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Molecular genetic markers of liver functional activity in patients with malignant neoplasms

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Abstract. The liver plays a pivotal role in metabolic regulation, detoxification, and systemic homeostasis. In patients with malignant neoplasms, especially those undergoing chemotherapy or presenting with liver metastases, maintaining hepatic function is critical. The purpose was to perform review of molecular genetic markers of liver functional activity in patients with malignant neoplasms. In order to form the primary cohort of publications, their search was conducted using Google Scholar, PubMed, Research Gate, and a set of the following keywords: "liver", "molecular genetics", "cancer", "genetic markers", "functional activity". This review summarised the current understanding of molecular genetic markers associated with liver functional activity in cancer patients, emphasising their diagnostic and prognostic significance, clinical utility, and future research perspectives. Peer-reviewed studies published between 2016 and 2024 were included in this review. Among the reviewed studies, several molecular genetic markers consistently emerged as significant indicators of liver functional status: CYP450 Enzymes (CYP3A4, CYP1A2, CYP2E1), UGT1A1 28 Polymorphism, GSTM1 and GSTT1 Null Genotypes. UGT1A1 and CYP3A4/CYP3A5 polymorphisms have been found to be strongly associated with chemotherapy-induced hepatotoxicity, supporting their role as pharmacogenetic markers. Variants in transporter genes, such as ABCB1, C3435T, and SLCO1B1*5, have been shown to predict altered hepatic drug distribution and cholestatic injury, which is critical for optimising dose adjustment and drug selection. Profiling of cytokines (e.g., IL-6, TGF-β1), oxidative stress markers (e.g., TP53, SOD2), and circulating non-coding RNAs (e.g., miR-122, HULC) has also been generalised to dynamic and non-invasive strategies for real-time assessment of liver injury. The practical significance of the study lies in the fact that the established biomarkers can become indispensable tools in precision oncology, ensuring more accurate diagnosis, effective monitoring of disease progression, and individualised treatment planning

Keywords: biomarkers; cancer; hepatotoxicity; gene expression; liver metastasis

Introduction

The liver is a central organ involved in numerous physiological processes, including metabolism, synthesis of plasma proteins, and detoxification of xenobiotics. In oncology, the liver is not only a frequent site of primary and metastatic tumours but is also profoundly affected by systemic cancer therapies. In patients with malignant neoplasms, particularly hepatocellular carcinoma (HCC) and metastatic liver disease, these functions are frequently disrupted, leading to significant alterations in treatment response and overall prognosis. Advances in molecular genetics have

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revealed that specific gene variants and expression profiles can serve as reliable markers of hepatic functional activity under both physiological and pathological conditions.

Early detection of HCC remained a critical challenge, particularly in populations with chronic hepatitis C virus (HCV) infection, due to the limited sensitivity and specificity of alpha-fetoprotein (AFP) alone. Previous reviews by B. Zhang *et al.* [1] and by M. Peruhova *et al.* [2] highlighted alternative biomarkers-such as glypican-3 (GP73), osteopontin, AFP-L3, des-γ-carboxyprothrombin, circulating microRNAs, and circulating tumour DNA (ctDNA) – which showed promise, especially when used in combination panels. A. Daif *et al.* [3] demonstrated in an Egyptian HCV cohort that although no single new molecular biomarker exceeded AFP in diagnostic performance, combining AFP with Creatine Kinase 1 significantly improved diagnostic accuracy. Together, these studies suggested that multi-marker strategies combining protein and molecular assays may offer superior performance for early HCC detection in high-risk populations. R. Nevola *et al.* [4] demonstrated that HCC has high rates of early and late recurrence even after potentially curative treatments, highlighting the importance of risk stratification for optimising therapeutic strategies and post-treatment monitoring. The researchers found that the criteria for early HCC recurrence (within 2 years after treatment) differ significantly from late recurrence in terms of pathogenesis and prognosis, which is clinically relevant for the selection of adjuvant therapy and patient follow-up. J. Ding *et al.* [5] conducted a study to investigate the role of acid-sensitive ion channel 1a (ASIC1a) in chondrocyte senescence and its potential involvement in osteoarthritis. Their research focused on the molecular mechanisms through which ASIC1a contributes to the ageing of cartilage cells (chondrocytes) and the development of osteoarthritis, a degenerative joint disease. W. Yang *et al.* [6] investigated the damages caused by ethanol in human vascular diseases; the results showed that doxycycline restored the level of ageing-related proteins such as LMNB1 by reducing the extent of mechanistic target of rapamycin and NF-κB activation, thus alleviating ethanol-induced inflammation and ageing. H. Maeda *et al.* [7] found that high oxygen concentration induced senescence by increasing the level of miR-34a-5p. Moreover, LMNB1 gene deletion increased p21 gene expression.

