Undergraduate Thesis Prospectus

Prototyping multilayer cell encapsulation device

Controversies over implementation of universal healthcare in the U.S.

by

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On my honor as a University student, I have neither given nor received unauthorized aid on this assignment as defined by the Honor Guidelines for Thesis-Related Assignments.

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General research problem

How can cell and gene therapies more effectively treat disease?

Developments in tissue engineering have led to the emergence of novel gene and cell therapies. Gene therapy market experienced rapid growth over past few decades in conjunction with development in tissue engineering field. $2.3 billion in funding went to private gene therapy companies over the last decade and number of gene therapy trails has been increased since 1989 (Elverum & Whitman, 2019; Hanna, Rémuzat, Auquier, & Toumi, 2017). Advanced therapies, however, do not help patients who have insufficient access to care. Despite the ongoing technological development in tissue engineering, the number of uninsured Americans is increasing (Armour, 2019). Incomplete insurance coverage and high costs keep many patients from getting adequate medical treatment.

Prototyping a multilayer cell encapsulation device

How to design an automated cell encapsulation device?

The project is capstone project advised by Dr. Highley of the Biomedical engineering department. This is 3-man project is supervised by Noah Vanterve, Gabe Popescu, and I, 4th-year BME students. Our capstone project team aims to design and prototype a device that will automate the multilayering cell encapsulation process based on parameters that are input into an Arduino controlled program.

For many labs conducting biological research on the cellular level, cell encapsulation is a critical process required for effective cell delivery into a target medium (Murua et al., 2008). Specifically, cell encapsulation refers to the technique of enclosing the biological active material

within a polymeric matrix by a semipermeable membrane (Atala, Lanza, Thomson, & Nerem, 2008). Encapsulation is typically used for therapeutic purposes as well as cell transplantation and organ replacement as it can provide mechanical protection for the enclosed cells (Farina, Alexander, Thekkedath, Ferrari, & Grattoni, 2019; Uludag, De Vos, & Tresco, 2000). Additionally, encapsulation prevents immune reactions that arise from cell injection, therefore reducing the need for use of immunosuppressants (Olabisi, 2015).

Since the beginnings of cell encapsulation, which began when Chang et al. first reported encapsulating human erythrocytes in nylon microspheres, a variety of methods for cell encapsulation have been designed and developed over the years (Batorsky, Liao, Lund, Plopper, & Stegemann, 2005; Chang, MacIntosh, & Mason, 1966; Kampf, 2002; Orive et al., 2003; Peirone, Ross, Hortelano, Brash, & Chang, 1998). Depending on the purpose of the experiment, a different type of cell encapsulation may be used. Cell encapsulations may be classified into two main categories: macroencapsulation, which typically refers to the encapsulation of multiple cells within a larger bulk hydrogel using macroscale devices, and microencapsulation, which refers to encapsulating cells into a semipermeable polymer matrix (microsphere, microbead) or membrane (microcapsule) at the micrometer scale (Kang, Park, Ju, Jeong, & Lee, 2014; Olabisi, 2015). While macroencapsulations can be useful in providing cells with a 3D hydrogel scaffolding that can model the body, the density of cells within the hydrogel is much lower than in microencapsulations (Wang et al., 2017). Therefore, the Highley Lab is using a microencapsulation method to provide a protective cell coating with only a few layers of polymer, thus achieving a high cell density encapsulation.

Specifically, a multi-layer biointerface method for the microencapsulation of mouse neural stem cells (mNSC) is being developed by graduate student Jack Whitewolf, who conducts

research in the Highley lab. In this approach, the first coating layer, which is made up of a lipid-and-thiol- modified hyaluronic acid (HA), is attached to the cell membrane through lipid-insertion, and subsequent layers (also modified forms of HA) are bound to the previous layer. While other layer by layer cell microencapsulation methods have been developed, this method of using lipid-insertion to develop a multi-layer cell coating is a novel approach, allowing for the outer polymer layers after the initial layer to be easily modified (Caruso, 2003; Lvov, Antipov, Mamedov, Möhwald, & Sukhorukov, 2001; Sukhorukov et al., 1998; Veerabadran, Goli, Stewart-Clark, Lvov, & Mills, 2007). These modifications to the HA polymers allow for control over the thickness and mechanical properties of the coating, as well as the interchanging of degradable and non-degradable layers.

