R+H

application note

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Bioprinted Neuroblastoma Models for Pathology Studies

R-GEN 200 Showcased Features

Multiple printing technologies can be combined in a single process to mimic native tissue architecture, composition, and complexity

Pneumatic extrusion enables versatile processing of a wide range of different bioinks

Light-curing kit enables for a fast, in-process crosslinking of photocurable materials while minimizing the dose provided to cells

Easy-to-use, intuitive SHAPER software and accurate optical calibration systems allow the process to be easily and automatically repeated in multiple wellplates for high-throughput screening

Dedicated biosafety cabinet for fabrication of cell-laden

IBEC
Institute for Bioengineering of Catalonia

Monferrer, E., Martín-Vañó, S., Carretero, A. et al. A three-dimensional bioprinted model to evaluate the effect of stiffness on neuroblastoma cell cluster dynamics and behavior.

López-Carrasco, A., Martín-Vañó, S., Burgos-Panadero, R. et al. Impact of extracellular matrix stiffness on genomic heterogeneity in MYCN-amplified neuroblastoma cell line. J Exp Clin Cancer Res 39, 226 (2020)

Challenge & Current Limitations

- Tumors are not homogeneous structures, but rather highly complex tissues involving many cell types. In these tissues, cells respond to the biochemical signals of their ECM and to physical forces such as tension.
- Increased stromal stiffness is a classic hallmark of cancer as is the transformation of this stiffness into chemical signals for cell advantage. ECM stiffness and composition, along with mechanotransduction, are considered promising therapeutic targets in many cancer types, including neuroblastoma.
- Traditional 2D or monolayer cultures are unable to reproduce these complex interactions between cells and ECM feature.

Why 3D Bioprinting?

- In-vitro 3D model are emerging as good models for ECM-related biological studies also whilst reducing animal use and sacrifice.
- Bioprinted scaffolds can accurately reproduce the complex feature of 3D tissues, resulting in better modelling and comprehension of the physiopathological tumor microenvironment.

How IBEC leveraged REGENHU's technology

- In this study, researchers compared an animal-derived model with a previously optimized 3D bioprinted one, which had already proven to favor neuroblastoma cells proliferation and migration. They evaluated how tumor genomics patterns and clinal heterogeneity of neuroblasma cell lines are affected by tumor microenvironment stiffness.

Fig.1 Hematoxylin-eosin stains of the bioprinted models mimicking different ECM stiffnesses

- To mimic different stiffnesses, a REGENHU bioprinting platform was used to process 3D hydrogels composed of methacrylated gelatin (GelMA) and methacrylated alginate (AlgMA). The composite bioinks were processed by means of pneumatic extrusion and polymerized using the light curing options provided by the platform.
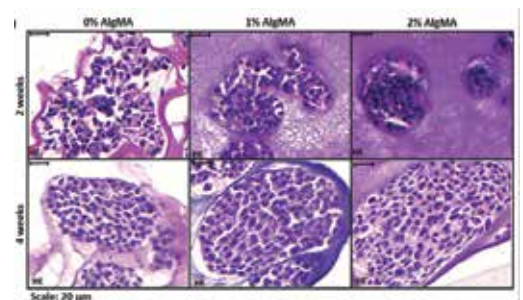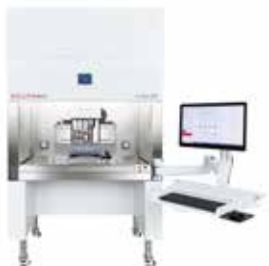
Results

- Biological significance: A similar genomic response of the neuroblastoma cell lines was observed in the two different models (xenograft and bioprinted hydrogels) making this approach a viable option to model different tumor microenvironments for pathology studies.
- In-vitro disease model: Biomimetic 3D scaffolds represent a useful tool to study genomics and clonal evolution of tumor cells under different stiffness conditions. A better understanding of the mechanotransduction pathways related to the tumor microenvironment has the potential to expand therapeutic possibilities.
- High-throughput screening platform: 3D bioprinted models were proved to be an excellent tool to test the efficiency, toxicity and impact of treatment on genomics and cell heterogeneity.

