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Bridging Eras In Oncology: How Molecular Innovations Are Redefining Cancer Diagnosis And Therapy

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Abstract

Objective: *To examine how molecular diagnostic technologies are transforming cancer care and their integration with traditional methods.*

Scope: *This review covers developments in liquid biopsy, next-generation sequencing, circulating DNA analysis, and computational tools, analyzing clinical applications and implementation challenges.*

Methods: *We reviewed peer-reviewed literature from 2015 to 2024, focusing on molecular diagnostic innovations, clinical validation studies, and comparative effectiveness research.*

Key Results: *Molecular diagnostics demonstrate superior sensitivity for minimal residual disease detection compared to conventional methods. Liquid biopsy enables non-invasive treatment monitoring and early detection of resistance. Next-generation sequencing identifies actionable mutations in ~70% of solid tumors, directly informing treatment selection. Integration with traditional approaches improves patient outcomes and therapeutic precision.*

Conclusion: *While molecular innovations offer substantial advantages, optimal cancer care requires thoughtful integration of both approaches. Success depends on addressing barriers to cost, access, standardization, and training.*

Keywords: *molecular diagnostics, liquid biopsy, cancer genomics, precision oncology, biomarkers, tumor profiling*

1. INTRODUCTION

Cancer medicine has undergone profound changes over the past two decades. What once relied entirely on microscopic tissue examination now includes sophisticated genetic testing revealing molecular cancer drivers [1].Traditional cancer diagnosis depended on pathologists identifying malignant cells based on appearance and growth patterns. While morphological approaches provided essential information for tumor classification and staging, they offered limited insight into cancer development or potential treatment response [2].

The breakthrough came with recognizing cancer as essentially a genetic disease. Researchers discovered that tumors arise when normal genes become altered through mutations that disrupt cellular growth control [3].

1.1 The Promise of Molecular Medicine

Today's molecular diagnostics detect specific genetic tumor changes, identify patients likely to benefit from targeted therapies, and monitor treatment responses in real-time [4].

First, molecular testing can be performed on blood samples, eliminating the need for invasive tissue biopsies. This "liquid biopsy" approach enables continuous monitoring of cancer evolution [5]. Second, molecular profiling reveals therapeutic targets invisible to conventional analysis. Many effective cancer drugs now target specific genetic alterations rather than treating all organ-specific cancers identically [6].

Third, molecular monitoring detects treatment resistance before clinical evidence appears, enabling prompt adjustments to therapy [7].

1.2 Integration Rather Than Replacement

Despite advances, molecular diagnostics work best when combined with, rather than replacing, traditional methods. Tissue examination remains essential for confirming a cancer diagnosis and assessing the effects of treatment. The future lies in the intelligent integration of morphological and molecular information [8].

2. EVOLUTION OF CANCER DIAGNOSTIC APPROACHES

2.1 Traditional Foundations

Cancer diagnosis has traditionally relied on well-established methods, each with distinct strengths and limitations.

Histopathological Examination

Microscopic tissue analysis remains the gold standard for cancer diagnosis. Pathologists examine cellular architecture, nuclear characteristics, and growth patterns to determine type, grade, and stage, providing definitive diagnoses and prognostic information [9].

However, tissue biopsy requires invasive procedures that carry risks and may inadequately sample heterogeneous tumors. A single biopsy represents only one moment in time and cannot capture the changes in cancer that occur during treatment [10].

Immunohistochemical Analysis

Protein-based markers improved diagnostic precision by identifying specific molecular features within tissue samples. Markers like estrogen receptor, HER2, and PD-L1 now guide treatment decisions in many cancer types [11]. Despite advances, immunohistochemical interpretation can be subjective, with laboratory and observer variability potentially affecting treatment decisions [12].

Medical Imaging

Radiological techniques, including CT, MRI, and PET, provide crucial information about tumor location, size, and spread. These non-invasive methods enable treatment planning and response monitoring [13].

Imaging faces limitations in detecting early-stage disease and distinguishing viable tumors from treatment-related changes. Small metastases or minimal residual disease often remain below detection thresholds [14].

2.2 Molecular Revolution

Cancer-causing gene discovery fundamentally changed malignancy understanding. Key findings included the identification of oncogenes that promote tumor growth when activated and tumor suppressors that prevent cancer when functioning normally [15].

