UTS UNIVERSITY OF TECHNOLOGY SYDNEY

# Applying microfluidics for industrial production of stem cells

**by Lin Ding**

Thesis submitted in fulfilment of the requirements for the degree of

**Doctor of Philosophy**

under the supervision of Prof. Majid Ebrahimi Warkiani
Adjuvant Prof. Graham Vesey

University of Technology Sydney
Faculty of Engineering and Information Technology

August 2022

# Certificate of Original Authorship

I, Lin Ding, declare that this thesis is submitted in fulfillment of the requirements for the award of Doctor of Philosophy, in the School of Biomedical Engineering, Faculty of Engineering and Technology at the University of Technology Sydney.

This thesis is wholly my own work unless otherwise reference or acknowledged. In addition, I certify that all information sources and literature used are indicated in the thesis.

This document has not been submitted for qualifications at any other academic institution.

This research is supported by the Australian Government Research Training program.

Signature: Production Note:
Signature removed prior to publication.

Date: 19-08-2022

# Acknowledgement

'There is neither wine of eternity nor fountain of youth. Life is pointless. Death loomed over all, and the ground beneath us all was the same. Humanity will one day be ended by the explosion of the Sun'. Thought the 15-year-old me. 'However, knowledge can be everlasting. If I can do research, contribute to even just one building block of human knowledge, or become a dancing byte in the database. Eventually, the human race will travel across the universe and find another oasis.'

Therefore, I am very grateful to my supervisors, Majid Ebrahimi Warkiani and Graham Vesey, for allowing me to work on my favourite stem cells topic, opening the gate of research for me, and providing the guidance to pursue my dream. I want to thank the school, faculty, and university for giving me the space and freedom to do my research and achieve what I would not be able to succeed in other places. I will never forget my colleagues' support during the hard times, the days we pursued excellence in work and dreams together. I would also like to express my gratitude to my family and friends. They have been my strong backing from the beginning, and they gave me the courage to go through the degree. I really appreciate my collaborators. They taught and helped me during my projects, shaped my papers and brought them to a higher level.

The taste of victory may be bittersweet, but the aftertaste lingers forever, a reminder of the journey, the struggle, and the triumph.

# Format of Thesis

The aim of this PhD thesis is to address the challenges faced by the stem cell industry using microfluidic devices. The thesis is presented in six chapters. In Chapter 1, an overview of the current stem cell production process is provided, along with a discussion of the industry's challenges. This is followed by a review of microfluidic devices used in stem cell research, along with potential applications in different processes of the stem cell industry. Chapters 2-5 present original research on the development and application of microfluidic devices to solve the challenges in the stem cell industry.

Chapter 2 describes the use of a high throughput microfluidic droplet generator to produce dissolvable and edible microcarriers for the cultivated meat industry, where no edible microcarriers are currently available. In Chapter 3, 3D printing technology is used to develop a microfluidic system for detaching stem cells from current commercial microcarriers and separating and concentrating cells for downstream applications. Industry-scale microcarriers detachment and harvesting rely on membrane-based technologies that cause significant cell loss.

Chapter 4 presents the development of a micromixer to homogeneously mix cryoprotectant and stem cells. This replaces the current industrial bulk mixing methods, which can potentially damage cells and cause batch-to-batch differences in the products. In Chapter 5, a static droplet array is used to evaluate the metabolism and senescence level of cells in industrial production culture.

Finally, Chapter 6 provides a summary of the thesis and highlights potential future works related to microfluidic applications in the stem cell industry. This thesis contributes to the development of innovative microfluidic devices that can address the challenges faced by the stem cell industry and potentially enhance the quality and efficiency of the stem cell-based products.

# Table of Content