Bioprinted Skin Equivalents

R-GEN 200 Showcased Features

Multiple printing technologies can be combined in a single process to mimic native tissue architecture, composition, and complexity

Highly accurate, stable temperature control in the range of 5-37°C applied independently to each printhead and workzone for controlled processing of thermosensitive materials

Pneumatic extrusion enables versatile processing of a wide range of different bioinks

Volumetric dispensing enables full control over material flow rate and to avoid effects due to inhomogeneous material viscosity

Drop-on-demand technology with precise valve control provides unmatched accuracy in processing low-viscosity bioinks and patterning cells

Cell agitator provides a solution to cellular sedimentation and guarantee homogeneous distribution

Easy-to-use, intuitive SHAPER software and accurate optical calibration systems allow the process to be easily and automatically repeated in multiple wellplates for high-throughput screening

Dedicated biosafety cabinet for fabrication of cell-laden constructs in a sterile environment

Challenge & Current Limitations

- International regulations mandate that skin products cannot be tested on animals and must be evaluated using alternative skin models.
- Excised skin models from human donors have been used for ex-vivo testing of compounds, but they've presented challenges in availability and variability.
- Therefore, in-vitro skin models are now being engineered for toxicity testing of skin products and therapeutics.

Why 3D Bioprinting?

- 3D bioprinting has the potential to increase the reproducibility, scalability, and complexity of the fabricated architecutres.
- The ability to produce bioprinted skin equivalents in a multiwell-based platform enables the robust testing of compounds for toxicity effects and the development of skin disease models for drug testing in a standardized, automated and high-throughput fashion.

How NIH leveraged REGENHU's technology

- Researchers fabricated Bioprinted Skin Equivalents (BPSEs) by combining 3 different printing technologies in a single process:
  - Volumetric dispensing for the dermis layer, in an ad-hoc developed bioink composed of gelatin, collagen, Elastin and Fibrinogen, embedding Human Dermal Fibroblasts.
  - Drop-on-demand technology for the basement membrane layer, composed of laminin/entactin, processed at 5°C.
  - Pneumatic extrusion for the epidermis layer, composed of a solution of Human Epithelial Keratinocytes.
- The bioprinting process was replicated in an automated manner in multiwell plates (12 or 24 wells) for the fabrication of high-throughput in vitro models for drug screening and discovery applications.
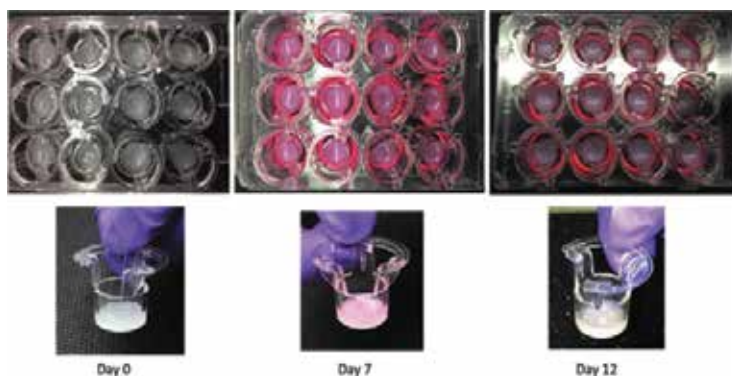

Fig.1 Automated fabrication of BPSEs in multiwell plates and maturation within 2 weeks.

Results

- Biomimetic, physiologically relevant constructs: Bioprinted organoids were viable for up to 10 days in culture and expressed hepatic functionality comparable to regular Matrigel cultures.

Fig.2 Histological comparison between BPSEs and native human skin tissue

- Drug responsive in-vitro model: Exposure to well-known hepatotoxic compounds strongly decreased cell viability and caused high level of damage markers expression.

- High-throughput screening platform: The ability of the liver models to metabolize pharmaceuticals compounds make them ideal for drug discovery and personalized medicine applications.
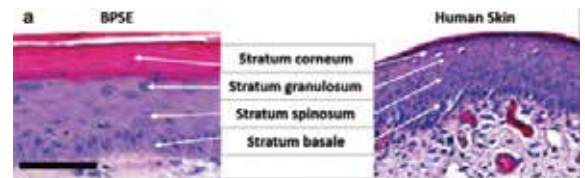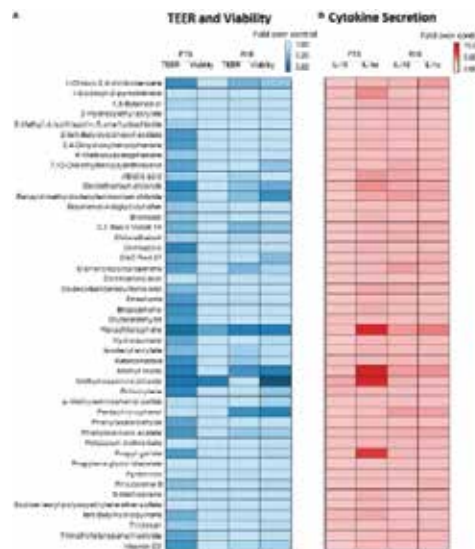

Fig.3 Comparison TEER and cytokine secretion for engineered (RhE) and bioprinted (FTS) tissue models.

