How do race and sex, independently and in tandem, contribute to the genetic risk of glioblastoma

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Abstract:

Glioblastoma is the most common primary brain cancer, of which around 15,000 people are diagnosed annually, with a very narrow survival rate of 6.9%. The various factors that contribute to glioblastoma have been slowly but steadily unveiled; we're aware of environmental factors that potentially affect pathways leading to glioblastoma. More and more research looks at the effect of sex or race on glioblastoma, but not both. There is a clear gap in knowledge about the pathways altered/caused by sex and race that lead to glioblastoma, as well as the genetic solutions. This review paper will cover the genetic causes of glioblastoma and their pathway for women of color, as well as the solutions present both surgically and therapeutically.

Introduction:

Glioblastoma (GBM) is the most common primary brain cancer, of which around 15,000 people are diagnosed annually, and has a very narrow survival rate of 6.9%. GBM starts as the growth of cells in either the spinal cord or the brain. The location can further specify the subtype it belongs to and display accelerated growth into healthy tissue. GBM is commonly located in the supratentorial region of the brain (frontal, temporal, parietal, and occipital lobes) and is rarely located in the cerebellum [36]. GBM forms from healthy cells called astrocytes, which serve to support nerve cells. Most cases (>90%) are primary GBM that develop without clinical evidence of a less malignant precursor lesion or de novo. [12] The unexpected switch from support to harm is what makes GBM so deadly; its unexpected new role leaves nerve cells supportless and at risk. The various factors that lead to GBM have been slowly but steadily unveiled; we're aware of environmental factors potentially affecting pathways leading to GBMs. Common symptoms of GBM can include headaches, nausea, difficulty speaking, altered senses, and seizures (Mayo Clinic).

Unfortunately, Survival from GBM is poor; only a few patients survive 2.5 years, and less than 5% of patients survive 5 years following diagnosis [36]. However, as noted in many cancers, there is a clear sex bias. A review of data that sex hormones have and can impact cancers outside of the reproductive system has gone underway with the linkage between sex hormones and GBM and even leading to different trends in the epidemiological pathway to GBM[6, 41] Race also has a profound role in cancer, with non-Hispanic whites having higher incidence and lower survival rates for GBM compared with individuals of other racial or ethnic groups [28] These trends have not gone unnoticed with more research exploring the specific genetic pathways each variable influences. Research investigating sex and race effects on genetics does exist and attempts to bridge a division of knowledge; however, much of this research focuses on the role sex and race play in survival [7]. More and more research looks at the effect

of sex or race on GBM individually, but in combination. There is a clear gap in knowledge about how these variables give rise to or contribute to the risk of GBM. Thus, the present review will explore the intersectional effect of race and sex on the genetics of GBM.

Methods

The database PubMed was searched using the terms “Glioblastoma” or “sex” and “race” or “ethnicity”. In this Review, we included studies that were available in English and that were relatively recent (2010-2025). The studies covered in our review included patients with GBM, as well as a few control groups of healthy older adults. Studies that were excluded from this review consisted of studies relating solely to GBM treatment, rather than the genetic pathway, sex, and/or race.

Results

Background of Glioblastoma

What is glioblastoma?

Glioblastoma is the most common and aggressive form of glial tumor and makes up almost 50% of primary malignant central nervous system tumors. Classified as a grade 4 tumor in the World Health Organization, it belongs to a variety of classes of tumors called the adult-type diffuse glioma. Sadly, the diagnosis typically has a median survival rate of 8 months and an overall 5-year relative survival of 5.5%. [2,27] “By definition, GB, IDHwt lacks mutations in IDH1 codon 132 and IDH2 codon 172. Molecularly, demonstration of TERT promoter mutations, EGFR gene amplification, and/or a gain of chromosome 7/ loss of chromosome 10 genotype is sufficient for the diagnosis of GB.”

History of glioblastoma:

The history of glioblastoma is complex. As with many cancers, it wasn’t discovered until much later, nor was - or is it- understood. The complexity of GBMhas baffled scientists and doctors for decades. Originally, GBM weren’t even classified as astrocytic tumors by the World Health Organization but rather as differentiated embryonal tumors. Advancements in science, including immunohistochemistry, later confirmed the classification, and it was reclassified as an astrocytic neoplasm. Still, the divisions between types of GBM weren’t fleshed out; the separation of primary and secondary had remained conceptual up until the past decade. Evidence has recently accumulated that patients of different ages have developed through different genetic pathways due to histopathologically indistinguishable conditions. In 1940, Hans-Joachim Scherer made early observations distinguishing between primary and secondary GBM. [12]

Hospital protocol/ how to catch it early on:

Identifying glioblastoma is tricky due to the variety of symptoms that can show up in a patient. However, developments have been made to catch the cancer earlier, including the development of liquid biopsy, detection of serum biomarkers, and more. Diagnosis of GBM is made through an analysis of its many symptoms, such as headaches, seizures, memory problems, personality changes, vision problems, language difficulty, weakness, and paralysis. Nausea, sensory losses, and more general symptoms are associated with GBM, which makes it hard to diagnose.

To narrow the search down, GBM is also diagnosed by Computed tomography (CT) or Magnetic Resonance Imaging (MRI) scans, a biopsy, and consultations with specialists to confirm the prognosis. Many healthcare professionals understand the aggressive nature of GBM and face it with a personalized approach. Developing treatment plans with alterations to the patient's circumstances is key to the prevention and mitigation of GBMs, including "factors such as tumor location, extent of resection, molecular characteristics, patient preferences, and comorbidities."Current treatment strategies for GBM typically involve a multimodal approach including surgical resection, radiation therapy, and chemotherapy. [20]
The standard care regimen, known as the Stupp protocol, involves maximal surgical resection followed by concomitant, meaning together with, temozolomide and adjuvant Temozolomide. [35] When used with radiotherapy, it means that the drug is given at the same time as the radiation therapy. Temozolomide helps to enhance the effectiveness of radiation therapy by making cancer cells more sensitive to the radiation, increasing the effectiveness of radiation. However, it's not enough that the cancer is sensitive to radiation. It must also not recur. This is where adjuvant is necessary in the treatment plan. "Adjuvant" refers to additional treatment given after the primary treatment (in this case, after the initial phase of radiotherapy and concomitant temozolomide). Adjuvant temozolomide is administered to further reduce the risk of cancer recurrence. It is typically given as a series of cycles following the completion of radiotherapy and the initial course of temozolomide. Despite these approaches, the prognosis remains poor, highlighting the need for more effective therapeutic options.

