

**Biotechnologies for Cancer Diagnostics: Cell
Sorting, Protein Analysis and Imaging of
Cellular Metabolism**

Thesis by
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In Partial Fulfillment of the Requirements for the degree
of
Doctor of Philosophy



CALIFORNIA INSTITUTE OF TECHNOLOGY
Pasadena, California
2013
(Defended May 30th, 2013)

To my dearest wife,

Hana Kim

Acknowledgement

First of all, I would like to thank to my advisor, Professor James Heath. With great patience, he has guided and trained me to become a research scientist during my Ph. D. journey. He also granted me academic freedom and incredibly valuable resources, including the organization of Nanosystems Biology Cancer Center (NSBCC) between Caltech, UCLA and the Institute for Systems Biology (ISB). I appreciate him for giving me many chances to collaborate with brilliant senior scientists, including Professor Caius Radu (UCLA), Professor Paul Mischel (UCSD), Professor Raphael Levine (UCLA), Professor Arion Chatziioannou (UCLA), Professor Heather Christofk (UCLA) and Professor Michael Phelps (UCLA), who have helped and advised me during my graduate researches. Also, I would like to acknowledge my thesis committee members, Professor Long Cai, Professor Shu-ou Shan and Professor William Goddard III, who spent much time providing insightful comments and suggestions on my progress report and research proposals. Not to forget, I thank the Samsung Scholarship which has also been supporting my Ph.D. studies.

In Heath lab, I have been fortunately able to collaborate with a number of gifted past and present group members. I would like to thank Dr. Gabe Kwong, Dr. Young Shik Shin and Dr. Jun Wang, with whom I worked on NACS, SCBC and RIMChip projects, respectively. Through them, I have learned practical techniques for the preparation of bio samples and the fabrication of microfluidic chips, as well as the scientific way of designing experiments. I also appreciate Dr. Heather Agnew and Wei Wei in studying the application of RIMChip in clinical systems. Thanks to Dr. Habib Ahmad, Dr. Jen-Kan

Yu, Joey Varghese, Alex Sutherland, Ryan Henning and Blake Farrow for valuable scientific discussions. I appreciate Diane Robinson, Amy Crown, Elyse Garlock and Kevin Kan for processing all paper-work and managing lab facilities properly.

Also, I acknowledge many intelligent co-workers at UCLA, especially Dr. Daniel Braas, Alex Dooraghi, Dr. David Nathanson, Dr. Dean Campbell and Jessica Gu in working with the RIMChip project. Without their kind help and assistance, I could not obtain wonderful results at UCLA.

I am grateful to all of my Korean friends for sharing my personal life at Caltech, especially Dr. Oh-Hoon Kwon, Dr. Chang Ho Sohn, Dr. Christopher Chang, Dongwan Kim, Chung Whan Lee and Jake Kim.

Finally, I appreciate my family who always supported me with love and care. In particular, I thank my beloved wife, Hana Kim. Without her unconditional love and patience during the Ph.D. period, this work would never have existed. I dedicate this thesis to her.

Abstract

This thesis presents the development of chip-based technology for informative *in vitro* cancer diagnostics. In the first part of this thesis, I will present my contribution in the development of a technology called “Nucleic Acid Cell Sorting (NACS)”, based on microarrays composed of nucleic acid encoded peptide major histocompatibility complexes (p/MHC), and the experimental and theoretical methods to detect and analyze secreted proteins from single or few cells.

Secondly, a novel portable platform for imaging of cellular metabolism with radio probes is presented. A microfluidic chip, so called “Radiopharmaceutical Imaging Chip” (RIMChip), combined with a beta-particle imaging camera, is developed to visualize the uptake of radio probes in a small number of cells. Due to its sophisticated design, RIMChip allows robust and user-friendly execution of sensitive and quantitative radio assays. The performance of this platform is validated with adherent and suspension cancer cell lines. This platform is then applied to study the metabolic response of cancer cells under the treatment of drugs. Both cases of mouse lymphoma and human glioblastoma cell lines, the metabolic responses to the drug exposures are observed within a short time (~ 1 hour), and are correlated with the arrest of cell-cycle, or with changes in receptor tyrosine kinase signaling.

The last parts of this thesis present summaries of ongoing projects: development of a new agent as an *in vivo* imaging probe for c-MET, and quantitative monitoring of glycolytic metabolism of primary glioblastoma cells. To develop a new agent for c-MET

imaging, the one-bead-one-compound combinatorial library method is used, coupled with iterative screening. The performance of the agent is quantitatively validated with cell-based fluorescent assays. In the case of monitoring the metabolism of primary glioblastoma cell, by RIMChip, cells were sorting according to their expression levels of oncoprotein, or were treated with different kinds of drugs to study the metabolic heterogeneity of cancer cells or metabolic response of glioblastoma cells to drug treatments, respectively.

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