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Editorial Article

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Personalized and Precision Oncology (PPO) via Cancer Pathology-related Modeling and IT-Assisted Clinical Practice to Prevent, to Treat and to Get Cured Cancer and Its Complications: A Role of Precision Cancer Pathology in the Era of PPO

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ABSTRACT

A new systems approach to diseased states and wellness result in a new branch in the healthcare services, namely, **Personalized and Precision Medicine** (PPM). To achieve the implementation of PPM concept, it is necessary to create a fundamentally new strategy based upon the recogni-tion of biomarkers and thus the targets to secure the grand future of drug design and drug dis-covery.

Each decision-maker values the impact of their decision to use PPM on their own budget and well-being, which may not necessarily be optimal for society as a whole. It would be extremely useful to integrate data harvesting from different databanks for applications to provide more tai-lored measures for the patients resulting in improved patient outcomes, reduced adverse events, and more cost-effective use of the latest health care resources including diagnostic (**companion** ones or **theranostics**), preventive and therapeutic (targeted molecular and cellular) etc.

Meanwhile, along with the impact of **genomics and bioinformatics, pathology** is the central specialty of PPM-related resources. Coupled with IT, the upgraded tools are ever more efficient and robust within clinical cancer settings. The latest algorithms may be able to identify and vali-date patterns which humans are not capable of quantifying easily, such as slight differences in textures or morphologies. In this sense, the impact of pathology allows a modular approach, as its various aspects are under development in several areas of PPM.

Among the above-mentioned medical specialists involved in PPM, the **pathologists** play an im-portant and key role in the implementation and development of PPM-driven resources that are in the center of decision of many therapeutic choices. Recent advances in systems biology have tremendously affected the practice of **precision pathology,** gradually transforming it from a morphology-based into a precise molecular-based discipline.

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The enormous development of precision pathology research (integrating molecular OMICS and digital approaches) has raised great expectations concerning its impact on PPM aiming to custom-ize medical practice with a focus on the individual, based on the use of molecular tests, identifi-cation of genomic biomarkers, and development of targeted drugs.

The precision pathology process introduces a new paradigm in pathology by leveraging digital imaging and IT technologies, and provides significant advancements in accuracy, efficiency, and collaboration. Among the latest innovations the precision pathology supported by digital tools, would dictate the implementation of high-resolution imaging, image analysis tools and integra-tion with molecular OMICS data. Integration of the approaches and resources will provide a true challenge for the future, requiring collaboration between oncologists, pathologists, biodesigners and bioengineers and remaining a challenge to precision cancer practice and profiled bioindustry.

The latter requires precision pathologists highly trained in pre-analytic processes, tumor area mi-crodissection for tumor cell enrichment, methodology analysis and results. The in-depth study of molecular alterations in patients allows optimizing molecular diagnosis and selecting candidates for receive novel treatments against specific molecular targets. These patients would benefit from multidisciplinary approach and learning. In this sense, molecular diagnostics has a long tradition in pathology, especially in clinical one, where various OMICS-analyses of cancers are incorpo-rated into diagnostic and decision-making algorithms to secure a way where the pathologists con-tinue to play an essential role in developing and implementing molecular profiling tests in practice and communicate the results and their relevance with cancer practitioners.

Cancer pathology is the central specialty of **personalized and precision oncology (PPO)**. Meanwhile, the combination of comprehensive biobanking and the next wave of **theranostic** pathology technologies provides a natural, externally visible infrastructure that now allows pa-thology as a discipline – to engage directly with the biotechnology and pharma sector. We're at an exciting junction in precision cancer pathology's growth as a medical specialty, and pathology-driven biobanking is becoming both central to our core expertise and, even more importantly, a powerful enabler for many of the most promising growth areas of our discipline: PPM healthcare, clinical trials and drug development, theranostics, and functional assessment and monitoring of disease. In the context of these changes and challenges, the **precision cancer pathology** can play a fundamental role in both PPO-guided clinical practice and biodesign-driven cancer research.

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Introduction

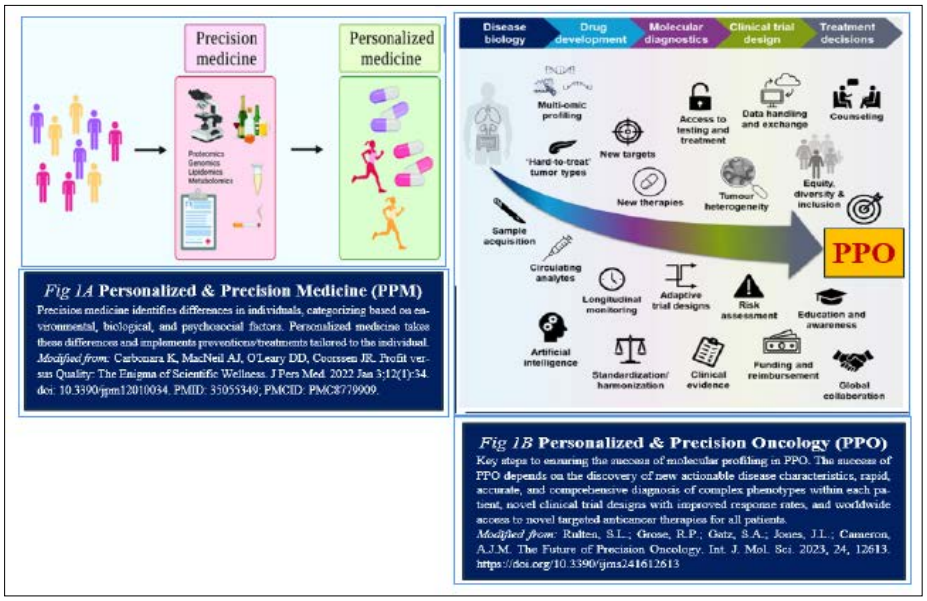
Cancer is a devastating disease that takes the lives of hundreds of thousands of people every year. Due to disease heterogeneity, standard treatments, such as surgery, chemotherapy or radia-tion, are effective in only a subset of the patient population. Meanwhile, over the course of its history, medicine and healthcare philosophy have given special attention to the already diseased individual, focusing on a type of clinically manifested disease (nosology) rather than on one's health or the so-called pre-illness conditions, whilst the latter left in the shade. Simultaneously, canonical cancer diagnosis hinged on the practice of traditional cancer pathology, relying on hu-man interpretations of patterns and morpholog. Daily oncology care has undergone a remarkable transformation over the past few decades. Today, advancements in biodesign-driven translational research and applications allow for a more nuanced understanding of cancer, leading to the de-velopment of PPM-guided cancer treatment plans. These plans are based on the individualized genetic makeup, lifestyle, and specific type of cancer.

Tumors can have different underlying genetic causes and may express different proteins as bi-omarkers in one patient versus another. The understanding of cancer biology has expanded, lead-ing to the development of targeted therapies. The latter has been shown significant success in certain types of cancer with improved outcomes and reduced side effects compared to conven-tional treatments [1].

Cancer immunotherapy has emerged as another pioneering approach, whilst using the body's im-mune system to recognize and attack cancer cells. Advances in PPM-guided cancer research, PPO and genomic profiling have enabled PPM-guided cancer treatment. By analyzing a tumor's genetic makeup, doctors can identify specific mutations or biomarkers and alter treatment ac-cordingly. This approach helps optimize treatment outcomes and minimize side effects.

In addition, innovative techniques such as minimally invasive surgery, robotic surgery, and im-age-guided radiation therapy have increased treatment accuracy, reduced complications, and im-proved patient recovery. This advancement in the field of cancer treatment has the potential to improve patient outcomes in the fight against cancer.

The shift towards personalized cancer treatment is driven by the realization that each cancer case is distinct. Factors such as genetic mutations, tumor biology, and patient health status play a cru-cial role in determining the most effective treatment strategy. This evolution in oncology care not only improves survival rates but also enhances the quality of life for patients.The practice of di-agnostic, predictive and prognostic cancer pathology has been substantially changed in the previ-ous years due to the advances in molecular diagnostics and targeted treatment (see below). For instance, there is an unmet need for novel and more reliable diagnostic, prognostic and predictive cancer tests given a low response rate and common resistance for most approved cancer targeted treatment modalities. By realizing along with precision genomics and the promise of digital and computational pathology with the use of intelligent software, some pathologists and labs will be in position to pursue limitless possibilities for their business, customers, cancer patients and even pre-cancer persons-at-. The improvement of methodology for genomic testing, for instance, has made it one of the cornerstones of Personalized and Precision Medicine (PPM) and PPM-guided Oncology, or Personalized and Precision Oncology (PPO), in particular (Figure 1A, B)!



PPM-guided clinical oncology or PPO, are evidence-based, individualized oncology that deliver the right care to the right cancer patient or pre-cancer persons-at-risk at the right time and results in measurable improvements in outcomes and a reduction on health care costs [2-6].

Our understanding of the molecular mechanisms underlying cancer development and evolution have evolved rapidly over recent years, and the variation from one patient to another is now widely recognized. While PPO has been very successful in the treatment of some tumors with specific characteristics, a large number of patients do not yet have access to precision cancer medicines for their disease. The success of PPO depends on the discovery of new actionable dis-ease characteristics, rapid, accurate, and comprehensive diagnosis of complex phenotypes within each patient, novel clinical trial designs with improved response rates, and worldwide access to novel targeted anticancer therapies for all patients.

The latter means that PPO encompasses a multifaceted approach to cancer treatment that inte-grates advanced genomic sequencing, molecular profiling (Figure 2),

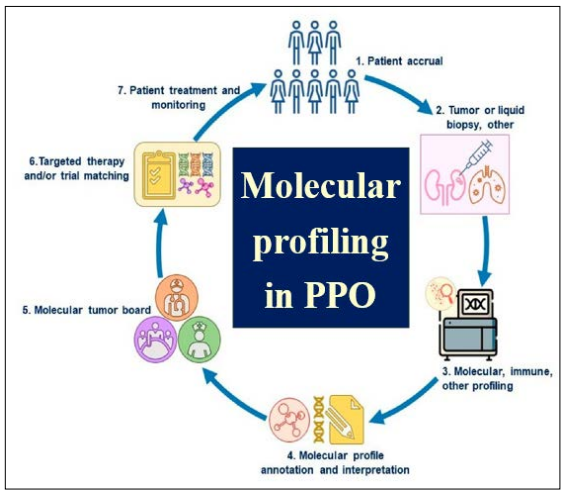


Figure 2: Overview of molecularprofiling in PPO

In the screening phase of a biomarker-driven trial, patients (1) undergo a tumor biopsy or blood draw (liquid biopsy) (2) that is used for tumor molecular profiling (3) to determine the drivers of carcinogenesis (genomic or protein level), if any (4). The molecular profile report is often discussed at a molecular tumor board (5) for the interpretation of tumor alterations and for matching with a targeted therapy or clinical trial (6). The patient is then treated with the assigned therapy (FDA-approved or inves-tigational drug after screening for clinical trial) and monitored for anti-tumor effects and toxicity (7). If the disease progresses, the next treatment can again be selected from a new round of tumor or blood analyses to identify evolving biomarkers.

Modified from: Song, I.-W.; Vo, H.H.; Chen, Y.-S.; Baysal, M.A.; Kahle, M.; Johnson, A.; Tsimberidou, A.M. Precision Oncology: Evolving Clinical Trials across Tumor Types. Cancers 2023, 15, 1967. https://doi.org/10.3390/cancers15071967

and computational analysis to identify targetable alterations driving tumor growth. By elucidat-ing the unique genetic mutations, gene expressions, and signaling pathways, identification of targets beyond standard of care, driving cancer progression, and potentially revolutionizing per-sonalized cancer management, including the clinical adoption of molecular profiling platforms, PPO enables clinicians to select therapies with greater likelihood of efficacy and minimal toxicity for each patient (canonical cancer therapies) or for a pre-cancer person-at-risk (preventive cancer therapies).

The developments in multi-OMICS technologies have improved PPO-driven clinical applications, making genomic analysis of tumors more affordable and accessible. And targeted NGS panels now enable the rapid identification of diverse actionable mutations, requiring clinicians to effi-ciently assess the predictive value of cancer biomarkers for specific treatments. Those techniques uncover genetic alterations, tumor heterogeneity, and the evolutionary dynamics of cancers. Ge-netic abnormalities and molecular markers that initiate and propagate distinct cancer types are classified according to tumor type. The integration of PPM resources with cancer genomics em-phasizes the significance of utilizing genetic data in treatment decision-making, enabling person-alized care and enhancing patient outcomes. Critical topics in cancer genomics encompass tumor diversity, alterations in non-coding DNA, epigenetic modifications, cancer-specific proteins, metabolic changes, and the impact of inherited genes on cancer risk.

The urgency for timely and accurate decision-making in PPO-guided clinical practice emphasizes the importance of reliable and profiled PPO-related software. Online clinical decision-making tools and associated cancer databases have been designed by consolidating genomic data into standardized, accessible formats. These new platforms are highly integrated and crucial for iden-tifying actionable somatic genomic biomarkers essential for tumor survival, determining corre-sponding drug targets, and selecting appropriate treatments based on the mutational profile of each patient's tumor. Future enhancements, incorporating AI algorithms, are likely to improve integration of the platforms with diverse big data sources, enabling more accurate predictions of potential therapeutic responses [7-21].

The applications of the above-mentioned modern approach, referred to PPO and PPM as a whole, are already becoming a staple in cancer care and will expand exponentially over the com-ing years. Practical guidelines on how to interpret and integrate OMICS-related information in the clinical setting, addressed to oncologists without expertise in cancer genomics, are currently limited. Building upon the genomic foundations of cancer and the concept of PPO, we are about to develop practical guidance to aid the interpretation of genomic test results that help inform clinical decision making for patients with cancer or pre-cancer persons-at-risk.

Personalized cancer treatment in particular stands to benefit from PPM-guided cancer therapies, since extensive variability between tumors presents a need to target each case in a personalized manner. Central to personalized cancer treatment is the comprehensive genomic profiling of tu-mors to identify actionable alterations and potential therapeutic targets. More precisely, genomic profiling of hundreds of cancer-associated genes is now a component of routine cancer care. The clinical adoption of molecular profiling platforms such as RNA sequencing better suited to iden-tifying those patients most likely to respond to immunotherapies and drug combinations will be critical to expanding the benefits of PPO-guided clinical practice.

Concurrently, biomarker discovery efforts aim to identify predictive biomarkers, such as muta-tions in genes like EGFR, ALK, and BRAF in lung cancer, to guide treatment selection and op-timize patient outcomes [22-29].

Underpinning PPO is the concept of somatic mutations as the foundation of cancer development. Mutations in oncogenes rendering them constitutively active are considered driver mutations and are central control points for progression of malignancies. Conversely, tumor suppressor genes, involved naturally in controlling tumor pathogenesis, can cause cancer progression when inacti-vated through mutation or allele loss. Multiple processes result in dysregulation of the genetic machinery in DNA RNA or protein, leading to altered expression of the protein coded for by the gene, whilst forming the endophenotype and thus a set of specific functions illustrating the phe-notype (Figure 3).

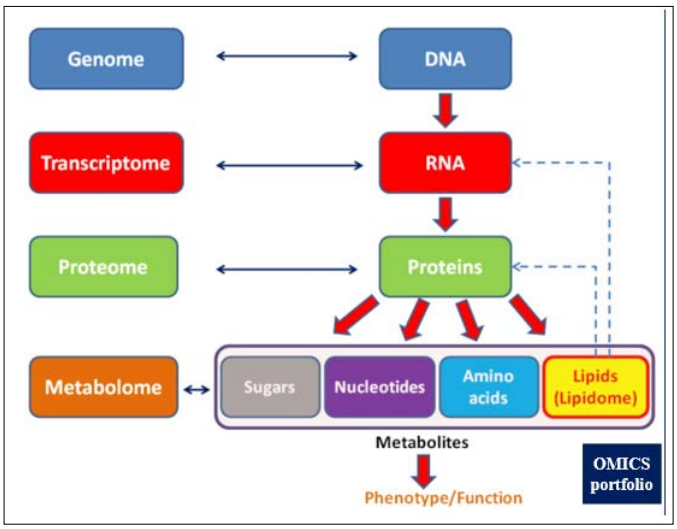


Figure 3: OMICS portfolio

OMICS sciences and PPO-guided cancer practice hold great promise for identifying new thera-peutic targets and developing more effective treatments for cancer. Studies integrating OMICS protfolio have shown early promise in enhancing prognostic and therapeutic outcomes for various cancer subtypes and providing insight into fundamental pathophysiological mecha-nisms occurring at different molecular levels. Multi-OMICS approaches are novel frameworks that integrate multiple OMICS datasets generated from the same patients to better understand the molecular and clinical features of cancers. A wide range of emerging omics and clustering algorithms now provide unprecedented opportunities to further classify cancers into subtypes, improve the survival prediction and therapeutic outcome of these subtypes, and understand key pathophysiological processes through different molecular layers.

Modified from: Xiao Y, Bi M, Guo H, Li M. Multi-omics approaches for biomarker discovery in early ovarian cancer diagnosis. EBioMedicine. 2022 May;79:104001. doi: 10.1016/j.ebiom.2022.104001. Epub 2022 Apr 16. PMID: 35439677; PMCID: PMC9035645, Nam AS, Chaligne R, Landau DA. Integrating genetic and non-genetic determinants of cancer evolution by

single-cell multi-omics. Nat Rev Genet. 2021 Jan;22(1):3-18. doi: 10.1038/s41576-020-0265-5. Epub 2020 Aug 17. PMID: 32807900; PMCID: PMC8450921, and Ma C, Wu M, Ma S. Analysis of cancer omics data: a selective review of statistical tech-niques. Brief Bioinform. 2022 Mar 10;23(2):bbab585. doi: 10.1093/bib/bbab585. PMID: 35039832.

To capture the entire spectrum of potential alterations, multiple technologies, termed a multi-OMICS approach, are best considered [30].

Nowadays, the increasing availability of OMICS and related data, due to both the advancements in the acquisition of biodesign-inspired translational application results and in systems biology simulation technologies, provides the bases for PPO and PPM as a whole. As you see from the above-mentioned, biomarker-driven targeted therapies constitute a cornerstone of personalized cancer treatment, designed to specifically inhibit molecular targets implicated in cancer patho-genesis. These therapies include small molecule inhibitors and monoclonal antibodies that selec-tively target oncogenic proteins or signaling pathways essential for tumor survival and growth. By precisely targeting the vulnerabilities of cancer cells, targeted therapies offer the potential for improved efficacy and reduced off-target toxicity compared to conventional chemotherapy. An-other groundbreaking advancement in personalized PPO-guided cancer treatment is the advent of immunotherapy, which harnesses the body's immune system to recognize and eliminate cancer cells. The development of targeted therapies is increasingly feasible due to tumor-agnostic treat-ments, such as PARP inhibitors in patients with BRCA1, BRCA2 or PALB2 alterations or im-munotherapies in patients with high microsatellite instability/tumor mutational burden. In addi-tion, other therapeutic molecules have been developed for patients with KRAS G12C mutation or fusions in NTRK or NRG1 [31-38].