Various types and different pathways leading to it:
As mentioned earlier, the complexity of GBM stems from its complex roots. The pathways leading to GBM are not homogenous and not always understood. As expected, many genes involved in GBM relate to the cell cycle, including TP53, COL3A1, and RAP1GDS1. TP53 is overexpressed in GBM, central to oncogenesis, connected with TGIF2 and EIF4A1I; COL3A1 is also overexpressed, involved in the extracellular matrix, and affects apoptosis and drug resistance; and RAP1GDS1, which is underexpressed, is associated with T-cell acute lymphocytic leukemia. [37] Something else doctors can look to genetically for GBM is the IDH (isocitrate dehydrogenase) gene, which is a marker that can predict a glioma's behavior. If they have mutations, they are IDH-mutate, and if not, they are classified as IDH-wildtype. This leads cleanly to the main types of GBM: primary and secondary. As mentioned earlier, Histologically, primary and secondary GBM are largely indistinguishable, but they differ in their genetic profiles. For example, secondary GBM progress from low-grade diffuse astrocytoma or anaplastic astrocytoma. They are found in younger patients, have a lesser degree of necrosis, are mostly located in the frontal lobe, and carry a significantly better prognosis than primary GBM. Secondary GBM have IDH1 mutations, which primary GBM lack. Primary GBMs typically exhibit EGFR overexpression, PTEN mutations, and whole chromosome 10 loss, while secondary GBMs are characterized by TP53 mutations and 19q loss. EGFR overexpression is rare in secondary GBMs, and TP53 mutations are uncommon in primary GBMs. These findings

suggest that primary and secondary GBMs develop through distinct genetic pathways. [12] The terms “primary GBM” and “secondary GBM” were first used by the German neuropathologist Hans Joachim Sherer in Antwerp in 1940 [23]

Who does it affect?

Glioblastoma affects individuals across a broad range of demographics. Most notably, GBM affect the older population. They are not commonly seen in children or adolescents. With a higher incidence observed in older adults and a slight male predominance, GBM are around 1.6 times more prevalent in males than females [29, 36]. Furthermore, GBM has an unequal effect on ethnicities. As previously mentioned, non-Hispanic whites have a higher incidence and lower survival rates for GBM compared with individuals of other racial or ethnic groups [28]. The rate of incidence is 2.0 times higher in Caucasians compared to Africans and Afro-Americans, with a lower incidence in Asians and American Indians [36]

Sex-linked Differences in GBM Pathways

(We understand that gender is much more fluid than chromosomes may imply. For this review paper, female refers to genetically female individuals, and male refers to genetically male individuals. .)

With the versatility of formation for cancer tumors, it comes as no surprise that there is a variation in the incidence of these tumors. Many cancers have already been found to differ in rates of incidence based on sex. For example, males are more likely to develop esophageal cancer, particularly esophageal adenocarcinoma, which has become more common in Western countries. The male-to-female ratio is around 3-1 for esophageal cancer.

We observe this phenomenon in GBM as well. Most notably, the incidence of gliomas is much higher in males than in females [28]. While males tend to have a higher incidence of GBM, females often exhibit a better prognosis [15]. However, the mechanisms behind these sex differences are not fully understood. Some potential hypotheses have been that hormones, specifically steroid hormones, are the root cause of this difference.

Steroid Hormones:

Before diving deep into hormones, it is necessary to have a solid understanding of the classification of hormones. Hormones are signalers in our bodies that outlast other communicators ([5]). From the fight-or-flight response to the feeling of hunger, hormones regulate many aspects of our body and often go unappreciated. Knowing that cancer can thrive in environments where miscommunication happens, many scientists look to communication signalers as a potential cause. Considering that hormones play a huge role in the differentiation of sex, scientists look to them as a potential pathway that may cause a greater likelihood of gliomas. It’s for this reason that many scientists have looked at specific sex-based hormones, steroid hormones. Steroid hormones are secreted by the gonads, which cross the blood-brain barrier and directly affect the tissues within [21]. The synthesis of gonadal steroid hormones is known as neurosteroids. [3] According to the data, GBM are more frequent in men than in

women in a 1.6/1 proportion both in children and adults. Furthermore, several studies indicate that pregnancy, a physiological state with the highest progesterone and estradiol levels, accelerates the progression of low-grade astrocytomas to GBM and increases the symptoms associated with these tumors. In vitro studies have demonstrated that progesterone has a dual role in GBM cells: physiological concentrations promote cell proliferation, migration, and invasion, while very high doses (out of physiological range) reduce cell proliferation and increase cell death. [3] Hanada and colleagues (2016) reported the fastest progression of diffuse astrocytoma during pregnancy, transitioning to GBM in a young woman. [11] Peeters and colleagues (2018) also found that pregnancy worsens glioma progression, with 87% of cases showing increased tumor growth during pregnancy and 38% experiencing clinical deterioration (e.g., seizures). [31] However, these clinical deteriorations are resolved after delivery, effectively tying pregnancy and worsening of symptoms together. [1, 14]

Furthermore, the MAPK (Mitogen-Activated Protein Kinase) pathway is commonly dysregulated in cancers like astrocytomas, driving excessive cell proliferation. In male mice studies, activation of the MAPK pathway is increased in certain brain regions, independent of gonadal steroid hormone status. In vitro studies of female astrocytes reveal heightened MAPK activation, with estradiol (E2) treatment inhibiting MAPK signaling more potently in females and triggering increased apoptosis [3]. These findings suggest that sex differences in MAPK signaling may contribute to divergent tumor behaviors between males and females. Diving deeper into how each hormone affects gliomas, estrogen (E2) has been identified as a potential protective factor against GBM in females and is thought to contribute to the male-to-female GBM incidence ratio of 1.6:1. E2-induced epithelial-mesenchymal transition (EMT) is a process that plays a key role in cancer progression, including GBM. However, this effect is less pronounced in secondary GBM, which are more common in females [3]. E2 acts through estrogen receptors (ER), particularly ERα and ERβ. ERα is linked to GBM progression, while ERβ is associated with tumor suppression, with reduced ERβ expression correlating with higher malignancy and worse survival outcomes. ERα activation increased cell migration and expression of EMT markers like vimentin and N-cadherin, but effects were blocked by ERα antagonist MPP, while ERβ agonist DPN had no impact.

