Preface

It used to be said that "All roads lead to Damascus," and this was subsequently changed to "Rome." Today, it might be more appropriate to say "All roads lead to cancer." Half a century of focused modern research efforts have failed to find a "cure" for cancer because of the plethora of causes and mechanisms that can instigate tumorigenesis. Despite these many roads, the resultant tumor cells nonetheless share a handful of characteristics. To proliferate, cancer cells must have reactivated the cell cycle and often cell cycle regulators and signaling pathways that maintain a differentiated state are altered in tumors. Loss of genome integrity may or may not be causative in the progenitor cell, but it clearly becomes a characteristic within the tumor with chromosome translocations, DNA damage, and significant changes in transcriptional profiles all characteristic of pretty much all tumors. Moreover, the degree of metastasis is often correlated with the extent of DNA damage and chromosome translocations. Component cells of metastatic tumors migrate to spread and so cytoskeletal changes that enable cell migration are highly characteristic of more malignant tumors.

Even before any of the above-mentioned characteristics of tumors were identified, it was noted that most tumor cells exhibited changes in the shape and size of the nuclear envelope. Thus in the modern era as soon as the first nuclear envelope proteins were discovered—the nuclear lamins—they became a focus of research. Many correlations between lamin levels and increasing cancer grade were observed, and so lamin levels were added to nuclear size and shape changes in tumor diagnostics and prognostics. However, in some tumor types increased metastasis correlated with increases in certain lamins, while in other tumor types it correlated with decreases in the lamins. Therefore, the nuclear envelope was dropped as a major focus of cancer research.

In recent years, the nuclear envelope has been found to play important roles in cell cycle regulation and signaling, genome organization, the regulation of gene expression, DNA damage repair pathways and genome stability, and cytoskeletal organization, cell mechanical stability, and cell migration—all of the above noted

general characteristics of cancer cells. Many recent studies revisiting the nuclear envelope as a player in tumorigenesis and cancer metastasis have found cancer associations through the above-mentioned central mechanisms/characteristics as well as several unexpected links. On this basis alone it is clearly time to make the nuclear envelope a major focus of cancer research. However, there may be an even more compelling reason in recent findings that nuclear envelope protein composition is highly tissue specific. Indeed, with the many general cancer functions already linked to the nuclear envelope this finding could be the Rosetta Stone that explains much of the tissue/tumor type-specific aspects of cancer and the reason that in the early studies certain nuclear envelope characteristics correlated with increased metastasis in one direction or another based on the tumor type.

This volume brings together many different researchers and perspectives covering the historical and current use of the nuclear envelope in cancer diagnosis and grading, clear and potentially relevant functions of the nuclear envelope in cell cycle regulation and signaling, chromatin organization and gene expression, genome stability, nucleocytoplasmic transport, cell mechanical stability and migration, as well as unexpected links between the nuclear envelope and tumorigenesis. We have tried to collect some divergent viewpoints as well as representing both clinical and basic research and both facts and conceptual ideas. Our hope is that this collection will inspire new directions in cancer research as well as a new focus on the nuclear envelope. We now know that the nuclear envelope is as complex a signaling node as the plasma membrane and perhaps the next phrasing of that old quote will be “all roads lead to the nuclear envelope.”

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