Ethnicity-Based Variations in Focal Adhesion Kinase Signaling in Glioblastoma Gene Expression: A Study of Puerto Rican Hispanic Population

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Background

Glioblastoma (GBM) is a highly aggressive brain tumor with poor prognosis, necessitating deeper understanding of its molecular mechanisms. Ethnicity and sex have been identified as influential factors in cancer incidence and treatment response, with variations observed among different ethnic and racial groups. Studies have reported higher incidence rates of GBM in non-Hispanic populations compared to Hispanic populations. Furthermore, male patients have been shown to have a higher chance of developing GBM compared to females. Focal adhesion kinase (FAK) and proline-rich tyrosine kinase (Pyk2) play crucial roles in integrating signals from cell adhesion, growth factors, and receptors, impacting GBM migration and proliferation. Understanding the molecular basis for ethnic and sex-based disparities in GBM is essential for personalized treatment approaches.

Purpose

This study aims to investigate ethnicity and sex-based variations in gene expression patterns in GBM, specifically focusing on correlations between genes encoding FAK (PTK2 and PTK2B) and growth factor receptors (NGFR, PDGFRB, EGFR, and CXCR1) in Puerto Rican Hispanic patients. By exploring these correlations, the study seeks to elucidate the molecular underpinnings of GBM pathogenesis and address observed disparities in different patient populations.

Methods

Clinical Sample Collection

- 21 Tumor specimens from patients diagnosed with grade IV glioblastoma were obtained with informed consent and approval from relevant ethics boards.
- Inclusion criteria comprised individuals aged ≥21 years with confirmed CNS neoplasia.
- Tissue samples were collected immediately post-surgery for various analyses, including western blot, RT-PCR, and glioblastoma culture preparation.

Glioblastoma and Microglia Purification

- Glioblastoma cells and microglial cells were isolated from tumor tissue using Percoll density gradient centrifugation.
- Specific Percoll concentration layers were used to collect distinct cell fractions for further analysis.

Molecular Analysis Methods

- RNA extraction from purified cells was performed using a specific kit, followed by quality assessment and reverse transcription.
- Real-time RT-PCR and Western blot analyses were conducted to examine gene expression and protein levels in glioma cells under different experimental conditions.
- Analyzed gene expression of cytokines (PTK2, PTK2B, PDGFRB, NGFR, EGFR, and CXCR1) in microglia from 21 human GBM specimens using RT-PCR.

Statistical Analysis

- Pearson correlation analysis was employed to assess the correlation between gene expressions. A p-value of <0.05 correlations arising from multivariable analysis with an r value > ± .7 was considered significant. GraphPad Prism 9.1.0 software was used for statistical analysis.

Correlation Analysis

-Clinical data and expression values for PTK2, PTK2B, PDGFRB, EGFR, CXCR1, NGFR (Glioblastoma (GBM), The Cancer Genome Atlas Program (TCGA) Provisional for Cancer Genomes, mRNA expression (RNA Seq V2 RSEM) were obtained from the cBioPortal for cancer genomics which contains annotated TCGA data. Gene expression correlation analysis was conducted separately for males and females, as well as for Hispanic and non-Hispanic cohorts and contrasted against data from Puerto Rican patients.