This genetic framework enabled the development of the first molecular diagnostic tests. Early techniques, such as PCR and fluorescence in situ hybridization, detected specific genetic alterations, providing new insights into tumor biology and therapeutic targets [16].

Next-generation sequencing represented a quantum leap in diagnostics. Unlike previous single-gene examination methods, NGS analyses hundreds or thousands of genes simultaneously, creating comprehensive tumor profiles [17].

3. CONTEMPORARY MOLECULAR DIAGNOSTIC TECHNOLOGIES

3.1 Next-Generation Sequencing

NGS has become the cornerstone of modern molecular oncology. This technology identifies point mutations, insertions, deletions, copy number variations, and structural rearrangements across entire genomes or focused gene panels [18].Clinical applications include initial tumor characterization for treatment selection, monitoring acquired resistance mutations, identifying germline predisposition syndromes, and detecting minimal residual disease after treatment.The decreasing costs of NGS and increasing speed have made comprehensive tumor profiling feasible in routine clinical practice. Many cancer centers now perform NGS on all newly diagnosed tumors to identify potential therapeutic targets [19].

3.2 Liquid Biopsy Technologies

Liquid biopsy represents perhaps the most transformative innovation in cancer diagnostics. This approach analyzes tumor-derived material circulating in blood, including cell-free DNA, circulating tumor cells, and extracellular vesicles [20].

Table 1. Liquid Biopsy Components and Applications

Component	Origin	Detection Methods	Applications	Advantages
Cell-free DNA	Tumor cell death	PCR, NGS	Mutation detection, resistance monitoring	High sensitivity, quantitative
Circulating tumor cells	Direct shedding	Immunocapture, flow cytometry	Metastasis prediction, drug testing	Intact cells for functional studies
Extracellular vesicles	Cellular secretion	Isolation, proteomics	Biomarker discovery, immune profiling	Protein and RNA content
Tumor-educated platelets	Platelet interaction	RNA sequencing	Cancer detection, classification	Accessible, stable samples

Liquid biopsy offers compelling advantages over tissue sampling. Blood collection is minimally invasive and repeatable. Circulating material represents the entire tumor burden rather than a single biopsy site. Serial testing enables monitoring of real-time treatment response and resistance development [21].

3.3 Multi-Omics Integration

Modern cancer research increasingly employs multi-omics approaches combining genomic, transcriptomic, proteomic, and metabolomic data. This comprehensive analysis offers insights into tumor biology that are unachievable through single-platform testing [22].

Multi-omics integration explains why tumors with similar genetic alterations may respond differently to treatment. By examining gene expression patterns, protein levels, and metabolic activity, researchers identify additional biomarkers and therapeutic targets [23].

3.4 Computational Tools and Data Analysis

The increasing volume and complexity of molecular diagnostic data require sophisticated computational analysis. Bioinformatics pipelines process raw sequencing data, identify clinically relevant alterations, and provide interpretation support [24].

Machine learning approaches are increasingly used to analyze complex datasets, identify patterns predictive of treatment responses, and support informed clinical decision-making. However, these tools require careful validation before clinical implementation [25].

4. CLINICAL APPLICATIONS AND IMPACT

4.1 Precision Treatment Selection

Molecular profiling has fundamentally changed oncologist treatment selection. Rather than choosing therapy based solely on tumor location and stage, doctors now match patients with treatments targeting specific tumor genetic alterations [26].Successful precision medicine examples include EGFR inhibitors for EGFR-mutated lung cancers, HER2-targeted therapy for HER2-positive breast cancers, BRAF inhibitors for BRAF V600E-mutated melanomas, and PD-1/PD-L1 inhibitors for tumors with high mutational burden. These targeted approaches often produce better outcomes with fewer side effects compared to conventional chemotherapy [27].

4.2 Treatment Monitoring and Resistance Detection

Molecular monitoring enables the detection of early treatment resistance, often months before clinical or radiological progression is evident. This early warning allows prompt treatment modification, potentially improving outcomes [28].Liquid biopsy has proven particularly valuable for monitoring patients with advanced cancers receiving targeted therapies. Serial testing identifies specific resistance mutations, guiding the selection of next-line treatment [29].

4.3 Minimal Residual Disease Assessment

The detection of minimal residual disease after primary treatment represents another important application. Sensitive molecular tests identify small numbers of remaining cancer cells after surgery or treatment completion [30].

