REVIEW

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METABOLIC INHIBITORS AND THEIR IMPACT ON CANCER CELL MIGRATION, INVASION, AND METASTASIS

Cancer metastasis, the process by which cancer cells spread from the primary tumor to distant sites, remains the leading cause of cancer-related deaths. This complex process involves a series of steps, including cell detachment, migration, invasion, survival in the circulatory system, extravasation, and colonization of new tissues. A fundamental characteristic of cancer cells is their altered metabolism, often exhibiting increased glucose uptake and a preference for glycolysis even in the presence of oxygen, a phenomenon known as the Warburg effect. This metabolic shift provides cancer cells with a rapid source of adenosine triphosphate (ATP) and essential biosynthetic intermediates, supporting their rapid growth and proliferation. While early concepts attributed the Warburg effect to mitochondrial dysfunction, it is now recognized that mitochondria in cancer cells often remain functionally active, including oxidative phosphorylation, and critically regulate tumor progression. Notably, metastatic cells frequently depend on mitochondrial activity, reflecting metabolic plasticity that supports dissemination. Thus, targeting glycolysis–mitochondria crosstalk may represent a promising antimetastatic therapeutic strategy. This review aims to elucidate the mechanisms by which inhibitors of glycolysis and OXPHOS impact cancer cell migration, invasion, and metastasis, and to explore their potential therapeutic applications.

Keywords: glycolysis inhibitors, oxidative phosphorylation inhibitors, migration, invasion, metastasis.

Glycolysis inhibitors and their impact on metastasis

Several inhibitors targeting glycolysis have been investigated for their potential to impair cancer metastasis. These include sodium oxamate (SO), 2-deoxyglucose (2DG), 3-bromopyruvate, and others, each with distinct mechanisms of action (Fig. 1).

SO inhibits glycolysis by competitively inhibiting lactate dehydrogenase (LDH), a key enzyme catalyzing the conversion of pyruvate to lactate, thereby supporting tumor cell proliferation and metastasis [1]. This inhibition disrupts the final step of glycolysis, reducing the lactate production and decreasing the regeneration of NAD^+, which is es-

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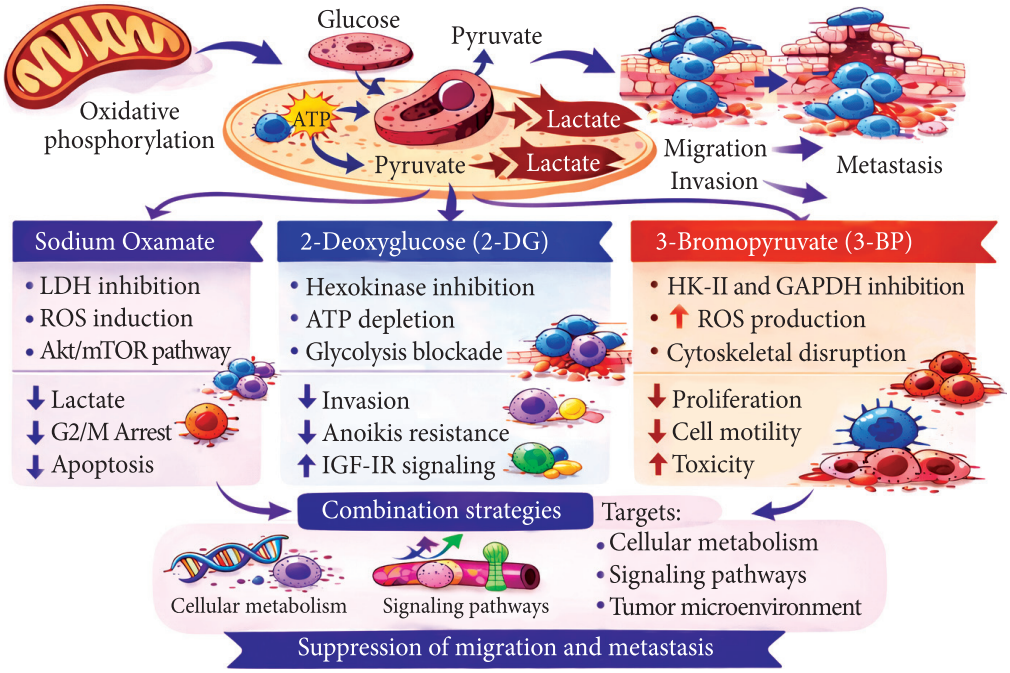

