Review

Discovery Medicine 2024; 36(190): 2143–2151
https://doi.org/10.24976/Discov.Med.202436190.197

Microgravity Effects on Glioma Cells: A Comprehensive Review

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Published: 20 November 2024

High-grade gliomas (HGGs) represent a formidable challenge in neuro-oncology due to their aggressive nature and resistance to current therapeutic interventions, which include surgery, radiation, chemotherapy, and emerging immunotherapies. Despite these efforts, the prognosis for patients remains poor, emphasizing the urgent need for novel treatment strategies. One promising avenue of exploration is microgravity, a condition experienced during spaceflight and simulated in laboratories on Earth, which induces significant physiological changes in cells and tissues. This review synthesizes relevant literature and provides a comprehensive overview of microgravity's effects on glioma cells, encompassing alterations in cell proliferation, apoptosis, gene expression, and a comparative analysis of its impact on other cancer cell types. Studies utilizing simulated microgravity techniques such as clinostats and rotating wall vessels have demonstrated that glioma cells exhibit reduced viability, altered growth patterns, and enhanced activation of apoptotic pathways compared to controls under normal gravity conditions. These findings are significant given the inherent resistance of gliomas to apoptosis; a process critical for the effectiveness of conventional therapies. Despite the challenges in accurately replicating the microgravity environment of space on Earth, simulated microgravity studies have elucidated molecular mechanisms underlying cellular responses. These mechanisms include DNA damage, impaired DNA repair mechanisms, and modulation of apoptotic pathways, which suggest potential vulnerabilities that could be targeted to improve therapeutic outcomes in glioma treatment. Moving forward, further research is essential to deepen our understanding of the specific molecular pathways involved in microgravity-induced effects on glioma cells. This knowledge could pave the way for the development of innovative therapeutic strategies aimed at enhancing apoptosis and overcoming treatment resistance in HGGs. Ultimately, microgravity research offers promising opportunities to advance neuro-oncology by identifying new therapeutic targets and improving clinical outcomes for patients with HHG.

Keywords: microgravity; glioma; cell proliferation; apoptosis; simulated microgravity; therapeutic targets

Introduction

High-grade gliomas (HGGs) are aggressive primary brain tumors posing a significant neuro-oncological challenge [1]. These tumors, originating from glial cells, are the most common and aggressive type of primary brain cancer in adults. Their uncontrolled growth, extensive infiltration into healthy brain tissue, and promotion of new blood vessel formation (angiogenesis) make HGGs particularly challenging to treat [1]. Despite advancements in cancer research and therapeutic approaches, the prognosis for patients with HGGs remains poor. For example, glioblastoma (WHO grade 4) has a median survival of less than two years following diagnosis [2]. One major reason for the dismal prognosis is the resistance of these tumors to treatment and their tendency to rapidly recur despite aggressive therapeutic interventions [2]. Current treatments, including surgical resection, radiation therapy, chemotherapy, and emerging immunotherapies, offer only limited extensions of survival and minimal improvements in quality of life [3,4].

A critical factor contributing to the treatment difficulty of HGGs is their inherent resistance to apoptosis, or programmed cell death, a natural safeguard against cancer [5]. The failure of glioma cells to undergo apoptosis undermines

the efficacy of conventional therapies such as radiation and chemotherapy [5]. Given the prevalence of HGGs and the limited effectiveness of current treatments due to impaired apoptosis, there is a pressing need for novel strategies to overcome therapeutic resistance by targeting these apoptotic barriers.

In this context, exploring the influence of microgravity on glioma cells offers a promising and innovative approach. Microgravity, which is prevalent in space during spaceflight missions, induces a range of physiological changes in astronauts, including alterations to musculoskeletal, immune, and cardiovascular systems [6,7]. Beyond its impact on human health, microgravity has been shown to affect various biological systems, from individual cells and tissues to entire organisms [8,9].

