Preface

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The human genome encodes hundreds of non-coding RNAs, such as microRNAs (miRNAs). MiRNAs have recently emerged as key regulators of gene expression during development and are frequently mis-expressed in human disease states, in particular cancer. MiRNAs act to promote or repress cell proliferation, migration and apoptosis during development, all of them processes that go awry in cancer. Thus, miRNAs have the ability to behave like oncogenes or tumour suppressors. Their small size and molecular properties make miRNAs amenable as targets and therapeutics in cancer treatment. MiRNAs thus present a paradigm shift in thinking about gene regulation during development and disease, and provide the oncologist with a potentially powerful new battery of agents to diagnose and treat cancer. This book brings together investigators from many distinct fields — namely RNA, bioinformatics, genomics and cancer biology — to facilitate new ideas regarding the means by which non-coding RNAs such as miRNAs impact tumour initiation and progression. The science discussed here has the potential to seed the next generation of anti-cancer diagnostics and therapeutics. While microRNAs have led the charge in the emergence of small RNA molecules functioning during development and

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disease, other small and large RNAs also contribute, and are also the subject of chapters in this book.

Cancer is a huge worldwide public health issue. The disease has recently become the greatest killer of older Americans, with hundreds of thousands of deaths annually. While oncologists have made progress in the early diagnosis and treatment of cancer, there is still room for improvement in this area. In many cases, novel therapies have emerged from an understanding of the basic biology of the disease. Most studies of the genetic causes of cancer have focused on mutations and alterations in protein-coding genes. However, scientists now appreciate that the genome generates a large diversity of non-coding RNAs, many of which have unknown functions, but which are increasingly implicated in cancer. Accumulating data suggests causal roles for miRNAs in human cancer, including observations of miRNA genes at tumour-associated chromosomal lesions and direct demonstrations that altered expression of miRNAs can cause tumour development. Analysis of miRNA expression signatures has also shown promise in contributing to cancer diagnosis, and miRNAs themselves are potential targets/agents for cancer therapy.

While hundreds of human miRNAs and non-coding RNAs are known, relatively little is understood about their roles and targets, and there is still a limited literature on using these molecules in the clinic. This book will focus on the exciting biology of non-coding RNAs, in particular, miRNAs in controlling developmental and cancer processes like cell proliferation, differentiation, cell cycle, apoptosis and metastasis. This book will highlight the best current research into the roles that miRNAs play in these fundamental processes and will provide the basic understanding that is driving the invention of powerful clinical tools.

Given the sheer number of miRNA genes, approaching 1,000 in humans, and our lack of understanding of all their roles, and given the need for a basic understanding of cancer mechanisms, it is hoped that this book will provide an important synthesis of the growing appreciation for miRNAs in development and cancer. It will highlight emerging roles of miRNAs in tumourigenesis and place these in the context of the normal roles for miRNAs in development and homeostasis. The book will involve chapters from the pre-eminent miRNA and non-coding RNA specialists, with discussions ranging from genomics of natural miRNA genes, to normal roles for

miRNAs and the consequences of their loss, to uses of miRNAs in the diagnosis and therapy of cancer. Non-coding RNAs, like miRNAs, have generated much excitement not only because they are intricately involved in cancer, but because they provide druggable targets as well as small molecule therapeutics that could see widespread use in treating cancer. This book will also focus on the latest efforts to harness the power of these small RNAs as agents in the fight against cancer. Discussions will range from the use of miRNAs as diagnostic and prognostic markers in cancer, to single nucleotide polymorphisms (SNPs) providing risk factors for cancer, to the delivery and effectiveness of small RNA therapeutics in clinically relevant settings. This book will advance the field and accelerate the benchside to bedside use of this technology.

The confluence of the superb group of basic and translational scientists assembled in this book is highly likely to stimulate exciting discussion and drive future discoveries in this important area.