

Cancer Biology: Foundations for Gastrointestinal Oncology Nursing Practice

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Abstract

Background: Gastrointestinal cancers including malignancies of the colon, rectum, stomach, pancreas, liver, and esophagus represent a significant global health burden with high morbidity and mortality. Advances in molecular oncology reveal that these cancers arise through complex genetic, epigenetic, microenvironmental, and metastatic processes. Understanding these mechanisms is essential for oncology nurses to support precision medicine and deliver effective, patient-centered care. **Methods:** This literature review employed a structured thematic analysis to synthesize knowledge on cancer biology concepts relevant to gastrointestinal oncology nursing. Comprehensive database searches (PubMed, CINAHL, Scopus, Google Scholar) targeted publications from 2000 to 2024 addressing genetic mutations, epigenetics, tumor microenvironment, metastasis, and nursing education. Eligible articles were critically reviewed and thematically coded to identify major themes and subthemes with clinical and nursing practice relevance. **Results:** Three primary themes emerged: (1) Genetic and Epigenetic Alterations, including oncogene activation, tumor suppressor inactivation, microsatellite instability, and DNA methylation; (2) Tumor Microenvironment and Immune Evasion, encompassing stromal barriers, angiogenesis, immune suppression, and intercellular signaling; and (3) Mechanisms of Metastasis, detailing local invasion, epithelial-mesenchymal transition, circulation, colonization, dormancy, and reactivation. Each theme includes nursing roles in patient education, decision-making support, therapy monitoring, and psychosocial care. **Conclusion:** Integrating cancer biology knowledge into nursing practice is essential for anticipating patient needs, supporting shared decision-making, and managing advanced therapies in gastrointestinal oncology. Nurses must engage in ongoing education and interdisciplinary collaboration to navigate the evolving landscape of precision oncology and improve outcomes and quality of life for patients facing these complex cancers.

Keywords: Gastrointestinal cancer- cancer biology- oncology nursing- precision oncology- genetic alterations

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Introduction

Gastrointestinal (GI) cancers including colorectal, gastric, pancreatic, hepatic, and esophageal malignancies remain a major global health burden with high morbidity and mortality [1]. Advances in molecular oncology show that these cancers arise from complex interactions among genetic mutations, epigenetic changes, microenvironmental influences, and metastatic processes that shape disease

progression, treatment resistance, and outcomes [2-4]. Precision oncology, which tailors therapy to tumor biology, has transformed GI cancer management and underscores the need for all members of the oncology team including nurses to understand the biological foundations of these diseases [5, 6].

Nurses are central to multidisciplinary oncology

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care, providing education, counseling, and symptom management across the cancer continuum [7, 8]. Yet many traditional nursing programs devote limited attention to molecular oncology, creating gaps that may hinder effective communication with patients and limit shared decision-making [8]. With the rapid integration of biomarkers, immunotherapies, targeted agents, and adaptive trial approaches into GI cancer care, these knowledge gaps become even more pressing [9,10].

This review addresses that gap by synthesizing essential cancer biology concepts most relevant to GI oncology nursing. We organize current evidence into three themes (1) Genetic and Epigenetic Alterations, (2) Tumor Microenvironment and Immune Evasion, and (3) Mechanisms of Metastasis and highlight how this knowledge informs nursing roles in patient education, treatment monitoring, and interdisciplinary collaboration.

Materials and Methods

We conducted a systematic thematic review to integrate current knowledge on cancer biology concepts relevant to GI oncology nursing practice. Peer-reviewed articles published in the last 20 years were searched in PubMed, CINAHL, Scopus, and Google Scholar using combinations of the following terms: gastrointestinal cancer, oncogenes, tumor suppressor genes, epigenetics, microsatellite instability, tumor microenvironment, angiogenesis, immune evasion, metastasis, nursing education, and precision oncology. Additional sources were identified by manually screening reference lists of seminal articles and guidelines.

Inclusion criteria were English-language articles that offered conceptual or clinical insights into genetic, epigenetic, microenvironmental, and metastatic mechanisms in GI cancers and their implications for patient care, treatment planning, or nursing practice. Non-GI or non-biologically focused articles were excluded. Eligible articles were critically appraised and

coded for key biological processes, clinical implications, and nursing roles.

Figure 1 shows the study selection process: database searches identified 2,345 records and manual/reference searches added 42, for 2,387 total. After removing duplicates, 1,812 unique records remained. Of these, 237 full-text articles were reviewed for eligibility, and 48 studies met all criteria and were included in the thematic synthesis.

The data were then thematically analysed to outline and categorise content into three main themes: (1) Genetic and Epigenetic Alterations, (2) Tumor Microenvironment and Immune Evasion, and (3) Mechanisms of Metastasis. In each of the themes, subthemes were created to explain the biological processes, how they apply to the selection of treatment and prognosis, and the implication of the same to nursing practice. The choice of this thematic structure was based on the need to facilitate a clear, practice-focused synthesis of the concepts of cancer biology with the practical nursing roles, which would inform educational planning and improve the provision of patient-centered oncology care.

