Automated and High Throughput Tissue Engineering

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The engineering of tissue substitutes and their application for in vitro drug testing and on human patients has become a reality. However, pharmaceutical industry and medical doctors are still struggling with problems of scalability for high throughput screening and lack of standardization for human implantation. CSEM is developing microsystems, automated tools and physiological environments for standardized tissue engineering.

Tissue engineering names the use of a combination of cells, engineering materials and suitable biochemical and physico-chemical factors to produce artificial tissues mimicking or replacing biological functions. With impressive progress in the last 5 years, tissue engineering has the potential to become a standard tool for drug discovery to assess the safety and/or efficacy of new compounds. Functional engineered 3D tissues have been proven to have a better predictive power compared to 2D cell culture or even animal models. Beyond drug discovery applications, tissue engineering holds promise to be used in regenerative medicine to replace organs (*e.g.*, skins, retina, liver…) made of patient cells with re-implantation. While remarkable progress has been realized in laboratory condition, this breakthrough technology has difficulties to reach the market due to the complexity of the manual processes involved.

Current obstacles for tissue engineering are tackled by combining autonomous self-assembly of cells in functional tissues and biomimicry to provide physiological conditions. Automated cell handling, sorting and seeding as well as microscale technologies such as bioprinting, microfluidics and micro-environments represent the technological bricks to build complex systems for in vitro testing or standardized tissue engineering platforms for implantation. CSEM supports biotech companies to transfer manual laboratory process to a scalable and automated manufacturing process. Two project examples are the development of multi-materials bio-printing and a skin-tissue producing machine

In vitro testing

RegenHU based in Villaz-St-Pierre is the market leader in bioprinting instruments with hundreds of users worldwide (Figure 1). Bio-printing is the method of choice to engineer complex 3D-structured tissues. By adding biological materials, layer after layer, a 3D arrangement of cells can be obtained. This initial positioning is essential to create the microenvironment in which the cells will migrate and differentiate to create the tissue. Recent examples of the use of this technology are the fabrication of skeletal muscle tissue [1] or even of a complete miniature heart [2]. CSEM supports its partner regenHU with its expertise in liquid handling and microfluidics to improve the ease-of-use of the technology while increasing the functionalities to create more complex tissue structures.

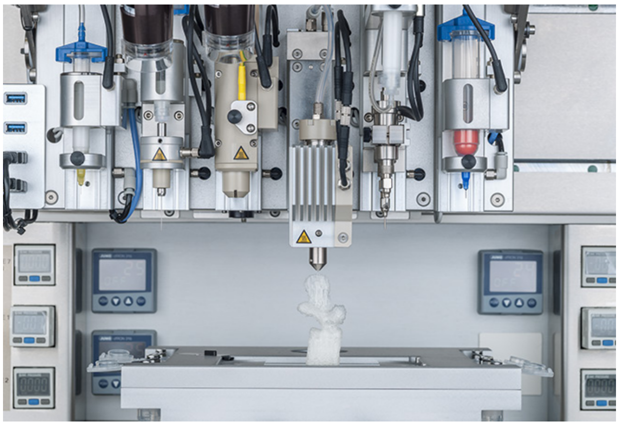

Figure 1: 3D discovery bioprinting platform from regenHU.

Artifical skin

The biotech start-up CUTISS has developed denovoSkin™ – a bio-engineered personalized, permanent skin graft. A small biopsy of healthy skin is harvested from the patient. The biopsy is processed to isolate epidermal and dermal cells. The cells are expanded in vitro, and thereafter used in combination with a hydrogel to create a dermo-epidermal skin graft. denovoSkin™ is now ready to be transplanted on the patient's wounds (Figure 2). Together with Cutiss, CSEM is now developing a cutting-edge technology that will enable to automate the production of the skin graft – thus decreasing costs, ensuring robustness and scaling up the process. Two main challenges are addressed. First, a disposable carrier is being developed, where the complete skin bio-engineering process is performed while ensuring sterility. Secondly, scaling up for the production of up to 100 skin grafts per patient in parallel requiring novel liquid handling processes that are investigated in the project.

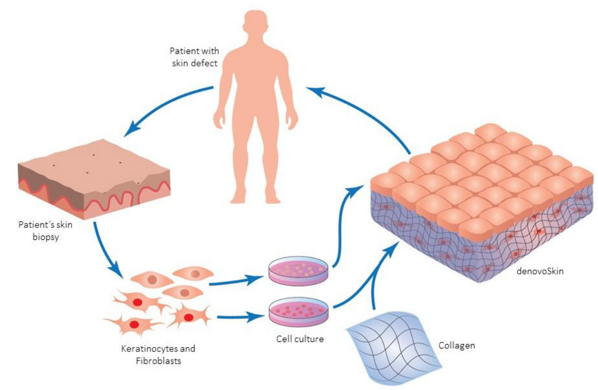

Figure 2: DenovoSkin™ engineering process from autologous skin graft.

[1] J. Goldowsky, V. Revol, Automated force measurement system for 3D printed muscle tissues, CSEM Scientific and Technical Report (2019) 18.

[2] N. Noor, *et al.*, 3D Printing of Personalized Thick and Perfusable Cardiac Patches and Hearts, Advanced Science, Vol. 6 (11), 1900344 (2019).