Fig. 1. Glycolysis inhibitors and their impact on metastasis. The scheme illustrates how inhibition of glycolysis affects tumor progression and metastasis. The key inhibitors — sodium oxamate, 2-deoxyglucose (2-DG), and 3-bromopyruvate (3-BP) — target enzymes involved in glucose metabolism, leading to ATP depletion, reduced lactate production, increased ROS generation, and disruption of signaling pathways. These effects suppress cancer cell proliferation, migration, and invasion. The main disadvantages of glycolysis inhibitors include low selectivity, systemic toxicity, metabolic adaptation of tumor cells (switching to OXPHOS), and limited efficacy due to tumor heterogeneity and compensatory metabolic pathways

sential for the continuation of glycolysis, ultimately resulting in reduced ATP levels [2]. Studies have shown that SO inhibits the viability of various cancer cell lines, including gastric, cervical, breast cancer cells, and others [3—8]. In gastric cancer cells, it induces protective autophagy [3]. Furthermore, SO treatment can lead to the enhanced production of reactive oxygen species (ROS), potentially contributing to cellular stress and inhibition of metastasis. It was also shown to inhibit the AKT-mTOR signaling pathway, which is crucial for cell growth and proliferation in many cancers [3]. In cervical and breast cancer cell lines, SO decreases LDH-A levels and activity, directly confirming its mechanism of action, and reduces superoxide dismutase (SOD) activity and the levels of reduced glutathione (GSH), further supporting an increase in ROS [4]. In nasopharyngeal carcinoma cells, LDH inhibition by SO induced a G_2/M cell cycle arrest and promoted apoptosis [5]. Notably, SO was found to decrease cell viability and migration in colorectal cancer cells by reducing lactate levels [6]. In esophageal cancer, it impairs TNF-α-dependent tumor cell migration [7], suggesting a role in counteracting inflammation-driven metastasis. Additionally, SO inhibits cell growth, suppresses tumor invasion, and induces apoptosis in gastric cancer cells [8]. Our recent studies have shown that the cytostatic effect of SO, observed under adherent growth conditions, persisted for up to 72 h after the transition to attachment-independent growth [9]. The clinical application of SO is limited to its low specificity, as it inhibits not only LDH-A but also other LDH isoforms, potentially disturbing metabolic balance in normal tissues. SO is a highly polar compound with restricted cell permeability, which reduces its intracellular efficacy. Its therapeutic effectiveness is further compromised by the metabolic plasticity of tumors [10]. Upon LDH-A blockade, cancer cells can shift to oxidative phosphorylation (OXPHOS) or alternative pathways such as glutaminolysis and fatty acid β-oxidation. Moreover, SO demonstrates a limited efficacy against migration and invasion: while glycolytic inhibition attenuates proliferation, tumor cells may maintain their motility through mitochondrial ATP production [10, 11].

2-Deoxyglucose (2DG) is another well-studied glycolysis inhibitor that, due to its structural similarity to glucose, competitively inhibits hexokinase and suppresses early glycolysis [12]. This leads to reduced ATP production and accumulation of 2-deoxy-glucose 6-phosphate (2DG-6P). Research shows that 2-DG inhibits aggressive triple-negative breast cancer cells by targeting their reliance on glycolysis and by reversing the cancer stem cell (CSC) phenotype. 2-DG enters cancer cells and then 2-DG-6P blocks glycolysis and causes a deficiency of energy. This metabolic blockade also reduces the aggressive characteristics of CSCs, such as their migration, invasion, and resistance to programmed cell death (anoikis) [13, 14]. Non-cytotoxic doses of 2-DG effectively diminished invasiveness in cell lines like MDA-MB-231, SUM149, and HCC1937 without causing cell death, suggesting 2-DG could be used as an adjuvant to target metastasis [13]. While effectively inhibiting glycolysis, 2DG activates multiple prosurvival pathways through IGF1R, which can potentially limit its efficacy as a single agent [15]. Furthermore, 2DG alters N-linked glycosylation, a process that can affect the function of proteins involved in cancer progression and metastasis [12]. Despite these complexities, 2DG has demonstrated the ability to inhibit proliferation, migration, and invasion of various cancer cell types, including colorectal and colon cancer [16]. It can also enhance the oncolytic effect of Coxsackie virus [17] and potentially boost T cell cytotoxicity [18], suggesting its utility in combination therapies. The low therapeutic selectivity of 2DG leads to glycolysis inhibition in both tumor and non-tumor cells, resulting in toxicity to normal tissues, particularly highly glycolytic cells, such as neurons and cardiomyocytes [19]. The treatment with 2DG induces the compensatory enhancement of the mitochondrial respiration, enabling tumor cells to adapt and maintain their migratory capacity. Moreover, its impact on the invasion appears insufficient, given that cytoskeletal and adhesion mechanisms are only partially dependent on the glucose availability. This is further supported by studies demonstrating that even under glucose-limiting conditions, cancer cells can adapt their metabolic pathways to utilize alternative energy sources, such as glutamine or fatty acids, to maintain cellular functions necessary for invasion. The redundancy in these pathways ensures that the cells retain invasive capabilities, albeit potentially at a reduced rate [20—22].

