach to optimizing human biological relevance. Incorporating organoids in drug development helps researchers better understanding the dynamic functions and responses of organs for drug evaluation and disease modelling studies.

Organoids are a type of 3D cell culture, human organoids are stem-cell derived 3D culture systems which can recreate the architecture and physiology of human organs in extraordinary detail. Animal models cannot mimic human physiology to the same degree as human organoids and leveraging the use of organoids promotes animal free experiments. Furthermore, organoids are self-organising.

3D Live Cell Imaging In Intestinal Organoids

Tamara Zietek (CSO, Doctors Against Animal Experiments) discussed the use of organoids as a model for biomedical research. She examined their application in gut hormone secretion and drug absorption. She introduced her background in nutritional physiology and intestinal absorption, emphasising her transition to working with organoids due to their ability to reflect human physiology accurately.

Zietek stated the importance of studying nutrient sensing and gut hormone secretion in enterocytes and enteroendocrine cells. She focused on peptides and glucose transporters and their role in regulating insulin release and blood glucose control.



One significant aspect of her presentation was the establishment of live cell imaging in three-dimensional organoids, which allows for the visualisation of intracellular signalling processes, such as calcium influx and pH changes. Zietek demonstrated the use of fluorescent dyes to track these signals and showed how drug absorption and transporter-specific inhibition studies could be conducted in organoids. High levels of red fluorescence indicate a low calcium signal. However, the addition of ATP increases calcium influx in the organoid.

She also discussed the importance of cell-specific signalling responses and how organoids allow for the analysis of such responses at the single-cell level. Zietek reiterated the versatility of organoids in studying various aspects of cellular physiology and drug responses, highlighting their potential as a tool for replacing animal testing in the long term.

Finally, Zietek mentioned her role as the product leader of the Nutri-Database, a free online database on non-animal technologies, and invited the audience to the upcoming MPS World Summit.

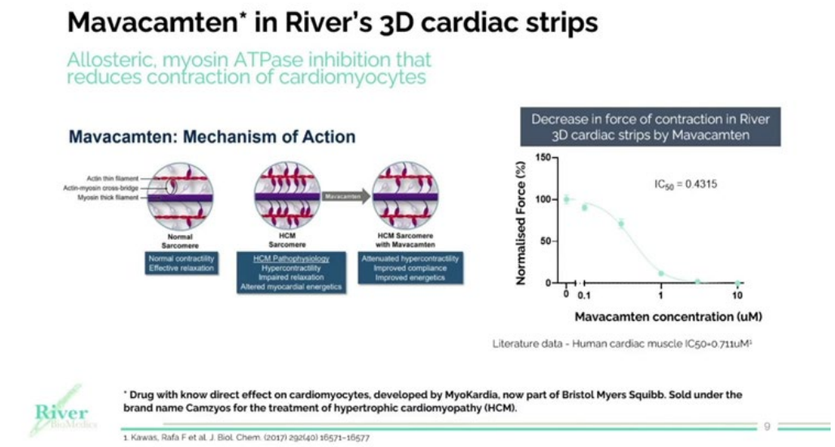
Modeling HFpEF Cardiac Stiffness Using Human 3D Cardiac Tissues and Its Application In Target Validation

Marcelo Ribeiro, (Co-Founder & Chief Scientific Officer, River Biomedics) introduced River Biomedics, a drug discovery company focusing on cardiovascular diseases, particularly heart failure. They employ a unique approach using 3D cardiac models to validate targets and compounds before advancing to animal or human models. Ribeiro emphasised the limitations of current preclinical models and stresses the need for more relevant and scalable alternatives.

He highlighted key points, including the company's focus on heart failure, the expertise of their team, and their funding status. Ribeiro discussed the challenges with traditional

preclinical models, such as rodents and cardiac organoids, in accurately mimicking heart failure.

River Biomedics develops 3D cardiac models using induced pluripotent stem cells (iPSCs) to replicate heart tissue, allowing for the measurement of force of contraction and relaxation, crucial for assessing cardiac function.



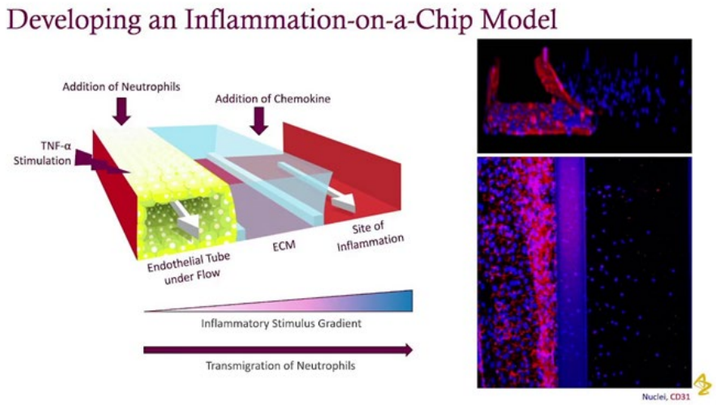
They validated their model by testing various drugs known to affect cardiac contractility. A key model that the team developed is one that mimics heart failure, this is particularly challenging to replicate in vitro because there are many other organs involved. Ribeiro aimed to model the decreased relaxation (passive stiffness) associated with heart failure. This model tackled this stiffness associated with cardiac arrest. The model is then used to validate the drug that will be found against the target.