Progesterone (P4) exerts a concentration-dependent effect on GBM progression. Low P4 levels promote GBM proliferation and migration. High P4 concentrations induce cell death processes, induce antiproliferative effects, decrease cell viability, and increase the cytotoxicity of temozolomide by promoting cell senescence, reducing glycolytic metabolism, and inhibiting the PI3K/Akt/mTOR signaling pathway. In in vivo models, P4 increased tumor size and infiltration in GBM-implanted rats, with these effects being blocked by progesterone receptor (PR) antagonists like RU486 or PR-targeting antisense oligonucleotides. Additionally, P4 stimulated the migration and invasion of GBMcells in U251 and U87 cell lines, which was also inhibited by PR blockers, suggesting PR signaling is crucial in these processes. P4 further promoted cofilin dephosphorylation, a key event in actin cytoskeleton remodeling, facilitating cell movement. On the molecular level, P4 enhanced the expression of EGFR and cyclin D1 in GBM cells through

PR and the SRC-1 coactivator. Moreover, P4 induced the expression of PIBF, a protein associated with immune suppression and tumor proliferation, leading to JAK1/STAT6 phosphorylation and further promoting GBM cell proliferation, potentially aiding in immune evasion. These findings highlight the complex, concentration-dependent roles of P4 in GBM progression. P4 signals through progesterone receptors (PR) or membrane-bound PRs (mPRs). In vivo studies show that P4 increases GBM tumor area and infiltration, promoting migration and invasion through PR signaling. P4 (10 nM) increased GBM cell proliferation, blocked by RU486 (PR antagonist), indicating P4 promotes GBM progression via PR.

Moreover, P4 induces the expression of genes like EGFR and cyclin D1, both associated with tumor growth [1.0]. Furthermore, progesterone receptors were found in 100% of GBM biopsies; the PR-B isoform was predominantly expressed over PR-A. Another interesting thing to note is that progesterone is found in different concentrations in different tumor types. Its expression was higher in GBM (grade IV) than in lower-grade astrocytomas (grades I and II) [22]. Testosterone (T) and its metabolites also contribute to GBM progression, similar to P4, by promoting tumor growth ([3])Studies have focused on the androgen receptor (AR) in GBM due to the location of the AR gene on chromosome X, often reported with shorter survival and higher prevalence of GBM among males they found that alterations of AR were more common in females. It also correlated with a difference in methylation levels for different CpG sites in males and females, but found no difference in expression. However, a survival analysis does show that AR overexpression correlated with a decrease in overall survival for females and a longer survival for males. For males, high AR is linked to DNA repair responses. [25] Once the role of gonadal steroid hormones and their receptors in GBM progression and prevalence have been completely demonstrated, new options for GBM therapy could be incorporated, for example, agonists or antagonists of gonadal steroid hormones receptors, enzyme inhibitors, the gonadal steroid hormones themselves in concentrations effective to suppress tumor growth, and their genes and protein targets.

Potential areas to consider as Therapies:

One potential target may be the androgen receptor as a therapeutic target. However, the strategies would need to be sex-specific, as for males, AR antagonists might inhibit DNA repair mechanisms, potentially making the tumor more susceptible to treatments. For females, AR modulation might need to be approached differently, as overexpression correlates with shorter survival, and therapeutic strategies might need to focus on reducing AR activity. [25]

Chromosomal:

Another area of concern for scientists is the chromosome. Many genetic links in the X chromosome cause diseases. For example, dyskeratosis congenita has been linked to the X chromosome. However, there is a difference in the effect of X chromosomal diseases between those with one X chromosome and those with two. Those with two X chromosomes undergo a process called X inactivation. In half the cells in the embryo, one of the pairs of X chromosomes is suppressed. This causes a wide variety of potential symptoms and effects of chromosomal diseases. However, those with one X chromosome do not have this saturation of symptoms.

Sex chromosomes, particularly the X and Y chromosomes, contribute significantly to the sex-specific genetic architecture of diseases, including brain tumors. The differential dosage of X-linked genes plays a critical role in various conditions, such as dyskeratosis congenita and severe combined immunodeficiency. These variations in X-linked gene expression have implications for disease susceptibility, with distinct mechanisms at play between males and females due to their differing sex chromosome compositions.

One key concept in this context is the EXITS theory, which focuses on genes on the X chromosome that escape X-inactivation. Normally, X-inactivation ensures that only one of the X chromosomes in females is fully active, but some tumor suppressor genes (TSGs) escape this process and remain active in both copies, referred to as EXITS genes. This biallelic expression of EXITS genes may provide a protective effect in females against certain cancers, as they benefit from the tumor-suppressing functions of both X chromosomes. In contrast, males, who only have one X chromosome, lack this protection, contributing to a male predominance in cancer susceptibility. In GBM, genes such as KDM6A, KDM5C, DDX3X, and ATRX exhibit biallelic expression in females, with higher gene expression in women compared to men, further suggesting significant sex-based genetic differences in tumor development.

The role of EXITS genes in GBM is particularly notable. Histone demethylases, such as KDM6A/B, play a crucial role in the maintenance of GBM stem cells (GSCs), which are key to the persistence of the tumor. Additionally, male and female astrocytes in GBM exhibit distinct patterns of tumor suppressor inactivation. Male astrocytes, particularly those from mesenchymal GBM, show greater inactivation of the RB tumor suppressor gene compared to female astrocytes. In contrast, female astrocytes tend to activate p16 and p21, cyclin-dependent kinase inhibitors, more robustly in response to serum deprivation or treatment with the chemotherapy drug etoposide. These differences in RB regulation and the activation of p16 and p21 may help explain the higher prevalence of GBM in males, further highlighting the complex role of sex chromosomes and associated genetic mechanisms in the disease's sex-specific architecture.

The tumor microenvironment significantly affects GBM progression and response to treatment, with notable differences between sexes. Males and females may exhibit distinct immune responses and cellular interactions within the tumor microenvironment, influencing disease outcomes. This understanding underscores the importance of considering sex differences when developing therapeutic approaches. [13, 17]

Potential Treatments for Sex-linked Differences:

Sex-specific differences extend to the effectiveness of treatments such as immunotherapy. Studies suggest that female patients may experience different levels of therapeutic response compared to male patients, affecting overall survival rates. This highlights the necessity of integrating sex-specific considerations into clinical decision-making for GBM management. [24]

Recognizing the impact of sex on GBM pathways is crucial for advancing research and clinical practices. Tailoring treatments to account for sex differences could potentially lead to improved outcomes and a more effective management strategy for patients diagnosed with GBM. Such personalized approaches are essential for addressing the unique challenges posed by this

aggressive brain tumor [34, 17]. However, in all of this analysis, there are still questions as to why sex differences in GBM rates occur. This is a rich area for research as it could lead to more personalized medication and more saved lives. Despite the low likelihood of one having GBM, the impacts of it are devastating and life-threatening. More research must be done to help as many as possible.