Results

Thematic Analysis results

Theme 1: Genetic and Epigenetic Alterations

Cancer is fundamentally a disease of the genome, driven by a complex interplay between genetic mutations and epigenetic modifications that disrupt normal cellular regulation. Oncogene activation, tumor suppressor gene inactivation, microsatellite instability (MSI), and Deoxyribonucleic Acid (DNA) repair defects collectively shape the biological course of GI malignancies, influencing tumor behavior and therapeutic responsiveness [2-4, 11-16]. Epigenetic alterations, including DNA methylation and histone modifications, further silence critical regulatory genes without altering DNA sequence,

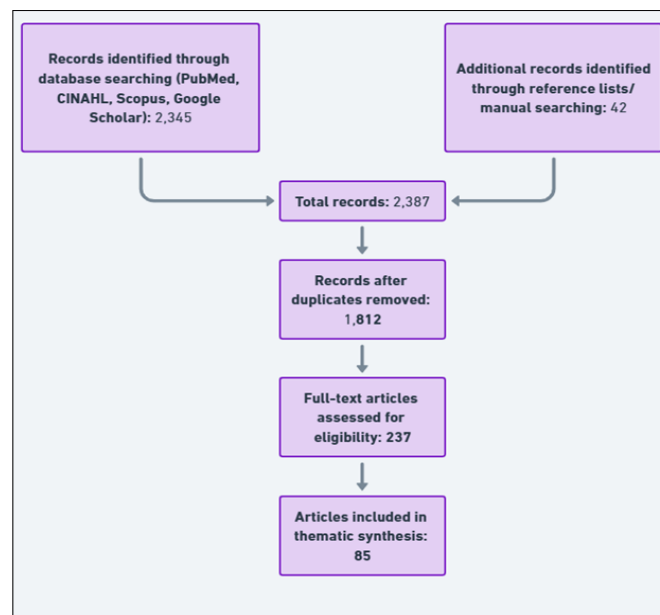


Figure 1. PRISMA-style Flow Diagram

creating opportunities for biomarker development and therapeutic targeting [19-21]. Molecular profiling and precision oncology translate these insights into practice by tailoring treatment to a tumor's molecular signature [5, 25-27]. For oncology nurses, this evolving landscape heightens responsibilities in patient education, genetic counseling support, interpretation of test implications, and monitoring of treatment responses so that complex advances are transformed into patient centered care [7, 8].

Oncogene Activation and Tumor Suppressor Gene Inactivation

Colorectal tumorigenesis exemplifies the multistep process of cascade mutations along the well-established adenoma carcinoma sequence, where progressive genetic and epigenetic alterations transform normal mucosa into invasive carcinoma [11]. Central to this process is the deregulation of the cell cycle and programmed cell death. Inactivation of critical tumor suppressor genes including Tumor Protein 53 (TP53), which normally

Table 1. Fundamental Concepts, Expanded Definitions, and Clinical Implications in Gastrointestinal (GI) Oncology

Concept	Expanded Definition	Clinical Implications in GI Cancer	References
Deoxyribonucleic Acid (DNA)	DNA is the hereditary material of all cells, encoding genes that regulate growth, repair, and cellular function. In GI cancers, DNA damage from mutations, replication errors, or environmental carcinogens drives genomic instability and malignant transformation.	Mutational burden underlies tumorigenesis, guides molecular profiling, and influences prognosis and therapy personalization.	[2-4]
Oncogenes	Oncogenes are normal genes that, once mutated or overexpressed, acquire the ability to promote uncontrolled proliferation and survival. In GI malignancies, key oncogenes include Kirsten Rat Sarcoma Viral Oncogene Homolog (KRAS) and B-Raf Proto-Oncogene (BRAF), which activate growth pathways independent of regulatory control.	KRAS mutations predict resistance to anti-EGFR therapy; BRAF V600E mutations signal poor prognosis and direct patients to combination targeted regimens.	[11, 12, 16]
Tumor Suppressor Genes (TSGs)	TSGs act as brakes of the cell cycle, maintaining genomic integrity by halting proliferation or triggering apoptosis in damaged cells. Commonly inactivated TSGs in GI cancers include Tumor Protein 53 (TP53), Adenomatous Polyposis Coli (APC), and Mothers Against Decapentaplegic Homolog 4 (SMAD4), whose loss dismantles key control pathways.	Their inactivation defines the adenoma–carcinoma sequence in colorectal cancer, shapes disease progression, and informs therapeutic strategy.	[2, 11–13, 16]
Microsatellite Instability (MSI)	MSI is a form of genetic hypermutability caused by defects in the mismatch repair (MMR) system involving MutL Homolog 1 (MLH1), MutS Homolog 2 (MSH2), MutS Homolog 6 (MSH6), and Postmeiotic Segregation Increased 2 (PMS2). It results in widespread insertion–deletion errors in short DNA repeat sequences.	MSI-high colorectal cancers respond favorably to immune checkpoint inhibitors (ICIs) and often signal Lynch syndrome, guiding both therapy and familial screening.	[14, 15, 17, 18, 36, 39]
CpG Island Methylator Phenotype (CIMP)	CIMP is an epigenetic pattern marked by widespread DNA hypermethylation at cytosine–phosphate–guanine (CpG) islands, often silencing TSGs. It represents a distinct colorectal cancer subtype with unique biological and clinical behavior.	CIMP-positive tumors define prognostic subgroups and open opportunities for demethylating or histone-modifying therapies.	[19–21, 23, 24]
Next-Generation Sequencing (NGS)	NGS is a high-throughput technology that simultaneously detects mutations, fusions, amplifications, and expression profiles from tumor or blood samples. It enables comprehensive tumor molecular profiling.	Identifies actionable targets (e.g., Human Epidermal Growth Factor Receptor 2 (HER2) amplification, Neurotrophic Tyrosine Receptor Kinase (NTRK) fusions) and tracks resistance evolution through liquid biopsy, guiding therapy selection and adaptation.	[25–27]
Extracellular Matrix (ECM)	The ECM is a network of proteins, glycoproteins, and signaling molecules that provides structural and biochemical support to cells. In GI cancers, it undergoes remodeling and stiffening that promotes invasion and blocks drug delivery.	In pancreatic cancer, dense ECM/desmoplasia impedes chemotherapy penetration, prompting trials of stroma-modulating therapies.	[22, 28, 29]
Tumor Microenvironment (TME)	The TME is a complex ecosystem of tumor cells, fibroblasts, immune cells, vasculature, and signaling molecules. Rather than passive, it actively interacts with cancer cells, shaping growth, invasion, immune escape, and therapy resistance.	Drives resistance, metastasis, and immune evasion; targeted by ICIs, anti-angiogenics, and stroma therapies in GI cancers.	[3, 28, 29, 31, 35, 44]
Angiogenesis	Angiogenesis is the process of forming new blood vessels from pre-existing vasculature, stimulated by tumor-secreted factors such as Vascular Endothelial Growth Factor (VEGF). Tumor vessels are often abnormal, leaky, and inefficient, fostering hypoxia and metastasis.	Anti-VEGF therapy disrupts angiogenesis, though associated toxicities (e.g., hypertension, bleeding) require management.	[28, 29, 31, 32]
Epithelial–Mesenchymal Transition (EMT)	EMT is a biologic reprogramming where epithelial cells lose polarity and adhesion, acquiring mesenchymal properties that enable motility, invasiveness, and resistance to apoptosis.	Facilitates invasion, metastasis, and resistance to targeted therapy; EMT inhibitors are under investigation as therapeutic strategies.	[33, 34, 42, 43]
Circulating Tumor Cells (CTCs)	CTCs are cells shed from primary or metastatic tumors that enter the bloodstream. They can circulate alone or in clusters, sometimes shielded by platelets, to evade immune attack and seed metastases.	Serve as prognostic biomarkers and noninvasive tools to monitor residual disease, resistance mutations, and therapy response in colorectal and esophageal cancers.	[5, 6, 46, 47, 49, 50]