Ribeiro also discussed their approach to modelling other cardiovascular diseases using genetic editing, environmental cues, and stressors like doxorubicin. Scaling up this process involves the miniaturisation of the 3D cardiac strip cells and using high-throughput screening to identify potential drug candidates. The ultimate goal is to improve preclinical to clinical translation efficiency in the cardiovascular field.

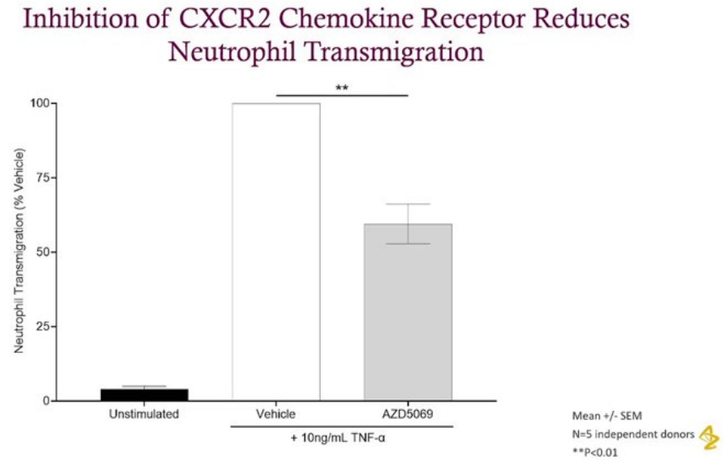
Inflammation-On-A-Chip Model of Neutrophil Transmigration

Rebecca Riddle (Scientist, Mestag Therapeutics) discussed her PhD research conducted at the University of Cambridge, in collaboration with AstraZeneca. Her research focused on developing an inflammation-on-a-chip model of neutrophil transmigration. She began by explaining the process by which immune cells leave the bloodstream to reach the site of inflammation and fight infections. This process can become dysregulated in chronic inflammatory diseases.

Using the Mimetas OrganoPlate, Riddle constructed a vessel in chip. She then aimed to build on this and develop her model into an inflammation on chip model. This requires inducing inflammation in the vessel. She achieved this by stimulating the endothelial vessel with TNF alpha, a common pro inflammatory mediator. Furthermore, she added chemokine, a chemoattractant molecule to stimulate neutrophil migration out of the vessels and into the surrounding extracellular matrix.



Riddle presented data validating the model's ability to test inhibitors of neutrophil transmigration, showcasing the effectiveness of compounds like AZD5069 and MCC950 in reducing neutrophil migration.



Additionally, she briefly discussed the model's usefulness in target discovery and validation by successfully knocking down a target gene within the endothelium, resulting in increased inflammatory gene expression. Riddle examined the adaptability of the model to different cell types, migratory cell types, inflammatory stimuli, and matrix compositions, highlighting its versatility in addressing various research questions and disease areas.

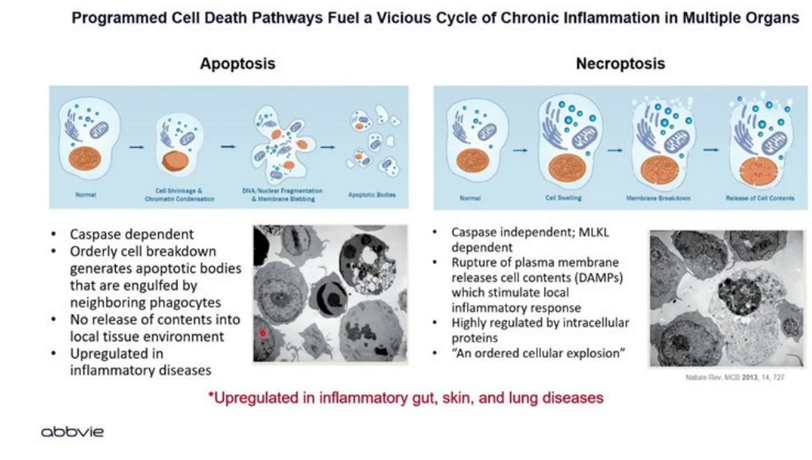
In conclusion, Riddle summarised her work, emphasising the development of a robust and effective inflammation-on-a-chip model that can be modulated by small molecule inhibitors or siRNA. The model can be modulated in different ways dependent on the specific research needs.

Microphysiological Systems In Drug Discovery: Does One Size Fit All?

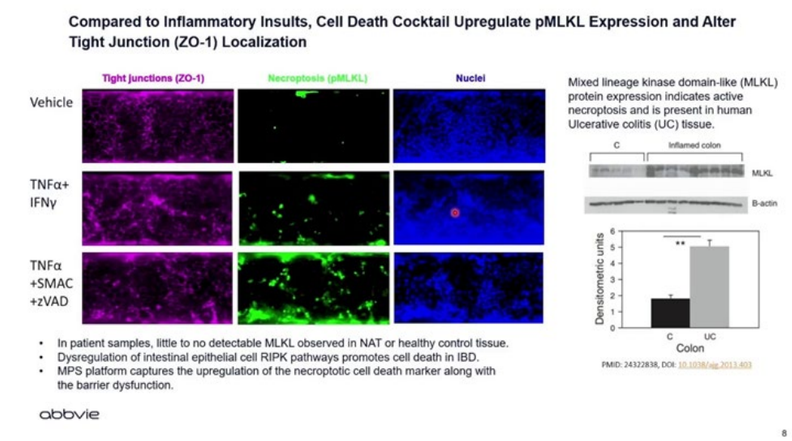
Abhinav Sharma, (Translational Human Models Lead, Immunology Discovery, AbbVie) focused on implementing complex in vitro models, specifically microphysiological systems (MPS), within the context of drug development at AbbVie.