Race

Another area where cancer rates can differ is ethnic background or race. For example, celiac disease is common among the ethnic group of Punjab. As other diseases have noted high rates of incidence in certain groups, cancer does as well. Ethnicity plays a vital role in delineating different genetic pathways in malignant gliomas. Variations in genetic expression and the prevalence of certain mutations can lead to distinct tumor characteristics and prognoses based on ethnicity. These differences highlight the importance of considering genetic diversity in GBM research and treatment efforts. [4]

Research has indicated that race influences survival rates in GBM patients, particularly those with a Karnofsky Performance Status (KPS) of 80 or above. Additionally, a correlation between race and specific genetic markers involved in retinoic acid metabolism suggests that these pathways may play a role in survival outcomes. This connection emphasizes the potential for targeted therapies that account for these genetic factors [39]

European:

Before diving into more prevalent ethnicities, we start with European descendants or white populations first for a couple of key reasons. Most notably, we start with this section as the data and studies available on this population far outweigh other ethnicities by a significant amount. This is because many studies have found that those of European descent have the highest incidence and poorest survival rates. The average Annual Age-Adjusted Incidence Rate (4.71 per 100,000) for GBM is the and the 5-year relative survival rate (4.8%) is the lowest of all racial groups. Even after receiving chemoradiation, non-Hispanic whites have the lowest 1-year and 5-year relative survival rates, and in patients undergoing surgery and chemoradiation, all racial or ethnic groups had significantly better survival than non-Hispanic whites. Although there may be a bias towards scientists focusing on white populations when it comes to GBM, there is an undeniable, large, and unfortunate impact on this population.

Table 1: Description of Genetic Pathways for Glioblastoma.

Gene/Pathway	Function	If Impaired	Also Associated With
TP53	Tumor suppressor regulating cell cycle, apoptosis, and DNA repair.	Uncontrolled cell proliferation, apoptosis resistance, and cancer.	

Glioblastoma, breast cancer, Li-Fraumeni syndrome.
COL3A1
Encodes type III collagen, vital for connective tissue integrity.
Vascular Ehlers-Danlos syndrome (fragile blood vessels and organs).
Aneurysms, spontaneous arterial ruptures.
RAP1GDS1
Involved in small GTPase signaling, regulating cell adhesion and proliferation.
Abnormal cell migration and tumor metastasis.
Cancer progression, immune signaling.
Isocitrate Dehydrogenase (IDH1/IDH2)
Catalyzes isocitrate to α-ketoglutarate in the TCA cycle; crucial for metabolism.
Produces oncometabolite 2-hydroxyglutarate, promoting tumorigenesis.
Gliomas, acute myeloid leukemia.
Mitogen-Activated Protein Kinase (MAPK)
Regulates cell growth, proliferation, differentiation, and survival.
Disrupted signaling causes cancers and inflammatory diseases.
Melanoma, colorectal cancer.
PI3K/Akt/mTOR Pathway
Controls cell growth, proliferation, and survival.
Dysregulation leads to cancer and metabolic disorders.
Breast, prostate, and glioblastoma cancers.
Cyclin D1
Regulates cell cycle transition from G1 to S phase.
Overexpression causes unchecked cell division.
Breast cancer, mantle cell lymphoma.
EGFR
Epidermal growth factor receptors regulate cell proliferation and survival.
Overactivation leads to tumorigenesis.
Glioblastoma, non-small cell lung cancer.
U251
Human glioblastoma cell line used in research.

Model for glioblastoma studies.
U87
Human glioblastoma cell line used in research.

Model for glioblastoma studies.
RU486

Progesterone receptor antagonist is used in cancer and reproductive research.
It may affect hormone-sensitive tumors.
Endometrial and breast cancer studies.
PR-B Isoform
Progesterone receptors are involved in transcriptional regulation.
Dysregulation is linked to hormone-driven cancers.
Breast and uterine cancers.
Androgen Receptor Gene
Encodes receptors for testosterone and dihydrotestosterone; regulates gene expression.
Mutations lead to resistance to androgen-deprivation therapies.
Prostate cancer.
Tumor Suppressor Genes
Suppress abnormal cell growth.
Loss-of-function mutations lead to cancer.
TP53, BRCA1/2, RB1.
KDM6A
Histone demethylase regulates gene expression.
Loss leads to chromatin remodeling defects and cancer.
Bladder cancer, glioblastoma.
KDM5C
Histone demethylase is important for transcription regulation.
Impairment associated with intellectual disabilities and cancer.
X-linked mental retardation, renal cancer.
DDX3X
RNA helicase is involved in translation and RNA metabolism.
Mutations linked to cancer progression.
Medulloblastoma, breast cancer.
ATRX
Chromatin remodeler is involved in telomere maintenance.
Mutations cause chromosomal instability.
Glioblastoma, alpha-thalassemia.
rs6010620
Genetic variant linked to glioblastoma risk.
Increases susceptibility to brain tumors.
Glioblastoma.
rs1412829
A genetic variant associated with glioma.
May increase glioma risk.
Glioma.
rs78378222

TP53 polymorphism linked to cancer susceptibility.
Alters TP53 function, increasing tumor risk.
Brain tumors, colorectal cancer.
rs55705857
Variant associated with glioma susceptibility.
Strongly linked to low-grade glioma risk.
Gliomas.
STK38L
Serine/threonine kinase is involved in signaling pathways.
Implicated in tumor progression.
Cancer biology.
RAB27A
Regulates vesicle trafficking and secretion.
Dysregulation is associated with tumor metastasis.
Melanoma, breast cancer.
CYP4F12
Cytochrome P450 enzyme is involved in lipid metabolism.
Altered expression linked to metabolic disorders and cancer.
Cancer metabolism.
PDGFR
Platelet-derived growth factor receptor, critical for cell proliferation and development.
Overactivation is linked to glioblastoma and other cancers.
Glioblastoma, leukemia.
MGMT Methylation
Epigenetic silencing of the MGMT gene.
Increases susceptibility to alkylating agents in cancer therapy.
Glioblastoma treatment response.
Loci 12p11.23, 15q15-21.1, 19p13.12
Genomic regions associated with glioblastoma risk.
Increased susceptibility to brain tumors.
Glioblastoma.
8q24.21, 1p31.3, 1q32.1
Genetic loci linked to glioblastoma risk.
Higher predisposition to glioblastoma.
Glioblastoma.
1p19q-IDH-TERT
Common co-deletions/mutations in gliomas.
Associated with a better prognosis in glioma patients.
Gliomas.
5p15.33, 7p11.2, 8q24.21

Loci linked to glioblastoma susceptibility.
Higher risk of glioblastoma.
Glioblastoma.

