Preface

The Medical Practice of Molecular Oncology Diagnostics

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Editor

Molecular diagnostics is a rapidly changing field. In a short period of time, molecular diagnostics for applications in cancer has evolved from a loose collection of investigational ancillary tests to redefine pathologic disease classification and usher in the era of precision medicine. Today, molecular testing, including the targeted sequencing of cancer genomes, is standard of care for confirming pathologic diagnosis, predicting clinical risk, and guiding the use of conventional and molecularly targeted therapies for most life-threatening human cancers.

The growing complexity of molecular applications, technology, and interpretation necessitates regular updates to help health care providers stay informed about standard clinical practices in molecular medicine. This special collection of review articles addresses the clinical challenges in molecular oncology diagnostics from expert molecular pathologists and geneticists who actively practice in the field. The issue is organized into four parts:

Part 1 provides updates in the clinical utility of molecular diagnostics, including the use of molecular testing to guide therapy selection in solid tumors (Willard, Sholl, and Aisner) and in the systematic classification of hematopoietic neoplasms (Hergott and Kim) with special considerations for molecular testing in pediatric cancers (Fisch and Church).

Part 2 focuses on the analytical aspects of clinical molecular testing. This section addresses issues that molecular diagnosticians face on a daily basis, including the selection of pathologic specimens (Gan and Roy-Chowdhuri), the principles of single-gene testing (Hanbazazh, Morlote, Mackinnon, and Harada) compared with multigene next-generation sequencing panels (Gindin and Hsiao), informatics pipelines that support

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the analysis of complex sequencing data (Roy), and best practices in clinical interpretation and reporting (Schubert, Wu, Li, and Cao).

Part 3 describes how laboratories use a variety of current and emerging molecular methods to detect structural alterations in cancer, such as gene rearrangements (Ordulu and Nardi) and copy number alterations (Spence and Dubuc), and the strengths and limitations of different molecular technologies used for this indication.

Part 4 highlights current and emerging hot topics in molecular oncology diagnostics, including biomarkers that predict response to cancer immunotherapy (Ritterhouse and Gogakos), molecular testing performance for cell free nucleic acids (Paulson, Konnick, and Lockwood), and strategies to identify cancer-predisposing germline variants (Ceyhan-Birsoy).

Multiple themes emerge in this collection of expert reviews. Molecular oncology diagnostics is a diverse field with multiple testing modalities, and the strengths and limitations of different molecular methods are highly complementary. The selection of molecular testing is complex and multifactorial, and the optimal testing strategy depends on clinical history, pathologic diagnosis, tissue availability, and pretest probability of clinically actionable molecular targets. An increasing volume of molecular data brings challenges in clinical interpretation but also opportunities to enhance patient care.

The purpose of this collection is to provide unique perspectives into molecular diagnostics and to aid pathologists, geneticists, and other clinicians in the field of medical oncology. I hope that the articles will also introduce imaginative young people, students, scientists, and resident physicians, to the world of molecular diagnostics, made possible by incredible scientific advances and the desire to help patients in need. Consider joining us in a riveting and rewarding career in molecular pathology, medical genetics, laboratory medicine, or bioinformatics. Ultimately, our collective expertise in molecular diagnostics is needed to fulfill the promise of precision medicine.

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