3-Bromopyruvate (3-BP) is a more potent glycolysis inhibitor for selective cancer treatment that acts by alkylating key glycolytic enzymes, such as hexokinase-II (HK-II) and glyceraldehyde-3-phosphate dehydrogenase [23, 24]. This leads to a significant reduction in ATP production and can also result in ROS generation. 3-BP has been shown to inhibit proliferation and metastasis in the preclinical models [23] and be able to disrupt the cytoskeleton, thereby inhibiting cell migration and colony formation [25]. Notably, 3-BP exhibits some selectivity for tumor cells due to their increased glucose consumption and overexpression of monocarboxylate transporters and HK-II [26]. However, the therapeutic application of 3-bromopyruvate (3-BP) remains severely limited by its high toxicity and poor selectivity, as the compound induces damage not only in tumors but also in vital organs, such as the liver and kidneys, at higher doses [27]. It should be noted that, to date, there have been insufficient data to fully characterize the pharmacokinetics of 3-BP, including its distribution, metabolism, and elimination, as previously noted [28]. Further research is essential to evaluate the potential toxicity of the drug in normal tissues, particularly those that are highly dependent on mitochondrial function and ATP levels. Resistance mechanisms also emerge upon treatment, most notably through metabolic rerouting toward glutaminolysis and fatty acid oxidation following hexokinase blockade [29, 30]. In addition, the antitumor activity of 3-BP is weakened by the intrinsic energetic flexibility of migrating cancer cells. Circulating tumor cells (CTCs) and invasive front populations often display a greater reliance on mitochondrial metabolism than on glycolysis, enabling them to escape glycolytic inhibition [31, 32]. These limitations underscore the need for next-generation analogs or delivery strategies that improve stability, enhance selectivity, and effectively target the metabolic adaptability of aggressive tumor cell subpopulations.

Other glycolysis inhibitors, including lonidamine [33, 34], inhibitors of pyruvate kinase, resveratrol [35], and various natural products, such

as kaempferol [36] and cantharidin [37], also show promise in targeting cancer metabolism and inhibiting metastasis by affecting different steps in the glycolytic pathway. The inhibition of glycolysis by these agents impairs the specific steps of metastasis by reducing the energy available for these processes. Cell detachment, migration, invasion, and colonization require significant ATP supply, and by disrupting glycolysis, these inhibitors can hinder these energy-dependent steps. Furthermore, the modulation of signaling pathways and the tumor microenvironment (TME), particularly the reduction of lactate production, can indirectly impede the metastatic cascade. Similar to other metabolic inhibitors, lonidamine and resveratrol exhibit low selectivity. Lonidamine has been reported to damage mitochondria in normal cells as well [38]; however, no direct evidence of cardiotoxicity or neurotoxicity has been documented in clinical or preclinical studies specifically for lonidamine. Importantly, lonidamine induces ROS, which may not always suppress but, in some contexts, rather promote cell migration and epithelial–mesenchymal transition (EMT) [39, 40]. Metastatic populations, including CTCs and cells at the invasive front, are often better adapted to elevated oxidative stress and may exploit ROS as a signal for enhanced motility [38]. Resveratrol, in addition to its low selectivity, suffers from poor in vivo bioavailability and is rapidly metabolized, which is reflected in low plasma concentrations [41]. It displays pleiotropic activity, modulating a wide range of pathways (including SIRT1, AMP-activated protein kinase (AMPK), and NF-κB), making its biological outcomes difficult to predict [42]. Resveratrol exerts only weak and reversible effects on tumor metabolism and does not induce sustained energetic collapse [43]. Evidence on its role in migration and invasion remains contradictory: while some models report suppression of EMT, others suggest it may facilitate stress adaptation and survival [44].

Taken together, metabolic inhibitors such as SO, 2-DG, 3-BrPA, lonidamine, and resveratrol possess antitumor potential, yet their major limitations include low selectivity, systemic toxicity, and the capacity of tumor cells to evade inhibition through metabolic plasticity. Therefore, an effective suppression of migration, invasion, and metastasis is likely to require combination strategies that concurrently target cellular metabolism, key signaling pathways (EMT, integrins, PI3K/AKT), and the tumor microenvironment.