However, replicating the true microgravity environment on Earth presents significant challenges. Although simulated microgravity techniques, such as clinostats and rotating wall vessels, have been developed, they may not perfectly replicate the biological responses observed in actual space conditions [10]. Despite these limitations, the potential therapeutic implications of microgravity on glioma cells warrant exploration. This review aims to investigate the multifaceted relationship between microgravity and glioma cells, emphasizing its potential as a novel therapeutic strategy. Specifically, it will address the epidemiological significance of gliomas, the physiological effects of microgravity on humans, and the broader impact of microgravity research on various cell cultures. Moreover, this review will analyze the influence of both real and simulated microgravity on glioma cell proliferation and apoptosis, providing insights into the underlying molecular mechanisms. Ultimately, this review emphasizes the critical need for further research to elucidate the effects of microgravity on glioma cells, which may uncover groundbreaking new treatment strategies for combating HGGs.

Microgravity and Its Physiological Effects

Exposure to microgravity, such as that experienced during spaceflight, induces a range of physiological changes in astronauts. These effects stem from the altered gravitational forces experienced in space, which differ significantly from those on Earth. Microgravity, often referred to as zero gravity, is not truly devoid of gravitational forces but represents a condition where gravitational effects are significantly reduced. In this environment, the body's normal physiological processes, which are adapted to Earth's gravity, are disrupted, leading to a variety of observed effects.

One of the prominent issues associated with space microgravity is space motion sickness (SMS). Affecting 60–80% of astronauts within the first few days of entering microgravity, SMS is characterized by symptoms such as vertigo, nausea, vomiting, appetite loss, headache, and pallor [11]. These symptoms bear similarities to traditional motion sickness but do not respond well to conventional antiemetic treatments. Several hypotheses have been proposed to explain SMS, including sensory conflict due to the loss of tilt-related otolith signals, fluid shift resulting in cephalad fluid movement and increased intracranial pressure, otolith asymmetry caused by mass differences between ears, and otolith adaptation where the brain reinterprets sensory inputs in the microgravity environment [12]. Evidence from Space Shuttle missions suggests that otolith asymmetry and adaptation are less likely to be the primary causes of SMS. Pharmacotherapy remains the primary countermeasure for SMS, with drugs like promethazine and scopolamine being used. Additionally, artificial gravity, achieved through rotating space habitats, is proposed as a potential effective countermeasure to alleviate SMS [13].

Microgravity also significantly impacts the cardiovascular system. Initially, body fluids shift from the lower body to the thorax and head, leading to facial puffiness, decreased leg volume, increased pulmonary capillary blood volume, and elevated intraocular pressure [14]. This fluid shift is associated with cardiovascular deconditioning, which manifests as postflight orthostatic intolerance. During the initial phase of spaceflight, heart rate, stroke volume, and cardiac output typically stabilize to preflight levels. However, long-term exposure results in a reduction in blood volume and heart size. This reduction in blood volume is attributed to fluid shifts from intravascular to interstitial spaces and decreased erythropoietin production, leading to a lower erythrocyte volume. Adaptations in the autonomic and endocrine systems, including increased sympathetic neural activity and decreased vagal activity, help stabilize blood pressure and fluid balance. Over time, the myocardial volume of the heart decreases by 8–10%, and blood pressure experiences a slight reduction. Additionally, aerobic capacity is affected, with maximal oxygen uptake decreasing by 22% after short-term spaceflights due to reductions in stroke volume and cardiac output [15]. These physiological adaptations pose challenges to astronauts' performance and health during and after space missions.

Simulated vs. Induced Microgravity

Simulated microgravity refers to laboratory methods and technologies designed to approximate the effects of true microgravity on biological systems. These techniques aim to replicate certain aspects of microgravity but may not capture all the complex interactions experienced in space. Key methods include:

- Clinostats: Clinostats continuously rotate biological samples at a constant speed to average out gravitational forces. This rotation minimizes gravity-induced sedimentation and distribution effects, simulating aspects of microgravity. However, clinostats cannot fully replicate fluid dynamics and mechanical forces experienced in space.