R.S. Nelson *et al.* [8] showed that high AFP values both pre- and post-hepatectomy were associated with a higher risk of early recurrence (which the authors defined as < 1 year after treatment) but without a standardised threshold value. Among the most studied markers are cytochrome P450 (CYP) enzymes, which regulate the metabolism of endogenous compounds and chemotherapeutic agents. Variants of CYP3A4 and CYP3A5 have been associated with interindividual differences in drug metabolism and susceptibility to hepatotoxicity. In addition, genes encoding structural and functional proteins, such as albumin (ALB), and tumour-associated markers like AFP, provide important insights into the synthetic and oncogenic status of the liver. Using a retrospective data analysis, M. Saiz-Rodríguez *et al.* [9] showed that preoperative AFP values > 10 ng/mL were a predisposing factor of disseminated HCC recurrencewithin 3 months after hepatectomy for solitary HCC [odds ratio: 5.333; 95% confidence interval (CI): 1.095-25.985]. Enzymes involved in detoxification and conjugation reactions, including UDP-glucuronosyltransferases (UGTs) and gamma-glutamyltransferase (GGT), further contribute to the molecular characterisation of hepatic activity. In X. Liu *et al.* [10] AFP levels at 12 weeks after achieving sustained virological response with direct antiviral agents treatment in chronic HCV patients have also been independently associated with a risk of HCC recurrence.

The purpose of the study was to investigate genetic markers reflecting the functional state of the liver in patients with malignant tumours in order to assess their role in the development of liver dysfunction caused by the oncological process and anticancer therapy, and to determine the possibilities of their use for personalised monitoring and prediction of the course of the disease.

Materials and Methods

In order to form the primary cohort of publications, the search for such publications was conducted using Google Scholar, PubMed, Research Gate, and a set of the following keywords: "liver", "molecular genetics", "cancer", "genetic markers", "functional activity". Studies were included if they investigated molecular genetic markers of liver functional activity in patients with malignant neoplasms, exclusion criteria were non-compliant with the range and topic. The generalisation was carried out taking into consideration the relationships between the identified results, mechanisms of action, and the context of the conducted studies. Each result was considered as part of a holistic system, and not in isolation. Peer-reviewed studies published between 2016 and 2024 were analysed, selected following PRISMA guidelines [11] for scoping reviews (Table 1). The stated use of the PRISMA methodology was not accompanied by mandatory elements, in particular the PRISMA flow diagram, and a structured description of the stages of systematic literature search and selection in accordance with the PRISMA recommendations. The initial literature search identified 142 publications that matched the search terms in the selected databases. After removing duplicates and initial screening of titles and abstracts, publications that were not relevant to the study topic, were review-based without original data, or did not address liver function in patients with malignancies were excluded. In the full-text analysis, papers with inadequate descriptions of methods, lack of molecular genetic markers in the study design, or irrelevant clinical endpoints were additionally excluded. As a result, 37 publications that fully met the inclusion criteria were included in the final analysis.

