

Preface

*Then Sleep and Death,
two twins of winged race,
of matchless swiftness,
but of silent pace*

[Homer](#), *The Iliad*, Book XVI. Pope's translation.

For several decades, cancer has been considered as a disease primarily characterized by unlimited and uncontrollable proliferation. Countless studies have drawn parallels between embryo and cancer cell growth [1], and cancer's "limitless replicative potential" is a milestone of the hallmarks paradigm [2].

In parallel with this view, a more nuanced description of cancer has gradually emerged. Laboratory experiments have shown that cancer cells are able not only to proliferate but also to alternate periods of quiescence with periods of rapid growth [3]. This reversible quiescent state is called "tumor dormancy" (from Latin *dormeo*: "I sleep"). In keeping with this paradigm, clinical observations have indicated that most neoplasms cannot be described in terms of unstoppable proliferation. For example, prostate cancer is characterized by prolonged iterative cycles of proliferation and dormancy (Fig. 1). Notably, during these periods of quiescence the neoplasm is often clinically indolent and therefore both patients and clinicians are less concerned about it.

The discovery of cancer dormancy paves the way for many unresolved questions. First of all: is cellular dormancy an inherited or acquired ability? How are cancer cells able to alternate proliferation and quiescence? And finally: why does tumor dormancy seem to be so critical for cancer cells' survival? Emerging evidence indicates that the mysterious phenomenon of cancer dormancy might hide the key for understanding the two deadliest attributes of cancer cells: their ability to resist anticancer treatments and their propensity to colonize distant organs. In the first two chapters of this book, Aguirre-Ghiso and Wang analyze the role of epigenetics and metabolic pathways in shaping the metastatic and drug-resistant potential of dormant cells.

Since dormant cells are generally overlooked by clinicians and resistant to conventional therapies, the "dormancy paradigm" paves the way for the development of

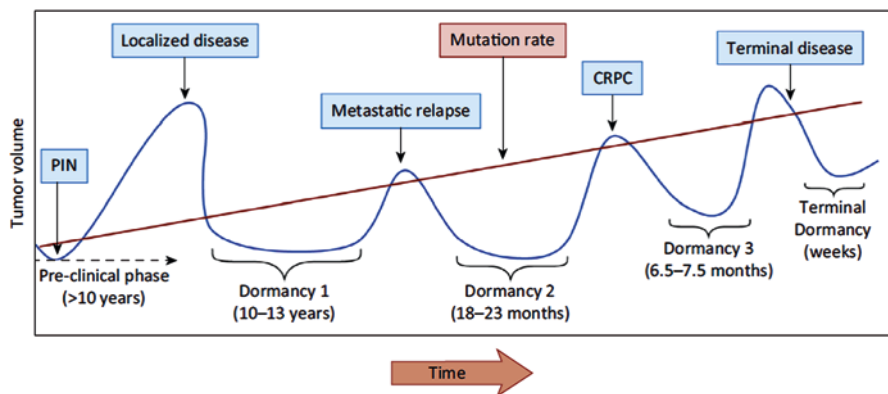


Fig. 1 The clinical course of prostate cancer is characterized by progressively shorter cycles of treatment–dormancy–relapse. The duration of the dormancy period is based on clinical evidence of progression-free survival after prostatectomy (1), androgen-deprivation therapy (2), and docetaxel treatment (3). An increased mutation rate (red line) correlates with shorter dormancy periods

a completely new class of therapies. In chapters “Tumor Dormancy, Angiogenesis and Metronomic Chemotherapy” and “Immunoncology of Dormant Tumors” of this book, Bocci and Bishop discuss the possible role of anti-angiogenic therapy and immunotherapy in targeting dormant cancer cells.

Finally, we decided to examine the roots of cancer dormancy by investigating the relationship between cancer proliferation, quiescence, and a thermodynamic description of biological processes (see chapter “Thermodynamics and Cancer Dormancy: A Perspective” by Tuszynski and Rietman). We hope that this chapter will identify new avenues of investigation for this fascinating research field.

We believe that this book is extremely timely and useful to everyone (students, clinicians, and scientists) who wants to understand more about the increasingly important concept cancer dormancy and recurrence. To produce an excellent text, we have decided to invite only outstanding contributors, with a strong track record of research in their specific area, and we have identified five key themes, corresponding to the chapters of this book. We hope that this first organic collection of essays on this topic will help to highlight the importance of this novel perspective, which has the potential to revolutionize our understanding of cancers and to pave the way for a new generation of therapies.

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Tumor Dormancy and Recurrence

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