Name(s)
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Project Number
S1303

Project Title
Nanotherapeutics Enhanced Artificial Liver against Antibiotic Resistant Bacteria

Abstract

Objectives/Goals
With the pressing issue of antibiotic resistant bacteria, anti-virulence therapies have emerged as a non-antibiotic strategy for bacterial elimination through removal of bacterial toxins. Usage of antibiotics has also provoked serious liver diseases, with the liver unable to metabolize large quantities of drugs. I aimed to develop a synergistic 3D bioprinted artificial liver platform containing cell membrane coated nanotherapeutics surrounding a liver cell scaffold. This artificial liver platform has the ability to eliminate antibiotic resistant bacteria through anti-virulence therapy and to reduce antibiotic toxicity through liver cell metabolism.

Methods/Materials
I started with the design of a hydrogel-based tubular platform with concentric cylinders. The inner cylinder contains HepG2 liver cells, while the outer cylinder encompassing the liver cells is a hydrogel wall embedded with red blood cell membrane coated nanoparticles (RBC-NPs). The RBC-NPs were synthesized through self-assembly methods and incorporated into the hydrogel monomer solution. Solutions containing cells and RBC-NPs were photopolymerized layer-by-layer using a light-based 3D bioprinting method, allowing for multi-layer printing of the cells surrounded by the nanoparticles.

Results
Through extensive 3D printing optimization, materials characterization and proof of concept testing, I have successfully 3D-printed the nanotherapeutics-enhanced artificial liver. The size and surface properties of the RBC-NPs can be well-controlled, while their function is maintained after the 3D printing process. I found that my platform promoted liver cell survival and neutralization of bacterial toxins. The liver cells successfully metabolized the drug rifampicin, while the RBC-NPs absorbed hemolytic toxins, demonstrating the ability for anti-virulence therapy and subsequent bacterial elimination.

Conclusions/Discussion
The nanotherapeutics-enhanced artificial liver platform demonstrates broad spectrum detoxification of bacterial toxins. It is time and cost efficient, and supports liver cell growth for enhanced drug metabolism. The 3D bioprinting method allows for rapid manufacture of the micro-liver scaffolds, while the combination of nanotherapeutics with liver cells provides a powerful platform to clear antibiotic resistant bacteria.

Summary Statement
I created the first nanotherapeutics-enabled artificial liver to enhance drug metabolism and eliminate antibiotic resistant bacteria.

Help Received
Used the lab equipment of Dr. Liangfang Zhang at the University of California, San Diego