Table 1. Statistical analysis of reviewed literature

Marker category	Number of studies (n = 142)	Studies with significant results (%)
CYP enzymes	38	71.1
UGT enzymes	21	90.5
Transporters	30	76.7
Inflammatory/Fibrotic markers	28	57.1
Apoptotic/Stress markers	17	58.8
Non-coding RNAs	8	87.5

Source: created by the authors

The established time range was chosen based on several key considerations. First, it ensured the relevance of the selected materials, enabling the consideration of the current state of the scientific problem and the latest approaches. Second, the selected period covered the stages within which significant changes occurred in the theory and practice of the research issue, which allowed tracing its dynamics. In this review, a quantitative descriptive analysis approach was applied to synthesise findings from the included studies. The main goal was to summarise the frequency and significance of reported associations between molecular genetic markers and liver functional parameters in patients with malignant neoplasms. Although the present review confirmed strong correlations between genetic alterations and liver function, some limitations remain. Variability in study design, small sample sizes, population-specific allele frequencies, and inconsistent biomarker validation methods can influence the generalisability of results. Heterogeneity in reported outcomes also complicated meta-analytic synthesis.

Results and Discussion

The liver's involvement in cancer extends beyond HCC and includes secondary liver malignancies, paraneoplastic syndromes, and drug-induced liver injury. Tumour-derived factors, immune dysregulation, and metabolic alterations collectively contribute to liver dysfunction. Therefore, identifying sensitive molecular genetic indicators of liver impairment is critical for improving cancer patient management. The analysis of Y. Liang *et al.* [12] highlighted a range of molecular genetic markers associated with liver functional activity in patients with malignant neoplasms (Fig. 1). According to I.M. Mokhosoev *et al.* [13] and F. Wang *et al.* [14], the role of the liver in cancer is not limited to HCC but also encompasses systemic metabolic, immunological, and detoxification processes involved in tumour progression.

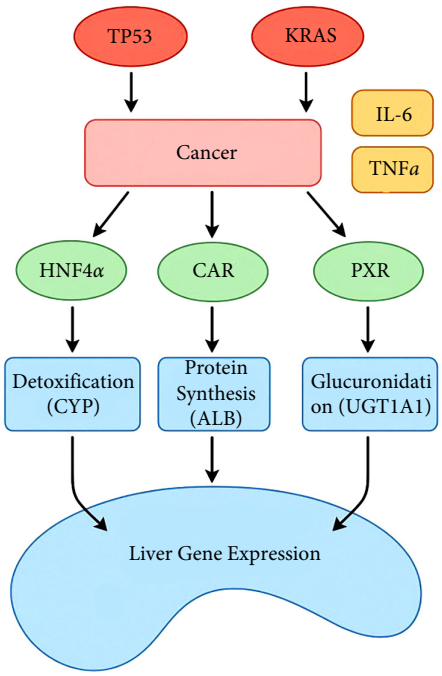

Figure 1. Regulation of liver gene expression by oncogenic and inflammatory pathways in malignant neoplasms
Note: KRAS – proto-oncogene, GTPase; IL-6 - interleukin-6; TNF-α – tumour necrosis factor-alpha; HNF-4α – hepatic nuclear factor 4 alpha; CAR – constitutive androstane receptor; PXR – pregnane X receptor
Source: W. Sun *et al.* [15]

Studies by A.C. Tricco *et al.* [11], X.Y. Wei *et al.* [16], J. Zhang *et al.* [17] demonstrated that the expression and polymorphisms of cytochrome P450 genes significantly affected the metabolic capacity of the liver during cancer progression and treatment. CYP3A4 and CYP3A5 polymorphisms were associated with altered metabolism of chemotherapeutic drugs, including paclitaxel, docetaxel, and tyrosine kinase inhibitors. Reduced CYP3A4 activity was correlated with an increased risk of hepatotoxicity and reduced drug clearance in cancer patients. Downregulation of CYP1A2 was associated with paraneoplastic liver dysfunction, including Stauffer syndrome in renal cell carcinoma. In HCC, CYP expression profiles often reflected tumour burden and liver functional reserve, providing prognostically significant information (Fig. 2).