• Rotating Wall Vessels (RWV): RWVs create a low-shear, rotating environment where cells are suspended in a rotating fluid. This setup simulates weightlessness by counteracting gravitational force with centrifugal force. While effective in reducing sedimentation, RWVs may not fully mimic the complex interactions of fluids and cellular forces in true microgravity.

• Random Positioning Machines (RPMs): RPMs use random rotational and tilting motions to prevent cells from experiencing consistent gravitational direction. By constantly changing the orientation, RPMs reduce the directional effects of gravity, simulating weightlessness. However, this method may not capture all aspects of the space environment.

Induced Microgravity, achieved through spaceflight or specialized facilities, provides an authentic representation of microgravity. Key methods include:

• Spaceflight: True microgravity is experienced during space missions on platforms like the International Space Station (ISS). The continuous free-fall state of the spacecraft and its contents creates genuine microgravity conditions, allowing researchers to observe real-time physiological and biological responses to this unique environment.

• Drop Towers: Drop towers allow experiments to experience brief periods of microgravity during free-fall from a significant height. Although the duration is short, it provides valuable insights into the immediate effects of true microgravity on biological samples.

• Parabolic Flights: Parabolic flight maneuvers in specially equipped aircraft create temporary microgravity during the descent phase of each parabola. While the microgravity period is brief, it offers valuable data on the effects of weightlessness on biological systems.

The primary difference between simulated and induced microgravity lies in their ability to replicate the full spectrum of space conditions. Simulated microgravity techniques approximate certain aspects of microgravity but may not fully capture the comprehensive range of physiological changes experienced in space. These methods are valuable for preliminary studies and large-scale screenings on Earth.

Induced microgravity provides a more accurate representation of the space environment, offering deeper insights into how organisms adapt to true microgravity. This approach is crucial for understanding real-world effects and developing effective countermeasures and therapeutic strategies.

Both simulated and induced microgravity play important roles in advancing our knowledge of biological systems under low-gravity conditions. Combining insights from both approaches enhances our understanding and contributes to the development of innovative solutions for space travelers and patients on Earth.

Effects of Microgravity on Glioma Cells and Microglia

Microgravity research has yielded significant insights into the physiological and molecular responses of glioblastoma cells and microglia, offering a deeper understanding of how altered gravitational conditions influence cellular behavior and function. These studies have particularly highlighted changes in cellular aggregation, proliferation, DNA damage response, apoptosis, and alterations in key signaling pathways related to cell survival and growth (Table 1).

Simulated microgravity (SMG) experiments have consistently demonstrated that within a relatively short period of 72 hours, both microglial and glioblastoma cells undergo notable changes. One of the primary observations is the formation of three-dimensional cellular aggregates, or spheroids, which occur as a response to SMG. This phenomenon is well-documented across various cell types and is thought to mimic aspects of tissue organization observed *in vivo* under conditions of reduced gravity [16–18].

In addition to structural changes, SMG significantly impacts cellular viability and proliferation. Studies have consistently shown that both microglial and glioblastoma cells exhibit reduced viability and proliferation rates under SMG conditions compared to normal gravity controls [16–18]. These findings are crucial as they indicate a potential impairment in cellular metabolic activity or growth signaling pathways that are sensitive to gravitational cues.

