Organogenesis 8:4, 101–102; October/November/December 2012; © 2012 Landes Bioscience

Organogenesis News and Views

Biomimicry in biomedical research

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Biomimicry (literally defined as the imitation of life or nature) has sparked a variety of human innovations and inspired countless cutting-edge designs. From spider silk-made artificial skin to lotus leaf-inspired self-cleaning materials, biomimicry endeavors to solve human problems. Biomimetic approaches have contributed significantly to advances biomedical research during recent years. Using polyacrylamide gels to mimic the elastic modulus of different biological tissues, Disher's lab has directed meschymal stem cell differentiation into specific lineages.[1] They have shown that soft substrates mimicking the elastic modulus of brain tissues (0.1–1 kPa) were neurogenic, substrates of intermediate elastic modulus mimicking muscle (8–17 kPa) were myogenic, and substrates with bone-like elastic modulus (25–40 kPa) were osteogenic. This work represents a novel way to regulate the fate of stem cells and exerts profound influence on stem cell research. Biomimcry also drives improvements in tissue engineering. Novel scaffolds have been designed to capture extracellular matrix-like structures, binding of ligands, sustained release of cytokines and mechanical properties intrinsic to specific tissues for tissue engineering applications.[2,3] For example, tissue engineering skin grafts have been designed to mimic the cell composition and layered structure of native skin.[4] Similarly, in the field of regenerative medicine, researchers aim to create biomimetic scaffolds to mimic the properties of a native stem cell environment (niche) to dynamically interact with the entrapped stem cells and direct their response.[5]

Biomimicry can be achieved at different levels: mimicking nature form or function, mimicking natural processes and mimicking natural systems.[6] Mimicking form or function are the most common biomimetics seen in biomedical research. A recent example can be drawn from cardiac research, where the field is poised for new breakthroughs. Published in *Biomaterials*, Dr Parker's group used micropatterned surfaces to build 2-dimensional engineered cardiac muscle from neonatal rat ventricular myocytes with distinct architectures that mimic in vivo hierarchal structures and electromechanical function of heart.[7] They combined image analysis of sarcomere orientation with muscular thin film contractile force assays to calculate the peak sarcomere-generated stress as a function of tissue architecture. Their data showed that increasing peak systolic stress in engineered cardiac tissues corresponds with increasing sarcomere alignment. Their results demonstrated that heterogeneities encoded in the extracellular space can regulate muscle tissue function, and that structural organization and cytoskeletal alignment are critically important for maximizing peak force generation. Their work suggested that engineering the extracellular space is an effective means of enslaving the cardiac myocyte's ability to self-organize its contractile apparatus to maximize the contractile strength of muscle. The conclusions of this research have important implications in how to maximize the physiologic function of engineered tissues.

While mimicking the form and function will likely lead to novel treatments, mimicking biological processes and systems are harder to achieve, but will bring greater impact. Exciting research by Dr Elvassore's group has been published in *PLOS ONE* November 2012 entitled "Micro-Arrayed Human Embryonic Stem Cells-Derived Cardiomyocytes for In Vitro Functional Assay."[8] In this study, Dr Elvassore's group developed for the first time an in vitro cardiac tissue assay using human cardiomyocytes (hCMs) and micro-technologies. hCMs were cultured onto a poly-acrylamide hydrogel with tunable tissue-like mechanical properties and organized through micropatterning in a 20 × 20 array. The features of the developed assay include: (1) 400 parallel experimental replicates through hCMs micropatterning in array of circular dots (300 μm in diameter) with a consistent and repeatable number of hCMs, (2) elastic substrate with physiological stiffness, able to support hCMs contractions and (3) electrophysiological stimulation assisting the online morphometric analysis of hCMs contractions. Their data showed that micropatterned hCMs maintained the expression of the major cardiac markers (cTnT, cTnI, Cx43, Nkx2.5 and α-actinin) and functional properties. They observed the spontaneously beating of micropatterned hCMs and showed the ability to increase beating frequency by exogenous electrical stimulation. To test the feasibility of using the developed system as an in vitro model for testing the effects of a pathological environment on human cardiac, they exposed the system to increasing level of hydrogen peroxide (H_2O_2) mimicking the oxidative stress during ischemia and reperfusion phases. The viability of hCMs was not compromised with exposure to 0.1 mM H_2O_2, however, their contractility was dramatically suppressed. This observation could be relevant for rational understating of why, after in vivo cellular injection into compromised or damaged heart tissue, the surviving cells do not integrate or have a poor functional integration with the host tissue. Overall the human cardiac assay could act as a cardiac system to examine pathological or toxicological conditions, which could dramatically expand our knowledge of cardiac diseases and treatments through high-throughput screening. Similarly, an engineered "lung-on-a-chip" biomimetic microdevice has been created most recently.[9] It was used not only to model pulmonary edema but also to screen drug that might treat the disease. The published results are still a proof of principle. However, with further improvement it could have a significant impact on drug development by replacing animal models used for drug screening.

Biomimicry has been the driving force in research for years. With the fast progress of biotechnology and the rapid growth of knowledge biomimicry at a deeper level could move the biomedical field forward.

References

1. Engler AJ, et al. Cell 2006; 126:677-89; PMID:16923388; http://dx.doi.org/10.1016/j.cell.2006.06.044.
2. Ravichandran R, et al. Macromol Biosci 2012; 12:286-311; PMID:22278779; http://dx.doi.org/10.1002/mabi.201100325.
3. Zhang G, et al. Adv Drug Deliv Rev 2007; 59:360-73; PMID:17513003; http://dx.doi.org/10.1016/j.addr.2007.03.018.
4. Jayarama Reddy V, et al. Wound Repair Regen 2012; PMID:23126632; http://dx.doi.org/10.1111/j.1524-475X.2012.00861.x.

5. Vinatier C, et al. Curr Stem Cell Res Ther 2009; 4:318-29; PMID:19804369; http://dx.doi.org/10.2174/157488809789649205.
6. Cramer MD. Libr J 1997; 122:92.
7. Feinberg AW, et al. Biomaterials 2012; 33:5732-41; PMID:22594976; http://dx.doi.org/10.1016/j.biomaterials.2012.04.043.
8. Serena E, et al. PLoS One 2012; 7:e48483; PMID:23152776; http://dx.doi.org/10.1371/journal.pone.0048483.
9. Huh D, et al. Sci Transl Med 2012; 4:ra147; PMID:23136042; http://dx.doi.org/10.1126/scitranslmed.3004249.