Interest in immunotherapy for cancer has surged due to its precise targeting of cancer cells and minimized impact on surrounding healthy tissues. The latter explores DNA and RNA-based vac-cines, T-cell modifications, adoptive cell transfer, CAR T cell therapy, angiogenesis inhibitors, and the combination of immunotherapy with chemotherapy, offering a holistic view of the poten-tial in cancer treatment. Additionally, it discusses the role of nanotechnology in increasing the efficacy of cancer-targeting drugs, as well as cytokine and immunoconjugate therapies for bol-stering immune system effectiveness against neoplastic cells. PPO-guided immunotherapies are a promising frontier in cancer treatment, offering the potential for more personalized and effective therapeutic strategies. Despite existing challenges, ongoing research and clinical trials are funda-mental for overcoming current limitations and enhancing the efficacy of immunotherapies in can-cer care. In-depth exploration of tumor biology, using novel technologies such as OMICS sci-ence, can help decode the role of the tumor immune microenvironment in producing a response to the immune blockade strategie, and can also help to identify biomarkers for patient stratification and personalized immunotherapies [39-50].

PPM and PPO have achieved remarkable successes in the treatment of cancer, having marked a significant change in the study of cancer mechanisms and approaches to treating cancer. A com-prehensive personalized cancer treatment plan involves several key components that work togeth-er to provide optimal care.

These components include: **genetic testing and genomic profiling:** understanding the genetic profile of the cancer helps in identifying targeted therapies that are most likely to be effective –

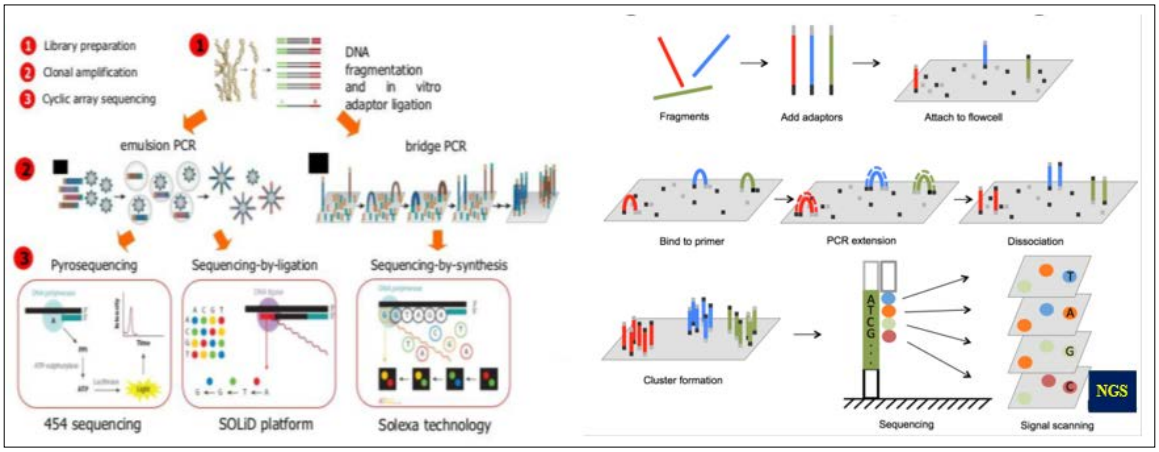


Figure 4: Next-generation sequencing (NGS)

Next-generation sequencing (NGS) technologies are high-throughput methods for DNA sequencing and have become a widely adopted tool in cancer research. The sheer amount and variety of data generated by NGS assays require sophisticated computational methods and bioinformatics expertise. NGS of tumor cell-derived DNA/RNA to screen for targetable genomic alterations is now widely available and has become part of routine practice in oncology. NGS testing strategies depend on cancer type, disease stage and the impact of results on treatment selection. By combining complementary methods with massively parallel DNA sequencing, a greater insight into the biological context of cancer and pre-cancer mechanisms is now possible. Emerging methodologies, such as advances in nanopore technology, in situ nucleic acid sequencing, and microscopy-based sequencing, will continue the rapid evolution of this area. These new technologies hold many potential applications for cancer and pre-cancer conditions, with the promise of precision and personalized cancer care in the future. Comprehensive annotated databases are available for clinicians to review the information detailed in the NGS report

Modified from: Gindin T, Hsiao SJ. Analytical Principles of Cancer Next Generation Sequencing. Clin Lab Med. 2022 Sep;42(3):395-408. doi: 10.1016/j.cll.2022.04.003. Epub 2022 Aug 22. PMID: 36150819, Schmid S, Jochum W, Padberg B, Demmer I, Mertz KD, Joerger M, Britschgi C, Matter MS, Rothschild SI, Omlin A. How to read a next-generation sequencing report-what oncologists need to know. ESMO Open. 2022 Oct;7(5):100570. doi: 10.1016/j.esmoop.2022.100570. Epub 2022 Sep 29. PMID: 36183443; PMCID: PMC9588890, and Larson NB, Oberg AL, Adjei AA, Wang L. A Clinician's Guide to Bioinformatics for Next-Generation Sequencing. J Thorac Oncol. 2023 Feb;18(2):143-157. doi: 10.1016/j.jtho.2022.11.006. Epub 2022 Nov 12. PMID: 36379355; PMCID: PMC9870988.

comprehensive genomic profiling of tumors through next-generation sequencing (NGS) (Figure 4)

will identify somatic mutations, copy number variations, and gene expression patterns;

- **Risk Assessment and Management:** evaluating the patient's family history and lifestyle fac-tors to assess cancer risk and tailor prevention strategies – bioinformatics algorithms will be employed to analyze complex datasets, including genetic information, clinical out-comes, and radiological images, which, by integrating data from various sources, will provide predictions on the effectiveness of specific cancer therapies, enabling the cus-tomization of treatment plans for individual cancer patients or pre-cancer persons-at-risk;
- **Targeted Therapy and Immunotherapy:** based on the molecular data obtained, the PPM- and PPO-driven model will recommend targeted therapies aimed at specific mutations and immunotherapies that activate the immune system to recognize and attack cancer cells;
- **Real-Time Monitoring and Adaptive Treatment Plans:** will leverage wearable devices and biomarkers to monitor patients' responses to treatment continuously - adaptive treatment strategies will be employed, adjusting therapies based on the real-time data to maximize effi-cacy and minimize adverse effects;
- **Multidisciplinary Team Approach:** collaboration among oncologists, biodesigners, radiolo-gists, surgeons, and other specialists ensures a holistic treatment plan – patients will be active-ly involved in decision-making, ensuring that treatments align with their preferences and val-ues;
- **Patient Preferences:** considering the patient's values and preferences in treatment decisions enhances satisfaction and adherence to the treatment plan.

In the context of those changes and challenges, the today's **cancer pathology** can play a funda-mental role in both clinical practice and research. Cancer pathology is the central specialty of personalized and precision oncology (PPO), which is an innovative approach to cancer treatment and ensuring the treatment to be specifically designed and targeted to the unique form of cancer. In this sense, molecular cancer diagnostics has deep roots in precision cancer pathology, where vari-ous OMICS-analyses of cancers are being incorporated into diagnostic and decision-making algorithms to secure a way where the pathologists continue to play an essential role in developing and implementing molecular profiling tests in practice and communicate the results and their rele-vance with clinician [52-61].

With innovative tools and making use of the collaboration of new professional figures, cancer pathologists can take today on a guiding role in the diagnostic-therapeutic process of cancer patients and pre-cancer persons-at-risk, allowing the combinatorial characterization of the individual tumors in a complete way. In this sense, precise diagnostics has a long tradition in cancer pathology. The improvement of methodology for genomic testing and molecular profiling as a whole has made it one of the cornerstones of PPM-related cancer medicine - various genomic analyses of human cancers are being incorporated into diagnostic and decision-making algorithms. In this context, clinical workflows in PPO rely on predictive and prognostic molecular biomarkers. However, the growing number of those complex biomarkers tends to increase the cost and time for decision-making in routine daily oncology practice; furthermore, biomarkers often require tumor tissue on top of routine diagnostic material.

In this sense, tumor and cell-free DNA profiling, immune markers, and proteomic and RNA analyses are used to identify these characteristics for optimization of anticancer therapy in individual cancer patients or pre-cancer person-at-risk. Consequently, clinical trials have evolved, shifting from tumor type-centered to gene-directed, precision pathology-agnostic, with innovative adaptive design tailored to biomarker and biomarker-driven targeted profiling with the goal to improve treatment outcomes [62,63].

Among many medical specialists involved in PPO today and in the nearest future, the pathologists would play a unique role in the implementation and development of PPO-driven resources that are in the center of decision of many therapeutic choices. The advances in systems biology have tremendously affected the practice of cancer pathology, gradually transforming it from a morphology-based into a precise molecular-based discipline.

Modern pathologists support biodesign-driven translational research and want to help their cancer patients and pre-cancer persons-at-risk enroll in clinical trials. The medical community believe regulators, pathologists, oncologists, investigators, and clinical trial sponsors can adjust current practices to alleviate these concerns and provide cancer patients and pre-cancer persons-at-risk with a much clearer understanding of the risks and benefits to them without compromising the ability of investigators and sponsors to efficiently conduct clinical trials and correlative science. Pathologists are becoming the caretakers of all tissues removed during clinical care. And there are national, state and local laws governing how pathologists must treat those tissues. So, **precision** pathologists have occupied an unusual position in this arena.

The advances in science and technology and focused interest in cancer research have provided ample opportunities for pathologists to participate in better understanding of the basic fundamen-tal cascade of events leading to tumorigenesis – they also partnered with their oncologists and drug designers to find more effective therapeutic options. The improvement of methodology for genomic testing in recent years has made it one of the cornerstones of PPO-guided clinical prac-tice and cancer care. The decisions related to cancer treatments are no longer solely based on the histopathological diagnosis. Various genomic analyses of human cancers are being incorporated into diagnostic and decision-making algorithms. This change has been possible with recognition of the fact that canonical and simple morphology alone may not be sufficient to tell the entire story of clinical behavior of cancer patients. In addition, the realization of heterogeneity of can-cer

endophenotypes and the differences in the expression of various biomarkers and the observed differences in response to therapy have resulted in extensive efforts to better define the charac-ters of each cancer subtype. This remarkable change in the role of the pathologist require the in-volvement in the modern taxonomy of cancer or pre-cancer conditions, and to rise to the chal-lenge of genomic profiling approaches and molecular diagnostics, which are the fastest growing areas of PPO-guided clinical care and PPM as a whole. Emphasis should be also placed to create a new precision pathology and to train pathologist of the next-step generation to expand beyond morphology and to embrace the power of molecular diagnostics, in order to be able to get effec-tive practice in the era of PPM (Figure 5) [64].

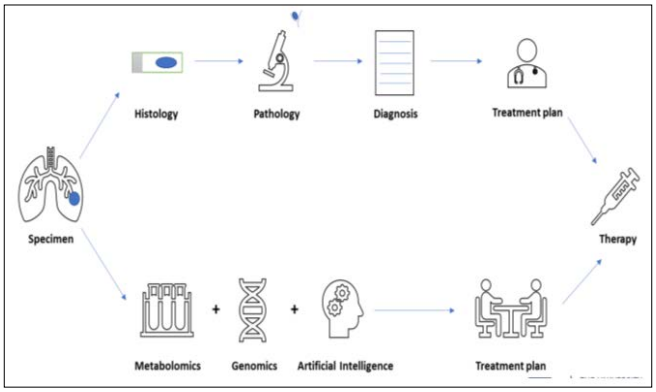


Figure 5: Traditional pathology versus precision pathology

The pathologists continue to play an essential role in developing and implementing molecular and ge-nomic tests in practice and communicate the results and their relevance with clinicians. Such activities are of utmost importance for successfully translating scientific advancements into a benefit to patients ("next-generation pathologists"). Modified from: Vranic S, Gatalica Z. The Role of Pathology in the Era of Personalized (Precision) Medicine: A Brief Review. Acta Med Acad. 2021 Apr;50(1):47-57. doi: 10.5644/ama2006-124.325. PMID: 34075763.

Personalized and Precision Medicine in Cancer [65-75].

The essence of PPO lies in the applications of cancer-related biomarkers, which can be from tis-sue, serum, urine or imaging, and must be validated. Three different types of biomarkers are of particular importance: predictive, prognostic and pre-early response biomarkers (Figure 6A-C).

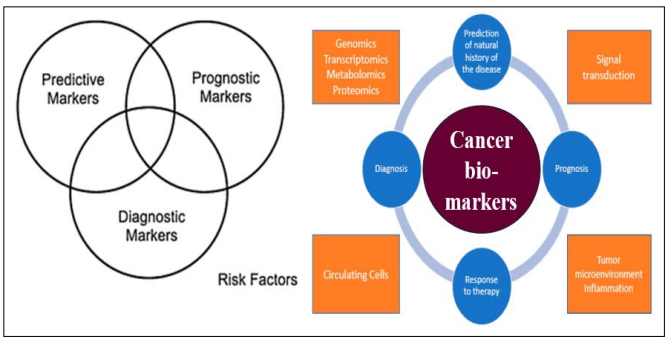
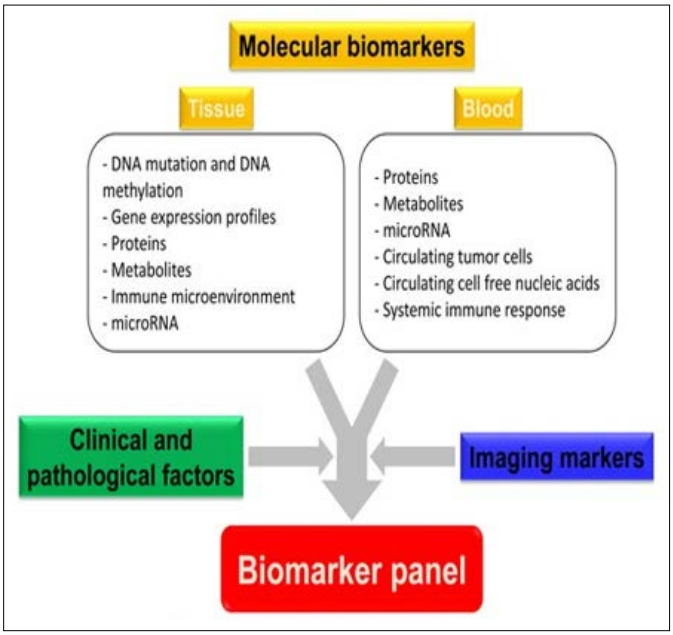


Figure 6A-C: Illustration of the Spectrum and Variability of Biomarkers Involved in the Diag-nosis, Prognosis, and Prediction of Cancer



Biomarkers, being genes, proteins, or other substances, have been identified as important tools in the diagnosis and management of cancer. Despite the increasing number of biomarkers described in the literature, most of them have demonstrated moderate sensitivity and/or specificity and are far from being considered as screening and/or monitoring tests. More efficient non-invasive bi-omarkers are needed to facilitate pre-early (subclinical) stage diagnosis and targeted interven-tions. Integration of diverse types of biomarkers including clinicopathological and imaging fea-tures, identification of links to tumor biology, and rigorous validation using samples which repre-sent disease heterogeneity, will allow to develop a sensitive and cost-effective molecular bi-omarker panel for PPO- and PPM-guided cancer practice. Multidisciplinary collaboration might be required to facilitate the identification of such markers.

Modified from: In terms of the above-mentioned terms, **molecular pathology and precision pathology** are utilizing **molecular** techniques, but the molecular one focuses on **cancer diagno-sis**, and the **precision** one does it on the **cancer therapy**. Molecular pathology provides support-ing evidence for cancer diagnosis (including predictive and prognostic aspects), precision pathol-ogy provides biomarker-driven therapeutic targets and pharmacOMICS for optimally managing cancer patients or pre-cancer persons-at-risk [76-78].

In this context, cancer biomarkers are the key to unlocking the promise of PPO, selecting which patients will respond to a more personalized treatment while sparing non-responders the therapy-related toxicity. In cancer, a biomarker refers to a substance or process that is indicative of the presence of cancer in the body (Figure 7A-C).

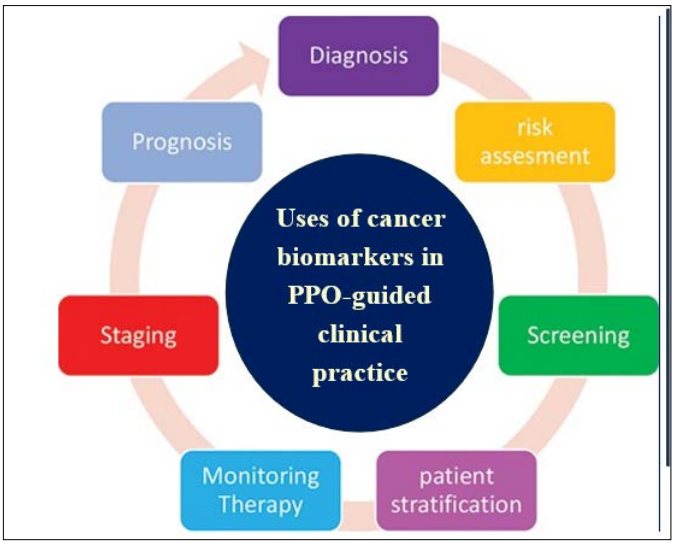


Figure 7A: Classification of cancer biomarkers on profiled criteria Several attempts have been made to define and classify cancer biomarkers using different approaches, but general consensus has yet to be established. Broadly, any biologically derived entity or processes which lead to a cancer diagnosis (in prognosis, screening and risk assessment), at the stage of diagnosis or post diagnosis (in therapy and treatment module) are potential candi-dates as cancer biomarkers. Due to the vast explosion of knowledge over the past several decades, collectively and in multiple spheres of the biomedical sciences and technology development, different methods have been suggested to classify cancer biomarkers. But these classifications should be considered contextual as identification of cancer biomarkers is one of the major multidisciplinary areas of the biomedical field.