Sharma discussed the importance of MPS platforms, which mimic biochemical and mechanical properties of organs, in understanding disease mechanisms and expediting drug development. He explained tissue engineering's role in creating these platforms, emphasising the need to replicate physiological features like barrier function, cell turnover, and immune responses.

The presentation then examined the implementation of an MPS platform for studying cell death pathways, particularly apoptosis and necroptosis, in a colon model.



Sharma demonstrated the platform's ability to measure barrier function and leakage, as well as its application in testing therapeutics and validating clinical findings.



He further explored the use of MPS platforms in modelling skin barrier function and alveolar epithelial barrier function, displaying their versatility across different organ systems. Sharma also discussed incorporating immune components into MPS platforms to study immune cell activation and migration.

In conclusion, Sharma highlighted the adaptability of MPS platforms across various applications within drug development, emphasising the importance of context-specific modelling and complexity-building.

MiNK-215, An IL-15 Armoured FAP-Targeting Allogenic CAR iNKT Cell Therapy, Effectively Targets Tumour Stroma While Enhancing T-Cell Antitumor Responses In A 3D NSCLC Model

Gerard Rubi-Sans's (Scientist, Mink Therapeutics) presentation focused on Mink Therapeutics' advanced CAR-T cell therapy program, particularly their use of 3D models to screen candidates and study their mode of action. They use invariant natural killer T cells (iNK T cells) for their therapies, emphasising their off-the-shelf nature and reduced risk of rejection.

Their approach involves engineering car and TCRs into iNK T cells to enhance their activity against tumour cells. They've demonstrated clinical benefits and safety in ongoing clinical trials across various diseases. Rubi-Sans aims to produce these therapies in-house using a scalable manufacturing platform.

Their most advanced project targets fibroblast activation protein (FAP), highly expressed in tumour-promoting stromal cells. By targeting FAP-expressing cells, they aim to modulate the tumour microenvironment and enhance immune cell activity.

To study the efficacy of their therapies, Rubi-Sans initially used animal models but transitioned to 3D models to predict efficacy and toxicity more accurately and efficiently. These models recapitulate the complexity of the tumour microenvironment, allowing for better preclinical assessments.

The preclinical data show promising results, with their iNK T cell therapy demonstrating strong efficacy against non-small cell lung cancer models by targeting FAP-expressing cells and enhancing T cell responses. Rubi-Sans plans to further enhance his models to study additional aspects of tumour biology and establish a drug screening platform.

Overall, his approach aims to develop effective and safe cell therapies for cancer treatment, leveraging innovative technologies and preclinical models to accelerate the development process.

Patient-Specific & Personalised Medicine Approaches

GMI's latest market report, highlights advancements in personalised medicine and 3D cell culture, as well as their wide range of applications that could reshape regenerative medicine approaches for numerous diseases. Personalised medicine in tissue engineering will allow clinicains to replace damaged tissues with patient-specific organs that are less likely to be rejected by the immune system.

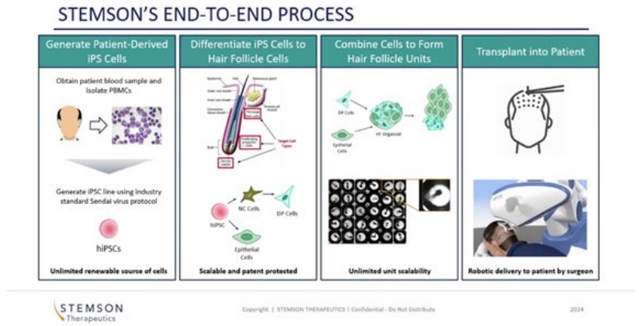
Source: GMInsights

A Hair Restoration Cell Therapy Leveraging iPSC-Derived Folliculogenic Organoids

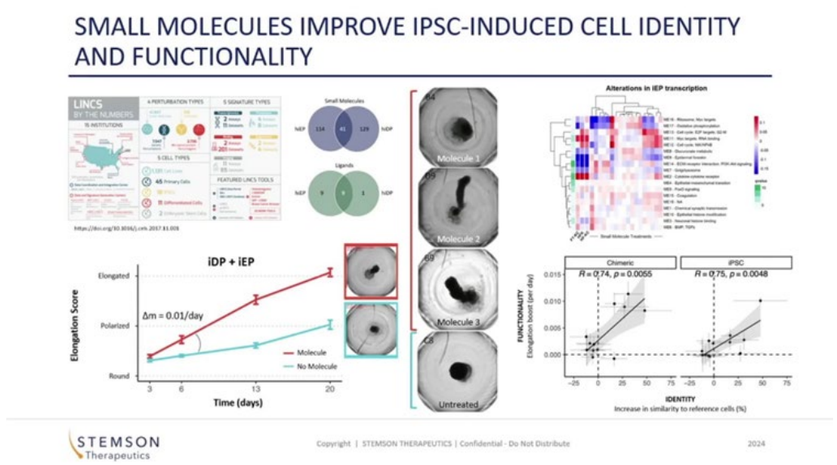
Sabrina Maisel, (Principal Scientist, Stemson Therapeutics) presented on hair restoration cell therapy using iPSC-derived follicular organoids. She began by highlighting the prevalence of hair loss, affecting tens of millions of people worldwide, including those who have undergone chemotherapy, suffer from immune disorders like alopecia areata, or experienced traumatic injuries. Sabrina stressed the need for therapeutic strategies to address tissue degeneration in hair follicles.

