

# Preface

In recent years, the strides made in understanding and elucidating both the origins and biological mechanisms responsible for driving cancer progression have been quite impressive. Specifically, the momentum that has coincided with the discovery and investigation of cancer stem cells (CSCs), tumor-initiating cells (TICs) or cancer-initiating cells (CICs) has been enormous. The investigation of every aspect of this deadly and lethal subpopulation has brought attention to its potential in a therapeutic light which we hope can translate into the clinic. The cancer stem cell hypothesis was first described with data from models of human leukemia by John E. Dick from the University of Toronto. The heterogeneity of human leukemia and the presence of stem cells in cancer was further translated into solid tumors by Al-Hajj et al. when they published a provocative paper in *Proceedings of the National Academy of Sciences* discussing the ability to distinguish tumorigenic (tumor-initiating) cancer cells from the nontumorigenic counterpart based on the expression of cell surface markers. The group reported that as little as 100 cells of this specific population were able to form a solid tumor when injected into the mammary fat pad of immunocompromised mice. The most critical aspect of this study was the data demonstrating that even tens of thousands of cells of the nontumorigenic cancer stem cell depleted fraction failed to produce a tumor.

Since this study, these cells have been heavily investigated and are now known to be the most aggressive cells within a solid tumor discovered to date. In recent years, many groups have demonstrated that in addition to being the most aggressive cells, they are highly resistant to current chemotherapy and radiation regimes employed in the clinic. The resistant nature of these cells has led many labs down the path of developing new therapies to eradicate them from patients. An interesting observation among our lab and others was that isolated CSCs express higher levels of DNA repair genes, and furthermore, lead to increased expression of crucial genes and pathways that contribute to their drug resistant characteristics. Thus, we have assembled a remarkable group of experts in both CSCs and DNA repair to discuss their research in light of the role of DNA repair genes and pathways in the CSC population. The common end goal is to contribute to the knowledge base and lead the field in investigating and studying additional mechanisms for potential therapies being designed to target this aggressive population of cells.

The concept of DNA repair conferring survival and progression is the overall theme of this book, and we believe provides a unique contribution to the CSC field in regards to developing new strategies to target this highly metastatic and resistant population. We hope this book can provide a foundation and support to future

scientists and clinicians working in the field of cancer resistance and cancer stem cells.

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