

The Use of Additive Printing to Develop Optimal Substrates for Regenerative Medicine

California Institute Of Technology
1200 E. California Blvd. Pasadena, CA

Keillen Lee

Caltech



BACKGROUND & MOTIVATION

Although regenerative therapy stem cell research have made great advancements, there are still issues that must be addressed before clinical studies can be possible.

- Most mammalian cells require a surface to adhere to for development and proliferation to occur.
- The organization of Stem Cells have an impact on how the cells mature
- *In Vivo* transplantation of Stem Cells for regenerative therapies would require means to deliver nutrients to the cells while without leaving surrounding tissue affected

INNOVATION

- In recent studies, polyacrylate polymers have been successfully used as surgical bonding and mesh materials for its bio-absorbability via hydrolysis
- In this study, we have explored the use of Poly(caprolactone) (PCL) as a polymer resin that can be developed into a substrate for living mammalian cells.
- Using two-photon laser etching (Nanoscribe 3D Printing) our hypothesis is that a non-cytotoxic PCLDA substrate can be functionalized with integrins that promote regeneration of tissues such as skeletal muscle

DESCRIPTION

Experimental design

Development of PCL diacrylate from PCL mn2000

Characterization of PCLDA through Nuclear Magnetic Resonance (NMR)

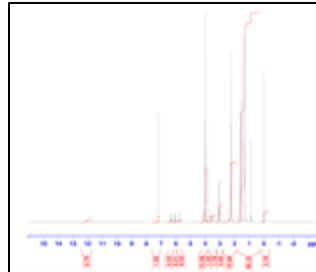
Development of PCLDA resin for Additive(3D) printing

Testing of various laser power and scan speeds to determine the best printing resolution.

Characterize using TEM

Print and develop substrates for cell cultures

Culture fibroblast with PCLDA substrates in 96 well plates



Characterization of PCLDA with NMR



photo courtesy of ecologyfortheresources.com



Ref.

Aditya, Mihai, et al. "Generation of Mesenchyme Free Intestinal Organoids from Human Induced Pluripotent Stem Cells." *Nature Communications*, vol. 11, no. 1, Nature Publishing Group, 2020. [ProQuest, https://doi.org/10.1038/s41467-020-18018-8](https://doi.org/10.1038/s41467-020-18018-8).

Green, M. D. et al. Generation of anterior foregut endoderm from human embryonic and induced pluripotent stem cells. *Nat. Biotechnol.* 29, 267-272. (2011).

Altay, Gizem, et al. "Self-Organized Intestinal Epithelial Monolayers in Crypt and Villuslike Domains Show Effective Barrier Function." *Scientific Reports*, vol. 9, no. 1, July 2019, p. 10140. [www.nature.com, https://doi.org/10.1038/s41598-019-46502-4](https://doi.org/10.1038/s41598-019-46502-4).

ANTICIPATED IMPACT

An alternative method of cell culturing were Cells can fully absorb the substrate during differentiation and proliferation

Developing new culturing protocols for 3D substrate structures to research their impact on cell/tissue development

More opportunity for scaffolding of soft-tissue in regenerative therapy research

PATH FORWARD

- **Functionalized Substrates with Integrins that will optimize regeneration of specific tissue such as skeletal muscle**
- **3D printing of organoids with living cells within the structure**
- **Functionalized substrates can be with different compounds for long-term assays**
- **Developing research for regenerative therapy transplation with PCLDA scaffolding**

Point of Contact: Kblee@caltech.edu