safeguards DNA integrity; Adenomatous Polyposis Coli (APC), a key regulator of the Wnt/ β -catenin pathway; and Mothers Against Decapentaplegic Homolog 4 (SMAD4), a mediator of TGF- β signaling removes essential checkpoints that restrain uncontrolled proliferation and survival of abnormal cells [12, 13]. In parallel, defects in the mismatch repair system give rise to microsatellite instability (MSI), creating a hypermutator phenotype that not only accelerates tumorigenesis but also serves as a predictive biomarker for responsiveness to immune checkpoint blockade therapies such as pembrolizumab in colorectal cancer [14, 15].

From a clinical perspective, these molecular events have profound therapeutic implications. Kirsten Rat Sarcoma Viral Oncogene Homolog (KRAS mutations) confer primary resistance to anti-EGFR monoclonal antibodies, rendering such targeted agents ineffective, while BRAF V600E mutations (B-Raf proto-oncogene, serine/threonine kinase, Valine-to-Glutamic Acid substitution at codon 600) signal aggressive disease biology and poorer prognosis, often necessitating combination targeted regimens to improve outcomes [12, 16]. The incorporation of these insights into routine practice has firmly established molecular profiling as a cornerstone of precision oncology enabling clinicians to align patients with the most effective, least toxic therapies while avoiding futile interventions [11-13].

For oncology nurses, this knowledge translates directly into patient care. Nurses play a pivotal role in explaining the rationale, scope, and limitations of molecular testing, clarifying to patients and families why specific treatments are recommended or withheld, and ensuring understanding during complex decision-making processes. They also guide patients toward appropriate genetic counseling when hereditary cancer syndromes are suspected, provide psychosocial support during testing and result disclosure, and reinforce adherence to individualized treatment plans. By bridging the scientific basis of tumor biology with compassionate communication, nurses enhance patient empowerment, participation, and trust in precision-guided cancer care.

Microsatellite Instability and DNA Repair Defects

Microsatellite instability (MSI) arises from defects in the DNA mismatch repair (MMR) system, most often involving MutL Homolog 1 (MLH1), MutS Homolog 2 (MSH2), MutS Homolog 6 (MSH6), and Postmeiotic Segregation Increased 2 (PMS2). When these proteins fail to correct replication errors, tumor cells acquire a hypermutator phenotype, resulting in abundant insertions or deletions within short DNA repeat sequences [15, 17]. This accumulation of errors drives tumor heterogeneity and progression, but also creates a large number of neoantigens abnormal proteins that appear “foreign” to the immune system. As a result, MSI-high tumors are particularly visible to T-cells and often show strong responses to immune checkpoint inhibitors (ICIs) such as pembrolizumab or nivolumab [18]. Beyond therapeutic implications, MSI testing also has genetic and familial relevance, as detection of MSI-high status can suggest

the presence of Lynch syndrome, a hereditary cancer predisposition that warrants cascade screening for at-risk relatives.

From a nursing perspective, the clinical and psychosocial dimensions of MSI are equally important. Nurses play a key role in educating patients about the purpose and process of MSI testing, clarifying what a positive or negative result means for treatment selection and family risk. They translate complex molecular findings into understandable language, reducing patient anxiety and supporting informed decision-making. During immunotherapy, nurses also provide vigilant monitoring for immune-related adverse events (irAEs) such as colitis, dermatitis, hepatitis, or endocrinopathies, which require early recognition and prompt management to ensure safety. By combining patient education, psychosocial support, and clinical surveillance, nurses bridge the gap between precision oncology advances and patient-centered care, ultimately enhancing adherence and outcomes.

