Middlegame Theory, Cancer Style: A Message from the Editor-in-Chief

Karen E. Knudsen, PhD

In more than 1,500 years since the inception of chess as a fascination of nobility, scholars, and gamers alike, theoreticians have proposed innumerable underlying strategies intended to exert control over the chaos of threats and offensives, and to eliminate opponents in short order. Suggested strategies are not uniform, and depend not just on the gambits offered, but the stage of the game being played—loosely categorized as opening, middlegame, and endgame theory. Of these, middlegame theory is perhaps the most critical and difficult to master; it defines the time when piece placement has developed, loose understanding of potential paths forward has emerged, action and reaction requires lateral thinking to gain advantage, anticipating next moves becomes essential, and the skirmishes begin. Successful middlegame play, albeit challenging, is the gateway to a successful endgame.

By parallel, 2013 brings us to the middlegame of cancer research, wherein key actors driving disease development and progression (e.g., oncogenes, tumor suppressors, cell-cycle perturbations) have been identified, weaknesses in the opponent that yield potential interventional opportunity (e.g., alterations in DNA repair and signaling addiction) have been discovered, appreciation for factors that challenge effective tumor cell elimination (e.g., pro-survival pathways, chromosome rearrangement, and epigenetic reprogramming) has been realized, and the concept that understanding not just the key pieces but the playing field as a whole (e.g., tumor microenvironment and role of the immune system) has become critical. It is therefore no surprise that the era of bioinformatics, systems biology, epigenetics, and genome-wide analyses is upon us, wherein the current challenge is not to understand each minute corner of the game, but to attain a greater understanding of the cancer cell and environment in its entirety, digging deep to connect the biochemistry to the cell biology, the cell biology to the tumor biology, and to extend this knowledge toward the greater goal of attaining a fluid understanding sufficient to identify weaknesses, anticipate reaction of tumor cells to challenges, and use comprehension of the collective whole to reach the endgame. Thus is the mission of Molecular Cancer Research (MCR).

Significant progress to the middlegame over the last 10 years can be attributed in part to the brilliant vision and success of Michael B. Kastan, whose term as the inaugural Editor-in-Chief oversaw major advances in the field, and highlighted the importance of interrogating the basic mechanisms that drive cancer development and progression. Findings of critical importance were reported; for example, MCR was among the first to report on differential effects of BRAF in cancer cells, provided a molecular justification for targeting K-ras function, and reported novel mechanisms that underpin neuroblastoma development. These influential studies provided transformative new insight into the molecular basis of disease, and underscore the importance of basic cancer research in providing the foundation for translational advances. In the last month alone at MCR, unexpected new findings revealed that a neuronal receptor regulates cellular processes directly linked to aggressive cancer cell phenotypes, that the integral membrane protein CD151 is a potent modulator of metastatic potential, and that c-Myc is a driving culprit in development of resistance to ERK1/2 suppression. All said, it has been an impressive decade of advances, and MCR has been at the forefront of reporting novel molecular research associated with human disease. To Mike, I would like to extend a wholehearted thanks for building this substantial foundation.

As I begin my term as Editor-in-Chief, it is the overarching goal of the journal to publish transformative basic cancer research discoveries of broad interest to the cancer biology field, prioritizing molecular and cellular studies that reveal novel mechanistic insight into pathways linked to cancer risk, development, and progression. I am fortunate to have an outstanding team of Senior and Deputy Editors to assist in this task, all leaders in their fields and fully vested in this mission before us. Areas of emphasis have been accordingly reshaped so as to highlight the areas of ongoing intensive investigation in contemporary cancer research. Moreover, in addition to the Research Articles of significance, in 2013, we will be launching a new "Rapid Impact" section, designed for short articles (3-figure limit)
of high impact, featuring studies showing unusual significance, timeliness, or novelty. Submissions meeting these criteria will be sent for rapid review (10 to 14 days to decision), with the goal of closing the gap between major fundamental discovery and dissemination to the cancer community. I look forward to working with the Senior and Deputy Editors, the Editorial Board, reviewers, and authors alike to facilitate publication of the highest quality fundamental, innovative basic cancer research.

In closing, it goes without saying that the need for basic cancer research could not be greater. We are indeed at the middlegame of the battle against cancer; fundamental research that will elucidate connectivity, and underpinning mechanisms of action is key to the development of preventative strategies and cures. The history of science is rich in examples of basic discoveries that transformed understanding of human disease, and this paradigm holds ever more true in the current era. In her acceptance banquet for the 2009 Nobel Prize in Medicine (given for the discovery of telomere function and telomerase, shared with Carol Greider and Jack Szostack), laureate Elizabeth Blackburn elegantly stated that "...our scientific journeys have taken us across a wide spectrum of biology. Why? Because we believe that basic science research is the key to continued advances in and applications to medicine." Three cheers, Elizabeth—we could not agree more, and your own example illuminates the way. At Molecular Cancer Research, we will continue to lead the effort by publishing outstanding, transformative basic discoveries, until the middlegame of cancer research transitions to the final goal, "Checkmate."

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Editor-in-Chief
Molecular Cancer Research
Published online January 18, 2013.
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