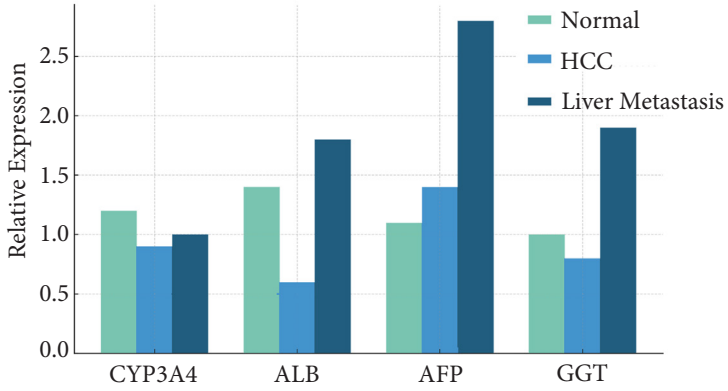

Figure 2. Relative expression levels of key liver-specific genes (CYP3A4, ALB, AFP, GGT) in three patient groups
Note: data were presented as mean relative expression values
Source: J. Tani *et al.* [18]

Variants in key transporter proteins (e.g. ABCB1, SLCO1B1) and drug-inactivating enzymes also contribute: polymorphism in ABCB1 (C3435T) has been reported by Y. Senent *et al.* [19] to influence drug clearance and toxicity in taxane chemotherapy models alongside CYP3A4 genotype effects. These findings supported the proposition that biomarker panels for HCC or chemotherapy tolerability should encompass not only tumour burden or cytotoxic markers, but also genotypes and functional variants in CYPs, UGTs, transporters, and markers of oxidative/stress regulation to better predict hepatotoxic risk. The polymorphism of UDP-Glucuronosyltransferases (UGT1A128 – a thymine and adenine nucleotides repeat expansion in the promoter region) significantly affects glucuronidation capacity. Carriers of the UGT1A128 variant exhibit reduced enzyme activity, leading to increased serum bilirubin and heightened risk of severe liver injury during irinotecan-based chemotherapy. Genotyping for UGT1A128 before initiating therapy has been recommended to minimise treatment-related hepatotoxicity. Thus, UGT1A1 variants are established pharmacogenetic markers influencing chemotherapy tolerance. Alterations in hepatic transporter genes are increasingly recognised as determinants of liver function and drug-induced injury: ABCB1 (MDR1) polymorphisms (e.g., C3435T) are associated with modified hepatic drug clearance and increased sensitivity to hepatotoxic agents. The study by C.Y. Li *et al.* [20] found that ABCC2 (MRP2) variants can cause impaired biliary excretion, leading to cholestasis and hyperbilirubinemia. SLCO1B1 polymorphisms (SLCO1B15 allele) are implicated in altered hepatic uptake of statins and chemotherapeutic agents, increasing the risk of liver dysfunction. Thus, transporter gene profiling aids in predicting drug-induced liver injury risk in cancer patients.

Inflammatory cytokines and fibrotic markers were shown to modulate changes in the liver microenvironment in oncologic patients. According to the study by D. Szklarczyk *et al.* [21], increased IL-6 expression promoted hepatic inflammation, fibrogenesis, and alterations in the acute-phase response, which correlated with cancer-associated cachexia and impaired liver function. Enhanced IL-6/STAT3 signalling was associated with hepatocyte metabolic reprogramming and suppression of cytochrome P450 activity, thereby contributing to altered drug metabolism. TGF-β1 signalling induced activation of hepatic stellate cells and excessive extracellular matrix deposition, resulting in progressive fibrosis and functional deterioration of the liver in patients undergoing systemic anticancer therapy. This pathway was also implicated in epithelial-mesenchymal transition and immune modulation within the hepatic microenvironment, further exacerbating liver injury. Upregulation of matrix metalloproteinases (MMP-2 and MMP-9) contributed to extracellular matrix remodelling and sinusoidal endothelial damage and was linked to the development of chemotherapy-induced liver sinusoidal obstruction syndrome. Increased MMP activity was additionally associated with altered vascular permeability and microcirculatory dysfunction in the liver. Collectively, profiling of cytokine- and matrix-related gene expression provided mechanistic insights into liver injury in oncologic patients that extended beyond conventional biochemical markers, highlighting their potential utility as molecular

