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A Call to Craft

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Abstract

Educational institutions must begin training tissue engineers to think as both biomedical investigators and fabricators.

Tissue engineering and regenerative medicine are on the cusp of a transformation. During the past 15 years, the field has metamorphosed from laboratory-based experimental studies in model systems to a mature discipline that is yielding products that are being evaluated and used in the clinical domain (1). Researchers are working to decellularize entire hearts, lungs, livers, and kidneys to yield protein matrices that can be loaded with stem cells and then coaxed to grow in vitro into functional organs (2, 3). Others are working with free-form fabrication technology to build fully vascularized tissues (4) that might eventually lead to off-the-shelf transplants. Some are even trying to grow organs in vitro from single cells (5). These are ambitious biomedical projects that, if successful, could radically alter how we think about and treat disease (6).

The success of such projects is fundamentally dependent on how we train our future tissue engineers to function in a field that requires a broad understanding of basic sciences (including biology, chemistry, and physics) and a sophisticated understanding of human pathophysiology, stem cell biology, and tissue mechanics. Accordingly, we now offer students broad graduate and undergraduate training: Indeed, we ask them to become proficient in physics, chemistry, biology, and engineering (7) and advise them to gain as much clinical experience as is possible. But tissue engineering, at its core, is devoted to designing and constructing physical objects, albeit of a vastly complex and organic nature. An exclusively investigative, reductionist approach is not enough to yield a clinically worthy product in this design-build discipline. Scientists attempting to create organs suitable for human transplantation must have the skills to build as well as biologically characterize their inventions along with facilities suitable for this type of interdisciplinary work. In short, we

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need to start training tissue craftsmen. Here, a veteran physician-scientist and a bioengineering student collaborate to envision ways to achieve this goal.

REDEFINING THE CURRICULUM

The ambition of whole-organ regeneration is best served by a broadly encompassing curriculum. Four defined skill sets are integral to training in this field at both the undergraduate and graduate levels (Table 1).

Biological insight

Current biomedical engineering programs already teach aspiring tissue engineers a concrete understanding of cell biology, chemical kinetics, and the ways in which cells respond to and interact with their environments. These core foundational studies provide a common basis for understanding the body and a starting point for those who seek to become whole-organ engineers.

Anatomical and histological insight

Educational institutions must begin offering in-depth gross anatomy and histology to our aspiring tissue engineers. It is crucial to explore the human body firsthand and to learn the tactile properties and living architecture of tissues and organs. In our experience, nothing can substitute for this kind of direct observation and manual learning. It also provides a direct introduction to handling and manipulating human tissue.

Tailored for whole-organ engineers, such coursework could teach students how to visualize tissues on multiple length scales—understanding how the structures of proteins determine their ability to organize, how that organization affects tissue architecture, and how that architecture manifests on a gross and physiological level. The opposite is also true: Intricate observation of tissues can help researchers connect a molecular goal to a manual action—that is, to deduce mechanical or physical inputs needed on a macroscopic scale to yield the desired chemistry, architecture, or tissue property. Researchers should be trained to understand the microscopic consequences of macroscopic actions and the macroscopic implications of microscopic observations. It is a language that allows people to physically realize ideas.

Technical design and development

The vast majority of tissue engineering endeavors have required the construction of specialized apparati as well as materials-processing techniques. We therefore propose that introductory courses in both materials science and design and fabrication be integrated into standard biomedical curricula at the undergraduate and graduate levels. Universities often require mechanical and chemical engineering students to study materials science. In parallel, classes focused on bioreactor design and biomedical-sensor development can teach valuable skills with computer-aided design; custom machining of metal, plastics, and glass; and build-out of controllers and electronic monitoring.

Physical and tactile skills

As projects grow more ambitious and clinically realizable, techniques for manipulating whole organs and designing and working with human-scale bioreactors will grow in importance. Simple cell-culture operations can become much more complex when dealing with large, three-dimensional constructs and billions of cells; therefore, and thus teaching the science behind large-scale cell culture and bioprocess manufacturing will be an important adjunct.

A quick survey of high-ranking biomedical departments shows that many institutions already have coursework in place that responds to some of these needs. Johns Hopkins encourages first-year biomedical engineering students to enroll in anatomy and pathobiology courses (8). The bioengineering department at the University of Pittsburgh offers biomaterials coursework tailored to tissue engineering (9). And Rensselaer Polytechnic Institute emphasizes the importance of courses in technical ability and computer-aided design for biomedical students (10). However, it is rare to find a department with a dedicated organ-engineering track that teaches the full scope of skills listed above. We hope to begin a larger conversation about the goals of tissue engineering and what new sets of training might be required in order to meet those aims.

REDEFINING THE LABORATORY

If we want to clear the path from concept to clinic, our laboratories need to be equipped to pursue a project all the way from idea to product. This means focusing on scientific investigation side by side with clinically minded construction. By creating spaces that are mergers of laboratories and fabrication facilities, we would be promoting the intersection of two equally valuable modes of thought.

Such a space has the potential to become an excellent training ground for young biomedical engineers, teaching the breadth of skills listed earlier. This means developing a space that teaches not just biological techniques and basic engineering but also polymer and metals processing, CAD, custom machining, electronic build-out, and any other tools that might be necessary both to investigate a tissue-engineering idea and to build a clinic-ready product.

A regenerative medicine laboratory or institute that allies scientific inquiry with production is a place where new technologies could be both invented and perfected. Such a lab would be well equipped to tackle questions of complex investigational science, but it also would be capable of refining fabrication techniques. It is a space that would facilitate the training of tissue engineers who are also craftsmen, generating inventors who are empowered to design and create with living cells.

The ultimate test of tissue engineering and regenerative medicine is going to be how quickly and effectively new technologies make it into the clinic. This requires bioengineers with the capacity to culture large, human-scale organs. It also requires advanced facilities tailored to turning a design into a living physical product ready for transplant. It took more than a century of medical history for modern surgery to develop into the fine-tuned process suited to organ replacement. It is time to encourage a commensurate push for regenerative medicine.

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Fig. 1. Room to breathe

Shown is a decellularized human lung in a custom-designed bioreactor. Turning this protein matrix into a viable organ for transplant will require medical scientists skilled at physical craftsmanship and working environments focused on both investigation and production.

Table 1

Expertises for training in regenerative medicine

In addition to the basic and biological sciences, engineers will benefit from experience in the rudiments of anatomy, histology, and surgery; a background in custom design, manufacture, and fabrication; and a working understanding of materials and chemical engineering.

Area	Examples	Impact
Biology	Cell biology Cellular mechanics Physiology, with lab Chemical kinetics, with modeling	Already at the core of many bioengineering curricula Provide an essential foundation for work in regenerative medicine
Anatomy/histology	Gross anatomy, with dissection Histopathology	Provide tactile experience working with living tissues and allow firsthand observation of tissue architecure
Physical and tactile skills	Principles of large-scale mammalian cell culture Introduction to surgical technique	Teach the manual techniques required for human-scale organ research
Technical design and development	Introduction to fabrication, with lab Bioreactor design, with lab Biomedical sensor design, with lab Introduction to biomaterials Biomaterials processing Large-scale cell culture/bioprocessing	Provide a much-needed technical basis for invention and custom fabrication