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Extended Abstract
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Regenerative Medicine 2018 & Synthetic Biology 2018: Development and optimization of complex liver models by 3D bio-printing- Marie Cuvellier- Research Institute for Environmental and Occupational Health, France

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The use of conventional 2D in vitro culture models is increasingly questioned and their ability to accurately mimic the complete physiological function of the organs or tissues of interest can be limited. For a few times now, 3D models have been successfully developed by the team Dymec of IRSET, with improved function and phenotypes of many cells type, including primary and transformed hepatic cells. The project aims to improve those 3D models by building a multicellular organoid-like liver model, with an organized architecture and in a reproducible and high-throughput way. We relied on extrusion based bioprinting technology, which allows the precise and spatially controlled deposition of a biological material containing cells to form definite microarchitectures. The first step of the work was to define the printing parameters: hydrogel concentrations, step of cross linking, printing temperature, pressure and speed, have been optimized to obtain a printable structure which remained stable over the long term. Secondly, the long-term biocompatibility of these structures was tested by encapsulation of transformed hepatic cells. They preserved their long-term viability (>30 days) and were able to proliferate in this biomatrix optimized for bioprinting. They organized themselves into spheroids/acini-like structures and displayed an apico-basal polarity after seven days of culture. The next step aim was to improve the liver function of the created structures, by bioprinting an architecturally organized co-cultures with parenchymal cells, by adding to the currents bioprinted structures non-parenchymal cells.

The liver is an intricate organ that requires consistent perfusion for the conveyance of supplements and oxygen and the expulsion of waste so as to endure. Endeavors to reproduce or mirror the liver microstructure by means of a ground-up approach are basic for liver tissue building. A decellularization/recellularization technique is one of the methodologies focusing on the chance of creating a completely utilitarian organ with in vitro-created development for clinical applications to supplant bombed livers, for example, end-stage liver malady (ESLD). Be that as it may, the unpredictability of the liver microarchitecture alongside the constrained appropriate hepatic segment, for example, the enhancement of the extracellular grid (ECM) of the biomaterials, the choice of the seed cells, and improvement of the liver-explicit three-dimensional (3D) specialty settings, represent various difficulties. In this part, we have given a complete attitude toward how the physiological, neurotic, and spatiotemporal parts of these disadvantages can be transformed into the present difficulties in the field, and set forward a couple of methods with the possibility to address these difficulties, predominantly concentrating on a decellularization-based liver recovery system. We estimate the essential ideas fundamental for building tissue-built liver organs dependent on either a flawless (from an innocent liver) or an incomplete (from a pretreated liver) structure by means of reproducing the normal turn of events and regenerative procedures.

Bioprinting is an added substance fabricating process where biomaterials, for example, hydrogels or different polymers are joined with cells and development factors, at that point printed to make tissue-like structures that mimic characteristic tissues.

The innovation utilizes a material known as bioink to make these structures in a layer-by-layer way. The procedure is broadly material to the fields of medication and bioengineering. As of late, the innovation has even made progressions in the creation of ligament tissue for use in recreation and recovery.

Generally, bioprinting works along these lines to ordinary 3D printing. A computerized model turns into a physical 3D object layer-by-layer. In this occasion,

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be that as it may, a living cell suspension is used rather than a thermoplastic or a gum.

The best significance of bioprinting lies in the subsequent tissue-like structures that emulate the genuine smaller scale and full scale condition of human tissues and organs. This is basic in tranquilize testing and clinical preliminaries, with the potential, for instance, to radically lessen the requirement for creature preliminaries.

When living tissues and organs need not originate from people, this sprouting innovation offers other enormous chances. One model is trying treatment for sicknesses utilizing falsely influenced tissues.

The procedure could likewise annihilate the cerebral pains related with organ gift and transplantation. Aside from the absence of accessible organs, the whole procedure is reprimanded from a good and moral point of view.

Organ substitution is the fundamental target, yet tissue fix is additionally conceivable meanwhile. With bioink, it's a lot simpler to take care of issues on a patient-explicit level, advancing less difficult activities.

3D bioprinting begins with a model of a structure, which is reproduced layer-by-layer out of a bioink either blended in with living cells, or seeded with cells after the print is finished. These beginning models can emerge out of anyplace – a CT or MRI check, a PC created plan (CAD) program, or a record downloaded from the web.

That 3D model document is then taken care of into a slicer – a particular sort of PC program which examines the geometry of the model and produces a progression of dainty layers, or cuts, which structure the state of the first model when stacked vertically. Cura and slic3r are instances of slicers regularly utilized in 3D printing. Allevi likewise has a particular slicer, streamlined explicitly for bioprinting, incorporated with our Allevi Bioprint programming.

When a model is cut, the cuts are changed into way information, put away as a g-code record, which can be sent to a 3D bioprinter for printing. The bioprinter adheres to directions in the g-code record all together, including guidelines to control for temperature of the extruders, expulsion pressure, bed plate temperature, crosslinking force and recurrence, and, obviously, the 3D development way created by the slicer. When the entirety of the g-code orders are finished, the print is done and can be refined or seeded with cells as a major aspect of a biostudy.