Oxidative phosphorylation inhibitors and their impact on metastasis

Inhibitors of OXPHOS, such as metformin (MTF) and others, have also demonstrated potential in combating cancer metastasis (Fig. 2) [45]. MTF, a widely used anti-diabetic drug, mildly inhibits mitochondrial complex I, the first complex of the electron transport chain [46]. This leads to reduced ATP production and activation of the-AMPK-dependent signaling pathway [47]. MTF has been shown to inhibit cancer invasion and migration through the AMPK signaling pathway [48] and to reduce the expression of transcription factors driving the EMT [49], a crucial process in metastasis. MTF can induce bioenergetic stress in cancer cells [47]. Treatment with MTF was associated with reduced morbidity and mortality in non-small cell lung cancer patients [50]. Its anticancer effects can be insulin-dependent and insulin-independent [50]. This energy deficit can impair metastasis. Activation of AMPK by MTF and its impact on EMT are the key mechanisms by which it inhibits cancer spread [49]. Inhibitors of mitochondrial dynamics can also affect cell migration and invasion by disrupting the proper distribution and function of mitochondria within the cell [46, 49, 51—54].

Other OXPHOS inhibitors include potent complex I inhibitors like IACS-010759 [55], mitochondrial electron transport inhibitors like NDUFA4L2 [56], TPP^+ (triphenylphosphonium-targeted compounds)-based drugs [57], oligomycin A [58], and antimycin A [59], and inhibitors of mitochondrial dynamics like Mdivi-1(inhibitor of DRP1) mediated mitochondrial fission [60]. These agents target different aspects of mitochondrial function and have shown promise in preclinical studies for inhibiting tumor growth and metastasis. Notably, metastatic colorectal cancer has been found to rely heavily on mitochondrial metabolism, suggesting that OXPHOS inhibitors could be particularly effective in this cancer type [54]. While inhibitors of OXPHOS and mitochondrial functions (including MTF, IACS-010759, NDUFA4L2 inhibitors, TPP^+-based compounds,