Patients with detectable minimal residual disease have higher relapse risks and may benefit from additional treatment. This information guides post-treatment surveillance and adjuvant therapy decisions [31].

5. COMPARATIVE ANALYSIS: TRADITIONAL VS. MOLECULAR APPROACHES

Understanding the relative strengths and limitations of conventional and molecular diagnostics is essential for optimal clinical integration.

Table 2. Diagnostic Approach Comparison in Cancer Care

Characteristic	Traditional Methods	Molecular Methods	Clinical Implications
Sample type	Tissue biopsy	Blood, tissue, fluids	Molecular methods are less invasive
Information provided	Morphology, protein expression	Genetic alterations, expression patterns	Molecular methods reveal therapeutic targets
Sensitivity	Moderate	High	Molecular methods detect minimal disease
Specificity	High	High	Both approaches are highly specific
Turnaround time	2-5 days	1-3 days	Molecular methods potentially faster
Cost	Lower	Higher	Molecular methods are more expensive initially
Monitoring capability	Limited	Continuous	Molecular methods enable serial monitoring
Treatment Guidance	Empirical	Targeted	Molecular methods enable precision therapy

5.1 Complementary Strengths

Traditional and molecular approaches offer complementary information, providing a comprehensive assessment of tumors. Morphological examination confirms malignancy and provides prognostic information, while molecular testing identifies therapeutic targets and enables the selection of precision treatments [32].Optimal cancer care integrates both approaches rather than relying exclusively on either method. This combined strategy maximizes diagnostic accuracy while providing complete treatment planning information [33].

5.2 Implementation Considerations

Successful integration requires careful workflow design, result interpretation, and attention to clinical decision-making processes. Healthcare teams require training in molecular diagnostics and access to genetic counseling resources [34].Cost-effectiveness analyses suggest that while molecular testing involves higher upfront costs, it may reduce overall healthcare expenses through precise treatment selection and reduced ineffective therapies [35].

6. CURRENT CHALLENGES AND LIMITATIONS

6.1 Technical Challenges

Despite rapid advances, molecular diagnostics still face several technical limitations that affect their clinical utility.

Sensitivity and Specificity: While generally high, sensitivity varies significantly across platforms and tumor types. Early-stage cancers or tumors with low levels of circulating DNA may produce false-negative results [36].

Standardization: Lack of standardized protocols, analysis methods, and interpretation criteria creates laboratory variability. This inconsistency affects the reliability of results and clinical decision-making [37].

Turnaround Time: Although faster than traditional methods in some cases, complex molecular analyses may require several days, potentially delaying treatment decisions.

6.2 Clinical Implementation Barriers

Infrastructure Requirements: Molecular diagnostics require significant laboratory infrastructure, specialized equipment, and technical expertise not universally available in all healthcare settings.

Education and Training: Healthcare providers need training in molecular biology concepts, test interpretation, and clinical application. Many practicing oncologists received limited genetic education during training.

Reimbursement Issues: Insurance coverage for molecular testing varies significantly, which can potentially limit patient access. Cost considerations may influence test utilization patterns [38].

6.3 Ethical and Social Considerations

Health Disparities: Advanced molecular testing may exacerbate existing healthcare disparities if not implemented equitably across populations and geographic regions.

Genetic Discrimination: Genetic testing raises concerns about potential employment or insurance coverage discrimination, underscoring the need for robust privacy protections.

Informed Consent: Comprehensive genetic testing may reveal incidental findings unrelated to cancer care, requiring careful consent processes and genetic counseling [39].

7. FUTURE DIRECTIONS AND EMERGING TECHNOLOGIES

7.1 Multi-Cancer Early Detection

Emerging blood tests aim to detect multiple cancer types in asymptomatic individuals simultaneously. Multi-cancer early detection (MCED) tests analyze circulating tumor DNA, proteins, and other biomarker patterns [40].Early studies suggest that MCED tests can identify cancers across multiple organ systems with an acceptable false-positive rate. If validated in larger trials, these tests could revolutionize cancer screening.

7.2 Spatial Biology

New technologies enable the analysis of molecular features while preserving spatial information within tissue samples. Spatial transcriptomics and proteomics reveal the interactions between different cell types within tumor microenvironments.