At the molecular level, SMG induces DNA damage in microglial and glioblastoma cells, characterized by increased levels of DNA strand breaks. This DNA damage triggers a cascade of cellular responses collectively known as the DNA damage response (DDR) pathway. A key marker of DNA damage, phosphorylation of histone H2A.X at Ser139 (γH2A.X), is consistently elevated under Stress-mediated genotoxicity conditions [19–21]. Activation of γH2A.X serves as a signal for recruiting repair factors to the site of DNA damage and initiating repair processes. Interestingly, the response of DDR pathways differs between normal microglial and glioblastoma cells. Normal microglial cells typically exhibit a suppressed ataxia-telangiectasia mutated/ATM- and Rad3-related (ATM/ATR)-Chk2/Chk1-dependent DDR pathway under SMG, suggesting a potential adaptation to reduced gravitational stress. In contrast, glioblastoma cells often show an activated ATM and Chk2 response, possibly indicating a heightened sensitivity to DNA damage in these cancerous cells [19,20].

Furthermore, SMG disrupts DNA repair mechanisms across both cell types. Processes such as base excision repair (BER), nucleotide excision repair (NER), mismatch repair (MMR), non-homologous end joining (NHEJ), and homologous recombination (HR) are inhibited or impaired under SMG conditions [19–21]. This impairment in DNA

Table 1. Effects of microgravity on glioma cells.

Step/mechanism	Effects of microgravity on glioma cells
Formation of 3D cellular aggregates	Induction of multicellular spheroid formation within 72 hours.
Cell viability	Decreased cell viability due to compromised metabolic activity and nutrient uptake.
Proliferation	Reduced cell proliferation rates, leading to slower growth and colony formation.
DNA damage	Increased DNA strand breaks, affecting genomic stability and integrity.
DNA damage response (DDR)	Activation of repair mechanisms varies between cell lines; some show impaired ATM/ATR pathways.
DNA repair inhibition	Suppressed repair pathways (BER, NER, MMR, NHEJ, HR), contributing to DNA damage accumulation.
Apoptosis and necrosis	Enhanced apoptotic pathways (e.g., upregulation of Bax, cleaved caspase-3) and increased necrotic cell death.
Mitochondrial function	Altered mitochondrial activity affecting energy production and cellular metabolism.
Signaling pathways (MAPK/ERK1/2, PI3K/AKT)	Modulation of MAPK/ERK1/2 and PI3K/AKT pathways influencing cell survival and growth.

ATM, ataxia-telangiectasia mutated; ATR, ATM- and Rad3-related; BER, base excision repair; NER, nucleotide excision repair; MMR, mismatch repair; NHEJ, non-homologous end joining; HR, homologous recombination; MAPK, mitogen-activated protein kinase; ERK1/2, extracellular signal-regulated kinase 1/2; PI3K, phosphatidylinositol 3-kinase; AKT, protein kinase B; Bax, Bcl-2-associated X protein.

repair pathways contributes to the accumulation of DNA damage within cells, posing a potential risk to genomic stability and cellular function over prolonged exposure to microgravity.

Cellular stress induced by microgravity also triggers apoptotic and necrotic pathways in both microglial and glioblastoma cells. Apoptosis, or programmed cell death, is characterized by distinct biochemical and morphological changes including DNA fragmentation, phosphatidylserine externalization (detected by annexin-V-FITC staining), and activation of caspases such as cleaved caspase-3 [20–22]. These apoptotic signals are often accompanied by a shift in the balance of pro-apoptotic (e.g., Bcl-2-associated X protein (Bax)) and anti-apoptotic (e.g., Bcl-2) proteins, favoring apoptosis in response to cellular stressors induced by microgravity.

Moreover, microgravity influences signaling pathways involved in cellular responses beyond survival and proliferation. Mitogen-activated protein kinase (MAPK)/extracellular signal-regulated kinase 1/2 (ERK1/2) and phosphatidylinositol 3-kinase (PI3K)/protein kinase B (AKT) signaling pathways, known regulators of cell growth and survival, exhibit altered activity in microglial and glioblastoma cells under SMG conditions [19–22]. While the specific roles of these pathways in mediating cellular responses to microgravity are still being elucidated, their differential modulation suggests complex interactions that may impact DDR and apoptosis regulation under altered gravitational environments.