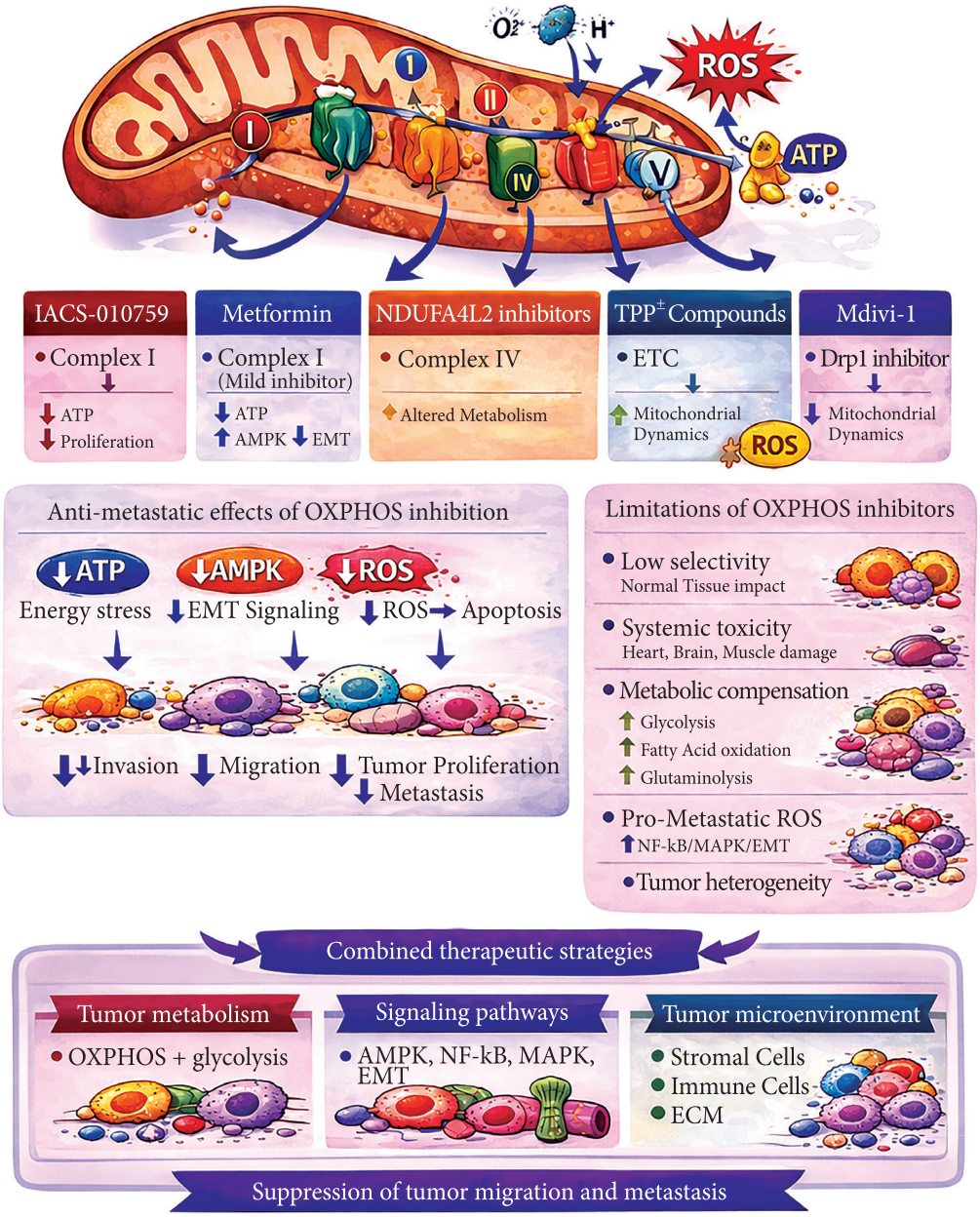

Fig. 2. OXPHOS inhibitors and their impact on metastasis. This scheme shows how mitochondrial OXPHOS inhibitors suppress tumor progression. The inhibition of the electron transport chain, particularly complex I, by metformin and IACS-010759, reduces ATP production and activates AMPK, suppressing EMT, invasion, and migration. Other agents increase ROS, inducing oxidative stress and apoptosis. However, their use is limited by low selectivity, systemic toxicity, metabolic compensation, and potential activation of pro-metastatic pathways (NF-κB, MAPK, EMT)

oligomycin A, antimycin A, and Mdivi-1) show promise in suppressing tumor growth, they also possess significant limitations that restrict their application in antimetastatic therapy. In particular, MTF requires suprapharmacological concentrations to inhibit tumor OXPHOS in vitro, while clinically achievable doses are often insufficient [61]. Moreover, systemic metabolic effects such as AMPK activation and reduced hepatic gluconeogenesis complicate the interpretation of its antimetastatic activity [62]. Many cancer cells adapt to OXPHOS inhibition by upregulating glycolysis or glutamine metabolism, thereby preserving motility and invasion [51, 63—64]. Consequently, MTF typically exerts stronger effects on proliferation than on invasion or migration in many models. Its effectiveness is also highly dependent on the genetic background of tumor cells, including the LKB1/AMPK status [65]. The drawbacks of other OXPHOS or mitochondrial dynamics in-

hibitors (IACS-010759, NDUFA4L2 inhibitors, TPP^+-based compounds, oligomycin A, antimycin A, Mdivi-1) parallel those of MTF. Tumor cells frequently develop resistance to these agents due to their intrinsic metabolic plasticity, which enables them to switch between OXPHOS, glycolysis, fatty acid oxidation, and glutaminolysis [63, 64]. Furthermore, OXPHOS inhibitors induce systemic toxicity, as mitochondria are indispensable for energy production in vital tissues such as the heart, brain, and skeletal muscle. Although these agents can increase ROS production and trigger apoptosis, ROS may also activate pro-metastatic signaling pathways, including NF-κB, MAPK, and EMT [40, 66]. The heterogeneity of tumors further complicates therapeutic outcomes, since metastatic subclones often differ in their reliance on OXPHOS. Importantly, inhibitors of OXPHOS or mitochondrial dynamics reduce proliferation but do not directly target key metastatic processes such as adhesion, EMT, or extracellular matrix remodeling. Finally, several OXPHOS inhibitors, including IACS-010759, MTF, and phenformin, have been associated with severe adverse effects, most notably lactic acidosis [55, 67].

Thus, the disadvantages of OXPHOS and mitochondrial dynamics inhibitors (MTF, IACS-010759, NDUFA4L2 inhibitors, TPP^+-based compounds, oligomycin A, antimycin A, Mdivi-1) in tumor growth suppression include low selectivity, systemic toxicity, metabolic compensation, and paradoxical pro-invasive effects mediated through ROS and metabolic adaptation. The heterogeneous toxicity profiles of these agents highlight the importance of carefully assessing the risk–benefit ratio for each inhibitor and developing more targeted compounds with reduced adverse effects [68]. Findings from studies on OXPHOS and mitochondrial dynamics inhibitors support the conclusion that combined targeting of tumor metabolism, signaling pathways, and the TME is a more rational strategy for anti-metastatic therapy.