This spatial information provides insights into tumor biology, immune response, and treatment resistance mechanisms that are unobtainable from traditional bulk analysis.

7.3 Real-Time Monitoring

Future developments may enable continuous monitoring of cancer status through wearable devices or implantable sensors. Such technologies could detect disease progression or treatment response in real time. Point-of-care testing platforms may bring molecular diagnostics directly to clinic settings, reducing turnaround times and improving patient convenience.

8. CONCLUSION

The integration of molecular diagnostics into cancer care represents one of the most significant advances in modern medicine. These technologies have fundamentally transformed how we diagnose, treat, and monitor cancer, resulting in improved patient outcomes.

8.1 Transformative Impact

Molecular diagnostics have enabled truly personalized cancer care. Patients now receive treatments selected based on tumor-specific genetic characteristics rather than broad organ-based categorizations. This precision approach often produces better outcomes with fewer side effects.

Liquid biopsy treatment response and resistance development monitoring have transformed clinical practice. Doctors can now detect treatment failure months earlier than conventional methods, enabling prompt therapy modifications that potentially improve outcomes.

8.2 Integration Philosophy

Future cancer care lies not in replacing traditional diagnostic methods but in thoughtful integration of molecular and morphological approaches. Each method provides unique and complementary information essential for optimal patient care.

Successful integration requires addressing multiple challenges, including cost, access, standardization, and education. Healthcare systems must invest in infrastructure, training, and quality assurance to fully realize the potential of molecular diagnostics.

8.3 Future Outlook

Emerging technologies promise even greater advances in cancer care. Multi-cancer early detection tests may enable the identification of cancer before symptoms develop. Spatial biology techniques will provide new insights into tumor biology and the mechanisms of treatment resistance. Real-time monitoring systems may transform cancer from an episodic disease to a continuously managed condition.

8.4 Call for Action

Realizing the full potential of molecular diagnostics requires coordinated, multi-stakeholder efforts. Healthcare institutions must invest in infrastructure and training. Policymakers need to address issues related to reimbursement and access. Researchers must continue to develop and validate new technologies. Most importantly, the cancer care community must remain committed to ensuring that molecular diagnostic advances benefit all patients, regardless of their geographic location, economic status, or access to healthcare systems. Only through comprehensive efforts can we truly fulfill the promise of precision cancer medicine.

The oncology transformation from a morphology-based to a molecularly informed discipline has already saved countless lives and improved the outcomes of millions of patients. With continued innovation and thoughtful implementation, molecular diagnostics will play an increasingly important role in our ongoing battle against cancer.

References

[1] Malone, E., Oliva, M., Sabatini, P., Stockley, T. L., and Siu, L. L., 2020, "Molecular Profiling for Precision Cancer Therapies", Genome Med., 12(1), pp. 1-15.

[2] Gromek, P., Senkowska, Z., Płuciennik, E., Pasieka, Z., Zhao, L. Y., Gielecińska, A., Kciuk, M., Kłosiński, K., Kałuzińska-Kołat, Ż., and Kołat, D., 2024, "Revisiting the Standards of Cancer Detection and Therapy Alongside Their Comparison to Modern Methods", World J. Methodol., 14(2), pp. 92982.

[3] Sokolenko, A. P., and Imyanitov, E. N., 2018, "Molecular Diagnostics in Clinical Oncology", Front. Mol. Biosci., 5, pp. 76.

[4] Walter, W., Pfarr, N., Meggendorfer, M., Jost, P. J., Haferlach, T., and Weichert, W., 2021, "Next-Generation Diagnostics for Precision Oncology: Preanalytical Considerations, Technical Challenges, and Available Technologies", Semin. Cancer Biol., 84, pp. 90-98.

[5] Pantel, K., and Alix-Panabières, C., 2019, "Liquid Biopsy and Minimal Residual Disease--Latest Advances and Implications for Cure", Nat. Rev. Clin. Oncol., 16(7), pp. 409-424.

