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Tissue Engineering Pre-Reads

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BME 310 Pre-Reads for Week 10: Tissue Engineering

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Basics of Tissue Engineering

Your pre-assessment this week will have some short-answer (not just true/false or multiple choice)!

This week, we are studying tissue engineering. You will see this incorporates hydrogels (similar to your Darcy flow lecture), materials testing (similar to your biomechanics lecture), and cell culture principles (which is why it's in the Cell Culture Module for the course!). Many BME fields and applications are interdisciplinary and incorporate many types of techniques.

Why?

Tissue engineers are motivated by:

-a shortage of organs available for transplant

-difficulty getting organs to far destinations

-compatibility of transplant to recipient (both graft vs. host disease and recipient rejection)

-circumstances when entire transplants are not necessary (e.g. wound healing, bone healing, etc.)

-to perform drug studies in organ-like structures as opposed to live-animal testing (e.g. organoids or lab-on-a-chip)

-are there others you can think of (examples of when a lab-grown organ may be better than human organs, or examples of where 3-dimensional cell cultures might be more useful than 2D?)

What?

"Tissue engineering is an interdisciplinary field that applies the principles of engineering and the life sciences toward development of biological substitutes that restore, maintain, or improve tissue function." Langer and Vacanti, Science, 1993

Indeed, Bob Langer (https://langerlab.mit.edu/) and Joseph Vacanti (https://www.massgeneral.org/research/regenerative-medicine/research-labs/tissue-engineering-organ-fabrication) are two of the pioneers and world leaders in Tissue Engineering. Check out their work if you are interested. Dr. Langer is one of the highest-cited engineers ever, and has over 1,000 patents, 1,000 publications, and has dozens of startup companies. Dr. Vacanti is a surgeon and world-leader in clinical translation of engineered materials.

Specifically, tissue engineering is the process of creating new tissues using a combination of biomaterials science/engineering at the interface of biology.

How?

Scaffolds, Cells, and Growth Factors

Scaffolds—can be synthetic or natural biomaterials. Which material to be used is determined by the final application (stiffness, location, size, porosity, pore size, degradation rate, etc). Common scaffolds are polymers like poly(lactic-co-glycolic acid) (PLGA) and polycapralactone (PCL); silicone; polysaccharides like chitosan and hyaluronic acid; metals or ceramics; or even decellularized tissues. Scaffolds can be formed by ionic crosslinking or temperature-based hydrogel formation (less stable), covalent crosslinking (more stable), or even 3D printing!

Growth factors—you've encountered these in the context of complete cell growth medium (in serum usually) and they give signals to cells to proliferate, differentiate, etc. In tissue engineering, some type of stem cells are often used, so these growth factors are typically differentiation signals (e.g. vascular endothelial growth factor, epidermal growth factor, bone morphogenetic protein, etc). They can be incorporated into or conjugated to the scaffold, or they can be added into the medium. Or sometimes they are manufactured by cells, for example cells are transfected with plasmids that direct them to make specific growth factors

Cells—Typically not cell lines or differentiated primary cells. More commonly use is stem cells of some sort. Can be adult stem cells or embryonic, however embryonic stem cells typically can differentiate into more types of cells. For regulatory/moral/ethical reasons embryonic stem cells are restricted, so induced pluripotent stem cells (iPSC) are most common (wherein a more differentiated type of cell is programmed to become a PSC through genetic engineering). Totipotent stem cells can divide into any type of cell (these are mostly early developmental type cells or in blastocysts). Pluripotent stem cells can divide into any type of non-embryonic cell. Multipotent stem cells can divide into any type of cell within a specific group, an excellent example is mesenchymal stem cells (MSCs). Unipotent stem cells can really only divide into one type of cell, it is a type of progenitor cell for terminally differentiated cells.

Characterization

Biological characterization—proliferation and growth assays (which you are familiar with), staining techniques and microscopy (both visible and fluorescence), antibody-based protein production assays (to be learned later)

Biomaterials-based characterization—commonly electron microscopy and rheometry (stress/strain) to evaluate the form and function of the scaffold, or the scaffold-cell construct. Young's modulus/stiffness/elasticity come into play again, though this is often in the MPa range for hydrogels as opposed to the GPa range for previous materials like bone, acrylics (some metal/ceramic scaffolds are of course in this range)