Epigenetic Modifications and Gene Silencing

Epigenetic mechanisms including DNA methylation, histone modification, and chromatin remodeling regulate gene activity without altering the underlying DNA sequence. In gastrointestinal (GI) cancers, aberrant DNA methylation frequently occurs in promoter regions of tumor suppressor genes, leading to their silencing and permitting uncontrolled cell growth, resistance to apoptosis, and therapeutic resistance [19, 20]. A notable example is the Cytosine-phosphate-Guanine (CpG) island methylator phenotype (CIMP), a molecular subtype of colorectal cancer characterized by widespread hypermethylation and distinct clinical behavior, including differential prognosis and treatment response [21]. Unlike fixed genetic mutations, epigenetic changes are potentially reversible, which has inspired the development of therapies such as DNA-demethylating agents (e.g., azacitidine, decitabine) and histone deacetylase inhibitors (HDACis) that aim to restore normal gene expression [23, 24]. Beyond genetic and epigenetic targets, the interplay between tumor and stroma is increasingly recognized as an epigenetically influenced barrier; modifying tumor-stroma interactions can enhance drug delivery and treatment response, offering additional therapeutic opportunities [22].

For nurses, integrating knowledge of epigenetics into clinical practice is essential. They help patients understand the meaning of epigenetic test results, particularly in contexts such as CIMP classification or eligibility for targeted epigenetic drugs. Nurses also prepare patients for the uncertainties of clinical trials, explain potential benefits and risks, and provide emotional support during participation in novel therapeutic protocols. Furthermore, they monitor for adverse effects associated with epigenetic therapies such as cytopenias, gastrointestinal disturbances, and fatigue and communicate promptly with the care team to ensure patient safety. Through education, psychosocial support, and vigilant monitoring, nurses bridge complex scientific advances with compassionate,

Table 2. Nursing Learning Needs and Corresponding Nursing Roles in Gastrointestinal Oncology (Cancer Biology Focus)

Nursing Learning Needs	Nursing Roles in This Regard
1. Molecular Drivers of Disease – Oncogene activation (KRAS, BRAF) and tumor suppressor loss (TP53, APC, SMAD4) – Microsatellite instability (MSI) and mismatch repair (MMR) deficiency (MLH1, MSH2, MSH6, PMS2) – Epigenetic changes such as DNA methylation and CpG island methylator phenotype (CIMP)	– Explain the purpose and implications of molecular testing to patients and families – Support informed decision-making regarding targeted therapy or immunotherapy – Facilitate timely referral for genetic counseling in suspected hereditary cancer syndromes (e.g., Lynch syndrome)
2. Tumor Microenvironment (TME) – Stroma, desmoplasia, and extracellular matrix (ECM) remodeling – Angiogenesis driven by VEGF signaling – Immune evasion through regulatory T cells (Tregs), tumor-associated macrophages (TAMs), and myeloid-derived suppressor cells (MDSCs) – Reciprocal tumor–stroma signaling	– Educate patients on why some GI cancers (e.g., pancreatic cancer) are difficult to treat – Clarify the rationale for multi-agent, stroma-modulating, or experimental regimens – Monitor and manage adverse effects of anti-angiogenic agents, immunotherapy, and stroma-targeting drugs
3. Metastatic Cascade – Local invasion and epithelial–mesenchymal transition (EMT) – Intravasation, circulating tumor cells (CTCs), and survival in blood – Extravasation, colonization, and organ tropism (e.g., hepatic spread in colorectal cancer) – Tumor dormancy and reactivation	– Assess and document symptoms suggestive of metastasis (pain, jaundice, weight loss) – Explain the role of surveillance imaging, biomarkers, and liquid biopsy in follow-up – Provide emotional support during discussions about recurrence, progression, or palliative planning
4. Translating Biology into Practice and Communication – Converting genomic and molecular findings into patient-friendly explanations – Supporting shared decision-making with patients and families	– Simplify molecular concepts into accessible, culturally sensitive language – Ensure patients understand therapy goals, limitations, and expected outcomes – Foster trust and empowerment through compassionate, transparent communication
5. Monitoring and Managing Advanced Therapies – Mechanisms and monitoring of immunotherapies (e.g., PD-1/PD-L1, CTLA-4 blockade) – Targeted therapies (anti-EGFR, anti-HER2, BRAF/MEK inhibitors) – Use of next-generation sequencing (NGS) and liquid biopsy in guiding care	– Educate patients about therapy mechanisms, benefits, and potential risks – Monitor for immune-related adverse events (irAEs) and targeted therapy toxicities – Support adherence to treatment plans and timely reporting of complications
6. Continuing Education and Interdisciplinary Collaboration – Staying current with evolving molecular oncology and precision medicine – Engaging in collaborative learning with multidisciplinary teams	– Participate actively in tumor boards, journal clubs, and case discussions – Share updated knowledge with peers to strengthen team capacity – Advocate for lifelong professional development and integration of evidence-based advances into practice

patient-centered care.