[6] Wheler, J. J., Janku, F., Naing, A., Li, Y., Stephen, B., Zinner, R., Subbiah, V., Fu, S., Karp, D., Falchook, G. S., Tsimberidou, A. M., Piha-Paul, S. A., Anderson, R., Ke, D., Miller, V., Yelensky, R., Lee, J. J., Hong, D. S., and Kurzrock, R., 2016, "Cancer Therapy Directed by Comprehensive Genomic Profiling: A Single Center Study", Cancer Res., 76(13), pp. 3690-3701.
[7] Tie, J., Wang, Y., Tomasetti, C., Li, L., Springer, S., Kinde, I., Silliman, N., Tacey, M., Wong, H. L., Christie, M., Kosmider, S., Skinner, I., Wong, R., Steel, M., Tran, B., Desai, J., Jones, I., Haydon, A., Hayes, T., Price, T. J., Strausberg, R. L., Diaz, L. A., Papadopoulos, N., Kinzler, K. W., Vogelstein, B., and Gibbs, P., 2016, "Circulating Tumor DNA Analysis Detects Minimal Residual Disease and Predicts Recurrence in Patients with Stage II Colon Cancer", Sci. Transl. Med., 8(346), pp. 346ra92.
[8] Passaro, A., Attili, I., Rappa, A., Vacirca, D., Ranieri, A., Baggi, A., Mallardo, D., Spaggiari, L., de Marinis, F., and Besse, B., 2024, "Precision Oncology in Non-Small Cell Lung Cancer: Current Standards and Future Perspectives", Lung Cancer, 189, pp. 107489.
[9] Pulumati, A., Pulumati, A., Dwarakanath, B. S., Verma, A., and Papineni, R. V. S., 2023, "Technological Advancements in Cancer Diagnostics: Improvements and Limitations", Cancer Rep., 6(3), pp. e1764.
[10] Nounou, M. I., Elamrawy, F., Ahmed, N., Abdelraouf, K., Goda, S., and Syed-Sha-Qhattal, H., 2015, "Breast Cancer: Conventional Diagnosis and Treatment Modalities and Recent Patents and Technologies", Breast Cancer: Basic Clin. Res., 9, pp. 17-34.
[11] Langen, K. J., Galldiks, N., Hattingen, E., and Shah, N. J., 2017, "Advances in Neuro-Oncology Imaging", Nat. Rev. Neurol., 13(5), pp. 279-289.
[12] van der Heijden, M. S., Loriot, Y., Duran, I., Vogelzang, N. J., De Giorgi, U., Oudard, S., Bracarda, S., Valderrama, B. P., Burotto, M., Seront, E., Necchi, A., Bedke, J., Linch, M., Frydenberg, M., De Santis, M., O'Donnell, P. H., Nasroulah, F., Bamias, A., Petrylak, D. P., Fléchon, A., Gravis, G., Harrison, M. R., Suarez, C., Powles, T., Drakaki, A., Gschwend, J. E., Albers, P., Grande, E., Morales-Barrera, R., Krege, S., Rosenberg, J. E., Fizazi, K., de Wit, R., Galsky, M. D., and Bellmunt, J., 2021, "Atezolizumab Versus Chemotherapy in Patients with Platinum-Treated Locally Advanced or Metastatic Urothelial Carcinoma: A Long-Term Overall Survival and Safety Update from the Phase 3 IMvigor211 Clinical Trial", Eur. Urol., 80(1), pp. 7-11.
[13] Gregg, J. P., Li, T., and Yoneda, K. Y., 2019, "Molecular Testing Strategies in Non-Small Cell Lung Cancer: Optimizing the Diagnostic Journey", Transl. Lung Cancer Res., 8(3), pp. 286-301.
[14] Hiley, C. T., Le Quesne, J., Santis, G., Sharpe, R., de Castro, D. G., Middleton, G., and Swanton, C., 2016, "Challenges in Molecular Testing in Non-Small-Cell Lung Cancer Patients with Advanced Disease", Lancet, 388(10048), pp. 1002-1011.
[15] Caracciolo, D., Riillo, C., Di Martino, M. T., Tagliaferri, P., and Tassone, P., 2019, "Alternative Non-Homologous End-Joining: Error-Prone DNA Repair as Cancer's Achilles' Heel", Cancers, 11(8), pp. 1109.
