Tissue Engineered Artificial Organs

- After completing the reading and lectures of this module, discuss which human organ (other than the brain) you think would be the most difficult to artificially engineer using tissue engineering techniques and why?
- Respond to at least two of your classmates.

The major organs of the Gastrointestinal tract represent a challenge to replicate artificially. Take the stomach or the intestines; they have significant volume, and multi-complex functions resulting from the integration of neural, immune, secretory, absorptive and motility signals. The GI tract is composed of four concentric layers containing many different cell types: SMCs, enteric neurons, interstitial cells of Cajal (ICCs), mast cells (MCs), and various immune cells. The sourcing and proliferation of each of these types of cells is an on-going challenge for CTE.
Ideally an engineered scaffold aiming at reproducing the GI tract anatomy will:

- Be adequately porous to allow neovascularization, promote gas and nutrient exchange
- Exhibits degradation rates and biocompatibility w.r.t adhesion, proliferation, and host-immune response
- Shows a specific structural cellular alignment: the template scaffold must permit circular smooth muscle of the gut to concentrically align in syncytium and form a hollow tube that can contract to propel luminal contents. The scaffold must also allows the alignment of longitudinal smooth muscle in parallel sheets orthogonal to the circular smooth muscle layer (Bitar and Raghavan).
- Recreates highly coordinated to intracellular biochemical events peristaltic waves
- Contains different cell types with a distribution similar to the natural intestines
- Allows re-epithelialization to regenerate mucosal layers
- Maintains a patent lumen and prevents leakage during in use in the body as a replacement
- Due to the complex connection between CNS and enteric nervous system, it needs to integrate with the rest of the body
- Delivers nutrients in an orderly manner to facilitate absorption
- For the stomach, be able to handle highly acidic biological environment in order to reproduce the digestion process

In addition, the intestinal microbiome plays a critical role in the brain-gut axis which is actively investigated and not fully understood but must be replicated.

Today most of the CTE models are still in vitro and pre-clinical phases for intestinal disease applications, and very few have had success in the clinical field (Collier et al.).

<u>References</u>:

Bitar, Khalil N., and Shreya Raghavan. "Intestinal Tissue Engineering: Current Concepts and Future Vision of Regenerative Medicine in the Gut." *Neurogastroenterology*

and Motility : The Official Journal of the European Gastrointestinal Motility Society, vol. 24, no. 1, Jan. 2012, pp. 7–19. *PubMed Central*, https://doi.org/10.1111/j.1365-2982.2011.01843.x.

Collier, Claudia A., et al. "Tissue Engineering of the Gastrointestinal Tract: The Historic Path to Translation." *Journal of Biological Engineering*, vol. 16, no. 1, Dec. 2022, p. 9. *DOI.org (Crossref)*, https://doi.org/10.1186/s13036-022-00289-6.