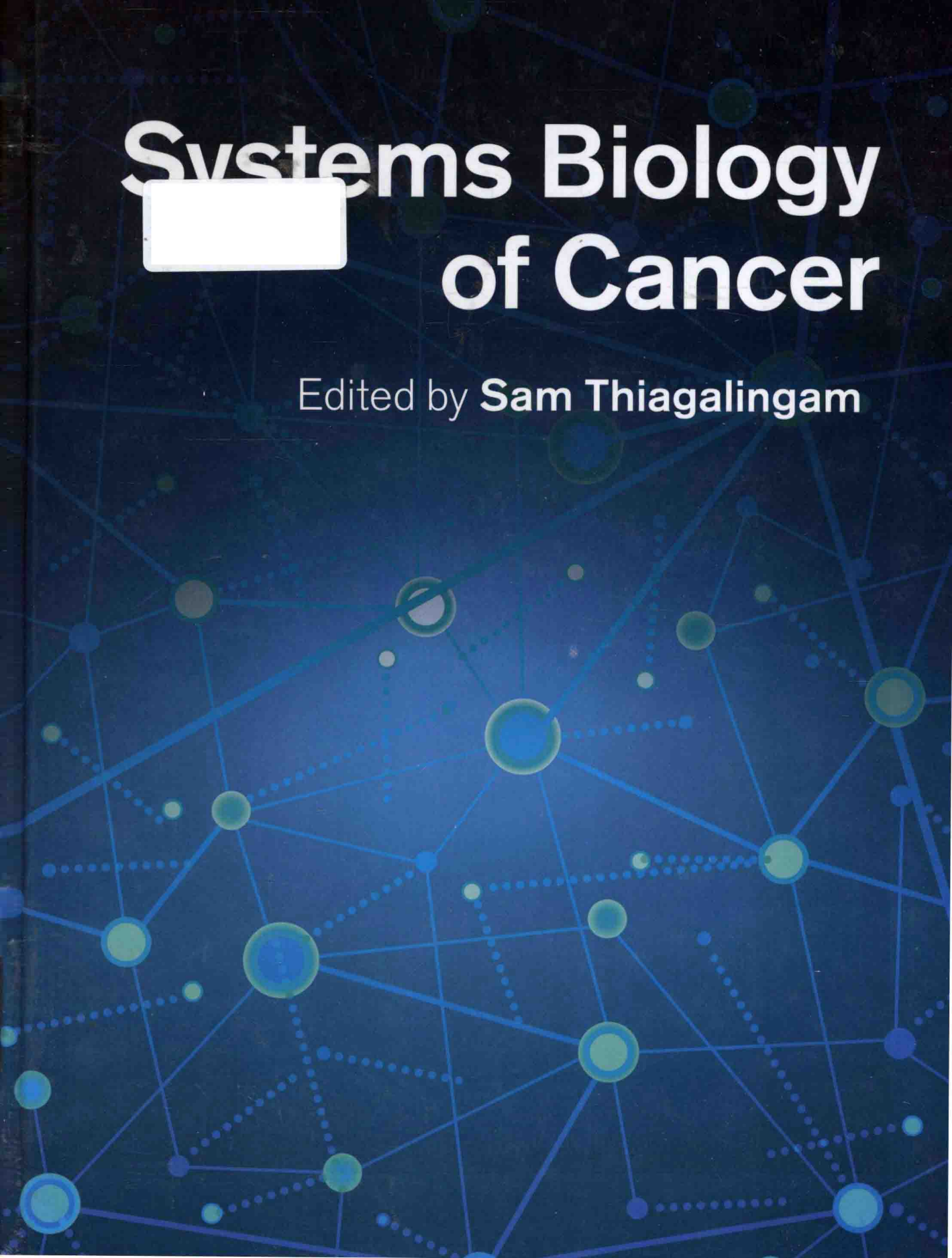
Systems Biology of Cancer

Edited by **Sam Thiagalingam**



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Systems Biology of Cancer

With over 200 types of cancer diagnosed to date, researchers the world over have been forced to rapidly update their understanding of the biology of cancer. In fact, only the study of the basic cellular processes, and how these are altered in cancer cells, can ultimately provide a background for rational therapies.