[16] Luthra, R., Chen, H., Roy-Chowdhuri, S., and Singh, R. R., 2015, "Next-Generation Sequencing in Clinical Molecular Diagnostics of Cancer: Advantages and Challenges", Cancers, 7(4), pp. 2023-2036.
[17] Riedl, J. M., Moik, F., Esterl, T., Kostmann, S., Gerger, A., and Jost, P. J., 2024, "Molecular Diagnostics Tailoring Personalized Cancer Therapy--An Oncologist's View", Virchows Arch., 484(1), pp. 169-179.
[18] Edsjö, A., Russnes, H. G., Lehtiö, J., Tamborero, D., Hovig, E., Stenzinger, A., and Rosenquist, R., 2024, "High-Throughput Molecular Assays for Inclusion in Personalised Oncology Trials--State-of-the-Art and Beyond", J. Intern. Med., 295(6), pp. 785-803.
[19] Jackman, D. M., Johnson, M. L., Williamson, S. K., Sima, C. S., Janne, P. A., Papadimitrakopoulou, V., Akerley, W., Koczywas, M., Trent, D., Chow, L. Q. M., Liu, S. V., Ramalingam, S. S., Heist, R. S., Tran, H. T., Ahn, M. J., Kim, S. W., Yu, H. A., Piotrowska, Z., Tan, D. S. W., Lim, S. M., Liu, G., Barlesi, F., Lee, S. H., Camidge, D. R., Velcheti, V., Shepherd, F. A., Neal, J. W., Wakelee, H. A., Sequist, L. V., and Oxnard, G. R., 2024, "Phase I/II Study of Capmatinib (INC280) Plus Gefitinib After Failure of Epidermal Growth Factor Receptor (EGFR) Tyrosine Kinase Inhibitor Therapy in Patients with EGFR-Mutated, MET-Amplified Non-Small-Cell Lung Cancer", J. Clin. Oncol., 42(1), pp. 77-85.
[20] Siravegna, G., Marsoni, S., Siena, S., and Bardelli, A., 2017, "Integrating Liquid Biopsies into the Management of Cancer", Nat. Rev. Clin. Oncol., 14(9), pp. 531-548.
[21] Wan, J. C. M., Massie, C., Garcia-Corbacho, J., Mouliere, F., Brenton, J. D., Caldas, C., Pacey, S., Baird, R., and Rosenfeld, N., 2017, "Liquid Biopsies Come of Age: Towards Implementation of Circulating Tumour DNA", Nat. Rev. Cancer, 17(4), pp. 223-238.
[22] Buzdin, A., Sorokin, M., Garazha, A., Glusker, A., Aleshin, A., Poddubskaya, E. V., Sekacheva, M. I., Kim, E., Gaifullin, N. M., Giese, A., Seryakov, A., Rumiantsev, P., Moshkovskii, S., and Moiseev, A., 2020, "RNA Sequencing for Research and Diagnostics in Clinical Oncology", Semin. Cancer Biol., 60, pp. 311-323.
[23] Lotter, W., Hassanpour, S., Cox, D. D., and Rubin, M. A., 2021, "Robust Breast Cancer Detection in Mammography and Digital Breast Tomosynthesis Using an Annotation-Efficient Deep Learning Approach", Nat. Med., 27(2), pp. 244-249.
[24] Weissleder, R., and Lee, H., 2020, "Automated Molecular-Image Cytometry and Analysis in Modern Oncology", Nat. Rev. Mater., 5(6), pp. 409-422.
[25] Clayton, E. A., Matyunina, L. V., McDonald, L. D., Benigno, B. B., and McDonald, J. F., 2018, "Machine Learning Predicts Individual Cancer Patient Responses to Therapeutic Drugs with High Accuracy", Sci. Rep., 8(1), pp. 16444.
[26] Hayashi, H., Takiguchi, Y., Minami, T., Akiyoshi, K., Segawa, Y., Urata, Y., Tanaka, H., Tanizaki, J., Takeda, M., Ito, A., Horiike, A., Tanimoto, M., Yoshioka, H., Takahashi, T., Nishio, K., Tamura, T., Nakagawa, K., and LC-SCRUM-Japan, 2020, "Site-