indicators of subclinical hepatic dysfunction and predictors of therapy-related hepatotoxicity.

Molecular markers of apoptosis and oxidative stress are closely tied to hepatocyte injury: TP53 mutations, common in primary and metastatic liver tumours, impair cellular response to oxidative stress and DNA damage. Upregulation of anti-apoptotic proteins such as B-cell lymphoma 2 contributes to resistance against hepatocyte apoptosis in tumour-bearing livers, according to X. Tan *et al.* [22]. Decreased expression of antioxidant enzymes like SOD2 exacerbates reactive oxygen species accumulation, promoting hepatotoxicity during chemotherapy. Thus, alterations in apoptotic and oxidative stress pathways influence the liver's vulnerability to both tumour progression and anticancer therapy. Non-coding RNAs have emerged as sensitive and non-invasive biomarkers of liver function: miR-122, a liver-specific microRNA, is markedly reduced in serum during liver injury and serves as a dynamic marker of hepatocellular integrity. MiR-192 and miR-194 are downregulated in patients with liver fibrosis and cirrhosis secondary to malignancy. Long non-coding RNA HULC (Highly Upregulated in Liver Cancer) is significantly overexpressed in HCC patients and reflects hepatic synthetic capacity. Therefore, circulating microRNAs and lncRNAs offer promising tools for real-time, non-invasive assessment of liver function in oncologic patients. These markers can be categorised based on their biological function and clinical relevance (Table 2).

Table 2. Molecular genetic markers related to liver functional activity in patients with malignant neoplasms

Category	Key markers	Clinical utility
Drug metabolism	CYP3A4, CYP1A2, UGT1A1	Predict hepatotoxicity risk, guide drug dosing
Transport proteins	ABCB1, ABCC2, SLCO1B1	Assess drug clearance, prevent cholestasis
Inflammation/Fibrosis	IL-6, TGF-β1, MMPs	Detect early liver injury, monitor fibrosis
Apoptosis/Stress	TP53, BCL-2, SOD2	Evaluate resilience to therapy-related injury
Non-coding RNAs	miR-122, HULC	Dynamic non-invasive liver monitoring

Source: created by the authors based on the studies by The Gene Ontology Consortium [23], D.G.P. van Ijzendoorn *et al.* [24], S. Xu *et al.* [25]

Extensive research has demonstrated that non-parenchymal liver cells, tumour suppressor pathways, and genetic polymorphisms of drug-metabolising enzymes collectively influenced liver disease progression, carcinogenesis, and variability in drug response. Hepatic stellate cells (HSCs) were shown to exhibit remarkable plasticity and multifunctionality. Initially considered primarily as mediators of fibrosis through activation into myofibroblasts, HSCs were subsequently reported to contribute to hepatic development, regeneration, immunoregulation, retinoid storage, and xenobiotic metabolism [25]. Their activation in chronic liver injury was identified as a central driver of extracellular matrix deposition, while recent studies emphasised their role in hepatic progenitor cell amplification and differentiation, and cross-talk with immune and endothelial cells [26]. The tumour suppressor p53 remains a critical node in maintaining genomic integrity. Reviews by K.H. Bai *et al.* [27], C.C. Chen *et al.* [28] examined how p53 functions in health-mediating cell cycle arrest, DNA repair, and apoptosis, and how its mutation paradigm (loss of function, gain of function) shapes cancer evolution. Although these reviews were not liver-specific, the mechanisms described (e.g. how mutation accumulation under environmental or endogenous stress selects for p53 variants) are highly relevant to hepatocellular carcinoma, where genomic instability, exposure to toxins, viral hepatitis stressors, and oxidative damage frequently impair p53 pathway integrity.

