The Development of Organ-on-a-Chip As a Therapeutic Approach to Treating Heart Disease

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Introduction

According to the Centers for Disease Control and Prevention [1], heart disease is the leading cause of death in the United States (Figure 1). Manufacturing of new drugs is a costly and time-consuming process. Heart disease can be treated using an innovative heart-on-a-chip approach.

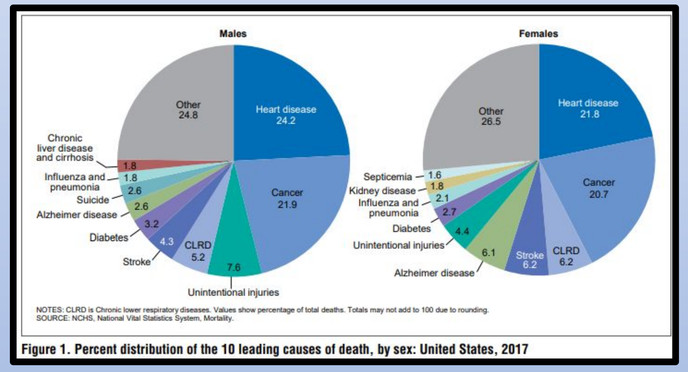

Figure 1

Background

Cardiac tissue is composed of cardiomyocytes, micro vessels, and fibroblasts. Cardiomyocytes regulate cardiac tissue contractions which allows blood to pump throughout the body. The functioning of cardiomyocytes is dependent on electrical, mechanical, and chemical stimuli. Proteins such as alpha-actinin, myosin, troponin I, troponin T and tropomyosin are expressed by cardiomyocytes [3]. In-vitro heart-on-a-chip allows for the control over the physiology of the above factors.

The heart-on-a-chip systems could be used to “culture cardiomyocytes and to obtain fully functioning, vascularized tissue of heart muscle” [4]. As a result the heart-on-a-chip system allows for the creation of heart models for drug testing and study of heart diseases.

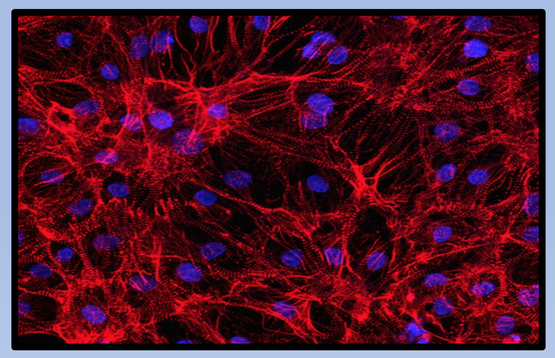

Figure 2 Cardiomyocytes-iPSC derived

Findings

Cells are accustomed to a warm 37 C, ¾ water-based, and tangibly soft environment. A computer chip is the opposite to that of the human body. Silicon is a material that is soft and is able to reach a temperature that human cells are accustomed to. Engineers have been able to take skin cells and biologically reprogram them to become heart cells [5].

Microfluidic environments lead to spatiotemporal control of the chemical, mechanical, and electrical stimuli (Figure 3). Bioreactor systems that allow for a steady-state/controlled oxygen supply can overcome the “limitations of diffusional transport in conventional culture systems”[6]. Polydimethylsiloxane (PDMS) is a widely used silicon-based organic polymer due to its properties. The siloxane bonds result in a flexible polymer with a high level of viscoelasticity (Figure 4).

An electrical stimulator can be produced via connecting carbon rod electrodes to the constructs. A developed microsystem was further evaluated by testing different concentrations of isoprenaline which is a commonly used drug for bradycardia to increase heartbeat frequency (Figure 5).

Data, Charts, and Graphics

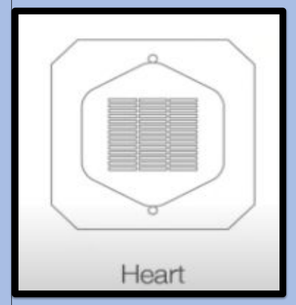

Figure 3
Heart-on-a-Chip

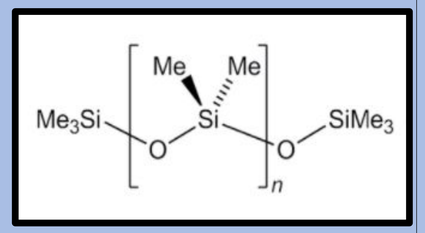

Figure 4

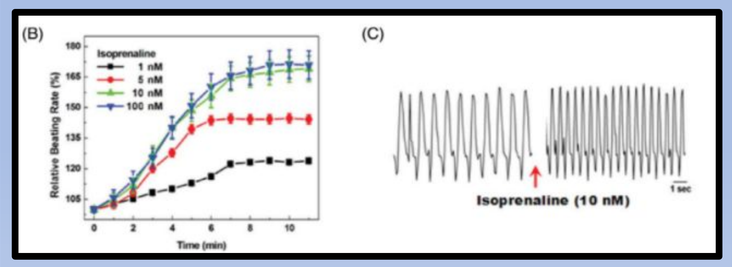

Figure 5

Discussion

Polydimethylsiloxane or PDMS is a high-performance polymer used as the foundation for the micro channels within the heart-on-a-chip.