She provided a detailed overview of hair follicle biology, explaining the importance of dermal papilla cells and epithelial bulge stem cells in hair follicle development. Maisel discussed existing hair loss treatments, such as Rogaine and Propecia, which focus on maintaining existing follicles, and hair transplantation, which is limited in its applicability, particularly for women.

Stemson Therapeutics aims to fill the niche in hair loss treatment by using iPSCs to generate dermal papilla and epithelial bulge stem cells and subsequently forming hair follicle units. Sabrina outlined the company's four-stage process.



She discussed the challenges of line-to-line and patient-to-patient variability in organoid morphology and functionality. There are differences in organoid elongation, matrix production and branching structures. Maisel described efforts to address this variability by leveraging big data. Using small molecules and scaffold-based systems scientists can improve organoid handling and transplantation outcomes. Organoids are evaluated based on their ability to elongate. Small molecules are able influence organoid morphology.

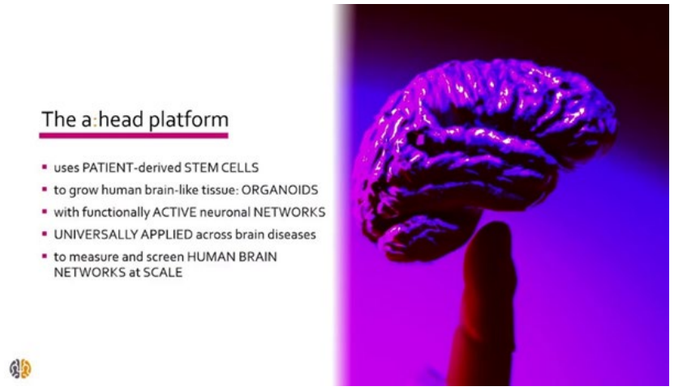


Additionally, Maisel highlighted the company's collaboration with academic institutions and the use of computational analysis and high-throughput screening to optimise organoid development. She presented data demonstrating the recapitulation of in vivo hair follicle morphology and functionality in Stemson Therapeutics' organoids.

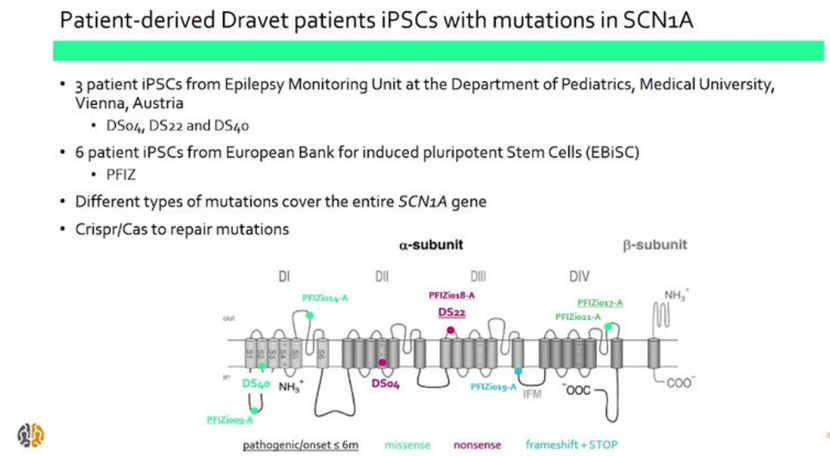
In conclusion, Maisel emphasised the company's commitment to developing a hair restoration therapy that is compatible with existing surgical techniques and can provide effective treatment for individuals experiencing hair loss.

Putting Our Human Brains In Drug Discovery

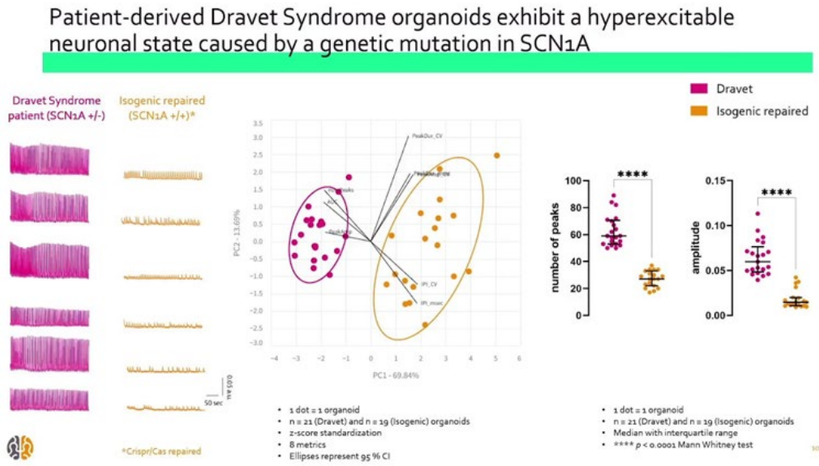
Bruno Fontinha, (Principal Scientist, a:head Bio) delivered a talk discussing the challenges and solutions in treating conditions like Alzheimer's, Parkinson's, and epilepsy. a:head Bio is an Austrian biotech focused of brain disroders. He highlighted the burden these disorders impose globally and the gap between needed treatments and available options. To address this, his company developed a platform called "a:head," leveraging brain organoids to screen potential therapies.