However, the current process is conducted manually and leads to a number of different inefficiencies, which we were able to identify through discussions with Dr. Highley and Jack Whitewolf. First, execution of the cell coating process by hand-pipetting the solutions containing the polymers and centrifuging is a tedious, time-consuming process, taking approximately two hours for a two-layer polymer coating, with 25-35 minutes added for each additional layer. Furthermore, the centrifugation process and the exchanging of solution can be extremely energy-intensive and place unnecessary strain on the cells. Finally, the manual coating process is prone to technician error from improperly pipetting or pipetting too forcefully, causing damage to the cell samples. If the manual cell coating process is continued, labs must continue to wield large amounts of money and resources to perform the energy-intensive procedures involved in the process. Therefore, our capstone group is attempting to automate the cell coating process by designing, constructing, and testing a device that will account for inefficiency in the current manual process.

Controversies over implementation of universal healthcare in the U.S.

How do advocates and critics of universal healthcare in the U.S. advance their agendas?

The United States is the only developed country without universal health care. Attempts to establish universal healthcare have failed (Quadagno, 2010). Americans can obtain coverage through the Affordable Care Act, which is equivalent to Obamacare, Medicaid, and Medicare, however, benefits do not reach all and do not provide full medical. About 28 million people in the United States (8.5% of the U.S. population) are uninsured according to the census data to 2017 (Armour, 2019). The U.S. spends two to three times as much per capita on healthcare as other industrialized countries (Merelli, 2017). Healthcare is expensive; the burden of paying for medical care causes economic insecurity in many families of middle to low income (Quadagno, 2010).

The notoriously high cost of the healthcare in the U.S. has several causes. Administrative costs are high. Drug costs in the United States are much higher than in other countries. Doctors in the United States tend to practice defensive medicine to avoid lawsuits. Medical treatment is expensive. Branding by individual healthcare providers drives healthcare costs higher. In countries in which the government is the single payers, governments can better control healthcare costs through their influence on drug, medical equipment and hospital costs. They can negotiate with private companies, and influence medical practice on patients (Epstein, 2019).

Participants in healthcare in the United States include pharmaceutical companies, insurance companies, medical professionals, hospitals, citizen groups, civil right groups, and patients. some favor universal healthcare. Pharmaceutical and insurance companies dominate the

healthcare market. Hospitals and medical practitioners, including physicians, serve the patients. Conservatives and civil right groups are also influential.

Medical businesses spend a lot on lobbying. From 1998 to 2018, the pharmaceutical and health products industry spent approximately $3.9 million. The insurance industry as a whole, spent roughly $2.7 million; health insurance companies specifically spent $1.6 million (Frankenfield, 2018).

Recently, senator Bernie Sanders of Democratic party proposed Medicare For All Act of 2019. In response, many healthcare interest groups, including insurance companies and medical professionals, formed the Partnership for America's Health Care Future to oppose it. Coalition members include the Blue Cross Blue Shield Association, PHrMa, the American Medical Association, and the Federation of American Hospitals. The coalition opposes overhauling U.S. healthcare. Charles N. Kahn III, the president of the Federation of American Hospitals, which represents investor-owned hospitals, said: "We have a structure that frankly works for most Americans. Let's make it work for all Americans. We reject the notion that we need to turn the whole apple cart over and start all over again" (Pear, 2019).

In 2017 the Republican-controlled Senate proposed to repeal Obamacare. Many healthcare groups, including American Hospital Association (AHA) and American Medical Association (AMA), opposed the efforts fearing its disruptive effect. Patient and provider groups, including the American Cancer Society, Cancer Action Network, and the American Heart Association, also opposed repeal, arguing it would limit patients' access to coverage and care. However, many insurance companies favored repeal so that they could charge their customers much more (Hellmann, 2017).

Conservatives and civil rights group fight over universal healthcare because conservatives see case as a commodity while civil liberties advocates tend to see it as a right. Freedom Partners, a conservative advocacy, opposes government control, seeing it as a threat to individual freedom and free market. It asserts that any government-supported healthcare, include Obamacare, is unconstitutional (Anderson, 2019). On the other end, a civil rights group, the American Bar Association (ABA), contends that healthcare is a human right. It criticizes the U.S. health system, calling it not a health care system at all but only a health insurance system (Gerisch, 2018).

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