Molecular Profiling and Precision Oncology

Next-generation sequencing (NGS) has revolutionized cancer diagnostics by enabling simultaneous detection of genetic, epigenetic, and transcriptomic alterations in tumor tissue and circulating DNA. This technology identifies actionable mutations, gene fusions, copy-number amplifications, and expression signatures, allowing clinicians to select therapies most likely to benefit individual patients [25, 26]. Clinically, NGS findings have transformed treatment strategies in gastrointestinal oncology: for instance, anti-Human Epidermal Growth Factor Receptor 2 (HER2) monoclonal antibodies are used in HER2-amplified gastric cancer, while Tyrosine Receptor Kinase (TRK) inhibitors target tumors harboring Neurotrophic Tyrosine Receptor Kinase (NTRK) fusions regardless of site [25]. In addition, longitudinal profiling through repeat biopsies or liquid biopsy enables real-time monitoring of resistance mutations, clonal evolution, and minimal residual disease, ensuring that therapy can be adjusted at the earliest sign of treatment escape [26, 27]. By bridging biology and practice, NGS has become a cornerstone of precision oncology, improving survival while minimizing unnecessary toxicity.

For nurses, the integration of NGS into patient care introduces both opportunities and responsibilities. They prepare patients for molecular testing by explaining

its purpose, procedures, and potential implications for therapy. Nurses help set realistic expectations about test outcomes, including the possibility of inconclusive or unexpected results, while providing psychosocial support to reduce anxiety during the waiting period. They also advocate for equitable access to testing and clinical trials, particularly for patients in resource-limited settings, ensuring that advances in precision oncology reach diverse populations. Furthermore, nurses facilitate multidisciplinary discussions, help patients interpret how molecular findings affect treatment decisions, and monitor emotional and physical responses when therapy plans change. In doing so, they serve as essential translators between genomic science and patient-centered care.

Theme 2: Tumor Microenvironment and Immune Evasion

The tumor microenvironment (TME) represents a dynamic ecosystem composed of malignant cells, stromal components, immune infiltrates, blood vessels, and soluble mediators that constantly interact to shape cancer progression. Rather than serving as a passive backdrop, the TME is actively remodeled by tumors to erect physical barriers (e.g., desmoplasia), alter vasculature through aberrant angiogenesis, and establish an immunosuppressive milieu that supports immune evasion and therapeutic resistance. These hallmark features dense stromal deposition, disorganized vessel networks, immune cell suppression, and reciprocal

tumor–stroma signaling collectively drive tumor survival, invasion, and metastasis, while simultaneously limiting drug penetration and efficacy [22, 28–31, 35–38]. Recognizing these processes has led to the development of stroma-modulating therapies, anti-angiogenic agents, and immune checkpoint inhibitors, which now form the foundation of modern gastrointestinal (GI) oncology treatment strategies.

For nurses, translating the science of the TME into practice is critical. They educate patients about why certain GI cancers are particularly resistant to treatment, explain the rationale behind complex regimens or participation in clinical trials, and manage expectations regarding therapeutic outcomes. Nurses also play a central role in monitoring toxicities such as hypertension with anti-angiogenics or immune-related adverse events with checkpoint inhibitors ensuring early recognition and timely intervention. By combining patient education, vigilant surveillance, and psychosocial support, nurses help bridge advanced molecular understanding with compassionate, patient-centered oncology care, ultimately maximizing therapeutic benefit and improving quality of life.

Stromal Components and Desmoplasia

The tumor stroma comprising fibroblasts, extracellular matrix (ECM), and support cells serves as both the structural scaffold and a signaling hub within the tumor microenvironment. In gastrointestinal malignancies, particularly pancreatic ductal adenocarcinoma, the stroma often becomes densely desmoplastic, creating a physical barrier that markedly impedes the penetration and distribution of chemotherapeutic agents. To address this challenge, stroma-modulating agents are under investigation, aiming to soften or remodel the stroma and thereby improve drug delivery while disrupting tumor–stroma crosstalk [22]. Additionally, tumor-secreted factors such as Vascular Endothelial Growth Factor (VEGF) drive abnormal angiogenesis, while ECM remodeling promotes a disorganized, leaky vasculature that fuels tissue hypoxia. Together, these processes enhance tumor aggressiveness and resistance while further restricting therapeutic access [28, 29]. Recognition of these stromal barriers has informed the rationale for combination strategies, integrating stroma-targeting therapies with chemotherapy or immunotherapy, as well as supporting enrollment in clinical trials testing novel approaches to overcome microenvironmental protection [22, 30].

For nurses, understanding stromal biology translates directly into patient care. They explain to patients why certain gastrointestinal cancers, such as pancreatic cancer, are so difficult to treat and why regimens often involve multiple or investigational agents. Nurses also provide emotional support, helping patients and families manage the stress of complex treatment plans and the uncertainties of trial participation. Through clear communication, expectation setting, and psychosocial care, nurses foster treatment adherence, engagement, and trust, ultimately bridging advanced science with compassionate oncology

practice.

Angiogenesis and Vascular Remodeling

Angiogenesis the formation of new blood vessels from pre-existing vasculature is a crucial mechanism by which gastrointestinal (GI) tumors secure oxygen and nutrients to sustain growth and expansion. Unlike physiologic angiogenesis, tumor-driven angiogenesis generates abnormal, fragile, and leaky vascular networks, which disrupt perfusion, exacerbate hypoxia, and promote resistance to chemotherapy and radiotherapy [31]. Targeted therapies that inhibit VEGF signaling aim either to suppress angiogenesis or to “normalize” vasculature, thereby improving drug delivery. However, these anti-angiogenic agents are associated with adverse effects such as hypertension, hemorrhage, impaired wound healing, and thromboembolic events, requiring close clinical surveillance [32]. A related process, the epithelial–mesenchymal transition (EMT), allows epithelial tumor cells to lose adhesion, acquire mesenchymal properties, and become more mobile and invasive. EMT frequently acts in concert with angiogenesis to accelerate invasion and metastasis, further complicating therapeutic control [33, 34]. Current clinical strategies increasingly evaluate combination regimens pairing anti-angiogenics with chemotherapy or immunotherapy to enhance treatment response and survival in GI cancers.