Fontinha detailed the process of growing brain organoids using established protocols and assessing their activity through high-throughput imaging and electrical recordings. He presented their efforts in modelling Dravet syndrome, a rare form of epilepsy, using patient-derived cell lines with mutations in the SCN1A gene.



By comparing organoids with and without the mutation, they observed that the Dravet cell lines were in a hyperexcitable neuronal state.



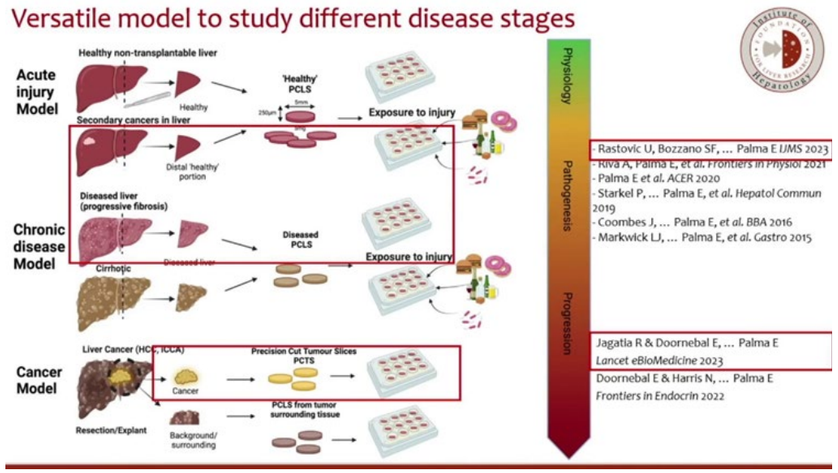
Furthermore, they demonstrated the effectiveness of clinically relevant anti-seizure medications in reducing organoid activity, indicating potential treatments.

In addition to calcium imaging, the scientists explored electrical recordings to closely mimic electroencephalogram (EEG) readings, enabling deeper insights into organoid activity and responses to treatments. By using various activity metrics and drug screening techniques, they gained a comprehensive understanding of disease models and potential therapeutic interventions. Fontinha concluded by encouraging further discussion and collaboration, particularly regarding pharmacological validation of neuroactive compounds.

Leveraging Precision Cut Tissue Slices To Advance Preclinical Research On Liver Disease And Malignancies

Elena Palma, (Principal Investigator, Foundation for Liver Research, The Roger Williams Institute of Hepatology) talked about the development of a 3D experimental model using precision-cut liver slices to investigate liver diseases, particularly alcohol-related liver disease (ALD) and primary liver cancer. She highlighted the global impact of liver disease and suggested that its increasing mortality rates are linked to the lack of effective therapies and biomarkers. Palma emphasised the limitations of animal models in studying liver diseases: animals are averse to alcohol, so it is challenging to recapitulate the stages of inflammation and fibrosis in their immune systems.

Therefore, she posited the need for alternative experimental models that better recapitulate human disease progression. The precision-cut liver slices model involves obtaining healthy liver tissue specimens from surgical resections, which are then processed and cultured.



To replicate the human disease in the precision cut liver slices (PCLS), alcohol is added to the slices alongside fatty acids and lipopolysaccharides (LPS). Palma explained the advantages of this model, including its organotypic nature, preservation of cellular heterogeneity, and versatility for studying various liver diseases and treatments.

Palma presented findings from studies using the liver slices model to investigate ALD progression. These studies involve treating the slices with alcohol and fatty acids to mimic aspects of human disease progression, including hepatocyte damage, inflammation, and fibrosis. She also discussed the formation of megamitochondria, a characteristic feature of ALD, observed in the liver slices.

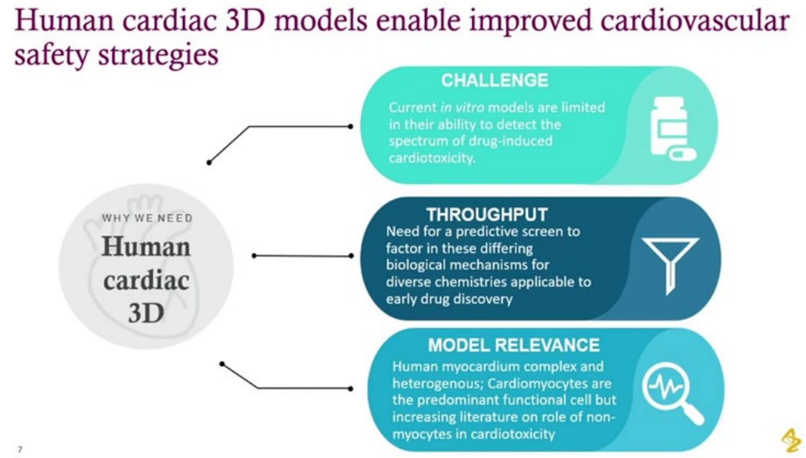
Additionally, Palma pointed to the application of the liver slices model for studying primary liver cancer. She presented data on drug screening and immunotherapy responses using the model, highlighting its potential for personalised therapy and predicting patient responses to treatment.

