Translational studies of engineered human tissues

Gordana Vunjak-Novakovic

Department of Biomedical Engineering, Department of Medicine, College of Dental Medicine, Columbia University, New York NY, USA

Keywords: Organ engineering; organs on chip; heart; lung; bone; vasculature

Hem. Ind. **78(1S)** 3 (2024)

Available on-line at the Journal web address: http://www.ache.org.rs/HI/

INTRODUCTION: This talk will discuss the applications of tissue engineering in two areas of medicine: regenerative engineering of whole organs at the clinical scale [1,2], and modelling of diseases and therapeutic modalities using micro-sized "organs on chip" platforms [3,4,5].

EXPERIMENTAL: Engineering of human tissues involves the use of human stem cells (in most cases derived from a sample of blood) and two engineering components that are "instructing" the cells how to form a specific tissue. Th first component is a tissue specific biomaterial scaffold that serves as a structural and logistic template for tissue formation. The second component is the bioreactor designed to provide homeostasis and tissue-specific molecular and physical regulatory factors, as well as sensing and imaging modalities necessary to monitor and measure tissue development and function. In all cases, we aim to recapitulate the cell niches, using bioengineering tools.

RESULTS AND DISCUSSION: To illustrate the state of the art in the field and reflect on the current challenges and opportunities, this talk will discuss representative examples of whole organ engineering and organs-on chip models of injury, disease and regeneration. At the clinical scale, the goal is to achieve regeneration by treating the whole organ damaged by injury of disease. We will discuss regenerative engineering of a joint (that can be engineered de novo), and the lung and heart (that are being regenerated with the use of therapeutic cells). In organs-on-chip platforms, micro-sized human tissues are matured to adult-like phenotypes and functionally linked by vascular perfusion containing circulating cells and factors.

At the micro-scale, we will focus on organs on chip models of cancer metastasis, radiation damage, and side effects of some common drugs. Finally, we will discuss the key challenges the field is currently facing.

CONCLUSIONS: Tissue engineering is increasingly successful in recapitulating human physiology in health and disease, in patient-specific settings, supporting the development of high-fidelity research models and treatment modalities tailored to the specific patient.

ACKNOWLEDGEMENTS – The studies discussed here are a result of long-term efforts of my research team and our many collaborators, with funding provided by the National Institutes of Health, National Science Foundation, National Aeronautics and Space Administration, Biomedical Advanced Research and Development Authority, Cystic Fibrosis Foundation, and Columbia University BiomedX program.

REFERENCES

[1] Chen D, Wu JY, Kennedy KM, Yeager K, Bernhard JC, Ng JJ, Zimmerman BK, Robinson S, Durney KM, Shaeffer C, Vila OF, Takawira C, Gimble JM, Guo XE, Ateshian GA, Lopez MJ, Eisig SB and Vunjak-Novakovic G. Tissue engineered autologous cartilage-bone grafts for temporomandibular joint regeneration. *Sci Transl Med.* 2020; 12(565): eabb668. https://doi.org/10.1126/scitranslmed.abb6683

[2] Hozain AE, O'Neill JD, Pinezich MR, Tipograf Y,Donocoff R, Cunningham KM, Tumen A, Fung K, Ukita R, Simpson M, Reimer JA, Ruiz EC, Queen D, Stokes JW, Cardwell NL, Talackine J, Snoeck H-W, Chen Y-W, Romanov A, Marboe CC, Griesmer AD, Guenthart BA, Bacchetta M and Vunjak-Novakovic G. Xenogeneic cross-circulation for extracorporeal recovery of injured human lungs. *Nat Med.* 2020; 26(7): 1102-1113. https://doi.org/10.1038/s41591-020-0971-8

[3] Vunjak-Novakovic G, Ronaldson-Bouchard K and Radisic M. Organs on chip models for biological research. *Cell.* 2021; 184: 4597-4611. https://doi.org/10.1016/j.cell.2021.08.005

[4] Ronaldson-Bouchard K, Ma S, Chen T, Yeager K, Sirabella D, Song LJ, Yazawa M and Vunjak-Novakovic G. Advanced maturation of human cardiac tissue grown from pluripotent stem cells. *Nature* 2018; 556(7700): 239-243. https://doi.org/10.1038/s41586-018-0016-3 Erratum in: *Nature.* 2019; 572(7769): E16-E17. https://doi.org/10.1038/s41586-019-1415-9

*Corresponding author E-mail: gv2131@columbia.edu

CC BY

[5] Ronaldson-Bouchard, K, Tavakol DN, Yeager K, Chramiec A, Teles D, Halligan SP, Summers M, Stylianos S, Tamargo M, Guo Z, Jackv≥w J, Tagore S, Lee BM, Shih J, Soni RK, Christiano AM, Califano A, Hirschi KK, Chen CS and Vunjak-Novakovic G. Inter-organ chips with matured tissue niches linked by vascular flow *Nature Biom Eng.* "022; 6: 351-371