For nurses, translating these complex biological processes into patient-centered education is essential. They explain in clear terms how angiogenesis fuels tumor progression and why targeted therapies are prescribed. Nurses also monitor for treatment-related toxicities, such as elevated blood pressure, bleeding, or clotting complications, ensuring early recognition and rapid intervention. By providing ongoing education, psychosocial reassurance, and vigilant toxicity monitoring, nurses strengthen treatment adherence and safety, while empowering patients to participate actively in their care.

Immune Cell Infiltrates and Immune Suppression

The tumor microenvironment (TME) harbors a diverse array of immune cells that can either exert tumoricidal activity or support tumor progression. While cytotoxic T cells and natural killer cells are capable of destroying cancer cells, their function is often undermined by the presence of tumor-associated macrophages (TAMs), regulatory T cells (Tregs), and myeloid-derived suppressor cells (MDSCs). These immunosuppressive populations release inhibitory cytokines, remodel the local milieu, and ultimately create a barrier that excludes or disables effector T cells, enabling tumors to escape immune destruction [35–37]. The advent of immune checkpoint inhibitors (ICIs) targeting pathways such as Programmed Death-1 (PD-1) / Programmed Death Ligand-1 (PD-L1) and Cytotoxic T-Lymphocyte–Associated Protein 4 (CTLA-4) has transformed treatment, as these agents can reverse immune suppression and restore anti-tumor immunity, achieving durable clinical benefit, particularly in microsatellite instability–high (MSI-high) gastrointestinal cancers [15, 38, 39]. Yet, because ICIs unleash immune

responses systemically, they can provoke irAEs across multiple organ systems, including colitis, pneumonitis, hepatitis, dermatitis, and endocrinopathies, making vigilant monitoring and rapid management essential [35, 36].

From a nursing perspective, the successful integration of immunotherapy into practice depends heavily on anticipatory guidance and surveillance. Nurses educate patients and families about the possibility of irAEs, emphasizing the importance of early reporting of symptoms such as diarrhea, cough, rash, or fatigue. They perform thorough and regular assessments to detect toxicity early, coordinate communication with the oncology team, and initiate timely supportive measures. By combining patient education, proactive monitoring, and interprofessional collaboration, nurses help maximize the therapeutic benefits of immunotherapy while safeguarding safety, adherence, and patient quality of life.

Signaling and Crosstalk with Cancer Cells

Reciprocal signaling between cancer cells and their surrounding microenvironment is a central driver of tumor progression, invasion, and resistance to therapy. This two-way communication involves a wide range of molecular messengers that reinforce tumor survival and blunt therapeutic responses. For instance, Fibroblast Growth Factor 2 (FGF2)-mediated activation of Vascular Endothelial Growth Factor (VEGF) signaling promotes angiogenesis and resistance in gastrointestinal stromal tumors (GISTs) [40]. Beyond growth factors, intricate signaling networks involving cytokines, circular RNAs (circRNAs), and the Wnt pathway contribute to immune suppression, epithelial-mesenchymal transition (EMT), and metastatic spread [41-45]. These insights have prompted the development of targeted strategies to disrupt tumor-stroma crosstalk, including EMT inhibitors, blockade of immunosuppressive cytokines, and modulators of stromal-derived signals. Such approaches are under active investigation in clinical trials and hold the potential to re-sensitize tumors to chemotherapy, targeted therapy, and immunotherapy [42-45].

For nurses, these scientific advances translate into specialized responsibilities within precision oncology. They play a pivotal role in supporting patient participation in clinical trials, beginning with education about investigational agents and the rationale behind novel approaches. Nurses also ensure that patients and families understand the details of informed consent, including potential risks and uncertainties. During trial participation, they conduct vigilant monitoring for complex and emerging toxicity profiles, communicate promptly with oncology teams, and provide psychosocial support to help patients cope with the stress of uncertainty. By serving as trusted advocates, nurses bridge innovation in cancer biology with safe, compassionate, and patient-centered care.

Theme 3: Mechanisms of Metastasis

Metastasis the principal driver of cancer mortality is a multistep cascade: local invasion, intravasation, survival

in circulation, extravasation, colonization of distant sites, and (for some cells) dormancy with potential reactivation. Each stage involves molecular reprogramming, EMT, immune evasion, and context-dependent interactions with local and distant microenvironments. In GI cancers, these mechanisms underlie aggressive behavior and characteristic patterns of spread (e.g., hepatic metastasis). Advances in liquid biopsy, molecular profiling, and real-time imaging are reshaping how clinicians track and target metastasis [5, 6, 27, 46, 47]. Nurses translate these insights into patient education, psychosocial support, and coordinated care across the metastatic trajectory.