Combined use of glycolysis and oxidative phosphorylation inhibitors

Simultaneously targeting both glycolysis and OXPHOS has emerged as a promising strategy to overcome the metabolic plasticity of cancer cells and enhance antitumor efficacy [69]. This dual inhibition can lead to a synergistic antitumor effect by creating a more profound energy depletion and preventing cancer cells from compensating for the inhibition of one pathway by upregulating the other [70] (Fig. 3). The combination can block the metabolic switch from OXPHOS to glycolysis that might occur when only one pathway is targeted [70]. Furthermore, it can enhance the antitumor effect of OXPHOS inhibitors by limiting the glycolytic backup and increasing the ROS production, leading to oxidative stress and cell death [70]. In some contexts, this combined approach, when used with radiotherapy, has shown the potential to overcome PD-1 resistance and enhance antitumor immunity [71]. Given that cancer cells can access a hybrid metabolic state, where both glycolysis and OXPHOS coexist, targeting both pathways simultaneously is a rational therapeutic strategy [72]. Inhibiting one pathway alone might trigger compensatory activation of the other, highlighting the importance of dual inhibition for achieving a more profound and sustained metabolic disruption. This comprehensive energy depletion can significantly hinder cancer cell survival and metastatic potential.

Combining glycolysis inhibitors with other antimetastatic therapies

Combining glycolysis inhibitors with conventional cancer therapies such as chemotherapy, radiotherapy, and immunotherapy has shown potential to enhance their efficacy against metastasis. Glycolysis inhibitors can synergize with chemotherapy by targeting the metabolic adaptations that lead to drug resistance and by normalizing the TME, thereby improving drug penetration [73, 74].

They can also enhance the sensitivity of cancer cells to radiotherapy by impairing energy-dependent repair mechanisms and by reversing hypoxia and reducing PD-L1 expression [71]. The key concept is that radiotherapy requires cellular energy (ATP) to support DNA repair processes; inhibition of glycolysis depletes ATP levels in tumor cells and thereby enhances their radiosensitivity. In addition, normalization of tumor hypoxia — through the suppression of the glycolytic flux and lactate accumulation — improves radiation efficacy by promoting reoxygenation and reducing hypoxia-induced radioresistance.