Research specifically focusing on glioma cells highlights that microgravity induces apoptosis in various glioma models. Studies have shown that SMG can inhibit proliferation and migration in human glioma cells, alongside inducing apoptotic pathways characterized by upregulated pro-apoptotic proteins and downregulated anti-apoptotic factors (Fig. 1) [23–25].

These findings are particularly significant given the intrinsic resistance of gliomas to apoptosis and the limited effectiveness of current treatment modalities [26]. Understanding the mechanisms by which microgravity influences apoptotic pathways in glioma cells not only enhances our understanding of cellular adaptations to altered gravitational environments but also holds potential implications for developing innovative therapeutic strategies. Targeting apoptotic pathways activated by microgravity could potentially enhance the efficacy of existing therapies, addressing the challenges posed by glioma resistance mechanisms [27–30].

Simulated microgravity studies using techniques such as the clinostat have been pivotal in advancing our understanding of cellular responses in microglial and glioblastoma cells [31–34]. These studies underscore the complexity of cellular adaptations to altered gravitational conditions and highlight the potential of microgravity as a tool for investigating and potentially manipulating cellular behaviors in health and disease contexts. Further research is essential to elucidate the specific molecular mechanisms underlying these responses and to translate these findings

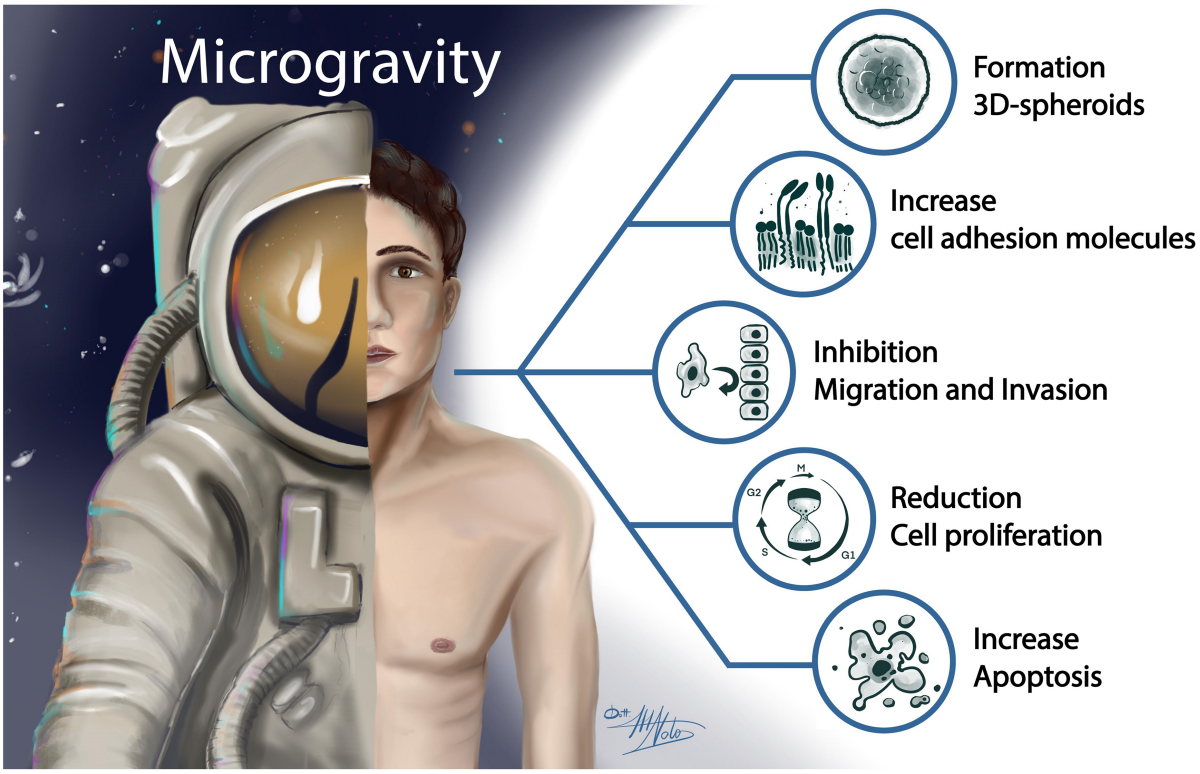

Fig. 1. Effects of Microgravity on Glioma Cells (Created using Procreate, Savage Interactive Pty Ltd., Version 5.3.5, Hobart, Australia). The figure illustrates the effects of microgravity on glioma cells, with one half depicting an astronaut representing space microgravity and the other half representing simulated microgravity on Earth. Key changes include 3D spheroid formation, increased cell adhesion, reduced migration and proliferation, and increased apoptosis.

into novel therapeutic approaches for conditions such as gliomas, where effective treatment options remain critically needed.

Effects of Microgravity on Other Cancer Cells

Comparative studies on the effects of microgravity across various cancer cell types provide valuable insights into both unique and shared mechanisms influenced by this altered environment. Cancer cells exhibit distinct responses to microgravity, affecting morphology, function, and molecular pathways. For instance, breast cancer cells rapidly form three-dimensional spheroids under microgravity, increasing the expression of cell-adhesion molecules such as vimentin, vinculin, and laminin [35–37]. Similarly, thyroid carcinoma cells show an enhanced expression of intermediate filaments and extracellular matrix components within hours of exposure to simulated microgravity [35].

