Coming Events

2016

National Society for Histotechnology: 42nd Annual Symposium/Convention
September 16–21, 2016
Long Beach, CA
www.nsh.org

Frontiers in Optics: The 100th OSA Annual Meeting and Exhibit/Laser Science XXXII
October 17–21, 2016
Rochester, NY
www.osa.org/en-us/meetings/global_calendar/events/frontiers_in_optics_the_100th_osa_annual_meeting_a

American Vacuum Society
November 6–11, 2016
Nashville, TN
www.avs.org

Neuroscience 2016
November 12–16, 2016
San Diego, CA
www.sfn.org

2016 MRS Fall Meeting & Exhibit
November 27–December 2, 2016
Boston, MA
www.mrs.org/fall2016

American Society for Cell Biology (ASCB) 2016 Annual Meeting
December 3–7, 2016
San Francisco, CA
http://ascb.org/future-ascb-annual-meetings

2017

Microscopy & Microanalysis 2017
August 6–10, 2017
St. Louis, MO
www.microscopy.org

2018

Microscopy & Microanalysis 2018
August 5–9, 2018
Baltimore, MD
www.microscopy.org

2019

Microscopy & Microanalysis 2019
August 4–8, 2019
Portland, OR
www.microscopy.org

2020

Microscopy & Microanalysis 2020
August 2–6, 2020
Milwaukee, WI
www.microscopy.org

2021

Microscopy & Microanalysis 2021
August 1–5, 2021
Pittsburgh, PA
www.microscopy.org

More Meetings and Courses
Check the complete calendar near the back of this magazine.

Carmichael's Concise Review

Microscopy Is Crucial to Building New Tissues from the Bottom Up

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A long-sought goal in the field of regenerative medicine is the creation of scalable methods to assemble and direct the development of complex tissues for use as models and implants. Methods used to date typically employ a "top-down" approach. In this context, "top-down" refers to creating a supporting scaffold, often made of biodegradable polymers or hydrogels, and then populating this scaffold with functional cells. The merits of this approach have been demonstrated, but it does impose some constraints on the ultimate architecture and development of the tissue. In a recent study Erik Vrij, Jeroen Rouwkema, Vanessa LaPoint, Clemens van Blitterswijk, Roman Truckenmüller, and Nicolas Rivron [1] described a "bottom-up" approach that uses only cells and cell products, allowing tissues to freely self-deform and remodel, similar to natural tissues. This method simulates the normal biological processes of self-assembly or directed assembly that stem cells undergo during tissue development.

Vrij et al. proposed a purely cell-based bottom-up approach that allows the building of stable tissue constructs with defined complex architecture. They used aggregates of cells as living self-scaffolding building blocks for the free-form fabrication of complex 3D tissues by sequential self-assembly. They developed a platform based on non-adherent hydrogel templates arranged in numerous microwells (several hundred to thousands). The basic idea was to introduce various growth factors (and other small molecules) and specific cells (for example, mesenchymal cells) and then use a high-throughput screening to define the factors directing assembly most effectively. Microscopy was crucial in order to extract information from the cellular aggregates (building blocks) in the microwells. For example, it was observed that the optimal time for aggregates of human mesenchymal stromal cells (hMSCs) to fuse into a continuous tissue while maintaining a precise geometry was 5 days. Different soluble factors that act on specific genetic circuits within the cells were introduced into the microwells.

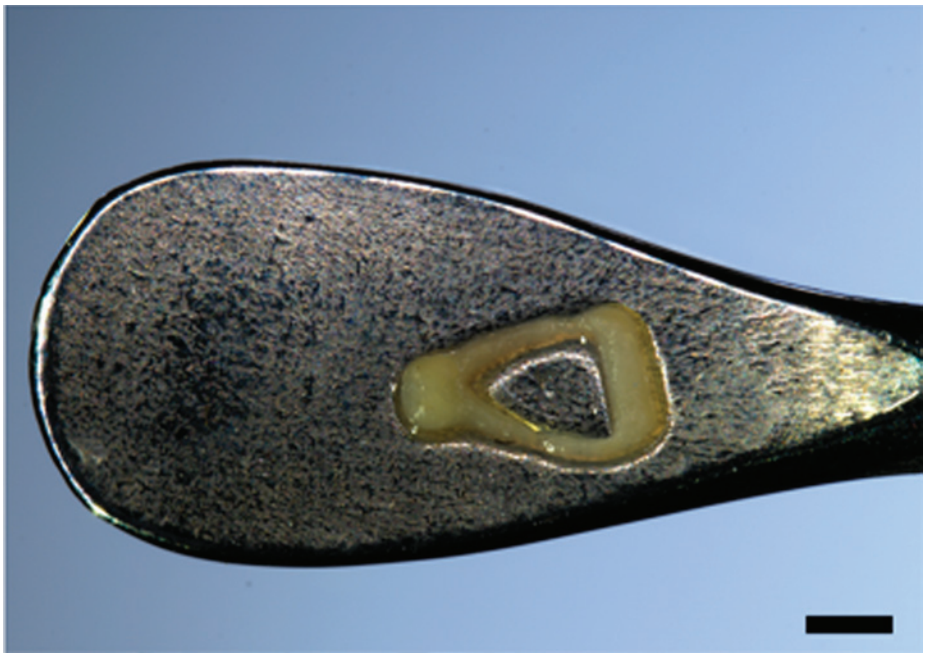

Figure 1: A macro photograph of tissue formed to resemble the stapes with clinically relevant size and 3D shape. Scale bar = 1 mm.

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Screening of the microwells showed that different factors directed the cell fate of hMSC aggregates toward forming bone, cartilage, fat, etc. On the other hand, human umbilical vein endothelial cells, upon fusion into a tissue, sprouted and self-organized to form a pre-vascular network spanning several cellular aggregates. Also, aggregates of mouse embryonic cells reproducibly formed structures called embryoid bodies.

As a proof of concept, Vrij et al. assembled tissues that mimic the smallest bone in the human body, the stapes, one of 3 ossicles in the middle ear. Upon assembly of cells and successively treating with specific factors, structurally stable tissues were formed with a size and 3D architecture resembling the stapes with unprecedented resolution (see Figure 1). This demonstrated the potential of forming precisely defined shapes using cellular building blocks.

In conclusion, Vrij et al. demonstrated an accessible and versatile microfabrication platform to build scaffold-free 3D tissues with complex architectures. The ability to screen a large number of these tissues to determine the optimal conditions for forming specific tissues is on the horizon. This has the promise to evaluate and thus properly recapitulate organogenesis *in vitro*. The possibility of forming organ-like structures and functional implants is very exciting! [2]

References

[1] E Vrij et al., *Advanced Materials*, DOI: 10.1002/adma.201505723 (2016).

[2] The author gratefully acknowledges Dr. Nicolas Rivron for reviewing this article.

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