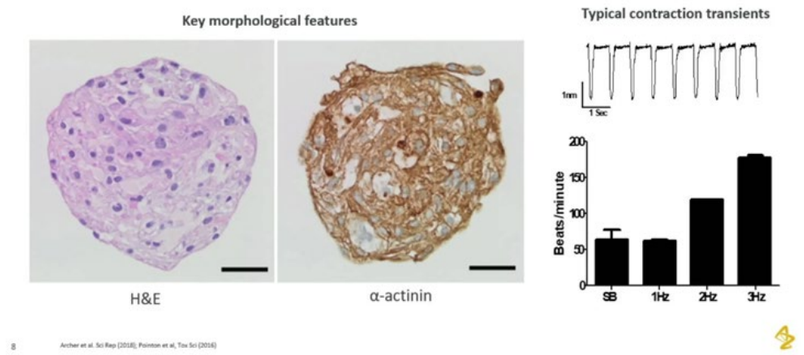
Finally, Palma acknowledged the limitations of the liver slices model, including sample availability and tissue quality. Overall, the presentation provided valuable insights into the development and applications of the precision-cut liver slices model for studying liver diseases and advancing therapeutic interventions.

Enhancing The Value Of Cellular Models Using Systems Modelling

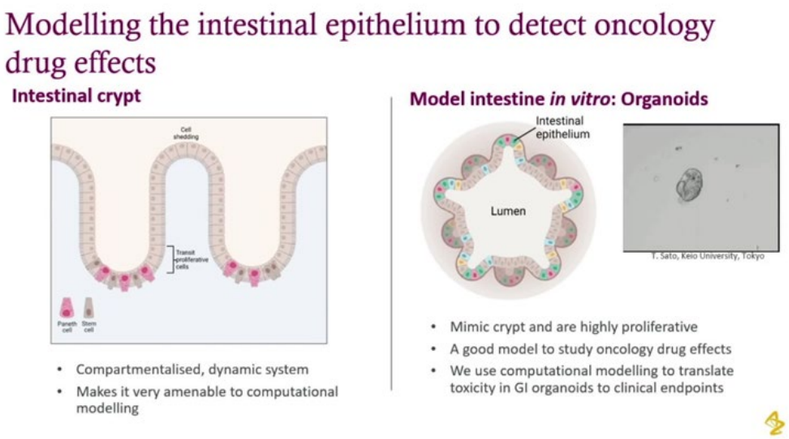
Stefan Platz, (Senior Vice President Clinical Pharmacology & Safety Sciences, AstraZeneca) highlighted the challenges faced in drug development, particularly the high rate of failures due to safety and efficacy issues. He discussed the current drug development model, which relies heavily on in vitro and in vivo screening methods but acknowledged the need for improvement. Platz advocated for the use of advanced cellular models to address these challenges, emphasising their potential to enable longer viable cell culture, repeat dosing, and the inclusion of multiple cell types to better mimic complex biological interactions.

He introduced specific examples of advanced cellular models, starting with a cardiac micro-tissue model designed to predict drug-induced cardiac toxicities more accurately. The model also predicts functional and structural changes. Furthermore, it integrates multiple aspects of cardiac function in a 3D structure, allowing for the detection of functional and structural changes induced by toxic drugs.





Next, Platz discussed a gastrointestinal (GI) organoid model, highlighting its ability to replicate the cellular composition and dynamics of intestinal crypts.



This model enables the study of specific cellular pathways and the prediction of GI toxicity, particularly in terms of diarrhoea, by integrating clinical data and computational modelling.

Finally, Platz presented a bone marrow model aimed at predicting haematological toxicities induced by drugs. This model, based on a 3D scaffold with dynamic flow, allows for the analysis of various cell types and their interactions, leading to the prediction of cytopenia risk in patients undergoing cancer treatment.

Throughout the presentation, Platz emphasised the importance of integrating advanced cellular models with computational modelling and clinical data to enhance preclinical assessment and ultimately replace animal testing in drug development. However, he also acknowledged the limitations, such as patient variability. However he expressed confidence in the potential of these models to improve drug development outcomes.

Collaboration & Inter-Disciplinary Research Efforts

How Adipoids Can Help Us In Immune Metabolism And Cardiac Disease Research

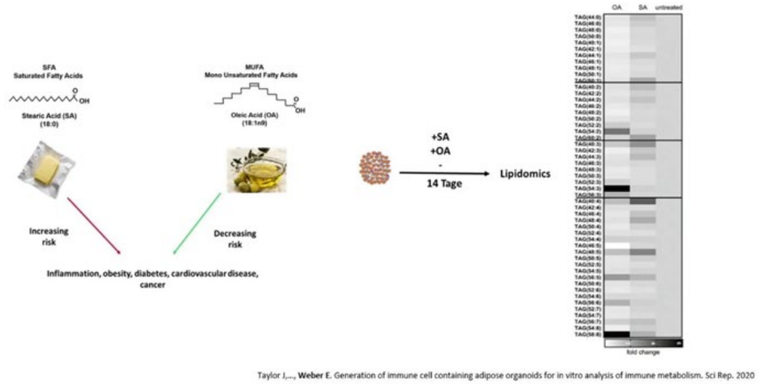
Elvira Weber's, (Head of the Lab, Universität Düsseldorf) presentation focused on the development and application of adipoids, immune-competent organoids derived from adipose tissue, for immune metabolism research. She pointed out the global rise in obesity, which is considered a public health crisis due to its association with various long-term diseases. Weber stated the importance of understanding adipose tissue and its communication with other organs in the body.