BPSE Application 1: High-Throughput Screening

- BPSE's were exploited in a two-step approach for large scale in-vitro compound testing. The first phase of involved the screening of 451 compounds for cytotoxic effects using 2D keratinocytes models, from which 46 toxic compounds were identified. These were further tested for skin irritation potential on both "traditional" 3D and bioprinted skin tissue models, by measuring tissue viability, transepithelial electrical resistance (TEER) and secretion of cytokines.

- The study highlighted advantages when using 3D bioprinted skin models compared to traditional methods in long-term culture, by preventing tissue contraction and avoiding the leakage phenomena from the side of the well, so allowing better preservation of barrier function.

BPSE Application 2: Skin Carcinoma Model

- In this study, researchers from NIH developed a high-throughput, 3-dimensional bioprinted model of cutaneous squamous cell carcinoma tumor to test chemotherapeutic effects efficacy and general toxicity in tissue.

- After 4 days of media submersion of the fabricated BPSEs models. cancer spheroids were introduced and invaded the constructs. The tumor models were shown to recapitulate native disease biology, exhibiting similar histology and gene expression to invasive cutaneous squamous cell carcinoma in vivo.

- This engineered platform enables testing of chemotherapeutics against tumor cell growth in a tissue specific context. This could eventually be adopted in a "bedside" manner and applied to cells form patient tumor biopsies.
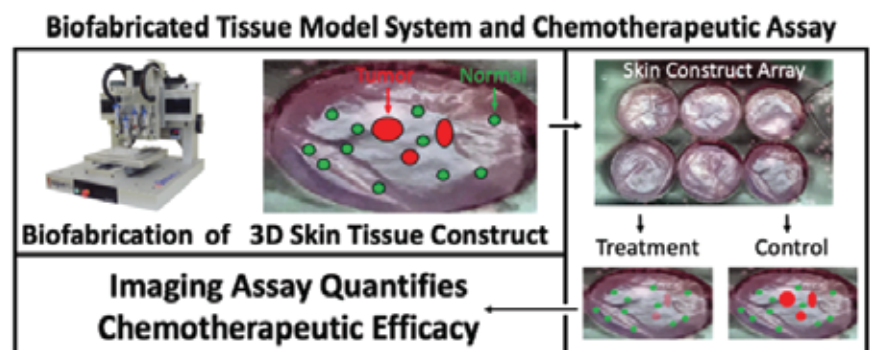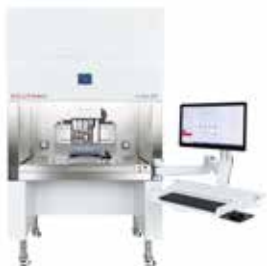

Fig.4 Schematic representation of bioprinted squamous carcinoma model fabrication and testing.

Organoid printing for drug-induced liver injury testing

R-GEN 200 Showcased Features

Multiple printing technologies can be combined in personalized configurations to enhance the complexity of fabricated constructs

Pneumatic extrusion enables versatile processing of a wide range of different bioinks

Highly accurate, stable temperature control in the range of 5-37°C applied independently in each printhead and workzone enabling controlled processing of thermosensitive materials

Light-curing kit can be used for a fast, in-process crosslinking of photocurable materials while minimizing the radiation dose provided to cells

Easy-to-use, intuitive SHAPER software and accurate optical calibration systems allow the process to be easily and automatically repeated in multiple wellplates for high-throughput screening

Dedicated biosafety cabinet for fabrication of cell-laden constructs in a sterile environment

Challenge & Current Limitations

- Drug-induced liver injury (DILI) is the most frequent (30%) reason for drug failure in clinical trials and post-marketing drug withdrawal.
- Compared to animal models, using human hepatic in vitro models gives better insight and provides an ethically less controversial model.
- Approaches based on single cell cultures present limitations such as rapid dedifferentiation (primary cells) or reduced enzyme expression (cell lines). Both of these approaches, moreover, do not exhibit interindividual differences
- Approaches based on single cell cultures present limitations such as rapid dedifferentiation (primary cell) or reduced enzyme expression (cell lines). Both approaches do not exhibit interindividual difference either.
- Organoids such as intrahepatic cholangiocyte organoids (ICOs) have a greater potential as liver models since they mimic native tissue architecture and function in vitro and reflect interindividual variability.

Why 3D Bioprinting?

- Increases complexity of the in-vitro constructs and their ability to mimic native liver environment through the precise placement of bioinks to promote cellular interactions, vascularization and enhanced exchange of nutrients.
- The possibility to converge bioprinting and self-assembled biological building units like organoids enables the creation of models at the tissue-like level scale. These novel models allow the implementation of robust testing platforms for personalized medicine and drug screening.