Modified from: Mishra, A.; Verma, M. Cancer Bi-omarkers: Are We Ready for the Prime Time? Cancers 2010, 2, 190-208. https://doi.org/10.3390/cancers2010190

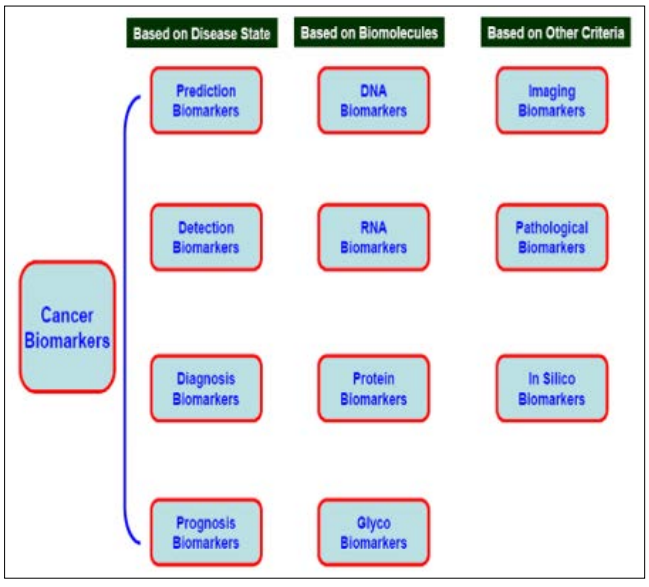


Figure 7B: Clinical utility and uses ofcancer biomarkers in PPO-guided clinical practice Clinical applications and uses of cancer bi-omarkers, as simply illustrated in Fig 4B, are screening and early detection, diagnostic confir-mation, prognosis and prediction of therapeutic response, and monitoring disease and recurrence. Another use of cancer biomarkers includes can-cer susceptibility and risk assessment markers which include the identification of individuals who are at a high risk of developing cancer or candidates for screening programs and early preventive applications.

Modified from: Kamel, Hala Fawzy Mohamed, and Hiba Saeed Bagader Al-Amodi. 2016. 'Can-cer Biomarkers'. Role of Biomarkers in Medi-cine. InTech. doi:10.5772/62421.

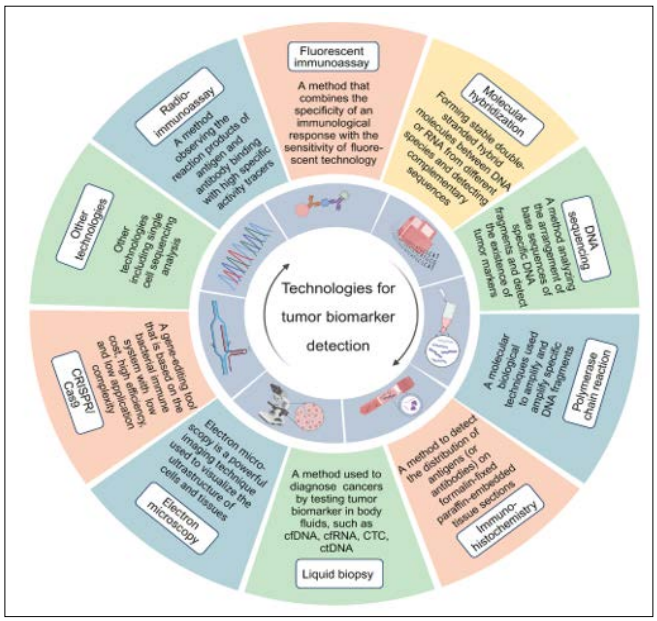


Figure 7C: Technologies for the detection of tumor biomarkers Cancer biomarkers are mostly found in body fluids including blood, urine, saliva, and also in cancer tissues. The detection of cancer biomarkers involves various advanced meth-ods, each tailored to identify specific types of biomarkers with high sensitivity and specific-ity. Techniques like immunohistochemistry, liquid biopsy, mass spectrometry and others have revolutionized the field, offering in-sights into the molecular and genetic under-pinnings of cancer. This allows for more personalized and targeted therapies, ultimate-ly improving patient outcomes.

Modified from: Zhou, Y., Tao, L., Qiu, J. et al. Tumor biomarkers for diagnosis, progno-sis and targeted therapy. Sig Transduct Target Ther 9, 132 (2024). https://doi.org/10.1038/s41392-024-01823-2

Genetic, epigenetic, proteomic, and imaging biomarkers can be used for cancer diagnosis, prog-nosis and epidemiology. Cancer patients and pre-cancer persons-at-risk must be placed firmly at the center of a cancer biomarker informed PPO-driven care agenda [79]. In this context, cancer biomarkers are any measurable molecular indicator of risk of cancer, occurrence of cancer, or pa-tient outcome. They may include germline or somatic genetic variants, epigenetic signatures, tran-scriptional changes, and proteomic signatures. These indicators are based on biomolecules, such as nucleic acids and proteins, that can be detected in samples obtained from tissues through tu-mor biopsy or, more easily and non-invasively, from blood (or serum or plasma), saliva, buccal swabs, stool, urine, etc. And thousands of species of RNAs, proteins, and metabolites are sug-gested as candidate tumor biomarkers alone or as constituents of multiplex signatures. If the pa-tient is already diagnosed with a certain cancer, RNA or protein biomarker signatures may help to select a specific therapy or to predict the probability of a relapse. Meanwhile, detection technolo-

gies have advanced tremendously over the last decades, including techniques such as next-generation sequencing, nanotechnology, or methods to study circulating tumor DNA/RNA or exosomes.

Biomarkers have many potential applications in PPO-guided cancer practice, including risk as-sessment, securing genetic risk prediction tools for a wide array of cancer, screening and differential diagnosis, determination of prognosis, prediction of response to treatment, and monitoring of progression of cancer. In addition, improved patient outcomes with the use of the biomarker tests must consider not only increased survival or quality of post-cancer life, but also improved clinical

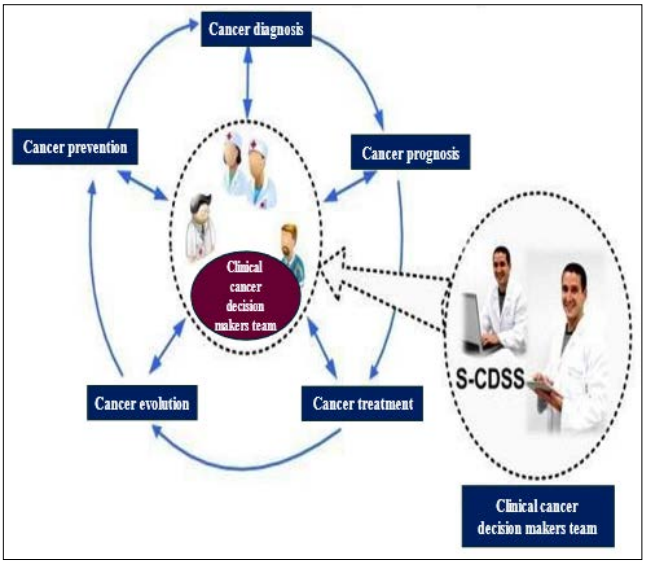


Figure 8: Clinical cancer decision support systems

Clinical decision support (CDS) tools has the potential to improve guideline adherence, cancer patient-centered care, and care delivery processes in clinical cancer care. A solution to this challenge is multifactorial CDSSs, contin-uously learning artificial intelligence platforms that integrate all available data - clinical, imag-ing, biologic, genetic, cost - to produce vali-dated predictive models. CDSSs compare the personalized probable outcomes - toxicity, tumor control, quality of life, cost effective-ness - of various care pathway decisions to ensure optimal efficacy and economy. DSSs can be integrated into the workflows both strategically (at the multidisciplinary tumor board level to support treatment choice, eg, surgery or radiotherapy) and tactically (at the specialist level to support treatment technique.

Modified from: Abdulwadud Nafees, Maha Khan, Ronald Chow, Rouhi Fazelzad, Andrew Hope, Geoffrey Liu, Daniel Letourneau, Srini-vas Raman. Evaluation of clinical decision support systems in oncology: An updated systematic review,
Critical Reviews in Oncology/Hematology, Volume 192, 2023, 104143, ISSN 1040-8428, https://doi.org/10.1016/j.critrevonc.2023.104143

decision support (CDS) & making (Figure 8)

leading to the avoidance of unnecessary therapy or toxicity captured within the rapid learning system. Each decision-maker values the impact of their decision to use PPM & PPO on their well-being, which may not necessarily be optimal for society as a whole.

The implementation of high-quality CDS is integral to ensuring the delivery of quality cancer care and subsequently achieving positive patient outcomes. Generating guideline-based recommenda-tions during multidisciplinary team (MDT) meetings in cancers is getting more complex due to increasing amount of information needed to follow the guidelines [80-85].

CDSSs are being continuously developed and integrated into routine clinical practice as they assist oncologists and oncoradiologists in dealing with an enormous amount of medical data, re-duce clinical errors, and improve diagnostic capabilities. They assist detection, classification, and grading of tumors as well as alert physicians of treatment change plans. It would be extremely useful to integrate data harvesting from different databanks for applications such as prediction and personalization of further treatment to thus provide more tailored measures for the patients resulting in improved patient outcomes, reduced adverse events, and more cost-effective use of the latest health care and diagnostic resources including diagnostic (companion ones), preventive and therapeutic (targeted molecular and cellular) etc. Moreover, the integration of biobanking with AI has the potential not only to expand the current understanding of cancer biology but also to pave the way for more precise, patient-centric healthcare strategies in pre-selecting the optimal PPO-guided multi-targeted therapy [86].

Moreover, biomarker-driven molecular subtyping has important prognostic and therapeutic impli-cations, and should guide cancer patient management, which is a molecularly driven disease. With the advancement of molecular sequencing techniques, genomic precision through the identi-fication of potential treatment targets and predictive biomarkers has been rapidly evolving. And advances in precision genomics have begun to propel PPM forward in the management of ad-vanced cancers, allowing for a more precise, biomarker-driven treatment selection with the goal of improving overall efficacy.

Remarkable progress has been made in the development of biomarker-driven targeted therapies for patients with multiple cancer types, including melanoma, breast and lung tumors. Systemic therapies for treatment of advanced/metastatic cancer should be biomarker-driven, when appro-priate, and thus current FDA approved treatments include HER2-targeted therapy, immunother-apy, and chemotherapy, but would require molecular profiling. Meanwhile, through investigating biomarkers of resistance and response, opportunities arise to discover new therapeutic targets and shape personalized treatment strategies [87-97].

Because of the critical role that biomarkers play at all stages of disease, it is important that they undergo rigorous evaluation, including analytical validation, clinical validation, and assessment of clinical utility, prior to incorporation into routine clinical care. In this review we address key steps in the development of biomarkers, including ways to avoid introducing bias and guidelines to follow when reporting results of biomarker studies. Meanwhile, biomarker testing isn't helpful yet for all types of cancer. But as more is learned about what causes cancer cells to grow and as new cancer treatments are developed, biomarker testing will become even more important for precision pathology-related diagnosis.

Some biomarkers can be useful in helping to determine if a person is at higher risk for cancer (pre-cancer persons-at-risk). Identifying cancer risk groups by multi-OMICS has attracted oncologists in their quest to find biomarkers from diverse risk-related OMICS.

Stratifying the individuals into cancer risk groups using genomics is essential for clinicians for prevention treatment to im-prove the survival time for patients and identify the appropriate therapy strategies [98-100].

Genomic technologies have facilitated the comprehensive characterization of the cancer genome and genetic biomarkers. Examples of genetic biomarkers include:
(i) detection of circulating tumor DNA (i.e. liquid biopsies) via blood samples provides a nonin-vasive method for detection and prognosis of cancer;
(ii) BRAFV600VE mutation in melanoma predicts sensitivity to BRAF inhibitors (e.g. vemuraf-enib, dabrafenib, or trametinib).
(iii) ALK gene rearrangement in lung cancer predicts response to crizotinib [101-102].

Epigenetic Biomarkers: Changes resulting from epigenetic modifications can accumulate throughout life and can be passed on through generations, whilst generating epigenomics-related risks, including the predisposition to disease. The role of epigenetics in human cancer has become an area of intensive research due to the growing understanding of specific epigenetic pathways, identification of epigenetic biomarkers, and rapid development of detection technologies. For instance, abnormal methylation can predispose cells to a precancerous stage by inactivating tumor suppressor genes and cell cycle regulatory genes (via hypermethylation) and reactivating onco-genes (via hypomethylation) within the promoter region.
The other example are **polygenic risk scores (PRS) (Figure 9A, B),**

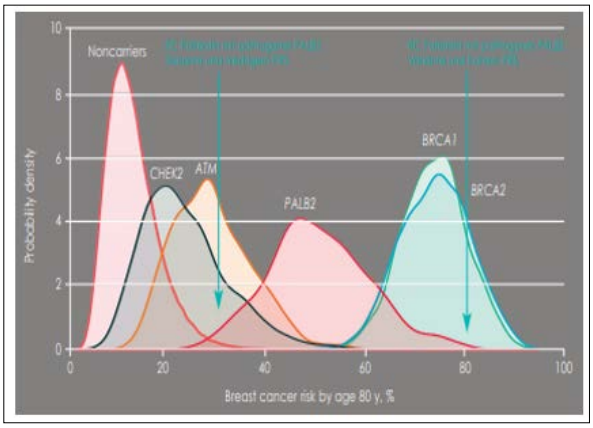


Figure 9A: Polygenic Risk Score (PRS) –Breast Cancer

Risk distribution for breast cancer as a function of PRS for different patient groups. Non-Carriers: distribution in the general population without pathogenic variants in BRCA or other genes. Risk distribution with pathogenic variant in one of the genes CHEK2, ATM, PALB2, BRCA1 or BRCA2 depending on PRS. (adapted from Gallagher et al. JAMA Netw Open. 2020;3(7):e208501. doi:10.1001/jamanetworkopen.2020.8501). Genetic factors contribute to breast cancer risk: (i) pathogenic variants in BRCA1 or BRCA2 are examples of monogenic factors; (ii) SNPs are polygenic factors: sequence variants that individually have a minimal effect on breast cancer risk; their combined effect is called a polygenic risk score (PRS). In the detection of high risk, PRS contributes in the following scenarios: (i) presence of a pathogenic variant in CHEK2 or ATM for which high-risk screening is not recommended per se; breast cancer prior to 45 years of age without evidence of a pathogenic variant in BRCA1, BRCA2, or PALB2; (iii) BOADICEA calculations for positive family history without evidence of pathogenic variants.

Modified from: https://www.mgz-muenchen.com/beyond-exome/polygenic-risk-score-breast-cancer

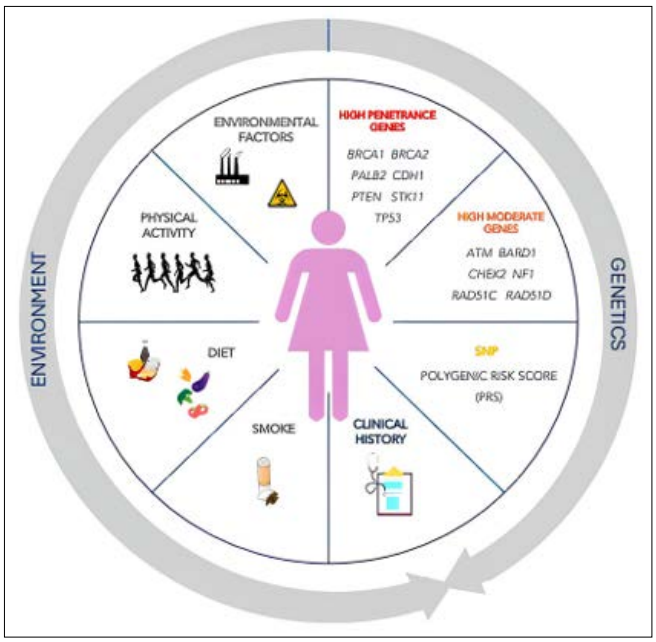


Figure 9B: Polygenic Risk Score (PRS) - outline of genetic and environmental factors influencing the polygenic risk of developing breast cancer

According to the WHO, subclinical diagnosis and treatment are key to improving outcomes and survival rates. Improved awareness of risk factors can contribute significantly to early diagnosis and better management of the disease. The pathogenesis of breast cancer is the result of a complex interaction of several factors. A small percentage of all women with breast cancer (5%-10%) have a genetic predisposition that gives them an increased risk of devel-oping the disease. This predisposition is due to the presence of pathogenic mutations in high- and moderate-risk breast cancer susceptibility genes, such as BRCA1/BRCA2 and other genes such as PALB2, CDH1, PTEN, STK11, TP53 (higher relative risk of cancer or highly actionable), and ATM, BARD1, CHEK2, RAD51C, RAD51D, NF1 (moderate relative risk of cancer or potential impact for therapy/change in medical management), or the presence of breast cancer-associated common SNPs, each weighted according to its association with breast cancer risk. Non-genetic risk factors include environmental and lifestyle factors such as alcohol consumption, obesity, lack of physical activity, exposure to radiation, use of exogenous female hormones [e.g., menopausal hormone therapy and hormonal contraceptives], and reproductive factors (early menarche and late menopause)

Modified from: Anaclerio F, Pilenzi L, Minelli M, Giansante R, Cicirelli M, Scorrano V, Antonucci I, Stuppia L. The polygenic risk score in the breast cancer treatment. J Transl Genet Genom. 2024;8:328-39. http://dx.doi.org/10.20517/jtgg.2024.60

which, being a new type of genetic predisposition, are a newer tool available in the clinical land-scape that can assign a level of risk to your patient in a disease, or phenotype-specific manner. In clinical reality, PGS have been developed for cancer risk-estimation and show potential as tools to prompt earlier referral for high-risk individuals and aid risk-stratification within cancer screen-ing programs.

For instance, identifying women at high epithelial ovarian cancer risk can inform personalized decisions on risk-reducing surgery and can facilitate early detection strategies. Meanwhile, in-cluding breast cancer-associated SNPs in risk assessment can provide more accurate risk predic-tion than family history alone and can influence recommendations for cancer screening and pre-vention modalities for high-risk women [103].

In this context, GWAS have identified associations between common genetic variants, SNPs and the risk of developing different cancers. Proponents argue that PRS testing, based on panels of risk SNPs, will revolutionize the prevention and early detection of cancer through individualized risk management strategies and streamlining of the current 'one-size-fits all' population screening programs [104-112].

Having access to genomic information and IT-driven and guided management of the latter will become increasingly important as oncologists and precision pathologists are progressively recep-tive to incorporating genomics and bioinformatics into PPO-guided clinical practice to predict cancer and pre-cancer risks. And a combination of genomic and phenotypic biomarkers are be-coming of great significance to be applied in PPO and need to be translated urgently into the daily PPO-guided practice.

As you see from the above-mentioned, OMICS technologies have expanded horizontally to in-clude single-cell genome, epigenome, proteome, and metabolome, while vertically, they have progressed to integrate multi-OMICS data and incorporate additional information such as spatial and **single-cell OMICS** approaches, representing a groundbreaking advancement in the cancer research and PPO-guided clinical practice, offering profound insights into the understanding of cancers [112.113]. (Figure 10).