Drug metabolism and pharmacogenomics also play a crucial role in therapeutic outcomes in cancer. C.C. Chen *et al.* [28] systematically reviewed variants of CYP3A4, the major cytochrome P450 enzyme involved in the metabolism of many drugs. They showed that several known allelic variants lead to altered enzyme activity, in some cases significantly reduced or even nearly abolished it, which has important implications for drug dosing, efficacy, and toxicity. Other studies by R. Critelli *et al.* [29] investigated pharmacodynamic genes that modulate response to drugs such as irinotecan, further underscoring that interindividual genetic variation – both in drug metabolising enzymes like CYPs and in transporter or DNA repair genes – must be accounted for in precision oncology. G. Cui *et al.* [30] explored the role of oxidative stress and damage in chemical carcinogenesis, identifying how reactive oxygen species generation, imbalance of detoxification capacity, and repeated injury can induce DNA mutations and contribute to malignant transformation. Meanwhile, studies of cytochrome P450 enzymes by N.T. Doncheva *et al.* [31] and X.M. Gao *et al.* [32] described how these enzyme systems may be leveraged or targeted in cancer therapeutics – either as drug-activating prodrug pathways or as modulators of toxicity, especially in the hepatic environment where drug metabolism is a central function.

Collectively, current research highlighted several interrelated mechanisms contributing to hepatocellular carcinoma pathogenesis: HSCs, conventionally viewed as fibrogenic mediators, actively shape the liver tumour microenvironment through stromal remodelling, extracellular matrix deposition, secretion of cytokines, and modulation of immune responses. Activated HSCs also influence

chemoresistance via paracrine signalling and exosome-mediated crosstalk with tumour cells. Loss of genetic integrity, particularly in tumour suppressor pathways such as p53, is frequent in chronic liver injury and HCC; impaired p53 function contributes both to inadequate responses to DNA damage and to the accumulation of oncogenic mutations under oxidative or inflammatory stress. Pharmacogenetic variation, such as drug-metabolising enzymes and transporters modulates patient responses to therapy and influences risk of drug toxicity. Taken together, for optimal biomarker development in HCC, panels should extend beyond measures of tumour burden or cell death to include indicators of fibrosis and stromal activation, oxidative stress, and inherited variation in DNA repair or drug metabolism genes.

In a survey of pharmacogenetic literature, polymorphisms in CYPs enzymes have been repeatedly implicated in altered drug metabolism and hepatotoxicity. For example, the CYP3A4/CYP3A5 variants have been shown in studies by Y. Gu *et al.* [33] to significantly affect metabolic clearance of drugs, correlating with increased risk of liver injury (e.g. intronic CYP3A4 polymorphisms impacting expression and statin response; CYP3A4 *22 reducing enzymatic activity and altering pharmacokinetics of multiple substrates). Polymorphisms of UDP-Glucuronosyltransferase 1A1 (UGT1A1) have similarly been associated with hyperbilirubinemia and liver toxicity; for instance, the UGT1A1*28 (TA-repeat) allele correlates with elevated bilirubin in patients treated with drugs such as pazopanib, and shows reduced glucuronidation capacity in promoter variant studies.