How UMC leveraged REGENHU's technology

- Combining multiple printheads in a single process, it was possible to bioprint liver organoids embedded in GelMA and create 3D structures with a pluronic support gel.
- The advanced temperature control and the light curing capabilities of REGENHU's bioprinter makes it possible to efficiently process thermosensitive and photocurable materials.
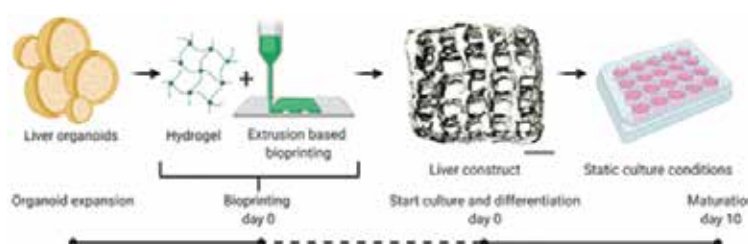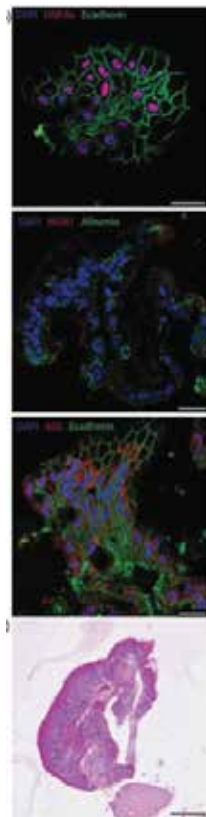

Fig.1 Schematic overview of the experimental procedure for bioprinting liver constructs.

Results

- Biomimetic, physiologically relevant constructs: Bioprinted organoids were viable for up to 10 days in culture and expressed hepatic functionality comparable to regular Matrigel cultures.

- Drug responsive in-vitro model: Exposure to well-known hepatotoxic compounds strongly decreased cell viability and caused high level of damage markers expression.

- High-throughput screening platform: The ability of the liver models to metabolize pharmaceuticals compounds make them ideal for drug discovery and personalized medicine applications.

Fig.2 Immunofluorescence staining and Glycogen accumulation in liver constructs.

UMC Utrecht

Bouwmeester, M.C., Bernal, P.N., Oosterhoff, L.A., van Wolferen, M.E., Lehmann, V., Vermaas, M., Buchholz, M.-B., Peiffer, Q.C., Malda, J., van der Laan, L.J.W., Kramer, N.I., Schneeberger, K., Levato, R. and Spee, B. (2021), Bioprinting of Human Liver-Derived Epithelial Organoids for Toxicity Studies. Macromol. Biosci., 21: 2100327.

Epidermis Model for Drug Discovery

R-GEN 200 Showcased Features

Multiple printing technologies can be combined in a single process to mimic native tissue architecture, composition, and complexity

Drop-on-demand technology with precise valve control (min. opening time 110 µs) provides unmatched accuracy in processing low-viscosity bioinks and patterning cells

Cell agitator provides a solution to cellular sedimentation and guarantees homogeneous distribution

Easy-to-use, intuitive SHAPER software and accurate optical calibration systems allow the process to be easily and automatically repeated in multiple wellplates or ad-hoc inserts for high-throughput screening

Dedicated biosafety cabinet for fabrication of cell-laden constructs in a sterile environment

L'ORÉAL

Madiedo-Podvrsan, S., Belaïdi, JP., Desbouis, S. et al. Utilization of patterned bioprinting for heterogeneous and physiologically representative reconstructed epidermal skin models. Sci Rep 11, 6217 (2021).

Challenge & Current Limitations

- Skin tissue models have been used for decades for efficacy & safety evaluation studies in the pharmaceutical and cosmetic industries. However, it is challenging to reproduce human skin high heterogeneity.
- Conventional culture-based models are still unable to accurately reproduce the complexity of native human skin due to the insufficient precision in the deposition of multiple cell types, resulting in limited predictability.

Why 3D Bioprinting?

- 3D bioprinting enables precise deposition of biological material into complex and functional 3D architectures, making it possible to fabricate physiologically relevant models that can reproduce skin heterogeneity.
- The capability to precisely combine multiple cell populations deposition makes it possible to reproduce keratinocyte heterogeneity for an accurate modelling of skin pathology and an improved understanding of skin physiology.
- The ability to create patterned models of healthy and pathological skin phenotypes in a single insert can accurately reflect the pathology heterogeneity and reduces inter-sample variability, thus improving the robustness of drug screening and evaluation studies.

