

PREFACE

Cancer is a crucial public health problem. According to the World Health Organization (WHO), 8.2 million people die each year from cancer, equivalent to >22,000 per day. Since more than 90% of cancer deaths result from metastasis, fully understanding how cancer spreads from the primary tumor to the secondary sites, and subsequently identifying ways to prevent metastasis, would have significant societal impacts.

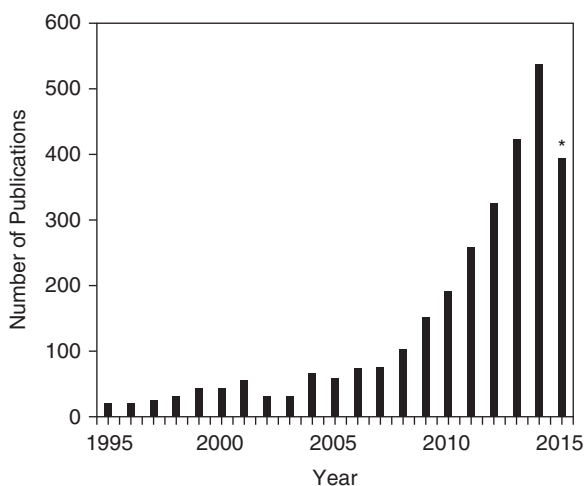
It is generally agreed that circulating tumor cells (CTCs) in the peripheral blood play a key role in cancer metastasis because cancer cells must transport through the circulatory system before colonizing the secondary sites. CTC enumeration is less invasive than biopsy while providing quantifiable information. It has been hailed as one of the potential “liquid biopsy” methods. It can also be used to monitor the response of an individual patient to a therapy and then tailor the treatment. Hence, CTCs have been advocated as potential biomarkers for cancer diagnosis, prognosis, and theragnosis or precision medicine. As a result, CTC isolation and analysis are an important topic in research, medical, and clinical communities.

The number of CTCs in the peripheral blood is extremely low. At large, there are a few CTCs in 1 mL of blood, which contains billions of red blood cells, millions of white blood cells, and hundreds of millions of platelets. Therefore, CTC isolation is truly a needle-in-a-haystack challenge.

The challenge makes CTC research exciting to many scientists and engineers who are developing various methods for efficient isolation and accurate enumeration of CTCs. Biomedical researchers have been studying CTCs for understanding the metastasis mechanisms, identifying cancer stem cells, and investigating their genomic and proteomic profile for helping develop therapeutic drugs. The significance of CTCs and potential market values make companies and investors interested

in the field. Many researchers, as well as students, are jumping into the field to make contributions.

Because CTC isolation and analysis are important topics that have attracted much interest recently from academics, government agencies, and industry, this field has been the subject of many international symposia, calls-for-proposals from funding agencies, and articles in high-impact journals. The strong interest of CTC-related research is partially indicated by the exponential increase in publications in the past decade. The figure below plots the number of publications in PubMed as a function of the year from 1995 to 2015, using “circulating tumor cells” in the title/abstract as the search term (the number for 2015 – indicated by a star at the top – is up to September of the year).



This book is aimed to those who are in the field – those entering the field – and those who just want to learn about the field. Readers who are new to this field will benefit from the introduction to CTCs and the historical perspectives offered in early chapters. Subsequent chapters explore a variety of state-of-the-art isolation methods, capture reagents used for CTC isolation and enumeration, the analysis of isolated CTCs, clinical translation, and commercial platforms. All of these chapters are written by experts who have developed remarkable techniques and made considerable contributions to the field.

The content in this book is organized into five parts.

- Part I is the introduction, which presents CTCs from historic perspectives. Chapter 1 is written by Professor Jonathan Uhr, whose pioneering research with his colleagues on CTCs in the 1990s led to the birth of CellSearch®. In Chapter 2, microfluidics is introduced, as it is a technology used for the work described in several chapters.
- Part II consists of 12 chapters, each of which describes different CTC isolation methods. The methods range from the macro- to the microscale, from positive isolation to negative depletion, and from biological-property-enabled to

physical-property-based approaches. These chapters are written by the inventors who developed the methods.

- Part III is comprised of three chapters, covering post-isolation analysis and clinical translation. Topics include tumor heterogeneity, single-cell analysis, regulatory policy, and clinical practice, all of which are important in realizing the full potential of CTCs and having impacts on clinical outcomes. The authors of these chapters are from the school of medicine, and they are pioneers in translating technologies from the bench to the bedside.
- Part IV focuses on commercialization. One commercialized platform is CellSearch, the only CTC platform currently approved by the US Food and Drug Administration (FDA). The majority of clinical studies on CTCs have been performed using this apparatus, and it has played a significant role in shaping the field. The other platform is DEPArray™, which is an instrument that can identify, quantify, and recover individual CTCs, and it has been placed in many laboratories in the world.
- Part V is glossary, consisting of the definition of scientific terms related to the field and those used in this book.

This is the first book focusing on CTC isolation and analysis. It grows out of and is a continuation of a CTC-themed issue of *Lab on a Chip* in 2014 (Vol. 14, Issue 1) that I edited with Professor David Beebe of University of Wisconsin and two invited symposia I organized at The Pittsburgh Conference in 2013 (Philadelphia, USA) and 2015 (New Orleans, USA). Some of the authors in this book, as well as other CTC investigators, contributed to the journal issues and presented their advancement at the conferences.

There are many people who deserve special thanks and recognition for their support of this book. Dr. Mark Vitha, the editor of the Chemical Analysis Series, initiated the conversation about this book after noticing my CTC session at Pittcon 2013. I am grateful for his help in the format guideline and content review and, more importantly, for nudging me to complete this book on time. I would like to thank all authors for their time and expert contribution. My appreciation also goes to Dr. Jinling Zhang for helping in the editorial work, to Ms. Lauren Miller for creating the cover art, and to all reviewers for their comments and suggestions. I am grateful to Dr. Klaus Pantel, who is an authority on CTCs with one book and dozens of review articles, for writing the forward. I am also thankful to Bob Esposito, Michael Leventhal, and their team at John Wiley & Sons, Inc. for their efforts in transforming the initial idea and the manuscripts into a viable book. Lastly, but not least, I appreciate my wife for her love and support by allowing me to spend time on this book.

Thanks for reading.

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