Bringing together the state-of-the-art contributions of international experts, *Systems Biology of Cancer* proposes an ultimate research goal for the whole scientific community: exploiting systems biology to generate in-depth knowledge based on blueprints that are unique to each type of cancer.

Readers are provided with a realistic view of what is known and what is yet to be uncovered on the aberrations in the fundamental biological processes, deregulation of major signaling networks, alterations in major cancers, and the strategies for using the scientific knowledge for effective diagnosis, prognosis, and drug discovery to improve public health.

Sam Thiagalingam is an Associate Professor of Genetics & Genomics, Medicine, and Pathology & Laboratory Medicine at the Boston University School of Medicine. He played a major role in establishing an association between genomic instability and loss of heterozygosity (LOH) in human cancers. He was the first to show that SMAD4 inactivation is a critical event during the late stages of colon cancer progression, and sustained TGFβ signaling events are required to maintain epigenetic memory during breast cancer progression. Dr. Thiagalingam also proposed a simple minded multi-modular molecular network (MMMN) cancer progression model as a road map to visualize the various gene alterations in modules of networks of pathways. His long-term goal is to identify novel cancer biomarkers and therapeutic targets by contributing to the "big picture" of interconnected networks of events that mediate cancer progression to metastasis using breast and colon cancers as the model systems.

To my parents

***Vanniyan* Sambunathan Seenithamby Sisupalapillai Sambasivamoorthy**

and

Paramsothy Thangaretnaammal Malar Eliyathamby Sambasivamoorthy

for their righteous living and the respect for freedom of expression.

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Preface

The heterogeneity in alterations and the failure to detect consistent changes in a unique set of gene(s) or gene products in similar and histologically well defined neoplasms pose a challenge for the accurate diagnosis, prognosis and therapy of cancer. Consequently, there is a need to integrate the individual observations made in tumor cells derived from numerous sources using the systems biology approach to identify a panel of alternate target genes/gene products as biomarkers for diagnosis and/or prognosis and as targets for therapy. This goal could be achieved with efficacy by dissecting alterations in cancer in interconnected modular networks of pathways represented in multi-modular molecular networks (MMMN) specific for progression of individual cancers. This landmark volume consisting of a collection of chapters examines the fundamentals of the molecular basis of the genesis of cancer in parts devoted to the overall big picture, basic biochemical events, manifestation of fingerprints of alterations, units of coordinated events, state of knowledge of the integrated progression of events for specific cancers and the future prospects and implications of the various MMMN cancer progression models in the fight against cancer.

My sincere thanks to the distinguished scientists for graciously contributing chapters on their expertise. My special gratitude to my doctoral thesis advisor, Professor Lawrence Grossman, for his guidance in shaping up my career as a molecular biologist and for stimulating my passion to undertake cancer research as the next step to studying DNA repair mechanisms, and to my post-doctoral advisor, Professor Bert Vogelstein, for being a role model and for sharing his wealth of knowledge and expertise in the field of cancer genetics and biology. My special appreciation to Allan Ross (Former Executive Editor, Medicine and Life Sciences, Cambridge University Press, New York) for inviting me to conceive this volume and for all his assistance at the initial stages of the development of this volume. I am indebted to my students, Arthur Lambert and Chen Wong for critical comments and proofreading and Panagiotis Papageorgis and Sait Ozturk for help with illustrations. I am thankful to Ilaria Tassistro (Assistant Editor, Life Sciences, Cambridge University Press, Cambridge, UK) and Katrina Halliday (Editor and Publisher, Life Sciences, Cambridge University Press, Cambridge, UK) for their patience with the last minute delays and guidance and Kath Pilgrem (Copy Editor) and Jessica Ann Murphy (Production Editor Academic Books, Cambridge University Press, Cambridge, UK) for their help with finalizing this volume for publication. On behalf of the authors, I would also like to thank the American Association for Cancer Research, Nature Publishing Group, Wolters Kluwer Health, and others for allowing partial or full reproduction of their previously published figures.

This project would not have been completed without the encouragement, support and the enduring love of my wife Arunthathi Cumaraswamy Thiagalingam and the unconditional love of my children Natasha Thivya Thiagalingam and Aaron Gajan Thiagalingam.

Contents

The color plate section appears between pages 320 and 321.