However, this impact has raised the question as to whether specific genetic markers have caused this higher incidence. A study by Jacobs 2012 found that rs6010620 and rs1412829 are associated with white populations, possibly indicating these SNPs (single-nucleotide polymorphisms) as a cause for the higher incidence rate. (see Table 1 for more information). Research further indicates that specific mutations, particularly in genes like TP53 and IDH1, contribute to the progression of GBM in European populations [12,16]. Some studies further find that white populations had a higher occurrence of PTEN alterations (48.67%, P = 0.045) [18]

Eckel-Passow et al.75 have also performed a large-scale glioma GWAS stratified by molecular subtypes defined by combinations of IDH mutation, 1p/19q co-deletion, and promoter mutation in TERT among White populations. Notably, they have identified 2 novel genetic loci and a GWAS-reported region associated with the risk of specific glioma molecular subtypes: rs5839764 (2q37.3; D2HGDH) for IDH mutation; rs1106639 (2q37.3; D2HGDH) for IDH mutation and 1p/19q non-codeletion; rs111976262 (7p22.3; FAM20C) for triple-positive (IDH mutation, TERT mutation and 1p19q co-deletion); and rs4809313 (20q13.33; GMEB2) for IDH wild-type. [8]

However, beyond genetic factors, environmental aspects also modulate GBM risk. Studies have suggested that exposure to certain chemicals or various lifestyle factors unique to European regions might play a role in GBM incidence [38]

Still, more research is needed to fully understand what causes European or non-Hispanic whites to experience worse prognosis and higher prevalence of GBM. Unfortunately for research, every individual has a unique genome and an even more unique environment. The interaction between the two results in a different impact on each patient and their genetic pathway to GBM. However, this does highlight the necessity of personalized medication. While many studies are available for the white populous, a white patient's genetic pathway is probably unique from the genetic pathways mentioned. Personalized medication can serve as a potential aid to the patient and help them combat this devastating cancer.

African:

The second group impacted by GBM that we will discuss is African descendants. This ethnicity faces a significant lack of data concerning the rates, treatment, and basic statistics concerning GBM. However, it has been noted that black females have a lower incidence. They also find that black non-Hispanic patients exhibit the highest rates of unplanned readmission within 30 days, adding complexity to their treatment and management scenarios. [18] The black population in the United States currently experiences lower incidence but higher survival rates when compared to other races. [9]

Studies have shown that certain genetic variants may confer increased susceptibility to glioma, with specific single-nucleotide polymorphisms (SNPs) identified that have varying prevalence across African ethnic groups [16]. However, the findings didn't find these prevalences statistically significant enough to report. It didn't fit frequency rates, though this may be due to the lack of African participants in the study.

They did find, though, that certain types of brain cancers were more prevalent in African populations in the United States. Lymphoma was the most common primary tumor subtype for black individuals ages 20-34, and GBM was identified as the most common tumor subtype for black individuals in the age group of 35-49. GBM was identified as the most common tumor subtype for black individuals in the age groups of 35–49, 50–64, 65–79, and 80+. [9]

In addition to genetic predispositions, environmental factors unique to African settings may further influence GBM risk. Factors such as exposure to toxins, socioeconomic conditions, and lifestyle choices could interact with genetic susceptibility, ultimately shaping the incidence and outcomes of GBM in specific populations. [32] Furthermore, many studies expose the large disadvantage black patients are in terms of access to care, which has been identified as strong evidence of the higher incidence and poorer prognosis in this population for almost all other types of cancer

These environmental factors may even contribute to the lack of attention on African populations. Although access to care is certainly a problem that warrants great resources and attention, the reversed disparity profile for brain cancer may suggest that the mechanisms behind the different primary brain tumors depend more strongly on other factors. Alternatively, the reversal of the typical disparity profile may reflect a negative, unintended consequence of the overuse of imaging by those with high access to healthcare, which increases the only well-known risk factor for brain cancer – ionizing radiation.

Conducting sub-analyses and molecular-level comparisons between populations with lower brain cancer incidence and higher survival (e.g., Black patients) and those with higher incidence and lower survival (e.g., White patients) could accelerate the identification of key etiological factors. For example, a recent study observed a 42% reduced risk of glioma in patients with a history of diabetes. Not only do Black patients experience lower incidence and better survival rates for brain cancer, but they also have a higher prevalence of diabetes in the U.S., a trend that has been well-documented. Therefore, it would be valuable to investigate and compare genetic polymorphisms between Black and White populations, aiming to uncover potential genetic differences and variations in signaling pathways that could inform future research and therapeutic strategies. Furthermore, if there is a genetic predisposition that causes this group to face a higher survival rate, it is worth exploring to help ethnicities who do not face those favorable odds. We must advocate for more research discussing the genetic pathways or causes of brain tumors in African populations. The bias within the scientific field has been present in an overproduction of research for white populations, but not for African populations. This leaves a population without much research that could potentially help lower their rates and

prevent remission, which has been noted in this population. It is imperative to open this research avenue up more to help those diagnosed with brain tumors.

There are many available methods to achieve this. Many research papers point out potential research methods that could provide an alternative to admixture mapping Figure 2). The candidate SNP approach used in Jacobs [33]. In the context of glioma research, the admixture method would ideally be applied to a set of African-American cases and controls, where excess European ethnicity shared among African-American cases would be suggestive of genetic regions that may play a role in glioma risk. [16]

Asian:

The next section to discuss is that of Asian descendants. Studies have correlated Asians with various genetic pathways, certainly more than Africans, but still less than whites.

East Asians do have a lower incidence of glioma than Whites, yet they tend to experience a younger age of onset and longer survival. Like Europeans, East Asians also exhibit specific SNPs associated with glioma risk. Xu et all 2012 find that the EGFR +61 G/A polymorphism may contribute to the susceptibility of glioma. However, some SNPs are shared. For example, only three risk loci—5p15.33, 11q23.3, and 20q13.33—are shared between East Asians and Whites, while others are population-specific. Loci 12p11.23, 15q15-21.1, and 19p13.12 are linked to East Asians, while 8q24.21, 1p31.3, and 1q32.1 are more prominent in Whites. Although the somatic mutational profiles of gliomas are largely similar between the two groups, East Asians show a lower incidence of EGFR amplification in GBM and a higher frequency of 1p19q-IDH-TERT triple-negative low-grade gliomas. Furthermore, East Asians have a lower standardized incidence rate of diffuse glioma across all major subtypes compared to Whites. Genome-wide association studies (GWAS) in East Asian populations have identified 12 SNPs in 10 loci associated with glioma risk, with odds ratios ranging from 1.18 to 3.55. Nine of these SNPs, including loci such as 5p15.33, 7p11.2, and 8q24.21, have also been identified in White populations, but significant racial differences in effect allele frequency (EAF) exist, with some SNPs, such as rs78378222 and rs55705857, being White-specific. These findings highlight genuine racial differences in glioma risk between East Asians and Whites, even within the same geographic regions. [26,40]

For the 3 East Asian GWAS-identified risk loci (i.e., 12p11.23, 15q15-21.1, and 19p13.12), the risk SNP (i.e., rs10842893) located on 12p11.23 was in the intronic region of the gene STK38L, and the expression of STK38L was higher in the glioma samples than the normal samples in the TCGA database. The rs4774756 SNP at 15q15-21.1 is located within the intronic region of RAB27A, a gene encoding a member of the Rab small GTPase family. Several studies have shown that Rab27a promotes proliferation and invasion, and represses apoptosis, based on functional assays in glioma cell lines 67,68. Another risk SNP (i.e., rs688755) located on 19p13.12 is near the genes CYP4F12, encoding a protein that oxidizes arachidonic acid; PGE2, encoding the omega-side chain of prostaglandin E2; and PGH2, encoding prostaglandin H269. Several studies have shown that PGE2 increases the survival, migration, and proliferation of glioma cells, thus indicating the critical role of CYP4F12 and PGE2 in the development of glioma

70. Nevertheless, further functional evaluations are needed to elucidate the roles of these SNPs and nearby genes to understand the development of glioma.

