Tissue engineering as an example of the need for interdisciplinary fields like bioengineering.

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Editorial

By definition Biomedical Engineering (BME) is multidisciplinary; being the application of math and science to clinical medicine. It is therefore important for a BME curriculum to have courses from multiple disciplines plus have the courses that are multidisciplinary. The discipline itself includes virtually all sub-specialties in math and science (biology, chemistry, physics, etc.) and applies it to all medical subspecialties (surgery, cardiology, rehabilitation medicine, etc.). Since different parts of BME emphasize different subspecialties in these other fields, this paper will just focus on Tissue Engineering/Regenerative Medicine which is part of biomaterials in BME.

For both Tissue Engineering and Regenerative Medicine the goal is to restore function by either regenerating the original structure or by using an "engineered" replacement that is close to the original structure. Tissue Engineering normally is building tissue and organs with cells and matrix materials (natural or synthetic); plus it usually adds strategies to speed healing (regenerative healing if possible) with biological response modifiers. Regenerative Medicine can be defined as including all of Tissue Engineering or more narrowly as strategies to regenerate tissue (stem cells, biological response modifiers, scaffolds, etc.).

Universities are a good place to both study and do research in multidisciplinary fields. Although there are many multidisciplinary fields in a university, BME brings the critical ones for Tissue Engineering/Regenerative Medicine all together. This is important, since a university does not always foster interdepartmental collaboration for either academics or research. Usually there are economic disincentives for sharing either tuition dollars or research dollars across departmental lines. Research centers, however, are frequently established to circumvent these barriers.

Even a BME program benefits from having strong programs outside the department for collaborations; such as a strong engineering school as well as biomedical sciences programs and either a med school or vet school. On the academic side, minors can help as well as project oriented classes such as senior design; allowing1easier collaboration across departmental lines. Graduate students can also set up multidisciplinary committees to provide expertise from many different disciplines, even if the funding is not spread around to all the different disciplines.

Specifically, Tissue Engineering/Regenerative Medicine requires knowledge in many different disciplines including biology (e.g. cell, developmental, comparative anatomy, physiology, evolutionary, and histology), biochemistry (e.g. molecular and recombinant), clinical medicine (e.g. surgery, rehabilitation medicine, and pathology), and engineering (e.g. materials engineering (biomaterials), mechanical and civil engineering (biomechanics), chemical engineering (biotransport and drug delivery), and electrical engineering (cell-cell interactions).

In general, the need is to understand how cells, matrices (synthetic and natural scaffolds), and biological response modifiers can help speed healing; particularly regenerative healing. There are disciplines for each of the three components as well as the interaction between them. For example, cells (e.g. cell biology), matrices (e.g. biochemistry and biomaterials), and biological response modifiers (e.g. biochemistry, biotransport, and mechanotransduction) have different main disciplines. In addition, there are similar disciplines for the interactions between these components: cell-cell interactions (e.g. cell biology and bioelectric phenomenon), cell-matrix interactions (e.g. biochemistry and biomaterials), and cell-soluble factors (e.g. cell biology and biochemistry).

One of the key overall areas is regeneration; the study of which helps to determine strategies to improve tissue-engineered products. In particular, two areas to look at are developmental biology and wound healing (both how it proceeds normally and how it works in regenerative animals). In developmental biology we see how regenerative ability decreases as we age; virtually all cells maintain the ability to turn-over (replace themselves) at some rate (days to years depending on the tissue); and changing the environment during development can alter the development process [1].

For example, babies up until about 6 months can regenerate an amputated finger and in utero surgery is essentially scarless [1,2]. In embryonic wound healing there is a higher concentration of hyaluronic acid and TGF-β_3 [3,4]. Research in this area has looked at questions like how to dedifferentiate cells as well as how to use biological response modifiers and matrix biochemistry to help differentiate cells along the desired lineage [1,2]; how changing electric fields during development can lead to asymmetrical growth (budding—how limbs are made) as well as how artificially changing the electrical fields can alter limb development [5]; and how changing the environment (e.g. electric fields, matrix (biochemical cues or scaffolding ability), or mechanical loading) can alter the healing process pushing more toward regeneration *vs*. scarring [1,2].

Understanding the mechanisms of regeneration can help provide clues to help in regenerative healing. In some cases, lessons learned can be similar to developmental biology with involvement of specific developmental features, such as nerve

dependence or specific gene expression [6,7]. In disparate taxa, however, regeneration (e.g. skin regeneration) can occur by similar processes; matrix metalloproteinases, enzymes involved in degrading or remodeling the extracellular matrix, are upregulated after wounding; bioelectric events can initiate regeneration; immune response genes are upregulated; cell signaling, especially Wnt and fibroblast growth factor signaling, is important for regeneration initiation and blastema development; and an important role has been demonstrated or suggested for innervation of the regenerating tissue [7]. There however, are differences among animal groups; e.g. regeneration can occur *via* a blastema of undifferentiated cells or through proliferation of existing cell types; without any proliferation [7]. A blastema, where one occurs, can be formed primarily through stem cells or dedifferentiation of mature tissue [7]. Also proton pumping or immune response suppression have been shown to be sufficient to rescue crucial aspects of tail regeneration during a transient non-regenerative period of development [7].

A number of studies have shown how the lessons learned from developmental biology and wound healing can help in enhancing regenerative healing. E.g. the use of stem cells [1,4,8], TGF-β_3 [1,4] and other growth factors [1,2], and electrical stimulation [5]. In addition studies to use and modify existing wound healing scaffolds have shown promise as well [1,2]. A key in this type of research is both the multidisciplinary nature of BME and the ability to find and work with local clinicians and basic scientist from multiple disciplines in a university setting.

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