Adipose tissue is heterogeneous, with differences in phenotype and function depending on its location in the body. Weber discussed the stromal vascular fraction, which includes progenitor cells, adult stem cells, and immune cells, such as adipose tissue macrophages. These macrophages play specific roles in adipose tissue, influencing adipocyte function, lipid metabolism, and inflammation.

Weber explained the limitations of current research models, including 2D cell culture systems and animal models, and introduced adipoids as 3D models that address these drawbacks. She described the process of generating and validating adipoids which involves culturing stromal vascular fraction cells in an ultra-low attachment plate, inducing adipogenic differentiation, and confirming the presence of adipocytes and macrophages.

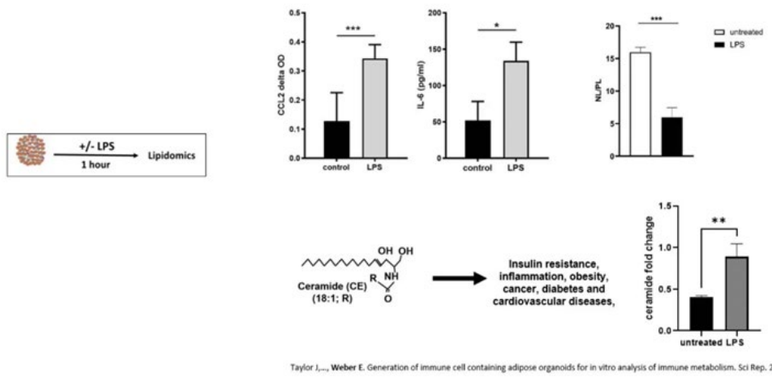
Weber presented examples of research applications for adipoids, including studies on dietary effects, inflammation, insulin resistance, and species-specific differences in adipose tissue metabolism.

A) Dietary research: Effect of distinct fatty acids on lipid metabolism



Taylor J.,.., **Weber E.** Generation of immune cell containing adipose organoids for in vitro analysis of immune metabolism. Sci Rep. 2020

B) Adipoids are a valuable tool for Inflammation in Adipose tissue



Taylor J.,.., **Weber E.** Generation of immune cell containing adipose organoids for in vitro analysis of immune metabolism. Sci Rep. 2020

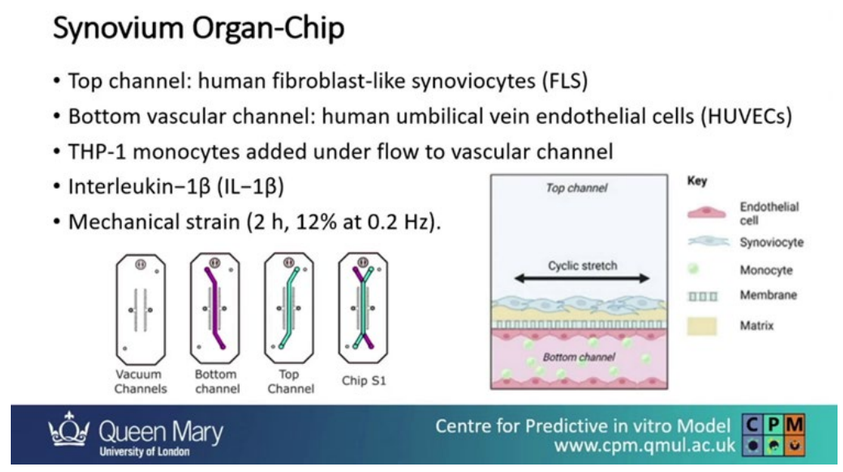
She also discussed ongoing research projects aimed at understanding the function of different adipose tissue types and investigating disease pathology, such as aneurysm development. In conclusion, Weber highlighted the collaborative nature of adipoid research.

Organ-Chip Models Of Musculoskeletal Tissues

Martin Knight, (Director, Queen Mary University) discussed the development of complex in vitro models, particularly for musculoskeletal tissues, to address the high attrition rate in drug discovery pipelines. Knight posited that developing reliable and predictive in vitro models could contribute to combatting the high rates of failure during clinical trials.

Knight demonstrated the need for musculoskeletal models due to the prevalence of musculoskeletal conditions and the lack of effective disease-modifying drugs. These models serve as ideal exemplars for building complex in vitro models due to their spatial heterogeneity, inflammatory components, biomechanical aspects, and interactions between multiple tissue and cell types.

He presented specific examples of in vitro models developed for studying synovial inflammation, cartilage-bone interaction, osteochondral tissue, and bone metastasis from breast cancer.