Moreover, a large study of 3,303 GBM patients, initially recruited for EGFR amplification screening in an EGFR antibody trial, found that EGFR amplification was more common in the overall population (about 56%) but less frequent in East Asians (around 35%). The classic glioma subtype in Chinese populations also showed weak EGFR expression. In a study of 90 Korean patients, whole-exome sequencing revealed a stronger enrichment of the p53 pathway compared to the TCGA cohort (n=250), though EGFR amplification was not reported. These findings suggest that EGFR-associated features may be less pronounced in East Asians. Additionally, a study of 188 patients with secondary GBM showed higher mutation rates in the White group.

A study by Das et all 2002 finds that GBM in Asian patients do not conform to currently accepted models of glioblastoma development and that clinically defined GBM in these patients show genetic changes consistent with both ‘primary’ and ‘secondary’ GBM. They found 3 mutations previously undocumented in GBM. Further, they expressed an unusual pathway. As discussed earlier, primary tumors have a high level of EGFR and mdm2, which was noted in these GBM. However, the levels of p35 and PDGFR-a were consistent with levels for secondary GBM. This is starkly different, as p53 mutations are less common in primary GBM, occurring in about 10% of cases, whereas secondary GBM have a high incidence of p53 mutations of greater than 65%, of which >90% are present in the first biopsy in the study. Further, 96% of samples overexpressed p35 with a monoclonal antibody pAb 240, which is usually seen in secondary brain tumors. Yet, there is still room to grow. Research on South Asians and Western Asians is severely lacking, with little to no primary sources discussing genetic pathways or rates noted in these groups.

Latino:

Finally, we take a look at the rates of glioblastomas in those of Latino or Hispanic descent. Latino patients have been noted to have a lower glioma incidence. We note that this group is arguably one of the more diverse ethnicities noted. Yet, data existing on this group often doesn’t explore the various ethnicities within the broad term Latino.. One study explored the broad term, Latino, breaking it up by countries or regions. Glioma incidence and outcomes differ in association with the geographic origins of Hispanic communities, with counties of predominantly Mexican/Central American origin at significantly reduced risk and those of Caribbean origin at comparatively greater risk. (Walsh et all 2022)

A study by Shabikhkani et all 2017 and colleagues examined the survival outcomes of Latino patients with GBM compared to non-Latino whites using a large database. The findings revealed that Latino patients, in general, had better survival rates at both 1 and 5 years after diagnosis. Specifically, South and Central Americans showed significantly better survival than non-Latino whites, while Mexican patients had higher 5-year survival rates, though no difference was seen at 1 year. While Latino patients were diagnosed at a younger age, age did not fully explain the survival difference. The study also found that factors like the extent of tumor removal and

radiotherapy did not account for the survival differences. Additionally, the researchers explored the genetic features of the tumors, such as MGMT methylation and IDH-1 mutations, to better understand the reasons behind these outcomes, but the results suggested that genetic factors alone did not explain the survival advantage. Ppatel et all 2019 review again, more research is needed for this ethnicity. [30] A common thread throughout all ethnicities is the undeniable need for more research exploring the genetic pathways of GBM and the possible differences between pathways between ethnicities.

The intersection between Race and Sex

Finally, we can explore the interaction between race and sex in tandem that affects genetic pathways in GBM. While data is, again, severely lacking in this department, some studies do account for this.

Unsurprisingly, black men in the United States continue to follow the same trend noted with men with a higher incidence of brain cancer, yet they didn't follow this pattern for malignant meningioma. Black women had a noted increase in the incidence of malignant meningioma. [9] Another study performed a comparison of the gender distribution of East Asians compared with Whites for each subtype. Beyond the divergence in incidence, the GBM onset age also varies by race. The incidence is significantly ($P < 0.005$) higher (1.59-fold) in males than in females in the USA among NHW16. Further studies in White populations also support a male preponderance,19,32,35–37,45. In the Korean population, the IRRs (male-female ratio) were 1.31, 1.32, 1.27, 1.3618,31,41,46. Four studies based on Chinese have reported IRRs of 1.57, 1.69, 1.43, and 1.34. [26]

Unfortunately, these handful of studies are all that exist on the intersectionality of race and sex on GBM. We must pour more research into this with the noted increase of diseases tied to cancers in certain races and sexes. Furthermore, the research can be utilized as personalized treatment. To overcome the stagnation in GBM survival, personalized treatment approaches, including standard molecular profiling and sex-specific regimens, are crucial. Studies highlighting sex-dependent molecular vulnerabilities and resistances provide valuable insights into tailoring treatments for male and female patients. By targeting these unique oncogenic drivers, therapies could become more effective at attacking GBM tumors on a cellular level, offering the potential for improved patient outcomes. For example, female patients have shown better 1-year overall survival with immunotherapy, suggesting these treatments may be more effective for them, while males may need customized immunotherapies to enhance their immune response. As molecular technologies evolve and our understanding of GBM deepens, it is essential to rethink the "standard of care" and embrace personalized therapies that address the tumor's heterogeneity, ultimately improving survival and quality of life for patients. (Jonovaich et all 2024)

Discussion/Conclusion:

This paper has discussed many different key points regarding sex and race. To recap, males are more likely to develop GBM than females, with a 1.6:1 ratio. Yet females have a better

prognosis, the mechanisms behind which are not fully understood. Steroid hormones, particularly sex-based hormones, have offered unique insight. Estrogen, thought to protect from GBM, inhibits MAPK signaling and promotes apoptosis in astrocytes, yet is linked to progression in secondary GBM. Progesterone and testosterone have a concentration-dependent effect; low levels promote proliferation while high levels induce cell death and increase the effectiveness of chemotherapies like temozolomide. Despite progress, the underlying causes of sex differences in GBM remain unclear, making this an important area for further investigation to develop better, more personalized therapies.

European-descended populations (non-Hispanic whites) have the highest incidence and lowest survival rates for GBM, with a 5-year survival rate of just 4.8%. Specific genetic factors, such as SNPs rs6010620 and rs1412829, along with mutations in TP53 and IDH1, may contribute to this higher incidence, along with a higher frequency of PTEN alterations (48.67%).

African-descended populations experience lower GBM incidence but better survival outcomes. Limited data and factors like healthcare access and environmental exposures complicate diagnosis and treatment, though these disparities may influence survival advantages.