How L'Oréal leveraged REGENHU's technology

- Exploiting the high levels of accuracy and cell viability provided by REGENHU's drop on demand technology, researchers were able to dispense different keratinocyte subpopulations in either semicircles or concentric circles to obtain controlled and reproducible reconstructed epidermis patterns, mimicking edge of lesions.

   • Printhead 1: healthy tissue, normal human keratinocyte (NHK) population.
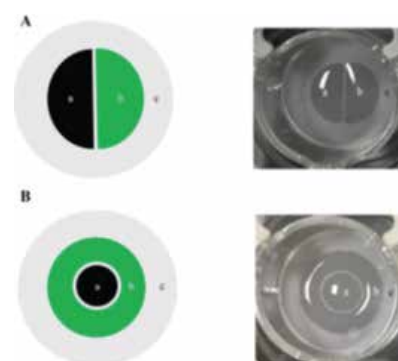   • Printhead 2: pathological skin, filaggrin (FLG) deficient keratinocyte model.

Fig.1 Macroscopic visualization of the fabricated models, where cells were printed in patterned suspensions in semi-circles or concentric rings

Results

- Physiologically relevant: The fabricated in-vitro models exhibited a well-organized epidermal structure, and each component presented the phenotypic characteristics of its constituent cells
- High-throughput models of skin pathology: Using transfected keratinocytes to model different skin conditions, this approach provides a stable and robust screening platform for evaluation studies that overcomes tissue usage related issues.
- Reduced sample size: The patterning approach of a dual population model can be used to test a compound of interest on both sides simultaneously. This creates the opportunity to use paired statistical approaches, reducing the inter-section variability and increasing the statistical power of evaluation studies.

Metastatic Bone Models for High-Throughput Screening of Prostatic Cancer Inhibitors

R-GEN 200 Showcased Features

Multiple printing technologies can be combined in a single process to mimic native tissue architecture, composition, and complexity

The Electrospinning and Writing Kit allows the convergence of bioprinting and electrospinning/writing in a single process, enabling different combinations for a multi-scale biofabrication process able to intregrate micro or submicrometric fibers with cell-laden hydrogels

Easy-to-use, intuitive SHAPER software and accurate optical calibration systems allow the process to be easily and automatically repeated in multiple wellplates or different substrates for high-throughput screening

Dedicated biosafety cabinet for fabrication of cell-laden constructs in a sterile environment

Thomas Bello, Claudia Paindelli, Luis A. Diaz-Gomez, Anthony Melchiorri, Antonios G. Mikos, Peter S. Nelson, Eleonora Dondossola, Taranjit S. Gujral: Computational modeling identifies multitargeted kinase inhibitors as effective therapies for metastatic, castration-resistant prostate cancer. Proceedings of the National Academy of Sciences Oct 2021, 118 (40) e2103623118.

Challenge & Current Limitations

- Metastatic, castration-resistant prostate cancer (mCPRC) is an advanced prostate cancer with limited therapeutic options and poor patient outcomes. The identification of proper treatment options would benefit from polypharmacology approaches that rely on large scale datasets.

- Bone metastasis is the most frequent and lethal complication of CPRC progression and therefore organotypic models mimicking bone environment would be of great interest for compound testing,

- Screenings are usually either performed on 2D culture models which are unable to recapitulate the complex tissue pathophysiology or in in-vivo assays requiring animal sacrifice, which raises ethical concerns and presents limitations in terms of availability and standardization of the outcome.

Why 3D Bioprinting?

- 3D bioprinting represents a valuable approach in recreating an organotypic bone mimetic environment (BME) of metastasis, able to mimic the metastatic bone niche and the in vivo–like mechanisms of response and resistance to therapy.

- The miniaturization capability as well as the high reproducibility of the fabricated constructs provides a robust, high throughput testing platform able to match the high number of samples required for multiple compound screening.

How Rice University leveraged REGENHU's technology

- Represents a valuable approach in recreating an organotypic bone mimetic environment (BME) of metastasis, able to mimic the metastatic bone niche and the in vivo–like mechanisms of response and resistance to therapy.

- The miniaturization capability as well as the high reproducibility of the fabricated constructs provides a robust, high throughput testing platform able to match the high number of samples required for multiple compound screening.

Results

- Biomimetic models to better mimic pathology: the 3D printed BME system was able to reproduce the well-known native bone tissue resistance to chemo and molecular therapy in metastatic cancer, requiring significantly higher doses of the tested Kinase Inhibitors to achieve the same growth suppression as in 2D monocultures.