Microgravity's influence extends beyond structural changes, impacting cancer cell functionality. In malignant glioma cells, microgravity inhibits invasion and migration—processes critical for metastasis—by upregulating apoptotic pathways [38]. Likewise, colon cancer cells exposed to simulated microgravity undergo apoptosis via early cleavage of caspase 3 and activation of the ATM/p53 signaling pathway [39].

The influence of microgravity on cancer stem cells is an emerging area of research. Initial findings suggest that microgravity increases apoptosis in lung cancer stem cells while also modulating key stem cell markers, such as Octamer-binding Transcription Factor 4 (*Oct4*) and *NanoG*, in colorectal cancer cells [40]. These insights highlight the potential of microgravity to unravel mechanisms driving cancer stemness and therapeutic resistance.

Breast cancer cells provide a particularly compelling case study of the multifaceted effects of microgravity. In cell lines such as MDA-MB-231, significant changes in cellular morphology and cytoskeletal organization have been observed, with microgravity disrupting F-actin and tubulin networks, leading to reduced adhesion and altered migration capabilities compared to cells cultured under normal gravity [36]. Gene expression studies further reveal complex responses in breast cancer cells, with the upregulation of genes involved in cytoskeletal differentiation, such as *VIM* and *RHOA*, and proliferation markers like *MAPK1*. This contrasts with the downregulation of genes like *VEGF*, reflecting a nuanced regulatory landscape under microgravity [37]. However, these gene expression changes do not always correlate directly with protein levels, underscoring the need for integrated analyses across different biological layers [37].

Cell cycle regulation and apoptosis are also impacted by microgravity. Breast cancer cell lines cultured in rotating wall vessels show inhibited proliferation, marked by decreased expression of cyclin D1, a key regulator of cell cycle progression [41]. Additionally, microgravity alters apoptotic pathways by modifying the expression of apoptosis-related proteins such as Bcl2 and Fas, shifting the balance toward pro-apoptotic signaling [41].

Interestingly, microgravity affects cancer cells differently depending on whether they are adherent or in multicellular spheroids. Adherent breast cancer cells exhibit distinct gene expression profiles related to focal adhesion molecules and extracellular matrix proteins, while multicellular spheroid cells show reduced expression of cell junction proteins like E-cadherin and altered cytoskeletal dynamics [36]. These adaptive responses demonstrate that cancer cells' reactions to microgravity are context-dependent, varying with spatial organization and environmental factors.