East Asians have lower GBM incidence than whites, developing the disease at younger ages with longer survival. Specific SNPs like EGFR +61 G/A are associated with glioma susceptibility. East Asians also show lower EGFR amplification and higher mutation rates in the p53 pathway compared to whites. Research on South and Western Asians remains scarce, highlighting a need for more studies.

Latino patients, especially those of Mexican and Central American descent, have better survival rates than non-Latino whites, but the reasons for this advantage are unclear. While tumor markers like MGMT methylation and IDH-1 mutations were explored, they didn’t fully explain the survival benefit.

There is a significant research gap for non-European populations, particularly African, Asian, and Latino groups. Further studies on genetic pathways, environmental factors, and treatment outcomes are crucial for advancing personalized therapies and improving survival rates across all ethnic groups affected by GBM.

This research paper has explored the complex intersection of sex, race, and genetic pathways in GBM, revealing how certain genetic factors are linked to specific populations. While progress has been made in identifying these associations, much remains unknown about the full genetic and molecular landscape of brain cancers. This knowledge gap becomes even more urgent as GBM incidence continues to rise.

As the rates of this aggressive cancer increase, the need for further research is critical. Without adequate funding, the momentum to uncover these crucial insights will be stifled, leaving us unprepared to tackle the growing burden of GBM. Investing in research is not just important—it's essential for developing more effective treatments and ultimately improving patient outcomes.

Furthermore, investigating the genetic pathways of GBM can drive advancements in personalized medicine. Tailored treatments that address genetic and sex-specific factors could

significantly enhance patient care, offering new hope in the fight against this devastating disease.

Works Cited

(APA)

Arcos-Montoya, Denisse et al. “Progesterone Receptor Together with PKCα Expression as Prognostic Factors for Astrocytomas Malignancy.” OncoTargets and therapy vol. 14 3757-3768. 16 Jun. 2021, doi:10.2147/OTT.S280314

Ah-Pine, F., et al. “On the Origin and Development of Glioblastoma: Multifaceted Role of Perivascular Mesenchymal Stromal Cells.” Acta Neuropathologica Communications, vol. 11, no. 1, 24 June 2023, doi:10.1186/s40478-023-01605-x.

Bello-Alvarez, Claudia, and Ignacio Camacho-Arroyo. “Impact of Sex in the Prevalence and Progression of Glioblastomas: The Role of Gonadal Steroid Hormones.” Biology of Sex Differences, vol. 12, no. 1, 22 Mar. 2021, https://doi.org/10.1186/s13293-021-00372-5.

Chen, Pengchin, et al. “Ethnicity Delineates Different Genetic Pathways in Malignant Glioma.” Cancer Research, vol. 61, no. 10, May 2001, pp. 3949–3954, aacrjournals.org/cancerres/article/61/10/3949/507468/Ethnicity-Delineates-Different-Genetic-Pathways-in. Accessed 28 May 2025.

Cleveland Clinic. “Hormones: What They Are, Function & Types.” Cleveland Clinic, 23 Feb. 2022, my.clevelandclinic.org/health/articles/22464-hormones.

Costa, Ana Raquel, et al. “The Sex Bias of Cancer.” Trends in Endocrinology and Metabolism: TEM, vol.. 31, no. 10, 2020, pp. 785–799, doi:10.1016/j.tem.2020.07.002.

Delfino, K. R., et al. “Therapy-, Gender- and Race-Specific MicroRNA Markers, Target Genes and Networks Related to Glioblastoma Recurrence and Survival.” Cancer Genomics & Proteomics, vol. 8, no. 4, 2011, pp. 173–183.

Eckel-Passow, J. E., Lachance, D. H., Molinaro, A. M., Walsh, K. M., Decker, P. A., Sicotte, H., Pekmezci, M., Rice, T., Kosel, M. L., Smirnov, I. V., Sarkar, G., Caron, A. A., Kollmeyer, T. M., Praska, C. E., Chada, A. R., Halder, C., Hansen, H. M., McCoy, L. S., Bracci, P. M., & Marshall, R. (2015). Glioma Groups Based on 1p/19q, IDH, and TERT Promoter Mutations in Tumors. New England Journal of Medicine, 372(26), 2499–2508. https://doi.org/10.1056/nejmoa1407279

Gabriel, Abigail, et al. “Adult Brain Cancer in the U.S. Black Population: A Surveillance, Epidemiology, and End Results (SEER) Analysis of Incidence, Survival, and Trends.” Medical Science Monitor: International Medical Journal of Experimental and Clinical Research, vol. 20, 25 Aug. 2014, pp. 1510–1517, doi:10.12659/MSM.890762.

González-Agüero, G et al. “Progesterone receptor isoforms expression pattern in human astrocytomas.” Brain research bulletin vol. 56,1 (2001): 43-8. doi:10.1016/s0361-9230(01)00590-1

Hanada, Tomoko et al. “Rapid malignant transformation of low-grade astrocytoma in a pregnant woman.” The Journal of Obstetrics and Gynaecology Research vol. 42,10 (2016): 1385-1389. doi:10.1111/jog 13072

Hiroko, Ohgaki, and Paul Kleihues. “Genetic Pathways to Primary and Secondary Glioblastoma.” The American Journal of Pathology, vol. 170, no. 5, 2007, pp. 1445–1453, https://doi.org/10.2353/ajpath.2007.070011.

Huang, Yingbo, et al. “Sex Differences in the Molecular Profile of Adult Diffuse Glioma Are Shaped by IDH Status and Tumor Microenvironment.” Neuro-Oncology, vol. 27, no. 2, 5 Oct. 2024, pp. 430–444, https://doi.org/10.1093/neuonc/noae207. Accessed 28 May 2025.

“Impact of Sex in the Prevalence and Progression of Glioblastomas: The Role of Gonadal Steroid Hormones.” Dntb.gov.ua, 2021, ouci.dntb.gov.ua/en/works/7Wa3mxDl/. Accessed 28 May 2025.

Ippolito, Joseph E., et al. “Sexual Dimorphism in Glioma Glycolysis Underlies Sex Differences in Survival.” JCI Insight, vol. 2, no. 15, 3 Aug. 2017, e92142, doi:10.1172/jci.insight.92142.

Jacobs, Daniel I., et al. “Leveraging Ethnic Group Incidence Variation to Investigate Genetic Susceptibility to Glioma: A Novel Candidate SNP Approach.” Frontiers in Genetics, vol. 3, 2012, https://doi.org/10.3389/fgene.2012.00203. Accessed 16 Nov. 2022.

Jang, Byunghyun, et al. “Integrative Multi-Omics Characterization Reveals Sex Differences in Glioblastoma.” Biology of Sex Differences, vol. 15, no. 1, 16 Mar. 2024, https://doi.org/10.1186/s13293-024-00601-7.