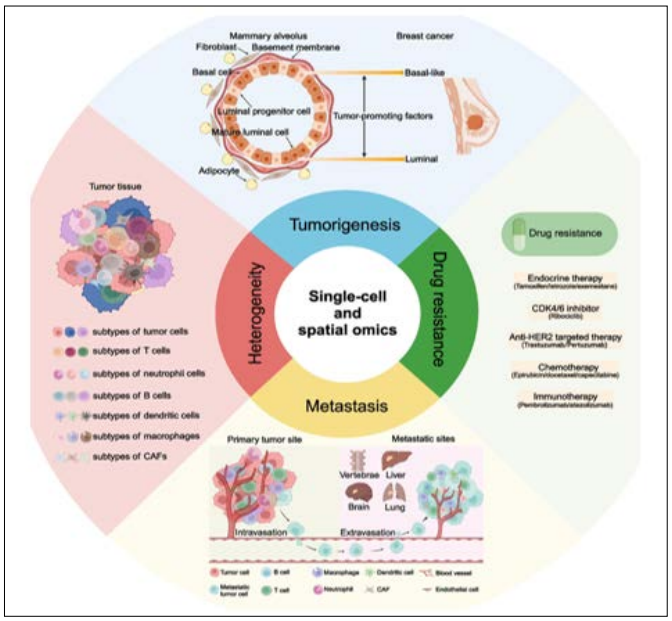


Figure 10: Overview of the application of single-cell and spatial OMICS in breast cancer

The emergence of single-cell sequencing (SCS) and spatial OMICS technology has introduced novel approaches for gaining comprehensive insights into the biological behavior of malignant tumors. The application of those technologies enables the elucida-tion of the origin, heterogeneity, and underlying mechanisms governing metastasis and drug re-sistance in breast cancer.

Abbreviations: CAF, Cancer-associated fibroblast

Modified and adapted from: Xiong, X., Wang, X., Liu, CC. et al. Deciphering breast cancer dynamics: insights from single-cell and spatial profiling in the multi-omics era. Biomark Res 12, 107 (2024). https://doi.org/10.1186/s40364-024-00654-1

Multi-OMICS approaches hold the promise of improving diagnostics, prognostics and personal-ized cancer canonical and pre-cancer preventive treatment. Thus, a fundamental computational approach for analyzing multi-OMICS data is differential analysis, which identifies molecular distinctions between cancerous and normal tissues. To deliver on this promise of PPO, appropri-ate bioinformatics methods for managing, integrating and analyzing large and complex data are necessary.

Advances in bioinformatics-driven technology have enabled the extraction of previously hidden information directly from routine histology images of cancer, providing potentially clinically use-ful information. For instance, molecular imaging analysis tasks include detection, grading and subtyping of tumor tissue in histology images; they are aimed at automating pathology work-flows and consequently do not immediately translate into clinical decisions. These advanced ap-proaches include inference of molecular features, prediction of survival and end-to-end predic-tion of therapy response. Predictions made by IT-driven systems could simplify and enrich clini-cal decision-making, but require rigorous external validation in clinical settings.

The practical integration of bioinformatics analysis and multi-OMICS datasets under complemen-tary computational analysis is having a great impact on the search for predictive and prognostic biomarkers and may lead to an important revolution in treatment. Moreover, integrating OMICS data with epidemiological data from well-defined cohorts improves our ability to associate genet-ic alterations with environmental exposures and specific clinical phenotypes, which has the poten-tial to improve our current understanding of cancer biology and ultimately patient management. Now that technological developments have enabled such multidimensional studies, much of the focus will shift to study design, interpretation, and clinical applicability [114,115].

This approach integrates data from various biological and life style layers, enhancing our under-standing of complex, heterogeneous cancers. The integration of multi-OMICS data into PPO-guided clinical practice has significantly advanced our knowledge of the cancer endophenotype and enabled the identification of valuable biomarkers for predicting treatment response from di-verse dimension levels, especially with rapid advances in design-driven biotechnological and AI methodologies [116]. Of particular interest are AI-based methods which have expanded the hori-zon for biomarker discovery, demonstrating the power of integrating multimodal data from exist-ing datasets to discover new meta-biomarkers. While most of the included studies showed prom-ise for AI-based prediction of benefit from cancer or pre-cancer immunotherapies, none provided high-level evidence for immediate practice change. A priori planned prospective trial designs are needed to cover all lifecycle steps of these software biomarkers, from development and valida-tion to integration into clinical practice [117,118].

Multi-OMICS accelerates PPM-guided oncology by identifying new biomarkers and therapeutic targets, potentially improving treatment options for cancer patients and pre-cancer persons-at-risk. We guess that the oncologists of the next-step generation

would need a highly informative computational framework to identify individualized risk-related sub pathway regions in cancer and then apply it to pan-cancer parsons-at-risk. The latter will be useful for precision cancer pa-thology and thus the evidence-based targeted treatment [119-127].

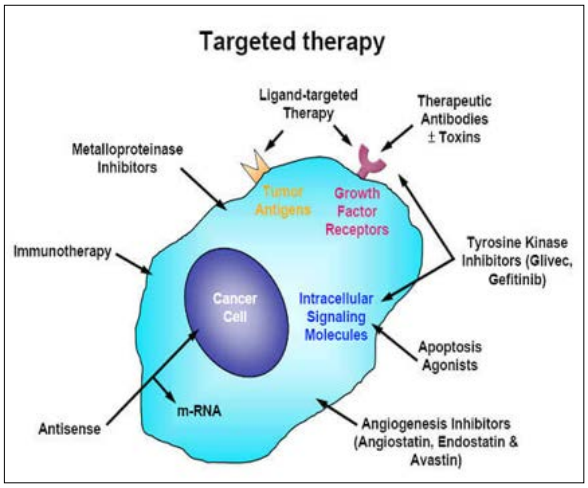


Figure 11A: Targeted treatments for cancer - targeted therapy Targeted therapy is a type of cancer treatment that targets proteins that control how cancer cells grow, divide, and spread. It is the foundation of PPM.

Modified from: https://www.cancer.gov/about-cancer/treatment/types/targeted-therapies

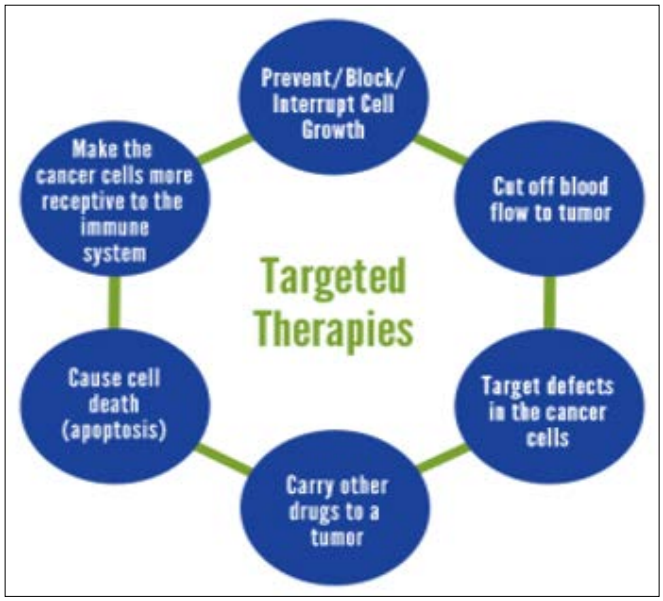


Figure 11B: Targeted treatments for cancer - targeted therapy

Targeted therapy is used in some types of cancer. Targeted therapy is a very effective treatment, but it isn't always suc-cessful as identifying a target for therapy is a challenging process.

Targeted therapy is cancer treatment that targets the genetic changes or mutations that turn healthy cells into cancer cells. Targeted therapy helps healthcare providers treat cancer cells without hurting healthy cells. Healthcare providers sometimes use targeted therapy as the front line or initial treatment. They may also combine targeted therapy with other treatments.

Some targeted therapies designed to keep cancer cells from growing, multiplying and surviving include:
Angiogenesis inhibitors: Just like all organs and tissues, can-cer cells have blood vessels that they rely on for the oxygen and nutrients to survive. To make sure they get enough oxy-gen and nutrients, cancer cells send out chemical signals encouraging their blood vessels to keep on growing.

Modified from: https://svastii.in/blog/targeted-therapy-for-cancer

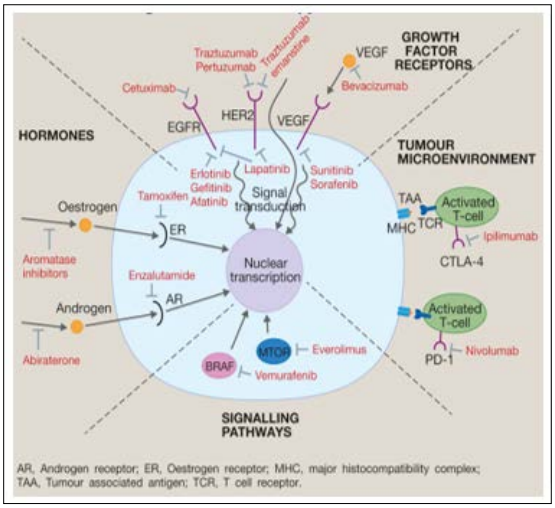


Figure: 11C Targets for cancer therapies

Targeted therapies affect specific cellular molecular mechanisms promoting cancer cell survival and proliferation, enabling treatment tailored to specific tumor characteristics. The key pathways include the hormonal axis, growth factor receptor-mediated tyrosine kinases and cellular immune system. Monoclonal antibodies can target extracellular ligands or cell surface growth factor receptors. Tyrosine kinase inhibitors prevent signal transduction from the intracellular portion of the receptors. Immune checkpoint inhibiting antibodies facilitate immune recognition and destruction of cancer cells by cytotoxic T cells. Various agents are used to reduce hormone synthesis or block activation of intracellular hormone receptors. These newer agents have a different pattern of adverse effects, but offer an improved therapeutic ratio for many patients. The highly targeted mechanism of activity means that an individualized pre-treatment characterization of the patient's tu-mour molecular profile is increasingly needed.

Modified from: Philip Charlton, James Spicer. Targeted therapy in cancer. Medicine, 2016, Volume 44, Issue 1, Pages 34-38. https://doi.org/10.1016/j.mpmed.2015.10.012

In this context, the identification of targetable genomic alterations in cancer subtypes is required as standard of care to guide optimal therapy selection. In particular, the analysis of upgraded cancer biomarkers in cancer patients and pre-cancer persons-at-risk is required to identify several types of cells, which carry a risk for a disease progression and subsequent post-therapeutic re-lapse. By integrating OMICS-driven cancer biomarkers into comprehensive diagnostic algo-rithms, clinicians can identify high-risk patients at the subclinical stage, enabling timely interven-tion and improved patient outcomes. Furthermore, the identification of specific biomarker-guided molecular targets has paved the way for the development of targeted therapies aimed at disrupting key pathways implicated in carcinogenesis. In conclusion, the evolving landscape of biomarkers and molecular targets presents exciting opportunities for advancing precision cancer pathology

and PPO as a whole. By harnessing those insights, precision cancer pathologists and clinicians can optimize treatment selection, enhance patient outcomes, and ultimately transform the management of this devastating disease [128].

For instance, CSCs that can drive tumor initiation and can cause relapses, and due to their im-portance, several biomarkers that characterize CSCs, have been identified and correlated to diagnosis, therapy and prognosis, whilst giving examples on how the CSC markers might be influ-enced by therapeutics, such as chemo- and radiotherapy, and the tumor microenvironment. Defining ways of targeting and destroying CSCs holds potential to impact significantly on cancer therapy, including prevention of metastasis and cancer recurrence [129-135].

Because of biomarker rarity, single-gene testing is not practical; next generation sequencing of hundreds of genes must be performed to obtain timely answers within the frame of OMICS-portfolio. Resistance to biomarker-driven therapeutics is often due to secondary mutations or co-driver gene defects; studies are now addressing the need for customized drug combinations matched to the complex molecular alteration portfolio in each tumor. Future investigation should expand tissue-agnostic therapeutics to encompass malignancies and include biomarkers beyond those that are DNA-based [136].

Some cancer biomarkers can be used to find cancer early in people without clinical manifesta-tions, or to help diagnose cancer in someone who already has pre-early signs or symptoms. Biomarker testing can also be used during or after treatment for some cancers to see how well the treatment is working. Moreover, some biomarker tests can be used after treatment, to look for possible signs of the cancer coming back [137-143].

Several guideline statements on the topic are currently available to help precision cancer pathologist and laboratory personnel best use the small specimens obtained from patients with cancer for ancillary molecular testing [144].

Over the past decades, continuous progress has been made in exploring and discovering novel, sensitive, specific, and accurate tumor biomarkers, which has significantly promoted PPM- and PPO-guided cancer care and improved the outcomes of cancer patients, especially advances in IT-supported OMICS technologies developed for the detection of tumor biomarkers. Collective-ly, the discovery and application of multiple tumor biomarkers may provide guidance on im-proved PPM and PPO, broaden horizons in future research directions, and expedite the clinical classification of cancer patients and/or according to their molecular biomarkers rather than organs of origin. Of particular interest is an accurate identification of cancer stem cells-based bi-omarkers, providing a theoretical basis for drug combinations of malignant tumors and offering a silver lining for patients with advanced malignancies. The development of PPM and PPO repre-sents a turning point and a new paradigm in cancer management, as biomarkers enable oncolo-gists to tailor treatments based on the unique molecular profile of each patient's tumor.

You might know that various genomic analyses and profiling of human cancers are being incor-porated into diagnostic and decision-making algorithms. So, the cancer precision pathologists continue to play an essential role in developing and implementing molecular and genomic tests in practice and communicate the results and their relevance with clinicians **(Figure 12)**.

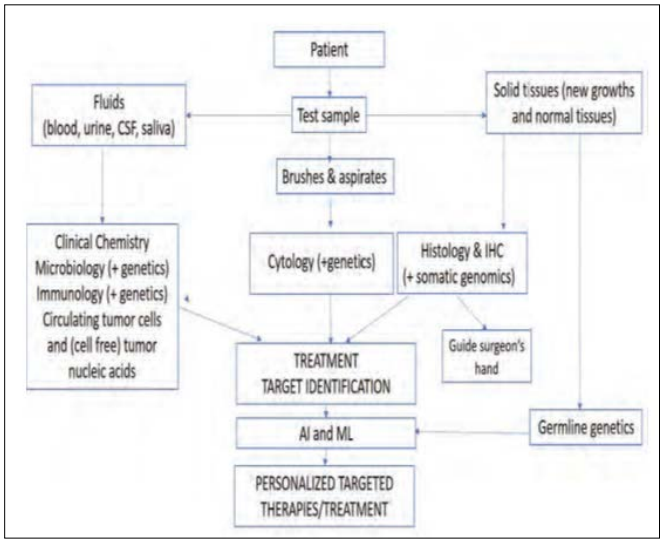


Figure 12: Precision Pathology in PPM- and PPO-guided Clinical Practice

The success of next-generation precision cancer pathology and PPO depends on the discovery of new actionable disease characteristics, rapid, accurate, and comprehensive diagnosis of complex phenotypes within each patient, novel clinical trial designs with improved response rates, and worldwide access to novel targeted anticancer therapies for all patients. Adaptive profiling strat-egies involving tissue- and liquid-based testing that account for the immense plasticity of cancer during the patient's journey and also include early detection approaches are already finding their way into clinical routine and will become paramount.

Modified from: Such activities are of utmost importance for successfully translating scientific advancements into PPM and PPO as a benefit to cancer patients or pre-cancer persons-at-risk ("next-generation pathologists"). In this setting, pathologists cover different academic and diag-nostic levels from biodesign-driven research projects and clinical trials of biomarkers of the next-step generation, to validation studies and diagnostic applications in a clinical setting [145]. With the reference to the use of biomarkers in clinical applications, several stages are needed and each of them requires pathologists' expertise and facilities [146]. These biomarkers arise as tumor-specific biomarkers, also through high through-output technologies.

Generally, both the detection technologies and modalities of interpretation are developed in a centralized pathology lab. Furthermore, biomaterials are associated with additional basic clinical and pathological information relating to canonical morphology and other biomarkers [Stanta G, Bonin S, Machado I, et al. Models of biobanking and tissue preservation: RNA quality in archiv-al samples in pathology laboratories and "in vivo biobanking" by tumor xenografts in nude mice-two models of quality assurance in pathology [147-149].

The traditional task of the pathologist is to assist physicians in making the correct diagnosis of diseases at the earliest possible stage to effectuate the optimal treatment strategy for each individual patient. Meanwhile, cancer and pre-cancer diagnostic applications in the clinical setting require the use of different technologies, namely OMICS portfolio, FISH, basic and complex molecular tests, such as multigene platforms. The use of molecular and genomic techniques al-ready demonstrates clear value in the diagnosis of cancer and pre-cancer conditions, with treat-ment

tailored specifically to individual cancer patients or pre-cancer persons-at-risk.

The ability to generate, analyze, interpret, and store huge amounts of data inevitably is changing the platform on which precision cancer pathologists perform their duties and deliver their ser-vices, with "informatics" now a recognizable subdiscipline, having a flourishing association and recognized training fellowships. However, for precision pathologists the challenge extends be-yond assimilation of the data generated by OMICS testing into the area of anatomic pathology and into the entire electronic medical record.

Molecular and genomic techniques are rapidly expanding whilst making the modern cancer pa-thology laboratories precision ones (Fig 13).

- Next generation sequencing (NGS)
- Omics:
  - Genomics
  - Transcriptomics
  - Proteomics
  - Kinomics
  - Metabolomics
- Biosensors
- Artificial intelligence (AI): deep thinking and machine learning

Figure 13: Cutting-edge tools of Precision Cancer Pathology Laboratories

One of the goals of precision cancer pathology is to standardize laboratory practices to increase the precision and effectiveness of diagnostic testing, which will ultimately enhance patient care and results. Standardization is crucial in the domains of tissue processing, analysis, and reporting. To enhance diagnostic testing, innovative technologies are also being created and put into use. Furthermore, although problems like algorithm training and data privacy issues still need to be resolved, digital pathology and artificial intelligence are emerging in a structured manner. Over-all, for the field of precision cancer pathology to advance and for patient care to be improved, standard laboratory practices and innovative technologies must be adopted. This innovation can help diagnose and treat cancers, potentially detecting otherwise invisible cancer cells. The future of PRECISION CANCER pathology is digital, and this work could not only transform how clinicians diagnose cancer, but also change how we train the diagnosticians of tomorrow.

Modified From:
Their use demonstrates clear value in the diagnosis and treatment of cancer tailored specifically to individual cancer patients or pre-cancer persons-at-risk. Active adaption and innovation is re-quired, driven by a sense of excitement and adventure. A passive or negative attitude is likely to marginalize pathologists with dire consequences for the discipline in the long term. So, PPM is the future, and PPM demands PPO and PPO-driven pathology be implemented into daily cancer practice. The need for integration of the flood of new molecular data, with surgical pathology, **digital pathology,** and the full range of pathology data in the electronic medical record has never been greater.