Local Invasion and Epithelial-Mesenchymal Transition (EMT)

Local invasion marks the earliest stage of metastasis, beginning when malignant cells breach the basement membrane and infiltrate surrounding tissues. This process is strongly influenced by the epithelial mesenchymal transition (EMT), in which epithelial tumor cells lose polarity and adhesion while acquiring mesenchymal traits that enhance motility, invasiveness, and resistance to apoptosis and therapy. EMT is orchestrated by transcription factors (e.g., Snail, Twist, Zeb), key signaling pathways, and cues from the tumor microenvironment, making it a central determinant of aggressive tumor behavior [33, 34, 42, 43]. Clinically, local invasion complicates management, often requiring multimodal strategies that integrate systemic chemotherapy, targeted therapies, and locoregional interventions such as hepatic artery infusion or radioembolization. Because tumor biology evolves over time, dynamic assessment is critical; here, liquid biopsies provide a minimally invasive method for monitoring real-time molecular changes, resistance mutations, and disease progression, complementing traditional imaging and pathology [1, 5, 46, 47].

For nurses, these biological processes translate into meaningful clinical interactions. They help patients and families interpret pathology reports that describe invasive characteristics, clarifying what such findings mean for prognosis, staging, and treatment intensity. Nurses also play a central role in facilitating shared decision-making, guiding discussions about treatment goals, and preparing patients for the complexity of multimodal care. In multidisciplinary settings, nurses act as communicators and advocates, ensuring that patients understand the perspectives of various specialists while receiving compassionate support to navigate the emotional challenges associated with invasive disease.

Intravasation and Circulating Tumor Cells

Intravasation the process by which malignant cells penetrate into blood or lymphatic vessels marks a pivotal step in enabling systemic dissemination and metastatic spread. Once in circulation, circulating tumor cells (CTCs) encounter formidable barriers, including hemodynamic shear stress and immune surveillance. To survive, CTCs adopt adaptive strategies such as forming clusters or cloaking themselves with platelets, thereby enhancing metastatic potential and evading

immune detection [46, 48]. Clinically, advances in liquid biopsy technologies now permit the detection of CTCs and circulating tumor DNA (ctDNA), offering noninvasive methods to monitor minimal residual disease, identify emerging resistance mutations, and evaluate treatment response in real time [47, 49, 50]. In gastrointestinal (GI) malignancies, CTC burden has been validated as both a prognostic and predictive biomarker, with higher counts correlating with worse outcomes and differential response to therapy in colorectal and esophageal cancers [49, 50]. This underscores the growing clinical relevance of liquid biopsy as a complement to imaging and tissue-based diagnostics.

For nurses, the integration of liquid biopsy into practice brings distinct responsibilities. They play a central role in educating patients about the purpose, benefits, and limitations of liquid biopsy testing, emphasizing that results supplement but do not replace conventional pathology. Nurses also set realistic expectations around interpretation and timelines, helping patients cope with anxiety during result waiting periods. In addition, they collaborate closely with oncologists and multidisciplinary teams to ensure that biopsy findings are explained in patient-friendly language and appropriately integrated into shared treatment decisions. By combining technical knowledge with communication and emotional support, nurses help patients navigate the evolving landscape of precision oncology diagnostics with clarity and confidence.

Extravasation and Colonization of Distant Organs

Extravasation marks the critical step in metastasis where circulating cancer cells exit the vasculature and invade distant tissues. Successful colonization requires tumor cells to adapt to foreign microenvironments, recruit or co-opt local stromal components, and stimulate angiogenesis to sustain growth. Foundational frameworks such as Paget's classic "seed and soil" hypothesis illustrate how metastatic cells (the seeds) thrive only in permissive host environments (the soil), explaining the organ-specific tropism of metastasis [51, 52, 53]. In gastrointestinal (GI) oncology, the liver is a predominant metastatic site, largely due to portal venous drainage, making hepatic involvement a defining factor for prognosis and therapeutic strategy. This clinical reality underscores the necessity of accurate staging and serial imaging (e.g., CT, MRI, PET) to detect early metastatic deposits, monitor progression, and guide timely treatment decisions [6, 50]. Moreover, the emergence of functional imaging and liquid biopsy technologies offers new opportunities to complement conventional imaging in detecting micrometastases.

From the nursing perspective, extravasation and colonization translate into important clinical monitoring responsibilities. Nurses remain on the frontline in identifying early signs and symptoms of metastasis, such as abdominal pain, jaundice, weight loss, or deranged liver function tests, which may signal hepatic involvement. They also play a vital role in educating patients and families about the purpose and meaning of staging and follow-up imaging, helping to bridge the gap between

complex radiology reports and patient comprehension. In addition, nurses provide compassionate support when therapy must be escalated, modified, or shifted toward palliative intent due to metastatic disease. By combining clinical vigilance with empathetic communication, nurses enhance patient engagement, reduce uncertainty, and contribute directly to the multidisciplinary management of advanced GI cancers.

Dormancy and Reactivation

Dormancy describes a state in which disseminated tumor cells persist in distant tissues but remain viable and non-proliferative for extended periods. These quiescent cells escape detection by traditional imaging and are largely resistant to conventional chemotherapy, which typically targets rapidly dividing cells. Their persistence poses a major clinical challenge, as reactivation can occur years or even decades later, driven by microenvironmental changes, angiogenic shifts, or loss of immune surveillance, ultimately leading to late metastatic recurrence [53]. This biological reality highlights the importance of long-term vigilance, even in patients considered clinically disease-free. Regular follow-up, sensitive biomarker assessments, and advanced imaging are essential to detect and address reactivation promptly [6].