- High-throughput, robust testing platform: the fabricated organotypic models were used to validate a multidisciplinary strategy that combines in-vitro models with machine-learning algorithms for rapid screening and identification of compounds that will result in the desired phenotypic effects.
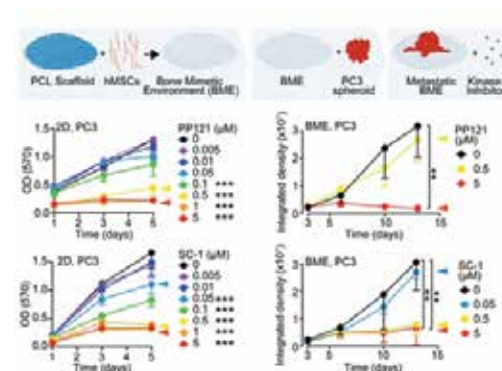

Fig.1 Schematic representation of the BME fabrication process and cell growth inhibition results for 2D and BME models with different doses of Kinase Inhibitors

Printed Microfluidic Chips for Neural Tissue Disease Models

R-GEN 200 Showcased Features

Multiple printing technologies can be combined in a single process to mimic native tissue architecture, composition, and complexity

Pneumatic extrusion enables versatile processing of a wide range of different bioinks

Easy-to-use, intuitive SHAPER software and accurate optical calibration systems allow the process to be easily and automatically repeated in multiple wellplates for high-throughput screening

Dedicated biosafety cabinet for fabrication of cell-laden constructs in a sterile environment

Challenge & Current Limitations

- The fabrication of human brain tissue models is very challenging due to the high number of simultaneous processes occurring at any one time. Microfluidic approaches such as tissue/organ on a chip are a preferable solution to reduce the complexity of the human brain and to study the neuronal microenvironment.

- Microfluidic devices are commonly fabricated using soft lithography of PDMS. However, this process is still reliant on some manual steps that increase its complexity and fabrication time and reduces the overall reproducibility of the outcome. There are also limitations in achieving designs that are useful for researchers.

Why 3D Bioprinting?

- A novel, versatile approach to the fabrication of microfluidic devices. Bioprinting makes it possible to simplify the process by minimizing the manual postprocessing of the fabricated devices and reducing the PDMS content through its controlled deposition.

- The high levels of accuracy and spatial control capability allow fast prototyping of devices with precisely defined features, that could be used in combination with the deposition of human-derived neural cells to model neuronal microenvironments.

How DTU leveraged REGENHU's technology

- Researchers used REGENHU's bioprinter in a multitool approach for the fabrication of the microfluidic chip, by combining extrusion of two different elastomer-based ink formulations.

- As a first proof of concept, different complex structures that would not be achievable with conventional soft lithography techniques were fabricated. The printing was performed directly onto the silicon wafer containing the master mold pattern, which was immobilized on the workzone by means of pneumatic suction.

- Subsequently, a proof-of principle nigrostriatal pathway on-a-chip was fabricated using the previously developed approach to separate dopaminergic neurons (representing midbrain) from astrocytes (representing forebrain) in a design facilitating directional outgrowth of dopaminergic projections through engineered microchannels.
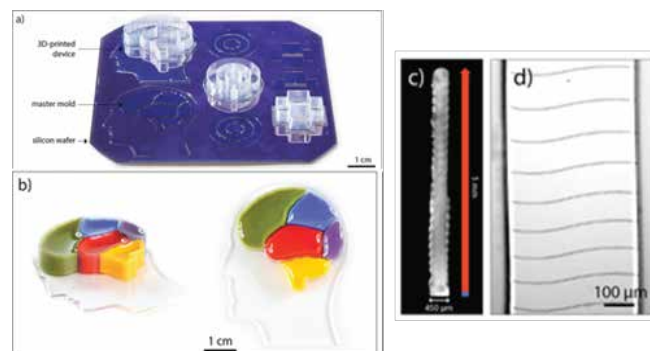

Fig.1 Images of the master mold, the fabricated devices and the compartment cross section with its patterned microchannels.

Results

- Fast, simplified fabrication process: The printing approach enables to minimize manual post processing, increasing standardization of the produced devices, and at the same time to expand design possibilities

- One step production of cell friendly in-vitro models: The possibility to fabricate chips using a bioprinting platform within a sterile environment, makes it possible for them to be combined with deposited cell-laden inks to realize in-vitro tissue and diseases models. This approach also reduces PDMS content in the chip, thus minimizing residual presence of uncured polymer that could affect cell viability.

- Biomimetic, functional tissue models: The test showcased the possibility to maintain cell viability in the microfluidic compartments for up to 40 days. Neuronal differentiation was also induced maintaining viability and function for up to 30 days without any detrimental effects.