Moreover, the successful implementation of IT-supported digital biomarker solutions guides the clinical selection of effective cancer-related immune therapeutics based on the retrieval and visu-alization of spatial and contextual information from cancer tissue images and standardized data. As such, digital pathology turns into "precision pathology" delivering individual therapy response prediction. Precision pathology does not only include digital and computational solutions but also high levels of standardized processes in the routine histopathology workflow and the use of mathematical tools to support clinical and diagnostic decisions as the basic principle of a PPO!!!

Consequently, the need to include molecular technologies in precision cancer pathology laborato-ries has required the training of specialized professionals. In the context of those changes, the precision cancer pathology can play a fundamental role in both clinical practice, translational re-search and biodesign-inspired applications. With innovative tools and making use of the transdis-ciplinary collaboration of new professional personnel, pathologists can take on a guiding role in the diagnostic-therapeutic process of cancer patients and pre-cancer persons-at-risk, allowing the morphological, molecular, and genetic characterization of the tumors in a complete way.

The Success of Precision Cancer Pathology: Multi-Omics and Bioinformatics are Building Blocks Towards Paving the Pathway Towards Guide Rational Diagnostic, Predictive, Prog-nostic, Preventive and Treatment Decision

Recent development of high-throughput methods enables detailed OMICS analysis of the mo-lecular mechanisms underpinning tumor biology, including identification of clinically actionable mutations, gene and protein expression patterns associated with prognosis, and provided further insights into the molecular mechanisms, indicative of cancer biology and new therapeutic strate-gies such as targeted therapy or immunotherapy. The development of PPM-guided precision can-cer pathology and PPM-guided PPO represents a turning point and a new paradigm in cancer management, as biomarkers enable oncologists to tailor treatments based on the unique molecular profile of each patient's tumor. In this context, personalized tumor molecular profiles, spec-trum of biomarkers, tumor disease site and other patient characteristics illustrating the funda-mentals for constructing treatment schedules, are then potentially used for determining optimum individualized therapy options and the final version of personalized cancer therapy [150-152]. (Figure. 14)

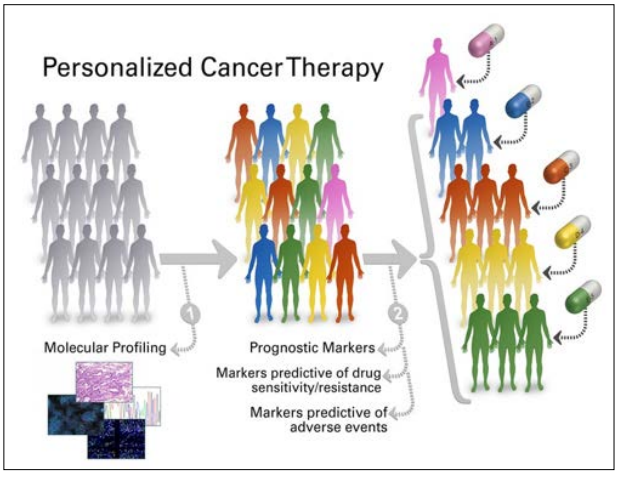


Figure 14: Cornerstones of personalized cancer therapy

Cancer treatment has evolved toward PPM-guided oncology. It is mandatory for oncologists to ascertain tumor biological features in order to optimize patients' treatment. Treatment of patients with cancer is currently undergoing a dramatic shift towards PPM-guided cancer therapy using molecular diagnostics.

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As cancer pathologists in the era of PPM and PPM-guided precision cancer pathology, we are uniquely positioned to participate in the integration of the histologic and molecular features of the malignancy and its microenvironment to provide the best prognostic information to clinicians, as well as to cancer patients and pre-cancer persons-at-risk. In the realm of PPO-guided care, the journey of a cancer patient or pre-cancer person-at-risk is profoundly personal and unique. The complexities of cancer diagnosis and treatment necessitate a shift from generic protocols to PPM-guided cancer treatment plans. Tailored care strategies not only enhance the outcomes but also ensure that each individual receives the most effective care for their specific condition [153].

In the future, with an improved understanding of the complex underlying molecular mechanisms via integrating various layers of genetic and functional analyses in a refined process of personalized clinical decision-making, alongside with an enhanced ability to dynamically detect and mon-itor individual cancer-driving molecular aberrations via liquid biopsies, personalized oncology will dramatically change our current concept of cancer therapy [154].

Currently, an individual cancer patient's biologic data is actively employed in a systematic way to predict the best course of biomarker-driven targeted cancer therapy. And the advent of individu-al biomarker-driven analysis and profiling provides hope that we are entering a new era of PPM-guided cancer care [155].

Tools for implementing cancer biomarkers and PPO-guided precision pathology-related OMICS-technologies based on molecular diagnostic and interventions, will improve cancer prevention [156]. Tumor biomarkers can be DNA, RNA, protein and metabolomic profiles that predict ther-apy response. Imaging technologies such as computed tomography (CT) and positron emitted tomography (PET) are already influencing the pre-early (subclinical) detection and management of the cancer patient or pre-cancer persons-at-risk (Figure 15A, B).

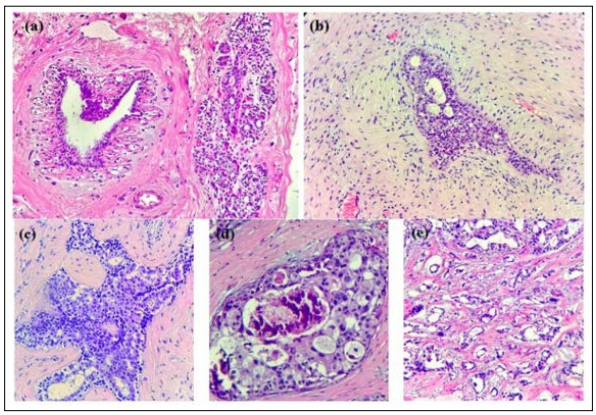

Figure 15A: Breast tissue progression towards invasive cancer: pre-early diagnosis, prediction and prognostication

(a) Normal breast tissue: ducts and lobules in a fibrous stroma, along with adipose tissue. (b) HE × 200. Usual ductal hyperplasia: benign intraductal epithelial proliferation with mild variation in cellular and nucle-ar size/shape. (c) HE × 200. Atypical ductal hyperplasia: intraductal clonal epithelial cell proliferation (<2 mm) with a cribriform pattern. (d) HE × 200. Ductal carcinoma in situ with high-grade atypia and cribriform growth pattern, comedonecrosis, and microcalcifications. (e) HE × 200. Invasive breast cancer of no special type (NST): infiltrative small nests and tubules of tumoral cells into a desmoplastic stroma

Modified and adapted from: Ionescu, A.-I.; Atasiei, D.-I.; Ionescu, R.-T.; Ultimescu, F.; Barnonschi, A.-A.; Anghel, A.-V.; Anghel, C.-A.; Antone-Iordache, I.-L.; Mitre, R.; Bobolocu, A.M.; et al. Prediction of Sub-clinical and Clinical Multiple Organ Failure Dysfunction in Breast Cancer Patients—A Review Using AI Tools. Cancers 2024, 16, 381. https://doi.org/10.3390/cancers16020381

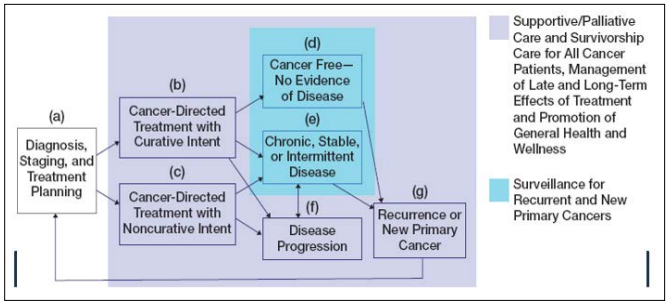

Figure 15B: The pre-cancer and cancer care trajectory

After a patient receives a diagnosis of cancer and begins treatment planning with the cancer care team (a) supportive and palliative care along with survivorship care should be initiated regardless of whether the patient is to be treated with curative intent (b) or noncurative intent (c). Patients who are cancer free after treatment (d) or who have chronic, stable, or intermittent disease (e) may be monitored for prolonged periods to assess for any recurrent or new primary cancers (g). Patients who receive noncurative treatments (c) may also have chronic, stable, or intermittent disease (e) and undergo surveillance for the development of cancer recurrence or a new primary cancer (g). Whether treated with curative or noncurative intent, some patients experience a progres-sion of their cancer (f).

Modified and adapted from: https://nap.nationalacademies.org/read/25956/chapter/6

The above-mentioned picture illustrates the interconnection between precursor lesions of breast cancer (typical ductal hyperplasia, atypical ductal/lobular hyperplasia) and the subclinical of multiple organ failure syndrome, both representing early stages marked by alterations preced-ing clinical symptoms, undetectable through conventional diagnostic methods. The illustration emphasizes the importance of pre-early (subclinical) identification and prevention of the multiple organ failure cascade at the inception of the malignant state, aiming to enhance the quality of life and extend survival. This pursuit contributes to a deeper understanding of risk factors and viable therapeutic options. Despite the existence of the subclinical multiple organ failure syndrome, cur-rent diagnostic methodologies remain inadequate, prompting consideration of bioinformatics as an increasingly crucial tool for early identification in the diagnostic process. Being summarized, we would stress that precision pathology is becoming one of the most important pillars for PPO and PPM-guided clinical oncology practice and cancer care. In this context, significant advances in molecular technologies, such as multiplex-polymerase chain reaction (PCR), NGS and mass spectrometry coupled with

computational medicine have identified new biomarkers for improv-ing disease classification and diagnosis (Li Q, Geng S, Luo H, Wang W, Mo YQ, Luo Q, Wang L, Song GB, Sheng JP, Xu B. Signaling pathways involved in colorectal cancer: pathogenesis and targeted therapy. Signal Transduct Target Ther. 2024 Oct 7;9(1):266. doi: 10.1038/s41392-024-01953-7. PMID: 39370455; PMCID: PMC11456611; The success of precision pathology: Multi-omics building blocks. Chan, Daniel W. Pathology, Volume 51, Supplement 1S, 2019; Gar-raway LA, Verweij J & Ballman KV Precision oncology: an overview. J. Clin. Oncol. Off. J. Am. Soc. Clin. Oncol. 31, 1803–1805 (2013; Garraway LA, Verweij J & Ballman KV Precision on-cology: an overview. J. Clin. Oncol. Off. J. Am. Soc. Clin. Oncol. 31, 1803–1805 (2013).

With significant advancements of OMICS technologies and IT-supporting algorithms, large amounts of multi-OMICS data, have been accumulated, offering an unprecedented oppor-tunity to explore the heterogeneity and complexity of cancer across various molecular levels and scales. One of the promising aspects of multi-OMICS as applicable to precision cancer pathology lies in its capacity to offer a holistic view of the biological networks and pathways underpinning cancer, facilitating a deeper understanding of its development, progression, and response to treatment. Addressing those challenges necessitates a multidisciplinary collaboration, paving the promising way for more precise, personalized, and effective treatments for cancer patients and pre-cancer persons-at-risk (Lusheng Li, Mengtao Sun, Jieqiong Wang, Shibiao Wan. Chapter Nine - Multi-omics based artificial intelligence for cancer research. Editor(s): Esha Madan, Paul B. Fisher, Rajan Gogna. Advances in Cancer Research, Academic Press, 2024, Volume 163, Pages 303-356, https://doi.org/10.1016/bs.acr.2024.06.005).

Being summarized, the confluence of new technologies with **artificial intelligence (AI)** and **machine learning (ML)** analytical techniques **(Fig 16A,B)**

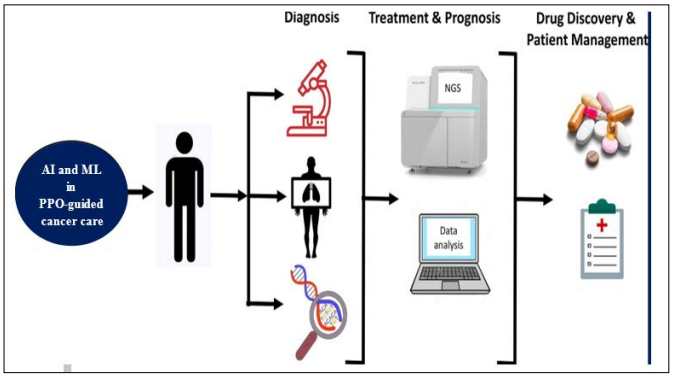

Figure 16A: Artificial intelligence (AI), machine learning (ML) and Big Data in cancer and PPO-guided clinical practice

Artificial intelligence (AI) and machine learning have significantly influenced many facets of the healthcare sector. With recent advances in the field of AI and ML, there is now a computational basis to integrate and synthesize this growing body of multi-dimensional data, deduce patterns, and predict outcomes to improve shared patient and clinician decision making. Through the applications of AI and ML, cancer diagnostics and prognostic prediction are enhanced with NGS and medical imaging that delivers high resolution images. Regardless of the improvements in technology, AI and ML have some challenges and limita-tions, and the clinical application of NGS remains to be validated. Bridging the AI-ML translational gap between initial model development and routine clinical cancer care by emphasizing and demonstrating three essential concepts: clinical validity, utili-ty, and usability. By continuing to enhance the progression of innovation and technology, the future of AI, ML and PPO show great promise. Modified and adapted from: Zodwa Dlamini, Flavia Zita Francies, Rodney Hull, Rahaba Marima. Artificial intelligence (AI) and big data in cancer and precision oncology. Computational and Structural Biotechnology Journal, 2020, Volume 18, Pages 2300-2311. https://doi.org/10.1016/j.csbj.2020.08.019 https://www.sciencedirect.com/science/article/pii/S200103702030372X, and Kann BH, Hosny A, Aerts HJWL. Artificial intelligence for clinical oncology. Cancer Cell. 2021 Jul 12;39(7):916-927. doi: 10.1016/j.ccell.2021.04.002. Epub 2021 Apr 29. PMID: 33930310; PMCID: PMC8282694.

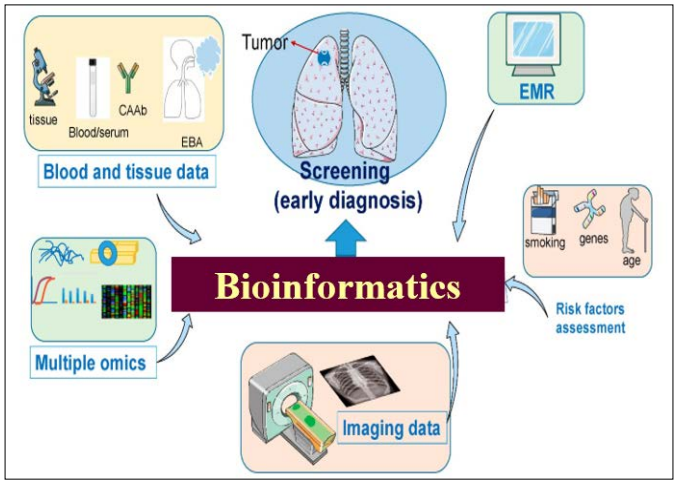

Figure 16B: Bioinformatics in cancer and PPO-guided clinical practice

Bioinformatics offers unique opportunities for enhancing such predictive capabilities in the lab and the clinic. By integrating multiple data, bioinformatics algorithms have the potential to improve the pre-early diagnosis of can-cer. The utility of IT tools interpreting medical images has been demonstrated in several settings and in several cancer cases. However, the usefulness of those algorithms in contributing to the pre-early diagnosis of cancer may extend beyond the interpretation of l images. For example, blood samples are currently interrogated for the presence of circulating autoantibodies, microRNAs, and various serum biomarkers, and some of these factors appear to be associated with cancer, thus algorithms could aid in the identification of specific patterns or signa-tures typical of cancer. Similarly, the data from Electronic medical records (EMR), which constitutes a formidable source of clinical, demographic, and biometric data, coupled with the algorithms could be a powerful diagnostic tool. Finally, high-throughput technologies such as metabolomics, transcriptomics, epigenomics, and the integra-tion of multiple "OMICS" together with information from medical images and clinical data will provide insightful information for the understanding of cancer conditions.

Modified and adapted from: Espinoza, J.L.; Dong, L.T. Artificial Intelligence Tools for Refining Lung Cancer Screening. J. Clin. Med. 2020, 9, 3860. https://doi.org/10.3390/jcm9123860, and Azuaje, F. Artificial intelligence for precision oncology: beyond patient stratification. npj Precision Onc 3, 6 (2019). https://doi.org/10.1038/s41698-019-0078-1

is rapidly advancing the field of PPO-guided precision pathology, promising to improve diagnos-tic approaches and therapeutic strategies for patients with cancer and pre-cancer persons-at-risk. By analyzing multi-dimensional, multi-OMICS, spatial pathology, and radiomic data, these tech-nologies enable a deeper understanding of the intricate molecular pathways, aiding in the identi-fication of critical nodes within the tumor's biology to optimize treatment selection [161-165].

The recent advancements in high-throughput technologies have enabled the generation of large-scale multi-OMICS datasets, providing a comprehensive view of the molecular landscape of can-cer. Integrating and analyzing these multi-OMICS layers can offer valuable insights into the un-derlying mechanisms of cancer development, progression, and response to therapy.

As you might see from the above-mentioned illustrations, once a cancer patient or a pre-cancer person-at-risk are diagnosed and the treatment plan is developed, several care pathways are pos-sible. Many cancer patients, particularly those with pre-early (subclinical)-stage disease, are treat-ed with the goal of being cured, respond to treatment, and may expect to have long-term, cancer-free survival. Others may not experience a successful treatment response and/or chronic, stable, or intermittent disease, and will experience a progression of their cancer. Some patients will be di-agnosed with advanced or metastatic cancer and be treated with palliative intent, rather than cu-rative intent, with the goal of improving their symptoms, quality of life, or length of life. Those who are cancer free with no evidence of disease and those with chronic, stable, or intermittent disease will typically undergo routine surveillance for recurrent and new cancers.

In this context, future advances in genomic predictive testing and profiling, as well as in theranostics-driven treatment and molecular imaging are expected to be in the field of integrated diagnostics, biology-driven interventional cancer-related radiology, targeted treatment and theranostics. The use of **theranostics (companion diagnostics)** as a result of the integration of treatment and diagnosis, involving a drug or technology that combines diagnostic imaging with targeted therapy, has become a standard in PPO-guided clinical practice in the context of ongo-ing therapeutic innovation, and shows huge potential to advance the battle against cancer. Mo-lecular diagnostics identify individual cancer patients who are more likely to respond positively to targeted chemotherapies. Molecular diagnostics include testing for genes, gene expression, proteins and metabolites. From the early concept of targeted drug delivery to the emergence of PPM and PPO, theranostics has benefited from advances in imaging technologies, molecular bi-ology, and nanomedicine [166-170].