From a nursing perspective, dormancy underscores the critical role of survivorship care. Nurses not only reinforce the importance of ongoing surveillance and follow-up appointments but also educate patients and families on subtle signs and symptoms that may suggest recurrence. At the same time, they help patients navigate the psychological burden of living with uncertainty by promoting balance between vigilance and quality of life. Through clear, compassionate communication, survivorship planning, and psychosocial support, nurses empower patients to remain proactive without being overwhelmed by fear, thereby fostering resilience across the cancer continuum.

Fundamental Concepts and Definitions for Nurses in Oncology

A clear understanding of fundamental cancer biology concepts is essential for oncology nurses, as these terms often form the basis of patient education, treatment discussions, and clinical decision support. Table 1 provides concise, nurse-oriented definitions of key biological concepts with references to guide further reading.

Nursing Learning Needs and Roles in Cancer Biology

Table 2 outlines priority biology learning needs for GI oncology nurses and corresponding roles. Mastery of molecular drivers, the TME, and metastatic processes enables nurses to interpret test results, justify treatment choices, and identify progression. Competencies include translating complex biology into patient-friendly terms, monitoring advanced therapies (immunotherapy, targeted agents), and engaging in continuing education and interdisciplinary collaboration [7, 8, 54-58].

Discussion

The biological foundations of GI cancers spanning genetic and epigenetic alterations, the TME, and metastatic processes are essential for nursing practice in precision oncology [2-4, 9]. Although oncologists have broadly adopted molecular profiling and targeted strategies [5, 25], nursing education and implementation remain inconsistent [8, 7]. Without strong grounding in cancer biology, nurses may be sidelined from conversations about therapy selection, trial enrollment, and emerging treatments [56].

Our synthesis underscores both opportunities and tensions. Biomarkers such as MSI and Human Epidermal Growth Factor Receptor 2 (HER2) amplification have reshaped algorithms and offer clear precision-medicine exemplars [26, 36, 39]. Conversely, the scope of MSI testing beyond colorectal cancer is debated [17, 18], and epigenetic therapies while scientifically compelling are constrained by heterogeneous data and variable uptake [19, 21, 23]. Similarly, stromal modulation and immune-microenvironment targeting are promising but remain protocol-dependent and often limited to research settings [22, 28, 30]. These realities require nurses to explain evolving evidence to patients while maintaining rigor and empathy [9, 55].

Educationally, traditional curricula seldom prepare nurses to interpret NGS reports, counsel on why one targeted therapy is preferred over another, or anticipate immunotherapy-specific toxicities [8, 57]. Targeted continuing education, simulation, and interdisciplinary workshops are needed to close the gap [7]. Molecular literacy enhances patient education, supports advocacy for appropriate testing, enables early adverse-event detection, and strengthens shared decision-making [59, 60].

From a policy perspective, cancer centers and accrediting bodies should recognize molecular oncology as a nursing core competency. As with infection control or chemotherapy safety, structured professional development in cancer biology should be required [56, 58]. Embedding nurses in tumor boards, genomic review meetings, and trial planning institutionalizes their roles as scientific interpreters and patient advocates [61, 62]. Linking career advancement to demonstrated competence in cancer biology may further motivate and sustain growth [59].

Practice implications are immediate. Nurses translate complex laboratory findings into patient-friendly explanations, guide families through genetic test results, and monitor subtle toxicities of immunotherapies and targeted agents [9, 55]. In anti-angiogenic therapy, vigilant monitoring of hypertension or bleeding can be pivotal for safe continuation [31, 32]. During immunotherapy, early recognition and management of irAEs prevents severe complications [24, 36, 35]. These roles demand integrated scientific knowledge and compassionate communication skills that reinforce each other in oncology nursing [7].

Looking ahead, innovation should shape delivery and application of this knowledge. Digital tools (e.g., AI-assisted decision support) can personalize education and anticipate complications [63, 64]. Shared-governance

structures can elevate nursing voices in implementing new therapies [59]. Integrating nursing scholarship within precision-oncology initiatives fosters a culture where practice and science co-evolve [65-68].

Oncology nursing practice in gastrointestinal cancer care is grounded in both biological understanding and organizational innovations that improve patient outcomes. Evidence highlights that organizational commitment and citizenship behavior foster retention and stronger professional culture among nurses [70, 71]. At the service level, referral process improvements, acuity-based tools, and lean management approaches strengthen care continuity and reduce inefficiencies [72-74]. Research has also advanced outsourcing strategies, fatigue assessment, and risk-reduction protocols in oncology settings, ensuring safer systems and minimizing errors [75-77]. Furthermore, studies on health literacy, patient learning needs, and patient-centered care emphasize the critical role of nurses in communication, education, and shared decision-making [78, 79]. Together, these insights provide a comprehensive framework for nurses to integrate cancer biology knowledge with practice innovations, ultimately supporting precision oncology and improving the patient experience.

In conclusion, in GI oncology, a solid grounding in cancer biology is essential to deliver effective, patient-centered care in the era of precision medicine. By understanding how genetic/epigenetic alterations, the TME, and metastatic processes shape disease and treatment, nurses can anticipate needs, support shared decisions, and promote equitable access to diagnostics and therapies. Ongoing professional development and cross-disciplinary collaboration are critical to sustain readiness for rapid scientific change and to preserve nursing's central role in improving outcomes and quality of life.

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Statement of Transparency and Principals

- Author declares no conflict of interest
- Study was approved by Research Ethic Committee of author affiliated Institute.
- Study's data is available upon a reasonable request.
- All authors have contributed to implementation of this research.

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