The micro channels serve as the compartments that house the cells. Reagents such as "growth factors, cytokines, and nutrients" are delivered to the cells [8]. Electrodes are implemented to measure the electrical activity of the cardiomyocytes. Micro channels can further be lined with Extracellular Matrix or ECM derived hydrogels to enhance the heart cell adhesion.

Future work

Cardiovascular organs-on-a-chip have not revolutionized the drug discovery process as of yet, as key challenges still lay ahead. Such as validating the data generated with these microscale platforms match human responses. Another related challenge is coupling heart-on-a-chip to other organ-on-a-chip systems.

These platforms are rapidly progressing as researchers continue to integrate breakthroughs in biology with cutting-edge engineering techniques. Properly designed heart-on-chips have the potential to truly revolutionize biomedical research, drug screening and have a significant impact on tackling a wide spectrum of cardiac diseases.

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Acknowledgements

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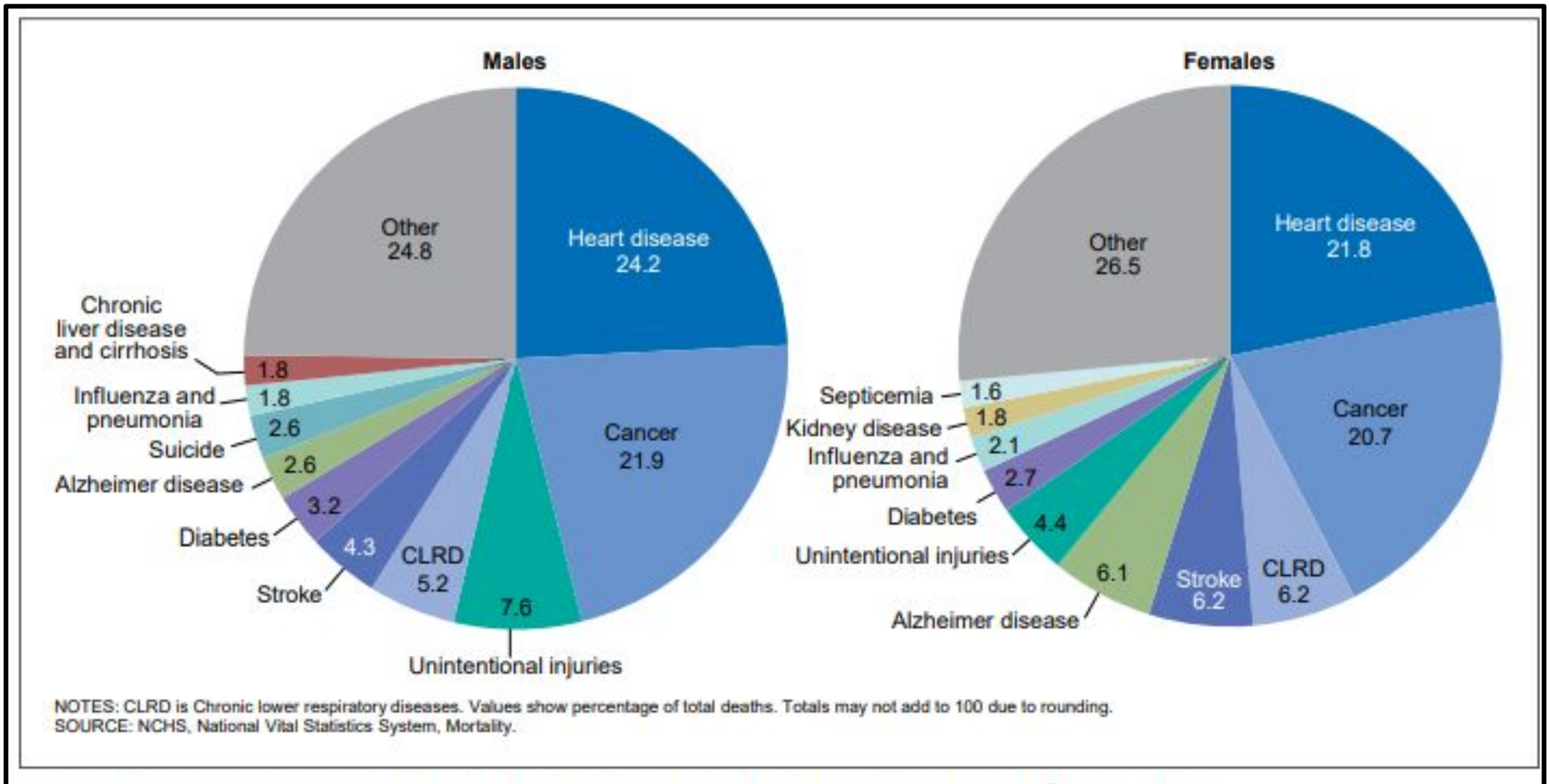
CDC Data of Mortality



NOTES: CLRD is Chronic lower respiratory diseases. Values show percentage of total deaths. Totals may not add to 100 due to rounding.
SOURCE: NCHS, National Vital Statistics System, Mortality.

Figure 1. Percent distribution of the 10 leading causes of death, by sex: United States, 2017

The Effects of Isoprenaline on Heart Beat Frequency