Theranostics has demonstrated its capacity to deliver targeted and real-time interventions, mak-ing it adaptable to diverse clinical domains. The integration of nanomaterials and advancements in molecular biology further enhance the capabilities of theranostics, promising a future where treatments are highly personalized, and cancers are understood and managed at a molecular level previously unattainable. The progression of theranostics represents a transformative phase in PPO-guided precision cancer pathology, providing new avenues for precise treatment and im-proved patient outcomes. Its multidisciplinary nature and continuous innovation have the poten-tial to profoundly impact the future of clinical practice, as well as revolutionizing the treatment and management of a wide array of cancer subtypes [170].

In this context, **radiotheranostics** explores the molecular targets expressed on tumor cells to tar-get them for imaging and therapy. In this way, radiotheranostics entails non-invasive demonstra-tion of the in vivo expression of a molecular target of interest through imaging followed by the administration of therapeutic radioligand targeting the tumor-expressed molecular target. There-fore, radiotheranostics ensures that only patients with a high likelihood of response are treated with a particular radiotheranostic agent, ensuring the delivery of PPO-guided care to cancer pa-tients and pre-cancer persons-at-risk [171-174].

The use of companion molecular diagnostics is expected to grow significantly in the future and will be integrated into new cancer therapies a single (bundled) package which will provide great-er efficiency, value and cost savings. This approach represents a unique opportunity for integra-tion, increased value in PPO-guided clinical cancer practice [175-184].

During the last decade, advances in cancer precision pathology has shown us the intricate cell signaling mechanisms that trigger oncogenesis are not dependent on a single factor, but instead the compound effect of OMICS-related alterations. In addition, significant advances in OMICS technologies, coupled with bioinformatics, have identified new biomarkers for improving cancer classification and diagnosis. Collectively, the discovery and application of multiple tumor bi-omarkers and upgraded OMICS-driven technologies to screen and monitor the latter, may pro-vide guidance on improved PPO-guided clinical practice and PPM as a whole, broaden horizons in future research directions, and expedite the clinical classification of cancer patients according to their molecular biomarkers rather than organs of origin. The ltarre outlined the biomarkers at multiple expression layers to tutor molecular classification and pinpoint tumor diagnosis, and ex-plored the paradigm shift in PPO-guided therapy: from single- to multi-OMICS-based subtyping to optimize therapeutic multi-targeted regimens.

Therefore, it is important for clinical, translational, and laboratory-based researchers and bi-odesigners to be acutely aware of the issues surrounding appropriate biomarker development, in order to facilitate entry of clinically useful cancer biomarkers into the clinic, while avoiding the introduction of biomarkers that have not been sufficiently evaluated and therefore may be useless or even potentially detrimental to patient care.

With the latest advent of OMICS technology and Big Data analytics, the oncologists can now gather detailed molecular information on the cancer cells, identify obscure patterns from the data effectively, and gather further insights into the biology and features of cancer progression in in-dividual patients and pre-cancer persons-at-risk. The recent availability of cancer "OMICS" data has created unique opportunities for characterizing the biological processes correlated with clini-cal cancer endophenotypes (Figure 17)

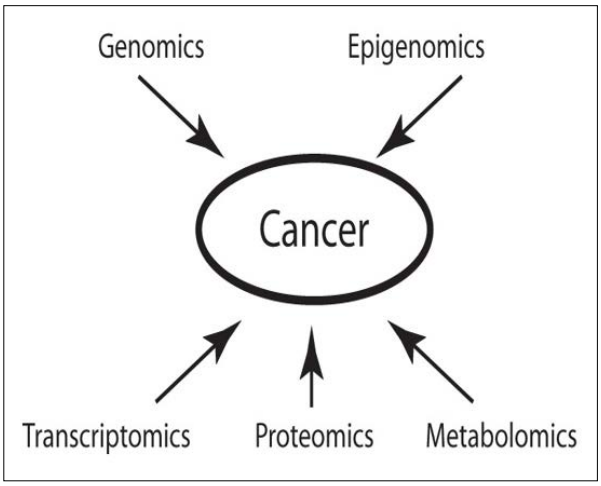

Figure 17: Schematic Diagram of OMICS Modalities in PPO

Genomics, epigenomics, transcriptomics, proteomics, and metabolomics methods provide com-plementary information on the biology of tumorigenesis and cancer development. OMICS revo-lution" provides great opportunities to link biological pathways to clinical cancer endopheno-types. The OMICS approach, initiated by genomics and transcriptomics studies, has revealed an incredible complexity with unsuspected molecular diversity within a same tumor type as well as spatial and temporal heterogeneity of tumors. The integration of multiple biological layers of OMICS studies brought oncology to a new paradigm, from tumor site classification to pan-cancer molecular classification, offering new therapeutic opportunities for PPO. Advancements in OMICS profiling techniques enable researchers to view the panorama of the biological pro-cesses underpinning cancer progression and health status, which not only renders further insights into cancer precision pathology, but also identifies biomarkers for clinical predictions.

Modified from

Each type of OMICS data adds to the list of molecular differences associated with cancer, re-vealing useful markers of disease process and providing insights into biological pathways. It built a tactic to tailor customized treatment informed by the tumors' molecular profile. Single-OMICS analysis dissected the biological features associated with carcinogenesis to some extent but still failed to revolutionize cancer treatment as expected. But individual strands of OMICS data are not sufficient to reveal the causal relationship between molecular signatures and the manifesta-tion of cancer. But most of those OMICS datasets are still assessed individually using distinct approaches and do not generate the desired and expected global-integrative knowledge with ap-plications in clinical diagnostics. Meanwhile, integrated OMICS analysis incorporated tumor bio-logical networks from diverse layers and deciphered a holistic overview of cancer behaviors, yielding precise molecular classification to facilitate the evolution and refinement of PPO-guided cancer care and PPM-driven clinical practice as a whole.

Multi-OMICS data play a crucial role in PPO-guided clinical practice, mainly to understand the diverse biological interaction between different OMICS, and the role of ML and AI approaches which have been extensively employed in this context over the years for integrating distinct OM-ICS datasets, providing valuable insights into their application, and highlighting their potential to harmonize diverse biological information layers. As a result, data harmonization, algorithm inter-pretability, and ethical considerations would pave the promising way for more precise, personal-ized, and effective treatments for cancer patients and pre-cancer persons-at-risk [185-189].

Of special attraction and interest is the potential of integrating radiological imaging with other data types, a critical yet underdeveloped area of PPO-guided cancer care in comparison to the IT-supported fusion of other multi-OMICS data. Radiological images provide a comprehensive, 3D view of cancer, capturing features that would be missed by biopsies or other data modalities due to the complexities of data integration models in the context of PPO [190-194].

Discussion and Conclusions

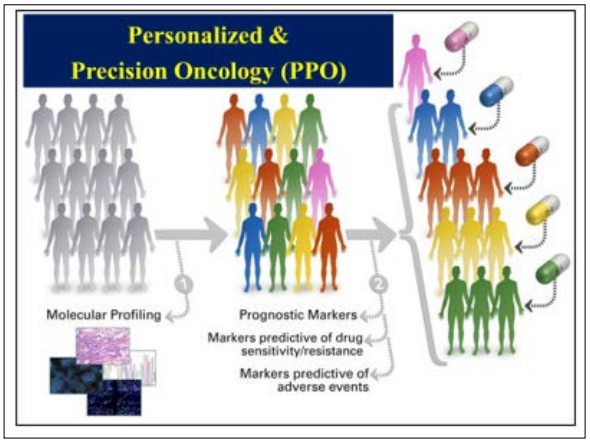

Fig 18A,B Personalized & Precision Oncology

PPO aims to offer individualized treatment to each cancer patient or pre-cancer person-at-risk by applying a comprehensive molecular, cellular, and functional analysis of tumors. We now know that biological properties differ greatly, not only from cancer to cancer but also from person-at-risk to patient.

One of the core competencies of our department is to investigate individual tumors in detail within the framework of specific programs and studies, and to provide access to customized, PPO-guided treatment to patients. In addition to the identification of new cancer biomarkers and biomarker-driven targeted drugs and the definition of rational drug combinations, we also support the precise use

of previously established forms of targeted treatment such as conventional chemotherapy, immunotherapy, radiation therapy, and surgical procedures.

Personalized cancer therapy is a treatment strategy centered on the ability to predict which patients are more likely to respond to specific cancer therapies. This approach is founded upon the idea that tumor biomarkers are associated with patient prognosis and tumor response to therapy. In addition, patient genetic factors can be associated with drug metabolism, drug response and drug toxicity. Personalized tumor molecular profiles, tumor disease site and other patient characteristics are then potentially used for determining optimum individualized therapy options.

Modified and adapted from: Boscolo Bielo L, Trapani D, Repetto M, Crimini E, Valenza C, Belli C, Criscitiello C, Marra A, Subbiah V, Curigliano G. Variant allele frequency: a decision-making tool in precision oncology? Trends Cancer. 2023 Dec;9(12):1058-1068, and Wahida A, Buschhorn L, Fröhling S, Jost PJ, Schneeweiss A, Lichter P, Kurzrock R. The coming decade in precision oncology: six riddles. Nat Rev Cancer. 2023 Jan;23(1):43-54

Presents principally new opportunities for patients with cancer and pre-cancer persons-at-risk as well, whilst emerging as the tumor treatment and prevention that consider the cancer variability in terms of gene expression patterns, tumor specific (immune) microenvironment, and patients' particular lifestyles and morbidities, covering huge Data Sets! As PPO introduces a Big Data analysis of PPO-guided OMICS approaches, there are still challenges in the translation of all these data into meaningful and equitable benefits to patients and health care. And each patient presents its specific preferences, needs, tolerances, and unique tumor vulnerabilities even when suffering from very similar diseases or course of treatment, which demands and highlight the importance of the PPO approach and the personalized cancer or pre-cancer care. In reality, it is time to recognize the possibility that advanced computer implementation could generate real-world data that expand our understanding of cancer, rapidly identify new treatments, and create personalized drugs or immune therapies.

The PPO global market research study consists of bioindustry trends, detailed market analysis, partnerships and collaborations analysis, and clinical trial analysis. The growth in PPO-related market size over the next decade is likely to be the result of an anticipated increase in patient population and rise in the demand for PPM and PPO for precision cancer care (Figure 19)

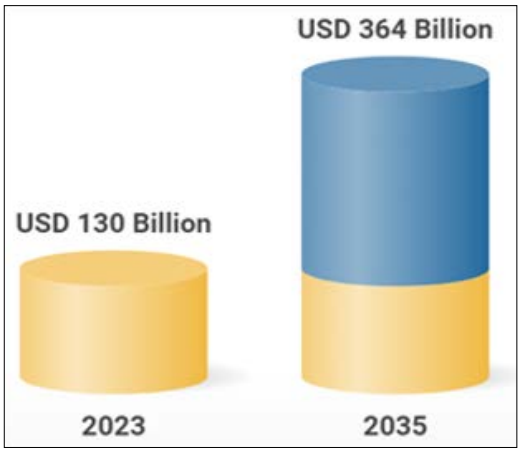

Figure 19: Personalized & Precision Oncology (PPO) Global Market

The global PPO market size is estimated to grow from USD 130 billion in 2023 to USD 364 billion by 2035, representing a CAGR of 8.93% during the forecast period 2023-2035

Modified and adapted from: https://www.globenewswire.com/news-release/2024/04/23/2867426/28124/en/Global-Oncology-Precision-Medicine-Market-Trends-and-Forecasts-Report-2024-A-364-Billion-Industry-by-2035-Amidst-a-Clinical-Trials-Boom-with-Over-6-500-Trials.html

A major challenge in PPO lies in establishing the relationship between biological data, disease, design-driven biotech and clinical translation: how can we interpret "Big Data," referring to the greater collection of healthcare data across thousands of patients and pre-cancer persons-at-risk, involving the tracking of various medical indicators and biomarkers (primarily clinical and OMICS data). High-throughput data collection enables researchers, bio designers and bioengineers to screen tissues for thousands of molecular targets, effectively capturing the response of a complex system over time. Statistically interpreting trends from Big Data is a discipline unto itself and is necessary for predictive modeling and clinical decision support [195-197]. PPO as the trend toward PPM in oncology continues, coordination of all health care stakeholders has become more important than ever. Oncologists, pathologists, and payers must work with pharmaceutical, biotech and diagnostic companies to develop products, services, and coverage policies that improve patient outcomes and, as we have begun to see, lower overall health care costs for institutions that put personalized regimens in place.

As precision cancer pathologists acquire PPM and PPO data, and companies develop PPM-guided cancer therapies, regulators, clinicians, cancer patients and pre-cancer persons-at-risk, and the public must consider the broader consequences of PPM and PPO. A major collaborative ef-fort between all associated groups - scientists, drug designers and biopharmaceutical companies, insurers, clinicians, regulators, and patients - will be necessary to keep driving precision cancer pathology forward and make it a viable field that benefits all [198].

Economic sustainability of genomic tests, access to drugs or clinical trials according to the MTB recommendation, and expanded use of existing anticancer drugs are required for MTBs to be-come a useful tool for the governance of precision cancer pathology and PPO as a whole in the real world. Continuing to work in collaboration with scientific societies, MTBs are poised to be-come a homogeneous and well-structured reality that can make the care pathway of the patient with cancer more efficient, with the ultimate goal to offer personalized therapy based on the most advanced scientific knowledge. Evidence is accumulating to support feasibility and survival benefit in patients treated with matched therapy [199-202].

The enormous development of precise cancer pathology research has raised great expectations concerning its impact on PPO aiming to customize cancer practice with a focus on the individual, based on the use of molecular tests, identification of genomic biomarkers, and development of targeted drugs. The latter requires precision pathologists highly trained in pre-analytic processes, tumor area microdissection for tumor cell enrichment, methodology analysis and results. The in-depth study of molecular alterations in cancer patients allows optimizing molecular diagnosis and selecting candidates for receive novel treatments against specific molecular targets. These pa-tients are expected to benefit from multidisciplinary approach and learning.

Although "the next-generation pathologists" have already been launched, further and continuous educational efforts must fully implement the paradigm shift into diagnostic molecular pathology practice and reinvent it as a leading diagnostic discipline in the PPM era. This approach men-tioned should be based on postulates, which will change the level of professional education and training, incarnate culture and social mentality [203-211]. And the above-mentioned PPM model and tools of PPO applied would need for novel training since the society is in bad need of large-scale dissemination of novel systemic thinking and minding. Upon construction of the new edu-cational platforms in the rational proportions, there would be not a primitive oncologist or traditional cancer pathologist created but a cancer-guided artist being teamed with precision cancer pathologist to be able to enrich flow-through medical standards with creative elements to gift for a cancer patient a genuine hope to survive but, in turn, for a pre-cancer person-at-risk – a trust for being no diseased.

References

1. Krzyszczyk P, Acevedo A, Davidoff EJ, Timmins LM, Marrero-Berrios I, et al. (2018) The growing role of precision and personalized medicine for cancer treatment. Technology (Singap World Sci) 6: 79-100.
2. Rulten SL, Grose RP, Gatz SA, Jones JL, Cameron AJM (2023) The Future of Precision Oncology. Int. J. Mol. Sci 24: 12613 https://doi.org/10.3390/ijms241612613.
3. J Clin (2013) Oncol. Off. J. Am. Soc. Clin. Oncol 31: 1803-1805.
4. Shin SH, Bode AM Dong Z (2017) Addressing the challenges of applying precision on-cology. NPJ Precis. Oncol 1: 20-28.
5. Schwartzberg L, Kim ES, Liu D, Schrag D (2017) Precision oncology: Who, how, what, when, and when not? In American Society of Clinical Oncology Educational Book; Amer-ican Society of Clinical Oncology: Alexandria, VA, USA 37: 160-169.
6. Villanueva L, Álvarez-Errico D, Esteller M (2020) The Contribution of Epigenetics to Cancer Immunotherapy. Trends Immunol 41: 676-691.
7. Song IW, Vo HH, Chen YS, Baysal MA, Kahle M, et al. (2023) Precision Oncology: Evolving Clinical Trials across Tumor Types. Cancers 15: 1960-1967.
8. Repetto M Fernandez N Drilon A Chakravarty D (2024) Precision Oncology: 2024 in Re-view. Cancer Discov 14: 2332-2345.
9. Van Schaik LF, Engelhardt EG, Van Harten WH, Retèl VP (2024) Relevant factors for policy concerning comprehensive genomic profiling in oncology: stakeholder perspectives. BMC Cancer 22: 1424-1441.
10. Akhtar K, Hassan MJ (2024) Personalized and Precision Medicine in Cancer. In: Aziz, M.A. (eds) Personalized and Precision Nanomedicine for Cancer Treatment. Springer, Singapore. https://doi.org/10.1007/978-981-97-3545-7_3.
11. Dougherty SC, Flowers WL, Gaughan EM (2024) Precision Oncology in Melanoma: Changing Practices. J Nucl Med 65: 1838-1845.
12. Tang X, Berger MF, Solit DB (2024) Precision oncology: current and future platforms for treatment selection. Trends Cancer 10: 781-791.
13. Rodríguez N, Viñal D, Rodríguez-Cobos J, De Castro J, Domínguez G (2020) Genomic profiling in oncology clinical practice. Clin Transl Oncol 22:1430-1439.
14. Kanbar K, El Darzi R, Jaalouk DE (2024) Precision oncology revolution: CRISPR-Cas9 and PROTAC technologies unleashed. Front Genet 15:143399-1434002.
15. Subbiah V, Gouda MA, Ryll B, Burris HA, Kurzrock R (2024) The evolving landscape of tissue-agnostic therapies in precision oncology. CA Cancer J Clin 74:433-452.
16. Gazola AA, Lautert-Dutra W, Archangelo LF, Reis RBD, Squire JA (2024) Precision on-cology platforms: practical strategies for genomic database utilization in cancer treatment. Mol Cytogenet 14: 17-28.
17. Zeng J, Shufean MA (2021) Molecular-based precision oncology clinical decision making augmented by artificial intelligence. Emerg Top Life Sci 5: 757-764.
18. Bhalla S, Laganà A (2022) Artificial Intelligence for Precision Oncology. Adv Exp Med Bio l1361: 249-268.
19. Subbiah V, Kurzrock R (2024) Precision oncology across the ages: Impact on children, adolescents, and young adults. Cancer Cell 42: 1473-1479.
20. Rodriguez H, Pennington SR (2018) Revolutionizing Precision Oncology through Collab-orative Proteogenomics and Data Sharing. Cell 173: 535-539.
21. Avci CB, Bagca BG, Shademan B, Takanlou LS, Takanlou MS, et al. (2025) Precision on-cology: Using cancer genomics for targeted therapy advancements. Biochim Biophys Acta Rev Cancer 1880: 189240-189250.
22. Chhabra R (2024) Molecular and modular intricacies of precision oncology. Front Immu-nol 23: 15-1476494.
23. Horgan D, Tanner M, Aggarwal C, Thomas D, Grover S, et al. (2025) Precision Oncology: A Global Perspective on Implementation and Policy Development. JCO Glob Oncol Jan;11:e2400416. doi: 10.1200/GO-24-00416. Epub 2025 Jan 23. PMID: 39847746.
24. Akhtar K, Hassan MJ (2024) Personalized and Precision Medicine in Cancer. In: Aziz, M.A. (eds) Personalized and Precision Nanomedicine for Cancer Treatment. Springer, Singapore. https://doi.org/10.1007/978-981-97-3545-7_3.
25. Abdalla AS, Rahman M, Khan SA (2024) Promising Therapeutic Targets for Recur-rent/Metastatic Anaplastic Thyroid Cancer. Curr Treat Options Oncol 25: 869-884.
26. Casolino R, Beer PA, Chakravarty D, Davis MB, Malapelle U, et al. (2024) Interpreting and integrating genomic tests results in clinical cancer care: Overview and practical guidance. CA Cancer J Clin 74: 264-285.
27. Tang X, Berger MF, Solit DB (2024) Precision oncology: current and future platforms for treatment selection. Trends Cancer 10: 781-791.
28. Rodríguez N, Viñal D, Rodríguez-Cobos J, De Castro J, Domínguez G (2020) Genomic profiling in oncology clinical practice. Clin Transl Oncol 22: 1430-1439.
29. Brown NA, Elenitoba-Johnson KSJ (2020) Enabling Precision Oncology Through Preci-sion Diagnostics. Annu Rev Pathol 15: 97-121.
30. Pallocca M, Betti M, Baldinelli S, Palombo R, Bucci G, et al. (2024) Clinical bioinformat-ics desiderata for molecular tumor boards. Brief Bioinform 25: 440-447.
31. Heo YJ, Hwa C, Lee GH, Park JM, An JY (2021) Integrative Multi-Omics Approaches in Cancer Research: From Biological Networks to Clinical Subtypes. Mol Cells 44: 433-443.
32. Bhoyar N, Chandu HN (2025) The future of precision medicine in personalized cancer treatment. J Neonatal Surgery 14: 373-377.
33. Brozos-Vázquez E, Toledano-Fonseca M, Costa-Fraga N, García-Ortiz MV, Díaz-Lagares Á, et al. (2024) Pancreatic cancer biomarkers: A pathway to advance in personalized treatment selection. Cancer Treat Rev 125:102710-102719.
34. Donisi C, Pretta A, Pusceddu V, Ziranu P, Lai E, et al. (2024) Immunotherapy and Can-cer: The Multi-Omics Perspective. Int J Mol Sci 25: 3560-3563.

