Memorandum

Ben Gerber
27 Nov, 2017

Status Report of Literature on the Subject of Microfluidic Cell Printing

Over the course of the semester, I have delved into research papers written on the topic of cell printing. There are many ways of attempting this including medium and high temperature 3D printing, but the focus of our research is on microfluidics and how to “print” cell spheroids based on these concepts.

According to one study, it is also very feasible to keep the cells alive in a microfluidic environment. HMSCs, bone marrow stromal cells were able to be kept alive for over 9 days and stimulated cell groups turned osteogenic (Rafael Gómez-Sjöberg, Anne A. Leyrat, Dana M. Pirone, Christopher S. Chen, & Stephen R. Quake, 2007). Although they had a different set up than us as in their microfluidic system was planar and linear. In contrast, our system is multi layered and a bit more complex in the microfluidic well design is nonlinear and has a much different flow design while also having a simpler system that doesn’t allow for mixing inside of the chip itself. According to this journal, PDMS is biocompatible and highly permeable to CO_2 and O_2, thereby guaranteeing rapid exchange of these gases between the atmosphere around the chip and the medium in the culture chambers (Rafael Gómez-Sjöberg et al., 2007). The exchange rate of their system was 9% of chamber volume every hour and each chamber is 60 nL which is a flow rate of 5.4 nL per hour in each chamber (Rafael Gómez-Sjöberg et al., 2007). According to Dr. Brooks, our research advisor, the linear design is more of a bioreactor style. Our method would be superior to a degree because it allows for fluid mixing, small scale, and potential reuse of the print head.

In another journal article, PDMS is further vetted as a standard in microfluidic chip design because of its properties such as transparency and the ability for extremely small channels being able to be laser cut in it (Matthias Mehling & Savaş Tay, 2014). Most of this article was about PDMS viability which, I found out, can have troubles being not fully cured and has can run into issues with lipids as it is a very porous material (Matthias Mehling & Savaş Tay, 2014). However, in our experiment, we need high visibility for the microPIV experiments. According to John-Luke Singh, another group member, even the transparent PDMS cannot support tracking via laser at a point where the channels are stacked. I have a suspicion that it may be because of the medium that the laser is going through so many times.

According to a paper titled “Microfluidic Cell Structure Systems,” bioreactors are used successfully in some cases due to their large surface to volume ratio and oxygen supply because of the laminar flow, but medium fluids and chemical don’t mix well because of the lack of turbulence (Ju Hun Yeon & Je-Kyun Park, 2007). However, laminar flow can be beneficial in cases of bacteria isolation, concentration gradients of drugs, etc… (Ju Hun Yeon & Je-Kyun Park, 2007); A further application of our well technology seems to be co-cultures of 3D cells to simulate organs where multiple cultures live in symbiotic relationships. We could possibly utilize a process called “Cell Docking” inside of our wells. Uses of this include realizing vital liver function simulation through the co-cultures of hepatocytes and endothelial cells (Ju Hun Yeon & Je-Kyun Park, 2007).

According to a paper on maximizing fibroblast adhesion, 15 to 30 uL/min flow rate would be optimal in our PDMS printhead device (S. N. Davidoff, D. Au, B. K. Gale, B. D. Brooks, & A. E. Brooks, 2015). Due to pressure buildup and deformation on our agarose gel mold, I found out that around 50 uL/min was the maximum flow rate before leaks started occurring between wells. According to another

study, submerged printing using our devices lead to a higher cell density(Sherry N. Davidoff, David Au, Samuel Smith, Smanda E. Brooks, & Benjamin D. Brooks, 2015). If we possibly combine submerged printing with our gel molds, maybe it would have an effect on cell density also.

This research gives me more insight into properties of PDMS including permeability processes. In addition there were more specifications into flow rate which can be modified and calculated with our chamber size. Also, more applications of our research that are future possibilities were great to learn about. This semester was some of the most I have ever learned outside of my major.

References:

Ju Hun Yeon, & Je-Kyun Park. (2007). Microfluidic Cell Culture Systems for Cellular Analysis. *Biochip Journal*, *1*(1), 17–27.

Matthias Mehling, & Savaș Tay. (2014). Microfluidic Cell Culture. *Current Opinion in Biotechnology*, (25), 95–102.

Rafael Gómez-Sjöberg, Anne A. Leyrat, Dana M. Pirone, Christopher S. Chen, & Stephen R. Quake. (2007). Versatile, Fully Automated, Microfluidic Cell Culture System. *Analytical Chemistry*, *79*(16), 8557–8563.

S. N. Davidoff, D. Au, B. K. Gale, B. D. Brooks, & A. E. Brooks. (2015). Maximizing Fibroblast Adhesion on Protein-Coated Surfaces Using Microfluidic Cell Printing. *RSC Advances*, *2015*(5), 104101–104109.

Sherry N. Davidoff, David Au, Samuel Smith, Smanda E. Brooks, & Benjamin D. Brooks. (2015). Comparison of Submerged and Unsubmerged Printing of Ovarian Cancer Cells.