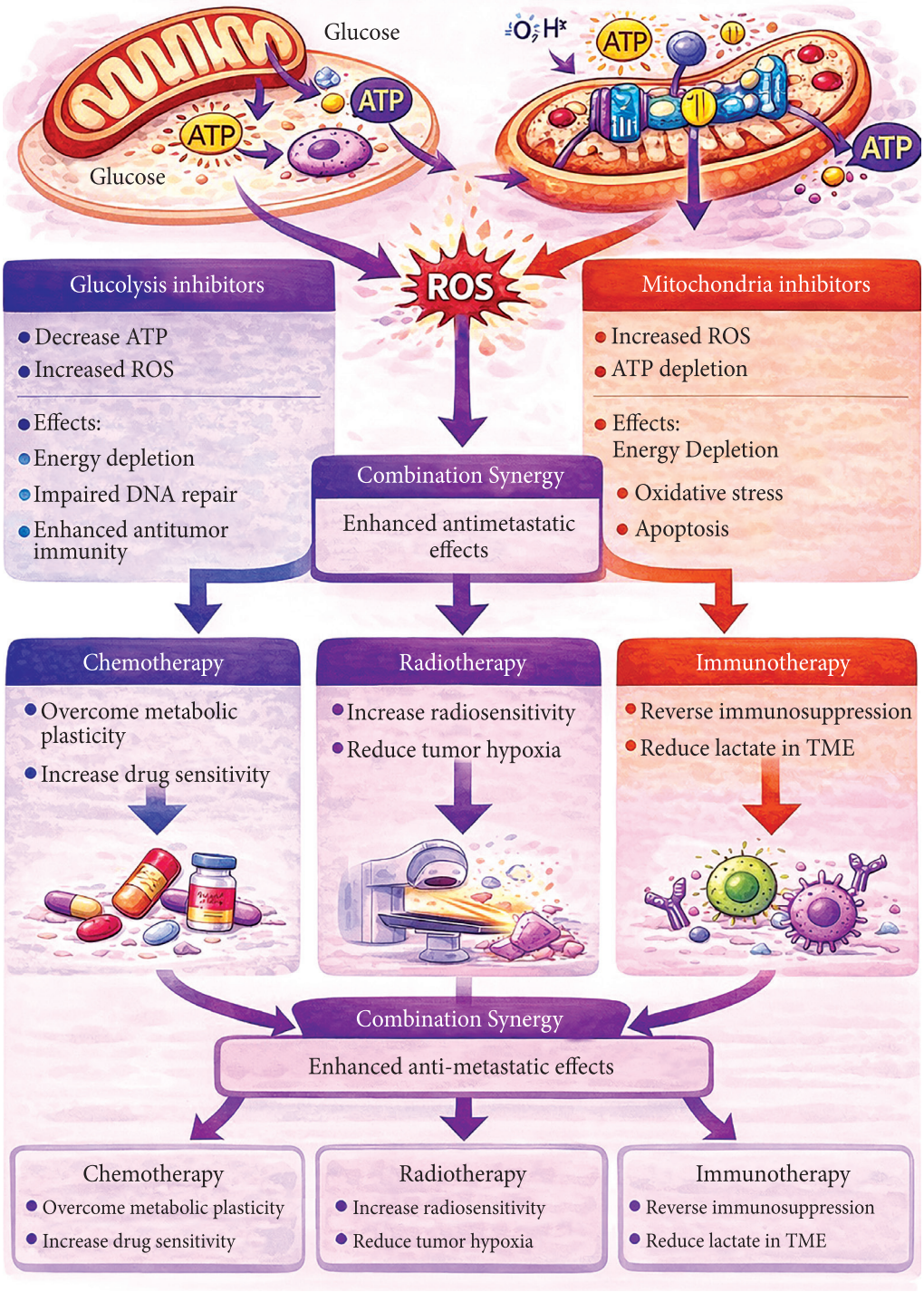

Fig. 3. Combined use of glycolysis and OXPHOS inhibitors against metastasis. The scheme illustrates the synergistic anti-tumor effects of simultaneously targeting glycolysis and mitochondrial OXPHOS. The dual metabolic inhibition prevents compensatory metabolic switching, causes ATP depletion, and increases ROS, leading to oxidative stress and tumor cell death. This strategy suppresses migration and metastasis while also modulating the tumor microenvironment, enhancing radiotherapy and chemotherapy responses, reducing PD-1/PD-L1 signaling, and promoting antitumor immune activity

Preclinical and early clinical trials demonstrated that 2-DG selectively sensitizes tumor cells to radiation by exploiting their elevated glycolytic flux, while sparing normal tissues that rely more on oxidative metabolism [75]. These studies reported that combining 2-DG with radiotherapy led to enhanced tumor regression and delayed regrowth in glioma and head-and-neck carcinoma

models, associated with depletion of ATP, inhibition of DNA repair enzymes, and accumulation of oxidative damage. Clinical phase I/II trials in patients with glioblastoma confirmed the feasibility and tolerability of such combination regimens [75]. Mechanistically, glycolytic inhibition by 2-DG leads to energy deprivation and redox imbalance. The reduced glycolytic flux limits NADPH regeneration through the pentose phosphate pathway, impairing antioxidant defenses and facilitating radiation-induced ROS accumulation. Elevated ROS levels cause oxidative DNA lesions and mitochondrial dysfunction, amplifying radiation cytotoxicity. Moreover, 2-DG reduces the repair of double-strand breaks by downregulating key repair proteins (Ku70/80, DNA-PKcs), thereby prolonging DNA damage signaling and promoting apoptosis.

Recent investigations have extended these findings to LDH-A inhibition by SO, which blocks conversion of pyruvate to lactate and disrupts NAD^+ recycling. It has been demonstrated that SO markedly enhances the radiosensitivity of lung and colorectal cancer cells both in vitro and in xenograft models [76]. LDH-A inhibition induced a metabolic shift toward mitochondrial OXPHOS, leading to overproduction of mitochondrial ROS and oxidative stress. This increase in ROS augmented radiation-induced DNA damage (γH2AX foci) and apoptosis, while suppression of lactate reduced the antioxidant buffering capacity of the tumor microenvironment. Notably, the combination of SO and irradiation suppressed the clonogenic survival more effectively than either treatment alone, and the effect was abrogated by ROS scavengers such as N-acetylcysteine, confirming the central role of oxidative stress in this synergistic interaction. Beyond ROS generation, SO-mediated ATP depletion appears to impair ATP-dependent DNA repair pathways and the activity of hypoxia-inducible factor-1α (HIF-1α), reducing the hypoxia-driven radioresistance commonly observed in solid tumors. This dual effect — metabolic collapse and redox imbalance — renders LDH-A inhibition a promising strategy for radiosensitization. Additional studies support the concept that targeting LDH-A enhances radiotherapy outcomes and reduces tumor repopulation between irradiation fractions [77, 78]. Collectively, these findings demonstrate that interfering with glycolytic metabolism — either by blocking upstream glucose utilization with 2-DG or downstream lactate production with SO — potentiates radiotherapy efficacy through converging mechanisms: ATP depletion, oxidative stress amplification, inhibition of DNA repair, and TME reoxygenation. Given the tumor-selective reliance on aerobic glycolysis (the Warburg effect), these strategies offer a rational approach to overcome radioresistance and improve therapeutic indices in solid tumors, including lung and colorectal carcinomas.