35. Massa C, Seliger B (2023) Combination of multiple omics techniques for a personalized therapy or treatment selection. Front Immunol 14: 125800-1258013.
36. In H, Park M, Lee H, Han KH (2025) Immune Cell Engagers: Advancing Precision Im-munotherapy for Cancer Treatment. Antibodies (Basel) 14: 10-16.
37. Rui R, Zhou L, He S (2023) Cancer immunotherapies: Advances and bottlenecks. Front. Immunol. New immune cell engagers for cancer immunotherapy. Nat. Rev. Immunol 24: 471-486.
38. Wu DW, Jia SP, Xing SJ, Ma HL, Wang X, et al. (2024) Personalized neoantigen cancer vaccines: current progression, challenges and a bright future. Clin Exp Med 24: 220-229.
39. Fayyaz A, Haqqi A, Khan R, Irfan M, Khan K, et al. (2024) Revolutionizing cancer treat-ment: the rise of personalized immunotherapies. Discov Oncol 15: 750-756.
40. Hoeben A, Joosten EAJ, Van den Beuken-Van Everdingen MHJ (2021) Personalized Medicine: Recent Progress in Cancer Therapy. Cancers (Basel) 13: 240-242.
41. Akhtar K, Hassan MJ (2024) Personalized and Precision Medicine in Cancer. In: Aziz, M.A. (eds) Personalized and Precision Nanomedicine for Cancer Treatment. Springer, Singapore. https://doi.org/10.1007/978-981-97-3545-7_3.
42. Bode AM, Dong Z (2017) Precision oncology- the future of personalized cancer medi-cine?. npj Precision Onc https://doi.org/10.1038/s41698-017-0010-5.
43. Garraway LA, Verweij J, Ballman KV (2013) Precision oncology: an overview. J. Clin. Oncol. Off. J. Am. Soc. Clin. Oncol 1803-1805.
44. Mei J, Liu X, Tian HX, Chen Y, Cao Y, et al. (2024) Tumour organoids and assembloids: Patient-derived cancer avatars for immunotherapy. Clin Transl Med 14: 1656.
45. Donisi C, Pretta A, Pusceddu V, Ziranu P, Lai E, et al. (2024) Immunotherapy and Can-cer: The Multi-Omics Perspective. Int J Mol Sci 25:3563.
46. Chen S, Xu H, Guo C, Liu Z, Han X (2022) Editorial: The role of multi-omics variants in tumor immunity and immunotherapy. Front Immunol 13: 1098820-1098825.
47. Porcu M, Solinas C, Mannelli L, Micheletti G, Lambertini M, et al. (2020) Radiomics and "radi-…omics" in cancer immunotherapy: a guide for clinicians. Crit Rev Oncol Hematol 154: 103060-103068.
48. Feng T, Hu J, Wen J, Qian Z, Che G, et al. (2024) Personalized nanovaccines for treating solid cancer metastases. J Hematol Oncol 17: 110-115.
49. Chick RC, Pawlik TM (2024) Updates in Immunotherapy for Pancreatic Cancer. J Clin Med 13: 6410-6419.
50. Wu DW, Jia SP, Xing SJ, Ma HL, Wang X, et al. (2024) Personalized neoantigen cancer vaccines: current progression, challenges and a bright future. Clin Exp Med 24: 220-229.
51. Abbasi AB, Wu V, Lang JE, Esserman LJ (2024) Precision Oncology in Breast Cancer Surgery. Surg Oncol Clin N Am 33: 293-310.
52. Yoon H, Lee S (2021) Integration of Genomic Profiling and Organoid Development in Precision Oncology. Int J Mol Sci 23: 210-216.
53. Maitland ML, Schilsky RL (2011) Clinical trials in the era of personalized oncology. CA Cancer J Clin 61: 365-381.
54. Repetto M, Fernandez N, Drilon A, Chakravarty D (2024) Precision Oncology: 2024 in Review. Cancer Discov 14: 2332-2345.
55. Herrera M, Pretelli G, Desai J, Garralda E, Siu LL, et al. (2024) Bispecific antibodies: ad-vancing precision oncology. Trends Cancer 10: 893-919.
56. Lee WG, Kim ES (2024) Preci-sion Oncology in Pediatric Cancer Surgery. Surg Oncol Clin N Am 33: 409-446.
57. Masina R, Caldas C (2024) Pre-cision Cancer Medicine 2.0-Oncology in the postgenomic era. Mol Oncol 18: 2065-2069.
58. Brown NA, Elenitoba-Johnson KSJ (2020) Enabling Precision Oncology Through Pre-cision Diagnostics. Annu Rev Pathol 15: 97-121.
59. Repetto M, Fernandez N, Drilon A, Chakravarty D (2024) Precision Oncology: 2024 in Review. Cancer Discov 14: 2332-2345.
60. Mack E (2024) Präzisionsmedizin in der Onkologie [Precision medicine in oncology]. Inn Med (Heidelb) 65: 194-201.
61. Chhabra R (2024) Molecular and modular intricacies of precision oncology. Front Immu-nol 15: 1476490-1476494.
62. Apostolia M, Tsimberidou, Fountzilas E, Nikanjam M, Kurzrock R (2020) Review of pre-cision cancer medicine: Evolution of the treatment paradigm. Cancer Treatment Reviews 86: 0305-7372.
63. Aziz MA Personalized and Precision Nanomedicine for Cancer Treatment. Springer, Sin-gapore. https://doi.org/10.1007/978-981-97-3545-7_3.
64. Ochi M, Komura D, Ishikawa S (2025) Pathology Foundation Models. JMA J 8: 121-130.
65. Doig KD, Fellowes A, Scott P, Fox SB (2022) Tumour mutational burden: an overview for pathologists. Pathology 54: 249-253.
66. Wen HY, Collins LC (2023) Breast Cancer Pathology in the Era of Genomics. Hematol Oncol Clin North Am 37: 33-50.
67. Masood S (2020) The changing role of pathologists from morphologists to molecular pathologists in the era of precision medicine. Breast J 26: 27-34.
68. Vranic S, Gatalica Z (2021) The Role of Pathology in the Era of Personalized (Precision) Medicine: A Brief Review. Acta Med Acad 50: 47-57.
69. Moch H, Blank PR, Dietel M, Elmberger G, Kerr KM, et al. (2012) Personalized cancer medicine and the future of pathology. Virchows Arch 460: 3-8.
70. Sharma S, George P, Waddell N (2021) Precision diagnostics: integration of tissue pathol-ogy and genomics in cancer. Pathology 53: 809-817.
71. Sanchez A, Bocklage T (2019) Precision cytopathology: expanding opportunities for bi-omarker testing in cytopathology. J Am Soc Cytopathol 8: 95-115.
72. Wang S, Pan J, Zhang X, Li Y, Liu W, et al. (2024) Towards next-generation diagnostic pathology: AI-empowered label-free multiphoton microscopy. Light Sci Appl 13: 220-254.
73. Giannis D, Moris D, Barbas AS (2021) Diagnostic, Predictive and Prognostic Molecular Biomarkers in Pancreatic Cancer: An Overview for Clinicians. Cancers 13: 1065-1071.
74. Dayde D, Tanaka I, Jain R, Tai MC, Taguchi A (2017) Predictive and Prognostic Molecu-lar Biomarkers for Response to Neoadjuvant Chemoradiation in Rectal Cancer. Int. J. Mol 18: 570-573.
75. Zhou Y, Tao L, Qiu J (2024) Tumor biomarkers for diagnosis, prognosis and targeted ther-apy. Sig Transduct Target Ther 9: 130-132.
76. Kim YS, Choi J, Lee SH (2023) Single-cell and spatial sequencing application in patholo-gy. J Pathol Transl Med 57: 43-51.
77. Collins LC (2021) Precision pathology as applied to breast core needle biopsy evaluation: implications for management. Mod Pathol 34: 48-61.
78. Mishra A, Verma M (2010) Cancer Biomarkers: Are We Ready for the Prime Time? Can-cers 2: 190-208.

79. Rao Bommi J, Kummari S, Lakavath K, Sukumaran RA, Panicker LR, et al. (2023) Recent Trends in Biosensing and Diagnostic Methods for Novel Cancer Biomarkers. Biosensors 13: 390-398.
80. Sarhadi VK, Armengol G (2022) Molecular Biomarkers in Cancer. Biomolecules 12: 1021.
81. Shinozuka T, Kanda M, Kodera Y (2023) Site-specific protein biomarkers in gastric can-cer: a comprehensive review of novel biomarkers and clinical applications. Expert Rev Mol Diagn 23: 701-712.
82. Pitt E, Bradford N, Robertson E, Sansom-Daly UM, Alexander K (2023) The effects of cancer clinical decision support systems on patient-reported outcomes: A systematic re-view. Eur J Oncol Nurs 66: 102390-102398.
83. Hendriks MP, Jager A, Ebben KCWJ, van Til JA, Siesling S (2024) Clinical decision sup-port systems for multidisciplinary team decision-making in patients with solid cancer: Composition of an implementation model based on a scoping review. Crit Rev Oncol He-matol 195: 104260-104267.
84. Nafees A, Khan M, Chow R, Fazelzad R, Hope A, et al. (2023) Evaluation of clinical de-cision support systems in oncology: An updated systematic review. Crit Rev Oncol Hema-tol 192: 104140-104143.
85. Pawloski PA, Brooks GA, Nielsen ME, Olson-Bullis BA (2019) A Systematic Review of Clinical Decision Support Systems for Clinical Oncology Practice. J Natl Compr Canc Netw 17: 331-338.
86. Mukherjee T, Pournik O, Lim Choi Keung SN, Arvanitis TN (2023) Clinical Decision Support Systems for Brain Tumour Diagnosis and Prognosis: A Systematic Review. Can-cers (Basel) 15: 3520-3523.
87. Voigt W, Trautwein M (2023) Improved guideline adherence in oncology through clinical decision-support systems: still hindered by current health IT infrastructures? Curr Opin Oncol 35: 68-77.
88. Frascarelli C, Bonizzi G, Musico CR, Mane E, Cassi C, et al. (2023) Revolutionizing Can-cer Research: The Impact of Artificial Intelligence in Digital Biobanking. J Pers Med 13: 1380-1390.
89. Shum B, Larkin J, Turajlic S (2022) Predictive biomarkers for response to immune check-point inhibition. Semin Cancer Biol 79: 4-17.
90. Mulvey E, Ruan J (2020) Biomarker-driven management strategies for peripheral T cell lymphoma. J Hematol Oncol 13: 50-59.
91. Li JJ, Rogers JE, Yamashita K, Waters RE, Blum Murphy M, et al. (2023) Therapeutic Advances in the Treatment of Gastroesophageal Cancers. Biomolecules 13: 790-796.
92. Liu EK, Sulman EP, Wen PY, Kurz SC (2020) Novel Therapies for Glioblastoma. Curr Neurol Neurosci Rep 20: 15-19.
93. Di Nicolantonio F, Vitiello PP, Marsoni S, Siena S, Tabernero J, et al. (2021) Precision on-cology in metastatic colorectal cancer - from biology to medicine. Nat Rev Clin Oncol 18: 506-525.
94. Mishra P, Laha D, Grant R, Nilubol N (2021) Advances in Biomarker-Driven Targeted Therapies in Thyroid Cancer. Cancers (Basel) 13: 6190-6194.
95. Gillette CM, Yette GA, Cramer SD, Graham LS (2023) Management of Advanced Pros-tate Cancer in the Precision Oncology Era. Cancers (Basel) 15: 2550-2552.
96. Deluce JE, Cardenas L, Lalani AK, Maleki Vareki S, Fernandes R (2022) Emerging Bi-omarker-Guided Therapies in Prostate Cancer. Curr Oncol 29: 5054-5076.
97. Karpel H, Slomovitz B, Coleman RL, Pothuri B (2023) Biomarker-driven therapy in en-dometrial cancer. Int J Gynecol Cancer 33: 343-350.
98. Shi DD, Guo JA, Hoffman HI, Su J, Mino-Kenudson M, et al. (2022) Therapeutic avenues for cancer neuroscience: translational frontiers and clinical opportunities. Lancet Oncol 23: 62-74.
99. Cai Z, Poulos RC, Liu J, Zhong Q (2022) Machine learning for multi-omics data integra-tion in cancer. iScience 25: 103790-103798.
100. Li J, Tian J, Liu Y, Liu Z, Tong M (2024) Personalized analysis of human cancer multi-omics for precision oncology. Comput Struct Biotechnol 23: 2049-2056.
101. Raufaste-Cazavieille V, Santiago R, Droit A (2022) Multi-omics analysis: Paving the path toward achieving precision medicine in cancer treatment and immuno-oncology. Front Mol Biosci 9: 962740-962743.
102. Saman DM, Chrenka EA, Harry ML, Allen CI, Freitag LA, et al. (2021) The im-pact of personalized clinical decision support on primary care patients' views of cancer prevention and screening: a cross-sectional survey. BMC Health Serv Res 21: 590-592.
103. Ou SH, Bartlett CH, Mino-Kenudson M, Cui J, Iafrate AJ (2012) Crizotinib for the treatment of ALK-rearranged non-small cell lung cancer: a success story to usher in the second decade of molecular targeted therapy in oncology. Oncologist 17: 1351-1375.
104. Shaw AT, Kim DW, Nakagawa K, Seto T, Crinó L, et al. (2013) Crizotinib versus chemotherapy in advanced ALK-positive lung cancer. N Engl J Med 368: 2385-2394.
105. Li H, Feng B, Miron A (2017) Breast cancer risk prediction using a polygenic risk score in the familial setting: a prospective study from the Breast Cancer Family Registry and k Con Fab. Genet Med 19: 30-35 https://doi.org/10.1038/gim.2016.43.
106. Sud A, Turnbull C, Houlston R (2021) Will polygenic risk scores for cancer ever be clinically useful?. npj Precis. Onc 50: 1212-1218.
107. Zhang Y D. Hurson AN, Zhang H, Choudhury PP, Easton DF et al. (2020) As-sessment of polygenic architecture and risk prediction based on common variants across fourteen cancers. Nat. Commun 11: 3350-3353.
108. Jia G, Yingchang Lu, Wanqing Wen, Jirong Long, Ying Liu, et al. (2020) Evaluat-ing the utility of polygenic risk scores in identifying high-risk individuals for eight com-mon cancers. JNCI Cancer Spectrum. https://doi.org/10.1093/jncics/pkaa021.
109. Thomas M, Sakoda LC, Hoffmeister M, Rosenthal EA, Lee JK, et al. (2020) Ge-nome-wide modeling of polygenic risk score in colorectal cancer risk. Am. J. Hum. Genet 107: 432-444.
110. Yanes T, Young MA, Meiser B James PA (2020) Clinical applications of polygen-ic breast cancer risk: a critical review and perspectives of an emerging field. Breast Cancer Res 22: 20-21.
111. Kachuri L, Graff RE, Smith-Byrne K, Meyers TJ,Rashkin SR, et al. (2020) Pan-cancer analysis demonstrates that integrating polygenic risk scores with modifiable risk factors improves risk prediction. Nat. Commun 11: 6080-6084.
112. Dannhauser FC, Taylor LC, Tung JSL, Usher-Smith JA (2024) The acceptability and clinical impact of using polygenic scores for risk-estimation of common cancers in primary care: a systematic review. J Community Genet 15: 217-234.
113. Chiang J, Chua Z, Chan JY, Sule AA, Loke WH, et al. (2024) Strategies to im-prove implementation of cascade testing in hereditary cancer syndromes: a systematic re-view. NPJ