- Open, flexible platform to study neurological diseases: The proof of concept enabled the reconstruction of the nigrostriatal pathway on a chip, opening new possibilities for in-vitro studies on relates diseases such as Parkinson's. This versatile approach could pave the way for multiple applications in neurosciences, such as studies on neural network formation and compound testing.
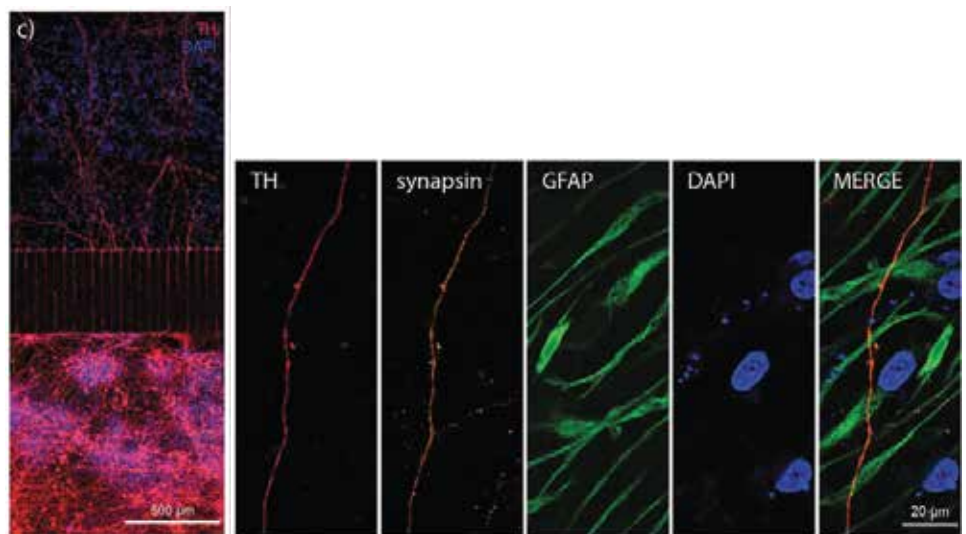

Fig.2 Fluorescent images showing directional growth of dopaminergic axons in the adjacent compartment within the nigrostriatal pathway on a chip and their interactions with astrocytes.

Kajtez, J., Buchmann, S., Vasudevan, S., Birtele, M., Rocchetti, S., Pless, C. J., Heiskanen, A., Barker, R. A., Martínez-Serrano, A., Parmar, M., Lind, J. U., Emnéus, J., 3D-Printed Soft Lithography for Complex Compartmentalized Microfluidic Neural Devices. Adv. Sci. 2020, 7, 2001150.

application note

Bioprinted Lung Models

R-GEN 200 Showcased Features

Multiple printing technologies can be combined in a single process to mimic native tissue architecture, composition, and complexity

Highly accurate, stable temperature control in the range of 5-37°C applied independently to each printhead and workzone for controlled processing of thermosensitive materials

Drop-on-demand technology with precise valve control provides unmatched accuracy in processing low-viscosity bioinks and patterning cells

Cell agitator provides a solution to cellular sedimentation and guarantee homogeneous distribution

Easy-to-use, intuitive SHAPER software and accurate optical calibration systems allow the process to be easily and automatically repeated in multiple wellplates for high-throughput screening

NANYANG TECHNOLOGICAL UNIVERSITY SINGAPORE

Ng WL, Ayi TC, Liu YC, Sing SL, Yeong WY, Tan BH. Fabrication and Characterization of 3D Bioprinted Triple-layered Human Alveolar Lung Models. Int J Bioprint. 2021;7(2):332. Published 2021 Apr 9. doi:10.18063/ijb.v7i2.332
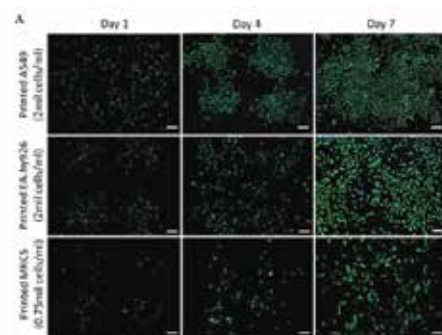
Challenge & Current Limitations

- The global prevalence of respiratory diseases caused by infectious pathogens has resulted in an increased demand for realistic in-vitro alveolar lung models to serve as suitable disease models
- Although numerous of these models have been developed based on 3D cultures or 3D constructs, the conventional production techniques are often laborious and lack repeatability and outcome standardization.

Why 3D Bioprinting?

- The high levels of accuracy, reliability, and control over spatial deposition achieved by bioprinting pave the way for a scalable and repeatable high throughput production of models for compound testing and disease study.