Recent preclinical studies have shown that targeting glycolysis can significantly reshape the immunosuppressive TME, consequently enhancing the efficacy of immunotherapy. For example, pharmacologic inhibition of LDH reduces lactate production, which, in turn, alleviates acidosis in the TME; this has been demonstrated to reverse immune suppression by increasing the cytotoxic T cell function and reducing regulatory T cell (Treg) activity in murine tumor models [79, 80]. It was shown that LDH inhibition decreases tumor cell glucose uptake and proliferation while boosting glucose availability in the TME, which enhances the infiltration and activation of effector T cells and impairs Treg-mediated suppression. Moreover, recent work has combined glycolysis inhibition with immunotherapy. In nanoplatform-based studies, the agents that deplete lactate in the tumor (e.g., lactate oxidase-based systems or inhibitors of lactate production/efflux) have been shown to shift macrophage polarization toward the M1 phenotypes and increase NK cell and cytotoxic T lymphocyte infiltration and activity [81]. For instance, an oxygen-generating nanoplatform combining lactate depletion with sonodynamic therapy promoted M1 macrophage polarization, improved antigen presentation by dendritic cells, and enhanced subsequent antitumor immune responses. Thus, inhibition of glycolysis and reduction of lactate production exert not only direct cytotoxic effects on tumor cells but also profoundly remodel the immunosuppressive TME. Suppression of LDH-A or lactate transporters normalizes extracellular pH, increases glucose availability for effector T lymphocytes, reduces the activity of Tregs and M2 macrophages, and enhances the antitumor immune response. Therefore, metabolic reprogramming

of the TME through glycolytic targeting represents a promising approach to improving the efficacy of immunotherapy and combination treatments for malignant tumors.

The synergistic effects observed highlight the fundamental vulnerability of cancer cells related to their altered metabolism, making metabolic targeting a potentially useful strategy to enhance existing antimetastatic therapies. Furthermore, the ability of glycolysis inhibitors to modulate the TME appears critical for improving the outcomes of combination treatments. However, careful investigation is needed to determine the optimal combinations, timing, and dosages to maximize therapeutic benefit while minimizing toxicities.

Conclusion and future perspectives

Inhibitors of glycolysis and OXPHOS have demonstrated significant potential in preclinical studies for impairing cancer cell migration, invasion, and metastasis by disrupting energy production and modulating key signaling pathways. The combined use of these inhibitors often results in synergistic effects, overcoming the metabolic plasticity of cancer cells. Furthermore, these metabolic inhibitors can enhance the efficacy of conventional cancer therapies like chemotherapy, radiotherapy, and immunotherapy. However, the clinical application of some of these agents is limited by their side effects. Future research should focus on developing more specific and less toxic inhibitors, optimizing combination therapies, and identifying biomarkers to predict patient response. Investigating novel drug delivery systems to enhance tumor-specific accumulation of these metabolic inhibitors is also crucial for improving their therapeutic index and ultimately translating these promising findings into effective treatments for metastatic cancer.

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МЕТАБОЛІЧНІ ІНГІБІТОРИ ТА ЇХ ВПЛИВ НА МІГРАЦІЮ, ІНВАЗІЮ ТА МЕТАСТАЗУВАННЯ РАКОВИХ КЛІТИН

Метастазування — процес, за допомогою якого ракові клітини поширюються з первинної пухлини у віддалені ділянки, залишається основною причиною смерті онкологічних хворих. Цей процес включає відшарування клітин, міграцію, інвазію, виживання в системі кровообігу, екстравазацію та колонізацію нових тканин. Фундаментальною характеристикою ракових клітин є їхній змінений метаболізм, який часто демонструє підвищене споживання глюкози та перевагу гліколізу навіть за наявності кисню, явище, відоме як ефект Варбурга. Цей метаболічний зсув забезпечує ракові клітини швидким джерелом аденозинтрифосфату та необхідних біосинтетичних проміжних продуктів, що підтримує їхній швидкий ріст та проліферацію. Хоча ранні теорії вважали дефект мітохондріального окисного фосфорилювання причиною ефекту Варбурга, зараз визнано, що мітохондрії в ракових клітинах часто функціональні та відіграють вирішальну роль у різних клітинних процесах. Примітно, що метастатичні клітини часто демонструють залежність від мітохондріального дихання та окисного фосфорилювання, що свідчить про потенційну метаболічну адаптацію, яка стимулює прогресування раку. Цей огляд розглядає механізми, за допомогою яких інгібітори гліколізу та окисного фосфорилювання впливають на міграцію, інвазію та метастазування пухлинних клітин, а також висвітлює перспективи їх терапевтичного застосування.

Ключові слова: інгібітори гліколізу, інгібітори окисного фосфорилювання, міграція, інвазія, метастазування.