John, Danny, et al. “Racial Disparities in Glioblastoma Genomic Alterations: A Comprehensive Analysis of a Multi-Institution Cohort of 2390 Patients.” World Neurosurgery, vol. 188, 4 June 2024, pp e625-e6300, https://doi.org/10.1016/j.wneu.2024.05.183.

Jovanovich, N., Habib, A., Chilukuri, A., Hameed, N. U. F., Deng, H., Shanahan, R., Head, J. R., & Zinn, P. O. (2023). Sex-specific molecular differences in glioblastoma: assessing the clinical significance of genetic variants. Frontiers in Oncology, 13, 1340386. https://doi.org/10.3389/fonc.2023.1340386

Kanderi, T., Munakomi, S., and Gupta, V. Glioblastoma Multiforme. StatPearls, updated 6 May 2024, StatPearls Publishing, 2025, www.ncbi.nlm.nih.gov/books/NBK558954/.

Kawata, Mitsuhiro. “Roles of Steroid Hormones and Their Receptors in Structural Organization in the Nervous System.” Neuroscience Research, vol. 24, no. 1, Dec. 1995, pp. 1–46, https://doi.org/10.1016/0168-0102(96)81278-8.

Khalid, H et al. “Immunohistochemical analysis of progesterone receptor and Ki-67 labeling index in astrocytic tumors.” Cancer vol. 80,11 (1997): 2133-40. doi:10.1002/(sici)1097-0142(19971201)80:11<2133::aid-cncr13>3.0.co;2-#

Kleihues, P., and H. Ohgaki. “Primary and Secondary Glioblastomas: From Concept to Clinical Diagnosis.” Neuro-Oncology, vol. 1, no. 1, 1999, pp. 44–51, doi:10.1093/neuonc/1.1.44.

Lee, Juyeun, et al. “Sex Differences in Glioblastoma Immunotherapy Response.” Neuromolecular Medicine, vol. 24, no. 1, 1 Mar. 2022, pp. 50–55, https://doi.org/10.1007/s12017-021-08659-x.

Łysiak, Małgorzata, et al. “The Sex-Dependent Role of the Androgen Receptor in Glioblastoma: Results of Molecular Analyses.” Molecular Oncology, vol. 16, no. 19, 2022, pp. 3436–3451, doi:10.1002/1878-0261.13262.

Mo, Z., Xin, J., Chai, R., Peter Y.M. Woo, Danny T.M. Chan, & Wang, J. (2022). Epidemiological characteristics and genetic alterations in adult diffuse glioma in East Asian populations. Cancer Biology & Medicine, 19(10), 1440–1459. https://doi.org/10.20892/j.issn.2095-3941.2022.0418

Ohgaki, Hiroko, and Paul Kleihues. “The Definition of Primary and Secondary Glioblastoma.” Clinical Cancer Research, vol. 19, no. 4, 2013, pp. 764–772, doi:10.1158/1078-0432.CCR-12-3002.

Ostrom, Quinn T., et al. “Adult Glioma Incidence and Survival by Race or Ethnicity in the United States From 2000 to 2014.” JAMA Oncology, vol. 4, no. 9, 2018, pp. 1254–1262, doi:10.1001/jamaoncol.2018.1789.

Ostrom, Quinn T., et al. “CBTRUS Statistical Report: Primary Brain and Other Central Nervous System Tumors Diagnosed in the United States in 2011–2015.” Neuro-Oncology, vol. 20, suppl_4, 2018, pp. iv1–iv86, doi:10.1093/neuonc/noy131.

Patel, N. P., Lyon, K. A., & Huang, J. H. (2019). The effect of race on the prognosis of the glioblastoma patient: a brief review. Neurological Research, 41(11), 967–971. https://doi.org/10.1080/01616412.2019.1638018

Peeters, Sophie et al. “Interactions between glioma and pregnancy: insight from a 52-case multicenter series.” Journal of Neurosurgery vol. 128,1 (2018): 3-13. doi:10.3171/2016.10.JNS16710

Porter, Alyx B., et al. “Socioeconomic Status and Glioblastoma Risk: A Population-Based Analysis.” Cancer Causes & Control, vol. 26, no. 2, 25 Nov. 2014, pp. 179–185, https://doi.org/10.1007/s10552-014-0496-x.

Price, Alkes L., et al. “Methods for High-Density Admixture Mapping of Disease Genes.” American Journal of Human Genetics, vol. ..., [Entry incomplete—please provide full details].

Qin, Shangyao, et al. “Identification and Characterization of Sex‐Dependent Gene Expression Profile in Glioblastoma.” Neuropathology, vol. 43, no. 1, 4 July 2022, pp. 72–83, https://doi.org/10.1111/neup.12845.

Stupp, Roger, et al. “Radiotherapy Plus Concomitant and Adjuvant Temozolomide for Glioblastoma.” The New England Journal of Medicine, vol.. 352, no. 10, 2005, pp. 987–996, doi:10.1056/NEJMoa043330.

Tamimi, A. F., and M. Juweid. “Epidemiology and Outcome of Glioblastoma.” Glioblastoma, edited by S. De Vleeschouwer, Codon Publications, 27 Sept. 2017, Chapter 8, www.ncbi.nlm.nih.gov/books/NBK470003/, doi:10.15586/codon.glioblastoma. 2017. ch8.

Tang, X., et al. “Therapeutic Prospects of mRNA-Based Gene Therapy for Glioblastoma.” Frontiers in Oncology, vol. 9, 2019, article 1208, doi:10.3389/fonc 2019.01208.

Wen, Patrick Y., et al. “Glioblastoma in Adults: A Society for Neuro-Oncology (SNO) and European Society of Neuro-Oncology (EANO) Consensus Review on Current Management and Future Directions.” Neuro-Oncology, vol. 22, no. 8, 17 Aug. 2020, pp. 1073–1113, doi:10.1093/neuonc/noaa106.

Wu, Meijing, et al. “Race Influences Survival in Glioblastoma Patients with KPS ≥ 80 and Associates with Genetic Markers of Retinoic Acid Metabolism.” Journal of Neuro-Oncology, vol. 142, no. 2, 31 Jan. 2019, pp. 375–384, https://doi.org/10.1007/s11060-019-03110-5.

Xu, X., Xi, L., Zeng, J., & Yao, Q. (2012). A Functional +61G/A Polymorphism in Epidermal Growth Factor Is Associated with Glioma Risk among Asians. PLoS ONE, 7(7), e41470. https://doi.org/10.1371/journal.pone.0041470

Yin, Jiale, et al. “Gender Differences in Gliomas: From Epidemiological Trends to Changes at the Hormonal and Molecular Levels.” Cancer Letters, vol. 598, 2024, article 217114, https://doi.org/10.1016/j.canlet.2024.217114.