Signaling pathways involved in cell survival and adaptation are also modulated under microgravity. For example, activation of the AKT pathway in breast cancer cells suggests a pro-survival response aimed at maintaining cellular homeostasis despite the challenges posed by altered gravitational forces [40,42]. This adaptive mechanism highlights the resilience of cancer cells and the complexity of targeting these pathways in microgravity environments.

In lung cancer (non-small cell lung cancer, H460 cell line), Pisanu *et al*. [40] found that cancer stem cells exposed to microgravity resist differentiation and show increased apoptosis compared to cells grown under normal gravity conditions. Additionally, microgravity leads to a loss of stem cell properties, with a reduction in *NanoG* and *Oct4* gene expression and decreased aldehyde dehydrogenase levels. In gastrointestinal stem cells (colon cancer, HCT116 cell line), Arun *et al*. [43] observed that microgravity increases the percentage of cancer stem cells expressing both CD44 and CD133 markers. Furthermore, microgravity impacts growth and differentiation control pathways, such as phosphatase and tensin homolog (PTEN), forkhead Box O3 (FOXO3), and AKT, enhances autophagy and increases the number of giant cancer cells with full nuclear localization of Yes-Associated Protein [40].

Overall, microgravity exerts profound effects on cancer cells, from morphological changes and cytoskeletal reorganization to modulation of gene expression and apoptotic pathway activation. These effects are both context-dependent and multifaceted, varying across cancer types, cell organization, and specific molecular pathways. Continued exploration in this area is critical for harnessing the full potential of microgravity research to advance cancer treatment strategies both in space and on Earth.

Discussion

HGGs, including glioblastomas, are among the most formidable challenges in neuro-oncology due to their aggressive growth, extensive infiltration into surrounding brain tissue, and resistance to conventional therapies [1]. Despite advances in multimodal treatment approaches—such as surgical resection, radiation therapy, chemotherapy, and emerging immunotherapies—the prognosis for patients with HGGs remains dire, with median survival rates typically falling below two years [1,2]. A critical obstacle in improving patient outcomes is the intrinsic resistance of glioma cells to apoptosis, a natural process of programmed cell death crucial for eliminating cancerous cells targeted by therapeutic interventions [5].

Anti-Apoptotic Properties of Glioma Cells

Glioma cells possess several unique characteristics that contribute to their resistance to apoptosis. One significant factor is their ability to evade apoptosis through various anti-apoptotic mechanisms. Glioma cells often exhibit overexpression of anti-apoptotic proteins such as Bcl-2 and Bcl-xL, which inhibit the activation of pro-apoptotic factors and prevent the initiation of the apoptotic cascade [5]. Additionally, the PI3K/AKT signaling pathway, commonly activated in gliomas, plays a crucial role in promoting cell survival and resistance to apoptosis by inhibiting pro-apoptotic proteins and enhancing cell proliferation [5]. The overactivation of the nuclear factor kappa B (NF-κB) pathway, another prevalent feature in gliomas, further contributes to resistance by promoting cell survival and inflammation [5].

Moreover, glioma cells often display altered apoptotic pathways and DNA repair mechanisms, which enable them to survive despite genotoxic stress induced by conventional therapies. For example, glioma cells may exhibit deficiencies in base excision repair (BER) and nucleotide excision repair (NER) pathways, leading to impaired repair of DNA damage and enhanced resistance to chemotherapeutic agents [5]. These characteristics underscore the need for innovative therapeutic strategies that can overcome the resistance mechanisms inherent in glioma cells.

Microgravity and Glioma Cell Behavior

Microgravity, experienced during space missions and simulated in laboratory settings, induces a range of physiological and cellular changes that offer a unique perspective on glioma cell biology [6–9]. Studies exploring the effects of microgravity on glioma cells have yielded promising insights into how altered gravitational conditions influence cellular behavior. Notably, microgravity has been shown to reduce glioma cell proliferation rates and induce changes in cell morphology and growth patterns [16–18]. These observations suggest that microgravity could potentially impact

the growth and survival of glioma cells in ways that differ from those observed under normal gravity conditions.