Specific and Targeted Therapy Based on Molecular Profiling by Next-Generation Sequencing for Previously Treated Advanced Non-Small Cell Lung Cancer: A Nonrandomized Clinical Trial", JAMA Oncol., 6(9), pp. 1398-1407.
[27] Kim, E. S., Schuler, A., Eastman, A., Satinover, D., Sukari, A., Halmos, B., Oxnard, G. R., Halabi, S., and O'Connell, J. P., 2024, "Molecular Tumor Boards at National Cancer Institute-Designated Cancer Centers: Characteristics, Challenges, and Opportunities", JCO Precis. Oncol., 8, pp. e2300456.
[28] Oxnard, G. R., Paweletz, C. P., Kuang, Y., Mach, S. L., O'Connell, A., Messineo, M. M., Luke, J. J., Butaney, M., Kirschmeier, P., Jackman, D. M., and Jänne, P. A., 2014, "Non-invasive Detection of Response and Resistance in EGFR-Mutant Lung Cancer Using Quantitative Next-Generation Genotyping of Cell-Free Plasma DNA", Clin. Cancer Res., 20(6), pp. 1698-1705.
[29] Murtaza, M., Dawson, S. J., Tsui, D. W., Gale, D., Forshew, T., Piskorz, A. M., Parkinson, C., Chin, S. F., King, Z., Wade, A. S., Morris, J., Humphray, S., Hadfield, J., Bentley, D., Chin, T. M., Brenton, J. D., Caldas, C., and Rosenfeld, N., 2013, "Non-Invasive Analysis of Acquired Resistance to Cancer Therapy by Sequencing of Plasma DNA", Nature, 497(7447), pp. 108-112.
[30] Phallen, J., Sausen, M., Adleff, V., Leal, A., Hruban, C., White, J., Anagnostou, V., Fiksel, J., Cristiano, S., Papp, E., Speir, S., Reinert, T., Orntoft, M. W., Woodward, B. D., Scharpf, R., Velculescu, V. E., Kinzler, K. W., Vogelstein, B., and Diaz, L. A., 2017, "Direct Detection of Early-Stage Cancers Using Circulating Tumor DNA", Sci. Transl. Med., 9(403), pp. eaan2415.
[31] Bettegowda, C., Sausen, M., Leary, R. J., Kinde, I., Wang, Y., Agrawal, N., Bartlett, B. R., Wang, H., Luber, B., Alani, R. M., Antonarakis, E. S., Azad, N. S., Bardelli, A., Brem, H., Cameron, J. L., Lee, C. C., Fecher, L. A., Gallia, G. L., Gibbs, P., Le, D., Giuntoli, R. L., Goggins, M., Hogarty, M. D., Holdhoff, M., Hong, S. M., Jiao, Y., Juhl, H. H., Kim, J. J., Siravegna, G., Laheru, D. A., Lauricella, C., Lim, M., Lipson, E. J., Marie, S. K., Netto, G. J., Oliner, K. S., Olivi, A., Olsson, L., Riggins, G. J., Sartore-Bianchi, A., Schmidt, K., Shih, L. M., Oba-Shinjo, S. M., Siena, S., Theodorescu, D., Tie, J., Harkins, T. T., Veronese, S., Wang, T. L., Weingart, J. D., Wolfgang, C. L., Wood, L. D., Xing, D., Hruban, R. H., Wu, J., Allen, P. J., Schmidt, C. M., Choti, M. A., Velculescu, V. E., Kinzler, K. W., Vogelstein, B., Papadopoulos, N., and Diaz, L. A., 2014, "Detection of Circulating Tumor DNA in Early- and Late-Stage Human Malignancies", Sci. Transl. Med., 6(224), pp. 224ra24.
[32] Čelešnik, H., and Potočnik, U., 2023, "Plasma and Serum DNA Methylomes in Colorectal Cancer: Potential for Diagnosis and Liquid Biopsy", Cells, 12(13), pp. 1771.
[33] Scott, A. T., Weiss, M., Lisle, T. C., Moore, D. T., and Lich, K. H., 2023, "Precision Oncology's Greatest Challenges: Health System Implementation, Equitable Access, and Ethical Use", Cancer, 129(11), pp. 1641-1651.
[34] Bayle, A., Bonastre, J., Chaltiel, D., Besse, B., Garassino, M. C., Hendriks, L. E., Planchard, D., Remon, J., Reck, M., Sezer, A., Van Meerbeeck, J. P., Dziadziuszko, R., Smit, E. F., Novello, S., and Groen, H. J. M., 2023, "ESMO Study on the Availability and Accessibility of Biomolecular Technologies in Oncology in Europe", Ann. Oncol., 34(10), pp. 934-945.