Genom Med 9: 20-26.
114. Sun F, Li H, Sun D, Fu S, Gu L, et al. (2025) Single-cell omics: experimental workflow, data analyses and applications. Sci China Life Sci 68: 5-102.
115. Matsuoka T, Yashiro M (2024) Bioinformatics Analysis and Validation of Poten-tial Markers Associated with Prediction and Prognosis of Gastric Cancer. Int J Mol Sci 25: 5870-5880.
116. Rosati D, Palmieri M, Brunelli G, Morrione A, Iannelli F, et al. (2024) Differential gene expression analysis pipelines and bioinformatic tools for the identification of specific biomarkers: A review. Comput Struct Biotechnol 23: 1154-1168.
117. Yang Z, Guan F, Bronk L, Zhao L (2024) Multi-omics approaches for biomarker discovery in predicting the response of esophageal cancer to neoadjuvant therapy: A mul-tidimensional perspective. Pharmacol Ther 254: 10850-108591.
118. Prelaj A, Miskovic V, Zanitti M, Trovo F, Genova C, et al. (2023) Artificial intel-ligence for predictive biomarker discovery in immuno-oncology: a systematic review. Ann Oncol 35: 29-65.
119. Hou W, Zhao Y, Zhu H (2023) Predictive Biomarkers for Immunotherapy in Gas-tric Cancer: Current Status and Emerging Prospects. Int J Mol Sci 24: 15320-15321.
120. Li J, Tian J, Liu Y, Liu Z, Tong M (2024) Personalized analysis of human cancer multi-omics for precision oncology. Comput Struct Biotechnol J 23: 2049-2056.
121. Xu Y, Wang J, Li F, Zhang C, Zheng X, et al. (2022) Identifying individualized risk sub pathways reveals pan-cancer molecular classification based on multi-omics data. Computer Struct Biotechnology J 20: 838-849.
122. Braytee A, He S, Tang S, Yuxuan Sun, Xiaoying Jiang, et al. (2024) Identification of cancer risk groups through multi-omics integration using autoencoder and tensor analysis. Sci Rep https://www.nature.com/articles/s41598-024-59670-8.
123. Vucic EA, Thu KL, Robison K, Rybaczyk LA, Chari R, et al. Translating cancer 'omics' to improved outcomes. Genome Res 22: 188-195.
124. Hachem S, Yehya A, El Masri J, Mavingire N, Johnson JR, et al. (2024) Contemporary Update on Clinical and Experimental Prostate Cancer Biomarkers: A Multi-Omics-Focused Approach to Detection and Risk Stratification. Biology 13: 760-762.
125. Liang XJ, Song XY, Wu JL, Liu D, Lin BY, et al. (2022) Advances in Multi-Omics Study of Prognostic Biomarkers of Diffuse Large B-Cell Lymphoma. Int J Biol Sci 18: 1313-1327.
126. Matsuoka Tb, Yashiro M (2024) Bioinformatics Analysis and Validation of Potential Markers Associated with Prediction and Prognosis of Gastric Cancer. Int J Mol Sci 25: 5870- 5880.
127. Xu Y, Su GH, Ma D, Xiao Y, Shao ZM, et al. (2021) Technological advances in cancer immunity: from immunogenomics to single-cell analysis and artificial intelligence. Signal Transduct Target Ther 6: 310-312.
128. Garg P, Krishna M, Subbalakshmi AR, Ramisetty S, Mohanty A, et al. (2024) Emerging biomarkers and molecular targets for precision medicine in cervical cancer. Biochim Biophys Acta Rev Cancer 1879: 189100-189106.
129. Walcher L, Kistenmacher AK, Suo H, Kitte R, Dluczek S, et al. (2020) Cancer Stem Cells-Origins and Biomarkers: Perspectives for Targeted Personalized Therapies. Front Immunol 11: 1270-1280.
130. Huang T, Song X, Xu D, Tiek D, Goenka A, et al. (2020) Stem cell programs in cancer initiation, progression, and therapy resistance. Theranostics 10: 8721-8743.
131. Talukdar S, Emdad L, Das SK, Sarkar D, Fisher PB (2016) Evolving Strategies for Therapeutically Targeting Cancer Stem Cells. Adv Cancer Res 131: 159-191.
132. Park JH, Pyun WY, Park HW (2020) Cancer Metabolism: Phenotype, Signalling and Therapeutic Targets. Cells 9: 2300-2308.
133. Li Q, Geng S, Luo H, Wang W, Mo YQ, et al. (2024) Signalling pathways involved in colorectal cancer: pathogenesis and targeted therapy. Signal Transduct Target Ther 9: 260-266.
134. Sudhalkar N, Rathod NP, Mathews A, Chopra S, Sriram H, et al. (2019) Potential role of cancer stem cells as biomarkers and therapeutic targets in cervical cancer. Cancer Rep Hoboken 2: 1140-1144.
135. Martin CM, Kehoe L, Spillane CO, O'Leary JJ (2007) Gene discovery in cervical cancer : towards diagnostic and therapeutic biomarkers. Mol Diagn Ther 11: 277-290.
136. Adashek JJ, Kato S, Sicklick JK, Lippman SM, Kurzrock R (2024) If it's a target, it's a pan-cancer target: Tissue is not the issue. Cancer Treat Rev 125: 102720-102721.
137. Henry NL, Hayes DF (2012) Cancer biomarkers. Mol Oncol 6: 140-146.
138. Zhou Y, Tao L, Qiu J, Jing Xu, Xinyu Yang (2024) Tumor biomarkers for diagnosis, prognosis and targeted therapy. Sig Transduct Target Ther https://pubmed.ncbi.nlm.nih.gov/38763973/.
139. Passaro A, Al Bakir M, Hamilton EG, Diehn M, André F, et al. Cancer biomarkers: Emerging trends and clinical implications for personalized treatment. Cell 187: 1617-1635.
140. Wang Z, Li R, Yang G, Wang Y (2024) Cancer stem cell biomarkers and related signalling pathways. J Drug Target 32: 33-44.
141. Wong CH, Ko IC, Ng CF (2025) Liquid biomarkers in prostate cancer: recent advancements and future directions. Curr Opin Urol 35: 3-12.
142. Kohaar I, Hodges NA, Srivastava S (2024) Biomarkers in Cancer Screening: Promises and Challenges in Cancer Early Detection. Hematol Oncol Clin North Am 38: 869-888.
143. Dong F (2024) Pan-Cancer Molecular Biomarkers: A Paradigm Shift in Diagnostic Pathology. Clin Lab Med 44: 325-337.
144. Roy-Chowdhuri S (2021) Molecular Pathology of Lung Cancer. Surg Pathol Clin 14: 369-377.
145. Walk EE. The role of pathologists in the era of personalized medicine. Arch Pathol Lab 133: 605-610.
146. Perl DP (2007) The role of the pathologist in translational and personalized medicine. Mt Sinai J Med 74: 22-26.
147. Biopreserv Biobank (2011) 9: 149-155.
148. Fabi A, Cortesi L, Duranti S, Cordisco EL, Di Leone A, et al. (2024) Multigenic panels in breast cancer: Clinical utility and management of patients with pathogenic variants other than BRCA1/2. Crit Rev Oncol Hematol 201: 104430-104431.
149. Passaro A, Al Bakir M, Hamilton EG, Diehn M, André F, et al. (2024) Cancer biomarkers: Emerging trends and clinical implications for personalized treatment. Cell 187: 1617-1635.
150. Giraldo NA, Peske JD, Sautès-Fridman C, Fridman WH (2019) Integrating histopathology, immune biomarkers, and molecular subgroups in solid cancer: the next step in precision oncology. Virchows Arch 474: 463-474.
151. Brozos-Vázquez E, Toledano-Fonseca M, Costa-Fraga N, García-Ortiz MV, Díaz-Lagares Á, et al. (2024) Pancreatic cancer biomarkers: A pathway to advance in personalized treatment selection. Cancer Treat Rev 125: 102710-102719.
152. Giraldo NA, Peske JD, Sautès-Fridman C, Fridman WH (2019) Integrating histopathology, immune biomarkers, and molecular subgroups in solid cancer: the next step in precision

oncology. Virchows Arch 474: 463-474.
153. Riedl JM, Moik F, Esterl T, Kostmann SM, Gerger A, et al. (2024) Molecular diagnostics tailoring personalized cancer therapy-an oncologist's view. Virchows Arch 484: 169-179.
154. Ely S (2009) Personalized medicine: individualized care of cancer patients. Transl Res. 154: 303-308.
155. Li Q, Geng S, Luo H, Wang W, Mo YQ, et al. (2024) Signaling pathways involved in colorectal cancer: pathogenesis and targeted therapy. Signal Transduct Target Ther 9: 260-266.
156. Chan, Daniel W. Pathology, Garraway LA, Verweij J, et al. (2019) Precision oncology: an overview. J. Clin. Oncol. Off 31: 1803-1805.
157. Lusheng Li, Mengtao Sun, Jieqiong Wang, Shibiao Wan (2024) Chapter Nine - Multi-omics based artificial intelligence for cancer research. Advances in Cancer Research, Academic Press 163: 303-356.
158. Fountzilas E, Pearce T, Baysal MA (2025) Convergence of evolving artificial intelligence and machine learning techniques in precision oncology. npj Digit. Med. 8:70-75.
159. Bhinder B, Gilvary C, Madhukar NS, Elemento O (2021) Artificial Intelligence in Cancer Research and Precision Medicine. Cancer Discov 11: 900-915.
160. Boehm KM, Khosravi P, Vanguri R, Gao J, Shah SP (2022) Harnessing multimodal data integration to advance precision oncology. Nat Rev Cancer 22: 114-126.
161. Bera K, Schalper KA, Rimm DL, Velcheti V, Madabhushi A (2019) Artificial intelligence in digital pathology - new tools for diagnosis and precision oncology. Nat Rev Clin Oncol 16: 703-715.
162. Kumar Am S, Rajan P, Alkhamees M, Holley M, Lakshmanan VK (2024) Prostate cancer theragnostics biomarkers: An update. Investig Clin Urol 65: 527-539.
163. Zou J, Zhang Y, Pan Y, Mao Z, Chen X (2024) Advancing nanotechnology for neoantigen-based cancer theranostics. Chem Soc Rev 53: 3224-3252.
164. Priyadarshni N, Singh R, Mishra MK (2024) Nanodiamonds: Next generation nano-theranostics for cancer therapy. Cancer Lett 587: 216701-216710.
165. Ferrari V, Mograbi B, Gal J, Milano G (2024) Companion Tests and Personalized Cancer Therapy: Reaching a Glass Ceiling. Int J Mol Sci 25: 9990-9991.
166. Abdel-Wahab M, Giammarile F, Carrara M, Paez D, Hricak H, et al. (2024) Radiotherapy and theranostics: a Lancet Oncology Commission. Lancet Oncol 25: 545-580.
167. Puccetti M, Pariano M, Schoubben A, Giovagnoli S, Ricci M (2024) Biologics, theranostics, and personalized medicine in drug delivery systems. Pharmacol Res 201: 107080-107086.
168. Giovanella L, Tuncel M, Aghaee A, Campenni A, De Virgilio A, et al. (2024) Theranostics of Thyroid Cancer. Semin Nucl Med 54: 470-487.
169. Song Y, Zou J, Castellanos EA, Matsuura N, Ronald JA, et al. (2024) Theranostics - a sure cure for cancer after 100 years? Theranostics 14: 2464-2488.
170. Lawal IO, Abubakar SO, Ndlovu H, Mokoala KMG, More SS (2024) Advances in Radioligand Theranostics in Oncology. Mol Diagn Ther 28: 265-289.
171. Bauckneht M, Ciccarese C, Laudicella R, Mosillo C, D'Amico F, et al. (2024) Theranostics revolution in prostate cancer: Basics, clinical applications, open issues and future perspectives. Cancer Treat Rev 124: 102690-102698.
172. Seifert R, Alberts IL, Afshar-Oromieh A, Rahbar K (2021) Prostate Cancer Theranostics: PSMA Targeted Therapy. PET Clin 16: 391-396.
173. Zou J, Zhang Y, Pan Y, Mao Z, Chen X (2024) Advancing nanotechnology for neoantigen-based cancer theranostics. Chem Soc Rev 53: 3224-3252.
174. Dutta B, Barick KC, Hassan PA, Tyagi AK (2024) Recent progress and current status of surface engineered magnetic nanostructures in cancer theranostics. Adv Colloid Interface Sci 334: 103310-103320.
175. Giammarile F, Paez D, Zimmermann R, Cutler CS, Jalilian A, et al. (2024) Production and regulatory issues for theranostics. Lancet Oncol 25: 260-269.
176. Zou J, Zhang Y, Pan Y, Mao Z, Chen X (2024) Advancing nanotechnology for neoantigen-based cancer theranostics. Chem Soc Rev 53: 3224-3252.
177. Wu R, Zhu W, Shao F, Wang J, Li D, et al. (2025) Expanding horizons in theragnostics: from oncology to multidisciplinary applications. Radiol Med https://pubmed.ncbi.nlm.nih.gov/40042756/.
178. Belge Bilgin G, Bilgin C, Burkett BJ, Orme JJ, Childs DS, et al. (2024) Theranostics and artificial intelligence: new frontiers in personalized medicine. Theranostics 14: 2367-2378.
179. Hua Y, Qin Z, Gao L, Zhou M, Xue Y, et al. Protein nanoparticles as drug delivery systems for cancer theranostics. J Control Release 371: 429-444.
180. Na L, Fan F (2024) Advances in nanobubbles for cancer theranostics: Delivery, imaging and therapy. Biochem Pharmacol 226: 116330-116341.
181. Lawal IO, Abubakar SO, Ndlovu H, Mokoala KMG, More SS, et al. Advances in Radioligand Theranostics in Oncology. Mol Diagn Ther 28: 265-289.
182. Lotter W, Hassett MJ, Schultz N, Kehl KL, Van Allen EM, et al. (2024) Artificial Intelligence in Oncology: Current Landscape, Challenges, and Future Directions. Cancer Discov 14: 711-726.
183. Li Q, Geng S, Luo H, Wang W, Mo YQ, et al. (2024) Signaling pathways involved in colorectal cancer: pathogenesis and targeted therapy. Signal Transduct Target Ther 9: 260-266.
184. Adashek JJ, Kato S, Sicklick JK, Lippman SM, Kurzrock R (2024) If it's a target, it's a pan-cancer target: Tissue is not the issue. Cancer Treat Rev 125: 102720-102721.
185. Xiong X, Zheng LW, Ding Y, Chen YF, Cai YW, Wang LP, Huang L, Liu CC, Shao ZM, Yu KD. Breast cancer: pathogenesis and treatments. Signal Transduct Target Ther 10: 40-49.
186. Piecoro DW, Allison DB (2024) Precision Medicine in Cytopathology. Surg Pathol Clin 17: 329-345.
187. Zhou Y, Tao L, Qiu J, Xu J, Yang X, et al. (2024) Tumor biomarkers for diagnosis, prognosis and targeted therapy. Signal Transduct Target Ther 9: 130-132.
188. Wang J, Zhang Z, Wang Y (2025) Utilizing Feature Selection Techniques for AI-Driven Tumor Subtype Classification: Enhancing Precision in Cancer Diagnostics. Biomolecules 15: 70-81.
189. Zhou Z, Lin T, Chen S, Zhang G, Xu Y, et al. (2024) Omics-based molecular classifications empowering in precision oncology. Cell Oncol (Dordr) 47: 759-777.
190. Yu KH, Snyder M (2016) Omics Profiling in Precision Oncology. Mol Cell Proteomics 15: 2525-2536.
191. Neagu AN, Whitham D, Bruno P, Morrissiey H, Darie CA, et al. Omics-Based Investigations of Breast Cancer. Molecules 28: 4760-4768.
192. Acharya D, Mukhopadhyay A (2024) A comprehensive review of machine learning techniques for multi-omics data integration: challenges and applications in precision oncology. Brief Funct Genomics 23: 549-560.
193. Li L, Sun M, Wang J, Wan S (2024) Multi-omics based artificial intelligence for cancer research. Adv Cancer Res

163: 303-356.

194. He X, Liu X, Zuo F, Shi H, Jing J (2023) Artificial intelligence-based multi-omics analysis fuels cancer precision medicine. Semin Cancer Biol 88: 187-200.
195. Paverd H, Zormpas-Petridis K, Clayton H, Burge S, Crispin-Ortuzar M (2024) Radiology and multi-scale data integration for precision oncology. NPJ Precis Oncol 8: 150-158.
196. Correa-Aguila R, Alonso-Pupo N, Hernández-Rodríguez EW (2022) Multi-omics data integration approaches for precision oncology. Mol Omics 18: 469-479.
197. Nicora G, Vitali F, Dagliati A, Geifman N, Bellazzi R (2020) Integrated Multi-Omics Analyses in Oncology: A Review of Machine Learning Methods and Tools. Front Oncol 10: 1020-1030.
198. Raufaste-Cazavieille V, Santiago R, Droit A (2022) Multi-omics analysis: Paving the path toward achieving precision medicine in cancer treatment and immuno-oncology. Front Mol Biosci 9: 962740-962743.
199. Donisi C, Pretta A, Pusceddu V, Ziranu P, Lai E, et al. Immunotherapy and Cancer: The Multi-Omics Perspective. Int J Mol Sci 25: 3560-3563.
200. Pandiella A, Calvo E, Moreno V, Amir E, Templeton A, et al. (2023) Considerations for the clinical development of immuno-oncology agents in cancer. Front Immunol 14: 1229570-1229575.
201. De Pauw T, De Mey L, Debacker JM, Raes G, Van Ginderachter JA, et al. (2023) Current status and future expectations of nanobodies in oncology trials. Expert Opin Investig Drugs 32: 705-721.
202. Parkinson JF, Ospina PA, Round J, McNeely ML, Jones CA (2023) Generic Health Utility Measures in Exercise Oncology: A Scoping Review and Future Directions. Curr Oncol 30: 8888-8901.
203. Fujiwara Y, Kato S, Kurzrock R (2024) Evolution of Precision Oncology, Personalized Medicine, and Molecular Tumor Boards. Surg Oncol Clin N Am 33: 197-216.
204. Incorvaia L, Russo A, Cinieri S (2022) The molecular tumor board: a tool for the governance of precision oncology in the real world. Tumori 108: 288-290.
205. Riedl JM, Moik F, Esterl T, Kostmann SM, Gerger A, et al. (2023) Molecular diagnostics tailoring personalized cancer therapy-an oncologist's view. Virchows Arch 484: 169-179.
206. Luchini C, Lawlor RT, Milella M, Scarpa A (2020) Molecular Tumor Boards in Clinical Practice. Trends Cancer 6: 738-744.
207. Munari E, Scarpa A, Cima L, Pozzi M, Pagni F, et al. (2024) Cutting-edge technology and automation in the pathology laboratory. Virchows Arch 484: 555-566.
208. Rafii A, Vidal F, Rathat G, Alix-Panabières C (2014) Circulating tumor cells: cornerstone of personalized medicine.J Gynecol Obstet Biol Reprod (Paris) 43: 640-648.
209. Riedl JM, Moik F, Esterl T, Kostmann SM, Gerger A, et al. (2024) Molecular diagnostics tailoring personalized cancer therapy-an oncologist's view. Virchows Arch 484: 169-179.
210. Yu KH, Snyder M (2016) Omics Profiling in Precision Oncology. Mol Cell Proteomics 15: 2525-2536.
211. Li J, Tian J, Liu Y, Liu Z, Tong M (2024) Personalized analysis of human cancer multi-omics for precision oncology. Comput Struct Biotechnol J 23: 2049-2056.