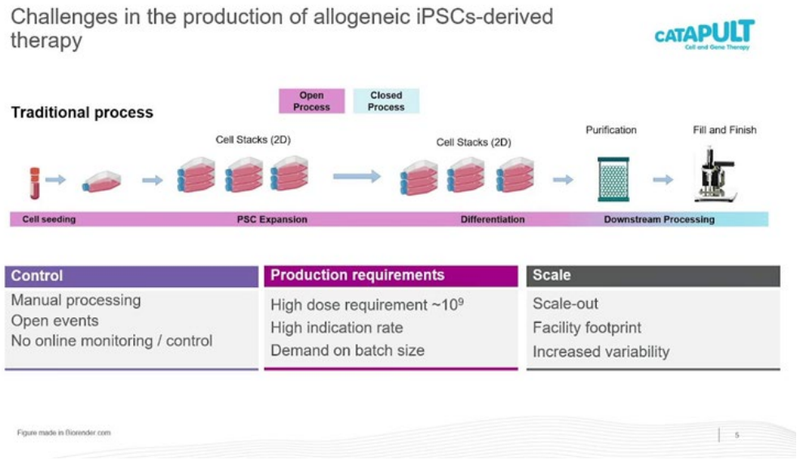
Knight described the design and validation of these models, highlighting their potential for studying disease mechanisms, testing therapeutic interventions, and predicting patient responses to treatment.

Additionally, Knight announced funding for a grant to develop techniques for building spatial patterning into these models, enhancing their complexity and predictive capabilities. He also discussed the establishment of a Centre for Doctoral Training in Next Generation Organ Chips, inviting industry collaboration to advance research in this field.

In conclusion, Knight pointed out the need to bridge the gap between technology providers and end-users to build biologically relevant models on advanced technology platforms. He also acknowledged collaborators and welcomed industry affiliates to join the Centre for Predictive In Vitro Models.

Industrialisation of iPSC derived allogeneic cell therapies using a scalable automated process for expansion and differentiation

Molly Tregidgo, (Associate Senior Scientist, Cell & Gene Therapy Catapult) gave an overview of Cell & Gene Therapy Catapult's (CGTC) allogeneic cell therapy development program which has had over 20 collaborators since its inception. She then discussed the typical challenges associated with the production of allogeneic iPSCs-derived therapy.



To overcome these challenges, the company is developing a modular automated production platform. This platform helps increase control and scale up.

She also introduced the key components of the iPSC perfusion platform: integrated flow rate control and correction, scalable cell retention device and cell specific perfusion rate. This platform is flexible and multiple cell lines can be used on the platform without compromising its function.

Tregidgo then introduced a recent project cell and gene therapy catapult collaborated with Plasticell to industrialise iNK manufacturing. The first step involved generating high quality iPSC starting material using the CGTC iPSC expansion platform which generates a consistent aggregate size and morphology. Their NK differentiation protocol led to a 10X improvement in NK-like cells produced per seeded iPSC compared to static controls. Furthermore, this NK differentiation protocol is adaptable to large-scale bioprocessing.

In conclusion, this presentation demonstrated that the CGTC expansion process displayed reproducibility across iPSC lines. The expansion process is capable of producing cytotoxic NK cells with improved yield and consistencies, displaying its potential to reduce manufacturing costs. This is particularly crucial when investigating scale up. Tregidgo finalised by mentioning the future directions for her project. She touched on the need for implementation of PAT and automation as well as the identification of novel biomarkers and building analytical capability.

Report Summary

This market report demonstrated the important shift from 2D to 3D cell culture. Expert opinions in this report showed that organoids and organ-on-chip technology are highly capable of physiological mimicry. Unlike animal models, these tissues can mimic the micro-environment of human cells. Examples of 3D cell models covered in this report ranged from gastrointestinal (GI) organoids to brain organoids.

Several presentations mentioned the use of advanced imaging and analysis techniques to study cellular responses and disease models. For example, Tamara Zietek's talk on 3D live cell imaging in intestinal organoids involves the visualisation of intracellular signalling processes, such as calcium influx and pH changes, using fluorescent dyes. These techniques provide insights into cellular physiology and drug responses at the single-cell level.

Furthermore, microphysiological systems (MPS) such as microfluidic organs-on-chips can be used in drug discovery. Sharma showed how MPS platforms mimic the biochemical and mechanical properties of organs in understanding disease mechanisms and expediting drug development. His application of MPS technology in modelling skin barrier function gave insight into their versatility across various organ systems and their potential in wider studies.

While these case studies demonstrate the important progress made in the 3D cell culture and organ modelling field, experts in this case study report addressed pressing challenges and the need for improvement in certain areas.

For instance, Sabrina Maisel, Tamara Zietek, and Marcelo Ribeiro highlighted the challenge of variability in organoid morphology and functionality. They mentioned that achieving consistent results across different organoid cultures, optimising growth conditions, and addressing patient-to-patient variability are crucial for reliable research outcomes and drug screening.

Scaling up production of 3D cell culture to meet commercial demands is a bottleneck; complexities in culturing and preserving 3D cell culture on a large scale is highly challenging. Recreating physiological features and immune response in MPS technology requires highly advanced tissue engineering methods. Furthermore, different cell types could require specific conditions for optimal growth and differentiation in 3D cultures, thus customising culture conditions for a variety of cell types complicates the scaling process.

Overall, these challenges illustrate the need for careful handling techniques and advanced tissue engineering methods. However important strides have been made towards developing advanced 3D cell cultures and this market report showed that continuous collaborations between scientists, engineers, academics and clinicians can address technical, biological, and translational hurdles effectively.