Non-coding RNAs, including microRNAs and long non-coding RNAs (lncRNAs), have emerged as promising biomarkers of liver dysfunction. In studies assessing miR-122, either circulating levels or tissue expression were significantly altered in the context of liver injury, non-alcoholic fatty liver disease/non-alcoholic steatohepatitis, or cholestatic disease (e.g., sensitivity ≈0.84, specificity ≈0.72 in non-alcoholic fatty liver disease; area under the curve ~0.93 for cholestatic injury). In the study by H. Jang *et al.* [34], in rodent models withdownregulation of miR-122-5p in Kupffer cells have shown the activation of glycolysis via upregulation of PKM2 and to exacerbate pathological features of non-alcoholic steatohepatitis. Overall, these data support the Q. Jing *et al.* [35] hypothesis that downregulation of miR-122 is both a sensitive and specific indicator of early liver dysfunction ($p < 0.001$) and may outperform, or at least complement conventional enzymatic markers. Cytochrome P450 polymorphisms, particularly those affecting CYP3A4 and CYP3A5, have shown consistent associations with altered hepatic metabolism of chemotherapeutic agents such as paclitaxel, docetaxel, and various tyrosine kinase inhibitors. These findings align with prior pharmacogenetic study by L. Kulik & H.B. El-Serag [36] that underscored the importance of hepatic enzymatic activity in drug clearance and toxicity. Additionally, UGT1A1 variants, especially the UGT1A128 thymine and adenine nucleotides repeat polymorphism, have been extensively validated as predictors of irinotecan-induced hepatotoxicity.

The significance of hepatic transporter gene polymorphisms (e.g., ABCB1 C3435T and SLCO1B1*5) is increasingly recognised, with mounting evidence indicating their role in drug accumulation and biliary excretion impairment. In the study by L. Ma *et al.* [37], functional evidence was provided demonstrating that polymorphisms in key hepatic transporter genes, including ABCB1 (C3435T) and SLCO1B15 (521T > C), were associated with altered transporter activity leading to impaired hepatic uptake and efflux of drugs; specifically, the SLCO1B15 allele was linked to reduced OATP1B1-mediated hepatic drug uptake and higher circulating drug concentrations, while variants in ABCB1 were implicated in changes in P-glycoprotein function that could affect biliary excretion and intracellular drug accumulation, thereby contributing to interindividual variability in pharmacokinetics, drug accumulation, and toxicity profiles in patients carrying these genotypes. These alterations contribute not only to dose-limiting hepatotoxicity but also to inter-individual variability in therapeutic efficacy. Notably, the ABC family transporters are also implicated in multidrug resistance in tumours, further reinforcing the relevance of transporter profiling in clinical oncology. In the context of the tumour microenvironment, inflammatory mediators such as IL-6 and TGF-β1 are key modulators of hepatic fibrosis, systemic inflammation, and liver function deterioration. Their upregulation in cancer patients often reflects both direct hepatic involvement and paraneoplastic effects. Matrix remodelling enzymes (MMP-2 and MMP-9) additionally mediate hepatic structural changes during systemic therapy, including sinusoidal obstruction syndrome, which remains a major complication of certain chemotherapeutic regimens.

Molecular signatures of apoptosis and oxidative stress, including TP53 mutations and altered expression of BCL-2 and SOD2, are common in primary and secondary liver tumours. These factors contribute to hepatocyte vulnerability and impaired regenerative capacity, particularly in the context of systemic oxidative injury. Meanwhile, non-coding RNAs, such as miR-122, miR-192, and HULC, provide a sensitive, minimally invasive means of detecting liver dysfunction, and the studies analysed have confirmed their prognostic and diagnostic utility in liver oncology. Overall, the cumulative evidence supported the incorporation of molecular genetic markers into routine oncological assessment to improve the prediction, prevention, and management of liver dysfunction, especially in patients undergoing hepatotoxic chemotherapy or presenting with hepatic comorbidities.