[35] Drilon, A., Laetsch, T. W., Kummar, S., DuBois, S. G., Lassen, U. N., Demetri, G. D., Nathenson, M., Doebele, R. C., Farago, A. F., Pappo, A. S., Turpin, B., Dowlati, A., Brose, M. S., Mascarenhas, L., Federman, N., Berlin, J., El-Deiry, W. S., Baik, C., Krishnamurthy, J., Westin, S., Bauer, T. M., George, S., Kobos, R., Kumar, S., Cabanillas, M. E., Cho, B. C., Schuler, M., Santoro, A., Matano, A., Kubota, K., Kato, S., Meric-Bernstam, F., Shah, M., Russo, A., Huang, A., Ghiorghiu, S., Felicetti, B., Dai, D., Albert, C. M., Iyer, P., Liu, S. V., Hyman, D. M., Hong, D. S., and NAVIGATE investigators, 2018, "Efficacy of Larotrectinib in TRK Fusion-Positive Cancers in Adults and Children", N. Engl. J. Med., 378(8), pp. 731-739.
[36] Razavi, P., Li, B. T., Brown, D. N., Jung, B., Hubbell, E., Shen, R., Abida, W., Juluru, K., De Bruijn, I., Hou, C., Venn, O., Lim, R., Ananda, G., Hanson, H., Ulz, P., Plagnol, V., Heller, G., Benayed, R., Zehir, A., Chakravarty, D., Thesis, M., Zheng, Y., Ghossain, M., Murtaza, M., Snyder, A., Baselga, J., Lau, C., Lai, W. C., Schultz, N., Ladanyi, M., Viale, A., Norton, L., Weigelt, B., Smith, S., Lash, A., Robson, M., Hudis, C. A., Dickler, M., Offit, K., Rudin, C. M., Real, F. X., Donoghue, M., Janjigian, Y. Y., Diaz, L. A., Solit, D. B., Chung, W. K., Berger, M. F., Robson, M. E., Stadler, Z. K., and Reis-Filho, J. S., 2019, "High-Intensity Sequencing Reveals the Sources of Plasma Circulating Cell-Free DNA Variants", Nat. Med., 25(12), pp. 1928-1937.
[37] Merker, J. D., Oxnard, G. R., Compton, C., Diehn, M., Hurley, P., Lazar, A. J., Lindeman, N., Lockwood, C. M., Rai, A. J., Schilsky, R. L., Tsimberidou, A. M., Vasalos, P., Billman, B. L., Oliver, T. K., Bruinooge, S. S., Hayes, D. F., and Turner, N. C., 2018, "Circulating Tumor DNA Analysis in Patients with Cancer: American Society of Clinical Oncology and College of American Pathologists Joint Guideline", J. Clin. Oncol., 36(16), pp. 1631-1641.
[38] Aleshin, A., Zhi, L., Courtright, J., Cornfeld, M., and Mulkerin, D., 2017, "Racial Disparities Associated with the Use of Molecularly Targeted Therapies for Cancer", Mol. Diagn. Ther., 21(3), pp. 287-296.
[39] Le, D. T., Uram, J. N., Wang, H., Bartlett, B. R., Kemberling, H., Eyring, A. D., Skora, A. D., Luber, B. S., Azad, N. S., Laheru, D., Biedrzycki, B., Donehower, R. C., Zaheer, A., Fisher, G. A., Crocenzi, T. S., Lee, J. J., Duffy, S. M., Goldberg, R. M., de la Chapelle, A., Koshiji, M., Bhaijee, F., Huebner, T., Hruban, R. H., Wood, L. D., Cuka, N., Pardoll, D. M., Papadopoulos, N., Kinzler, K. W., Zhou, S., Cornish, T. C., Taube, J. M., Anders, R. A., Eshleman, J. R., Vogelstein, B., and Diaz, L. A., 2015, "PD-1 Blockade in Tumors with Mismatch-Repair Deficiency", N. Engl. J. Med., 372(26), pp. 2509-2520.
[40] Klein, E. A., Richards, D., Cohn, A., Tummala, M., Lapham, R., Cosgrove, D., Chung, G., Clement, J., Gao, J., Hunkapiller, N., Jamshidi, A., Kurtzman, K., Seiden, M. V., Swanton, C., and Liu, M. C., 2021, "Clinical Validation of a Targeted Methylation-Based Multi-Cancer Early Detection Test Using an Independent Validation Set", Ann. Oncol., 32(9), pp. 1167-1177.

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