Microgravity-Induced Apoptosis

One of the most intriguing findings in microgravity research is the observed enhancement of apoptotic pathways in glioma cells. Microgravity conditions have been associated with the activation of pro-apoptotic signaling pathways and the upregulation of pro-apoptotic proteins, such as Bax and Bak, which promote apoptosis by inducing mitochondrial outer membrane permeabilization and cytochrome c release [23–25]. Conversely, the downregulation of anti-apoptotic factors, such as Bcl-2 and Bcl-xL, under microgravity conditions suggests a shift in the balance towards apoptosis [23–25]. These changes are particularly significant given the challenge of inducing apoptosis in glioma cells through conventional therapies.

Additionally, microgravity-induced alterations in DNA repair mechanisms have been observed, including impaired base excision repair and nucleotide excision repair pathways [19–21]. These vulnerabilities could potentially be exploited to enhance therapeutic outcomes by targeting the compromised DNA repair systems in glioma cells. The reduced viability and altered growth patterns of glioma cells under simulated microgravity conditions further support the hypothesis that microgravity could influence cellular responses in ways that may be therapeutically beneficial [16–18].

Challenges and Future Directions

Translating these findings into clinical applications poses several challenges. One major hurdle is the complexity of replicating true microgravity environments on Earth. While simulated microgravity techniques, such as clinostats and rotating wall vessels, provide valuable insights, they may not fully capture all aspects of the microgravity-induced changes observed in space [10]. For example, fluid dynamics, mechanical forces, and cell-cell interactions in true microgravity may differ significantly from those present in ground-based simulated methods.

Therefore, continued research is essential to elucidate the specific molecular mechanisms by which microgravity influences glioma cells and to optimize therapeutic strategies based on these insights. Future studies should focus on further characterizing the molecular pathways involved in microgravity-induced apoptosis, investigating the long-term effects of microgravity exposure on glioma progression, and exploring how these findings can be translated into clinical applications.

Microgravity research holds promise for advancing our understanding of glioma biology and improving therapeutic approaches. By uncovering the intricate interactions between altered gravitational forces and cellular responses, this field has the potential to identify new therapeutic targets and enhance the efficacy of current treatment regimens for HGGs. Ultimately, these endeavors aim to improve patient outcomes and quality of life in neuro-oncology through innovative approaches rooted in microgravity research.

Conclusion

Microgravity research has uncovered valuable insights into glioma biology, offering the potential to transform neuro-oncology. By influencing glioma cell proliferation and apoptosis, microgravity provides a unique perspective on developing new therapeutic strategies. While replicating authentic space conditions on Earth remains challenging, simulated microgravity studies have revealed crucial molecular mechanisms that could be therapeutically targeted. Future research should prioritize a deeper understanding of these mechanisms and their subsequent translation into clinical applications. Continued exploration of microgravity holds immense promise for enhancing treatment efficacy and improving outcomes for patients with HGGs.

Availability of Data and Materials

Not applicable.

Author Contributions

Conceptualization, RC and GS; methodology, GS, RC, GF and SM; software, GS and MN; validation, GEU, RM, GS and DGI; formal analysis, RC and GS; investigation, RC and SM; resources, RC; data curation, GS, RC, SM, MN and GS; writing—original draft preparation, GS and RC; writing—review and editing, GS, RC, GF and GEU; visualization, GS, DGI, GFN and GEU; supervision, GFN, GEU, RM and DGI; project administration, GS, RC and GEU. All authors were involved in the drafting and critical revision of the manuscript. All authors have read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

Not applicable.

Acknowledgment

Not applicable.

Funding

This research received no external funding.

Conflict of Interest

The authors declare no conflict of interest.

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