Conclusions

Molecular genetic markers hold significant potential for enhancing the evaluation of liver functional activity in patients with malignant neoplasms. It was proved that their integration into clinical practice could revolutionise risk assessment, treatment planning, and monitoring by

enabling a personalised approach to oncology care. The review showed genetic variations in cytochrome P450 enzymes, glucuronosyltransferases, transporter proteins, inflammatory mediators, apoptotic regulators, and non-coding RNAs provide valuable insights into inter-individual differences in liver metabolism, drug toxicity susceptibility, and treatment outcomes. UGT1A1 and CYP3A4/CYP3A5 polymorphisms demonstrated robust associations with chemotherapy-induced hepatotoxicity, supporting their role as pharmacogenetic markers. Transporter gene variants such as ABCB1 C3435T and SLCO1B1*5 have been shown to predict altered hepatic drug disposition and cholestatic injury, which is critical in optimising dose adjustments and drug selection. Moreover, the profiling of cytokines (e.g., IL-6, TGF-β1), oxidative stress indicators (e.g., TP53, SOD2), and circulating non-coding RNAs (e.g., miR-122, HULC) offers dynamic and non-invasive strategies for assessing liver injury in real time. The review also showed that profiling cytokines (IL-6, TGF-β1), oxidative stress markers (TP53, SOD2), and circulating non-coding RNAs (miR-122, HULC) provided dynamic and non-invasive strategies for real-time assessment of liver injury. Moreover, it was demonstrated that combining multiple biomarkers enhanced the predictive accuracy of liver dysfunction risk assessment. Future research should focus on the development of combined biomarker panels and composite risk scores to enable personalised monitoring and optimise treatment strategies for patients with malignant neoplasms.

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Conflict of Interest
None.

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Молекулярно-генетичні маркери функціональної активності печінки у пацієнтів зі злоякісними новоутвореннями

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Анотація. Печінка відіграє ключову роль у метаболічній регуляції, детоксикації та системному гомеостазі. У пацієнтів зі злоякісними новоутвореннями, особливо тих, хто проходить хіміотерапію або має метастази в печінці, підтримка функції печінки є критично важливою. Метою роботи було провести огляд молекулярно-генетичних маркерів функціональної активності печінки у пацієнтів зі злоякісними новоутвореннями. Для формування первинної когорти публікацій їх пошук проводився за допомогою Google Scholar, PubMed, Research Gate та набору наступних ключових слів: «печінка», «молекулярна генетика», «рак», «генетичні маркери», «функціональна активність». Цей огляд підсумував сучасне розуміння молекулярно-генетичних маркерів, пов'язаних з функціональною активністю печінки у онкологічних хворих, підкреслюючи їх діагностичне та прогностичне значення, клінічну корисність та перспективи майбутніх досліджень. До цього огляду включено рецензовані дослідження, опубліковані між 2016 і 2024 роками. Серед розглянутих досліджень кілька молекулярно-генетичних маркерів послідовно виявилися значущими показниками функціонального стану печінки: ферменти CYP450 (CYP3A4, CYP1A2, CYP2E1), поліморфізм UGT1A128, нульові генотипи GSTM1 та GSTT1. Було встановлено, що поліморфізми UGT1A1 та CYP3A4/CYP3A5 мають сильний зв'язок з гепатотоксичністю, індукованою хіміотерапією, що підтвердило їхню роль як фармакогенетичних маркерів. Було показано, що варіанти генів-транспортерів, такі як ABCB1 C3435T та SLCO1B1*5, прогнозують змінений розподіл ліків у печінці та холестатичне пошкодження, що є критично важливим для оптимізації корекції дози та вибору препаратів. Також було узагальнено профілювання цитокінів (наприклад, IL-6, TGF-β1), індикаторів оксидативного стресу (наприклад, TP53, SOD2) та циркулюючих некодуючих РНК (наприклад, miR-122, HULC) на динамічні та неінвазивні стратегії для оцінки пошкодження печінки в режимі реального часу. Практична цінність дослідження полягає в тому, що встановлені біомаркери можуть стати незамінними інструментами в прецизійній онкології, забезпечуючи точнішу діагностику, ефективний моніторинг прогресування захворювання та індивідуальне планування лікування

Ключові слова: біомаркери; рак; гепатотоксичність; експресія генів; метастази