**Limitations of Cell/Tissue Engineering Therapies**

* Please comment on the limitations of cell and tissue engineering therapies. Use your prior experience in the workplace to inform your comments if applicable.
  + Remember that we are interested in your point of view as a creative, thoughtful biomedical engineer.
* Respond to at least two of your classmates.

I identified these challenges that Cell/Tissue Engineering therapies must address:

* Difficulties in expanding stem cells in culture (for example difficulties to expand hepatocytes or pancreatic islet cells in culture).
* Be able to handle a vast range of exerted forces like in bone tissue.
* One repeated challenge faced by tissue engineering is the need for proper vascular and nerve supply which is a critical requirement for example in dentin/pulp engineering.
* Enduring extreme environments like the high acidity of the intestine.
* Defensive immune response from the receiving host leading to rejection of the cells or tissues.
* Safety and risk concerns like off target tumor formation.
* Delivery through highly protected parts of the human body like delivery through the brain-blood-barrier.
* Biomaterials to be biocompatible with the environment of intervention and with proper ligand adhesion for proper cell motility.
* Tissues with appropriate mechanical properties to sustain real-life biological stresses.
* Long life sustainability with self-regenerating and self-repairing capabilities. At the same time, in some situations, support materials need to be biodegradable after a specific time of biochemical exposure.
* Possibility of responding to biochemical signals for reprogramming i.e., turning off growth after complete healing. There is also the need to be able to monitor progression of regeneration.
* Scientific coordination and infrastructure development are required to accommodate the research in terms of biological, computational and data resources.
* Better quantitative methods to measure chance of success when translating therapies from animals, 2D-3D cell cultures or organ-on-chips models, to humans with faster delivery times.
* Manufacturing challenges in material sourcing, standardization and production to large scale.
* Speed during the bioprinting process, it is apparently not fast enough (I have never used a bioprinter).
* Clinical trials to design relevant to the drug therapies for FDA approval.

Hi Aarsh,  
  
Thank you for bringing the issue of vascularization and adding the reference. Since many of us also reported the vascularization challenge in tissue engineering, I looked for recent reviews and the one I have added mentions a combination of organ-on-chip, organoid technologies and 3D printing strategies and pre-vascularized scaffolds. It seems there is a recurrent issue to expand cells in 3-D structures. And one open challenge is to promote neural tissue growth in a specific direction with recruitment of different cell types related to motor or sensor functions.

[1]

Hi Nikita,

After you highlighted the risk of tumor with iPSC cells, I was curious how do they compare to mesenchymal cells (MSC) which are also used in regenerative medicine. MSC have many advantages: easy to isolate, high plasticity, high yield, immunomodulation and immunosuppression properties. They are also difficult to harvest, quickly lose their plasticity during expansion; on the other hand, iPSC cells are harvested using less invasive methods and pluripotent (MSCs are multipotent). Cross generation seem to address these issues: reprogramming MSC into iPSC cells is 200-fold more efficient and iPSC cell-MSC have greater expansion capacity, longer-term survival after transplantation and nontumorigenic.

[2]

[1] A. N. Frisch, “Advances in vascularization and innervation of constructs for neural tissue engineering,” *Current Opinion in Biotechnology*, p. 10, 2022.

[2] H. D. Zomer, A. S. Vidane, N. N. Gonçalves, and C. E. Ambrósio, “Mesenchymal and induced pluripotent stem cells: general insights and clinical perspectives,” *Stem Cells Cloning*, vol. 8, pp. 125–134, Sep. 2015, doi: 10.2147/SCCAA.S88036.