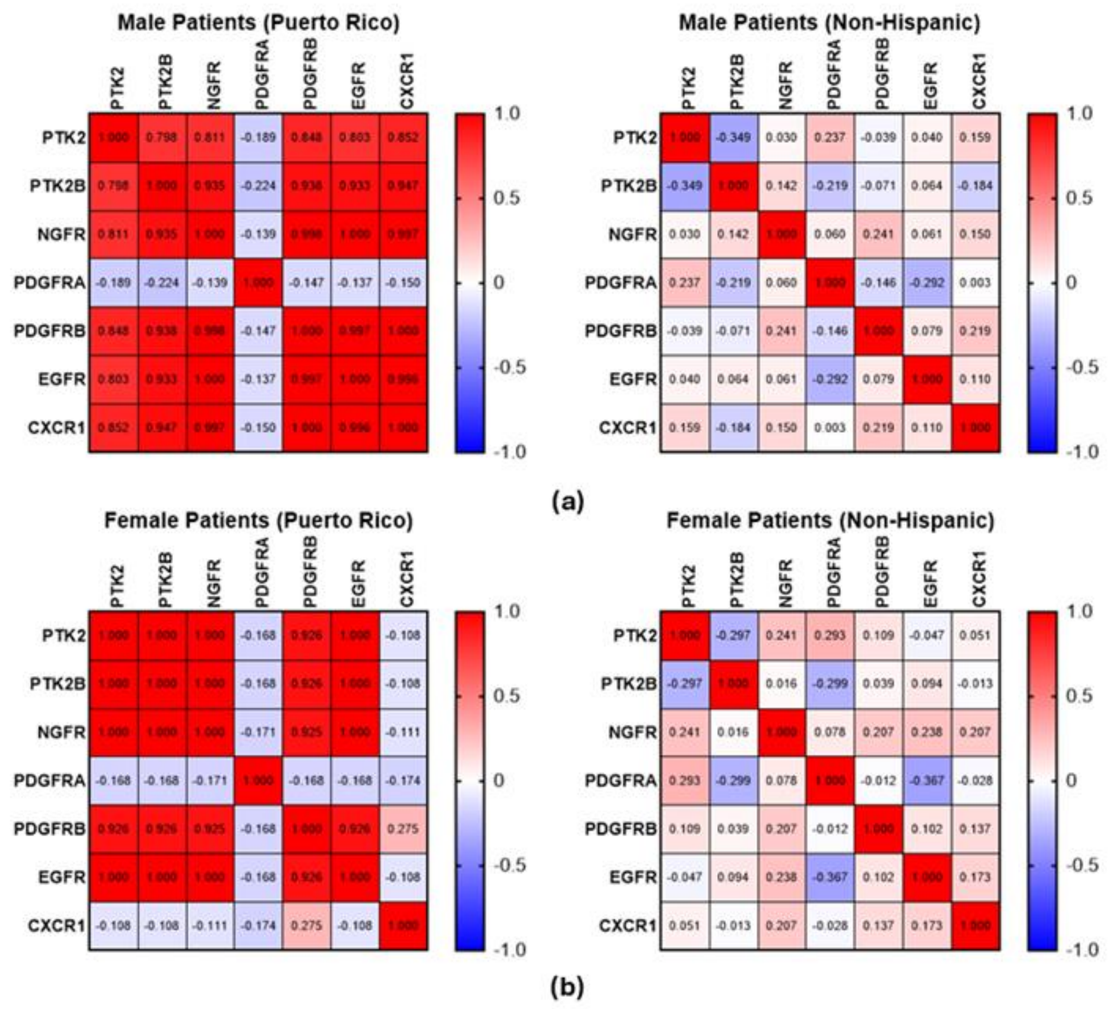

Figure 1. Heat map of Pearson correlation matrix for PDGFRB, NGFR, EGFR, and CXCR1 cell-surface receptors gene expression, assessed through the RT-PCR, as well as Pyk2 and FAK gene expression in human GBM cells, purified from tumors obtained from a cohort of patients from Puerto Rico (n=21). The Puerto Rican cohort was contrasted against non-Hispanic patient data from a micro-array dataset, containing 323 samples, downloaded from cBioPortal, Firehose Legacy microarray dataset. (a) Pearson correlation matrices comparing Puerto Rican males and non-Hispanic males. (b) Pearson correlation matrices comparing Puerto Rican females and non-Hispanic females.

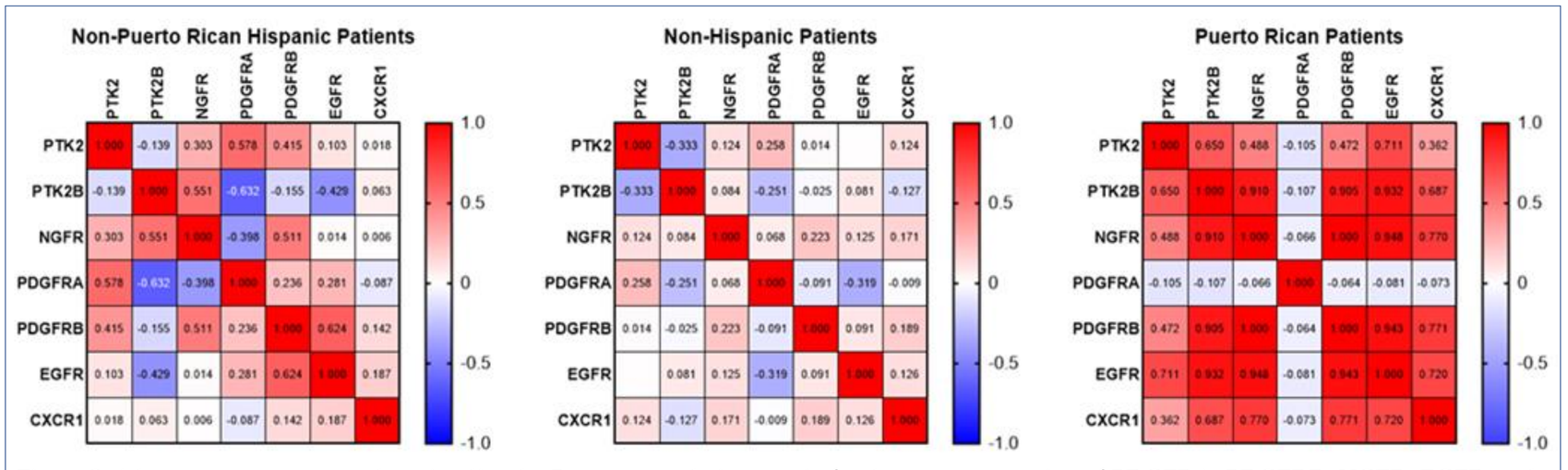

Figure 2. A heat map was generated to visualize the Pearson correlation matrix for the gene ex-pression of PDGFRA, PDGFRB, NGFR, EGFR, and CXCR1 cell-surface receptors, as well as Pyk2 and FAK, in human GBM cells. The analysis compared combined data from males and females across non-Puerto Rican Hispanic and non-Hispanic cohorts, with sample sizes of N=10 and N=313, respectively, obtained from the cBioPortal Firehose Legacy microarray dataset. Additional data from Puerto Rican patients (N=21) were obtained through RT-PCR analysis of GBM specimens.

Conclusions

This study reveals significant ethnicity-based variations in gene expression patterns within GBM tumors, particularly among Puerto Rican Hispanic patients compared to non-Hispanic counterparts. Distinct molecular signatures involving PTK2, PTK2B, NGFR, PDGFRB, and EGFR were identified in Puerto Rican patients, highlighting the importance of considering ethnicity and sex as critical determinants of GBM heterogeneity. These findings emphasize the potential for personalized therapeutic interventions tailored to individual patients' genetic profiles. Further research initiatives should prioritize multi-omic approaches and incorporate ethnicity as a crucial factor in cancer research to validate and clinically apply these findings.

References

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