How Nanyang leveraged REGENHU's technology

- Researchers were able to use REGENHU's bioprinter to fabricate a triple layer model using high precision patterning of multiple cell-laden biomaterials, alternating collagen layers with polyvinylpyrrolidone (PVP) bioink embedding human lung epithelial cells, endothelial cells and lung fibroblasts.
- The printing sequence of the different bioink and cell population layers was optimized to mimic the spatial arrangement of native lung alveolar cells.
- The capability of REGENHU's dedicated software to incorporate third party substrates in designs allowed for the printing to be performed directly into in Corning® culture dishes.
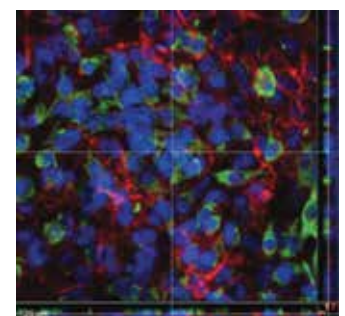

Results

- Physiological, functional models: The 3D bioprinted human triple-layered alveolar lung models maintained high levels of cell viability and, as showcased by their biomarkers' expression, retained their functionality over a period of 14 days which is a critical requirement for potential experimentation with respiratory viral infections.

Fig.1 Live and Dead assay performed on the fabricated constructs showing viability of the different cell types up to day 7

- High throughput, scalable testing platform: 3D bioprinting approach offers an attractive tool for the highly repeatable and robust fabrication of 3D in-vitro human alveolar lung models, that could be exploited for pathogen translocation studies and respiratory-related toxicological testing application.

Fig.2 Confocal imaging of 3D bioprinted human blood-air barrier model at day 14

Contractile muscle model for Drug Discovery

R-GEN 200 Showcased Features

Highly accurate, stable temperature control in the range of 5-37°C applied independently in each printhead and workzone. Enables controlled processing of challenging thermosensitive materials

Drop-on-demand technology with precise valve control (min. opening time 110 μs) provides unmatched accuracy in processing low-viscosity bioinks

Easy-to-use, intuitive SHAPER software and accurate optical calibration systems allow the process to be easily and automatically repeated in multiple wellplates for high-throughput screening

Dedicated biosafety cabinet for fabrication of cell-laden constructs in a sterile environment

NOVARTIS   zhaw

Alave Reyes-Furrer, A., De Andrade, S., Bachmann, D. et al. Matrigel 3D bioprinting of contractile human skeletal muscle models recapitulating exercise and pharmacological responses. Commun Biol 4, 1183 (2021).

Challenge & Current Limitations

- Drug development is a long and costly process mostly due to the very low success rate of new drug candidates entering clinical testing (taking on average 15 years and costing circa USD 2.5 billion).
- Current methods using 2D tissue culture are not able to assess muscle functions such as contractile force and fatigue.
- There are no 3D models that have been recognized to be sufficiently robust or reliable for routine use in drug screening.
- Ex-Vivo models are complex and scarcely reproducible. They are also dependent on animal sacrifice and often subject to ethical and regulatory critique.

Why 3D Bioprinting?

- Enhances translatability of preclinical drug discovery by engineering in vitro 3D microphysiological systems (MPS) for the identification and development of novel drugs with higher success rates in clinical tests.
- Allows the use of personalized, patient-derived tissue models using modern stem cell re-programming techniques.

How Novartis & ZHAW leveraged REGENHU's technology

- Matrigel is widely used in organoid technology and in hydrogels for muscle tissue models but very challenging when used as a bioink.

Fig.1 Macroscopic images of Matrigel/muscle cell model at different time points.

- Researchers exploited the advanced capabilities of the REGENHU platform in overcoming this challenge. Using the high precision Drop On Demand technology coupled with the accurate temperature control capability, they were able to process Matrigel as a bioink at 7°C in successfully bioprinting muscle models embedding muscle precursor cells.
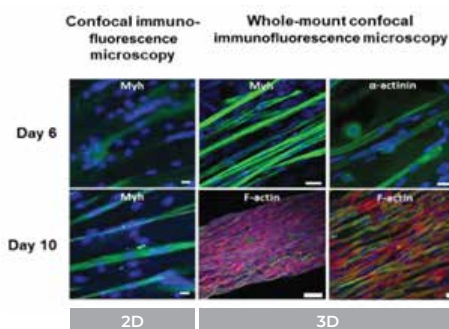

Fig.2 Histological analyses of the tissue models.

Results

- Faster fabrication of standardized 3D muscle models repeated directly in multiple 24-well plates for high-throughput functional compound screening
- In vitro-models able to express functionality: Formation of contractile, striated myofibers within one week
- Biomimetic model that meets ethical and regulatory compliance: The response of the bioprinted fibers were consistent with results achieved with ex-vivo fibers in relation to physical exercise and muscle stimulating drugs.