

HIV-1 glycoprotein gp120 upregulates activation of Pyk2 and Akt signaling pathways in mice glioma cells

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Human glioblastoma (GBM) cells infected with HIV-1 are more prone to... (GBMs). The median survival for GBM... for HIV-negative GBM patients, even... difference indicates that HIV infection is... or and with treatment resistance. Earlier... protein in the HIV shell, stimulates glycolysis

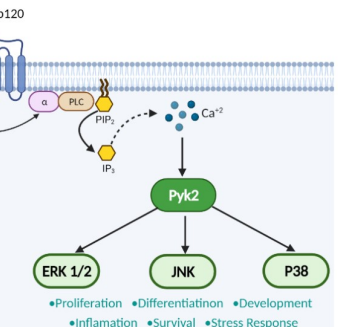
The underlying gp120-dependent signaling... GL-261 were continuously cultured for 7... 120 BaL III (100ng/ml) and collected for... blot analysis presented an increase in... (Pyk2(Y402)), p38(YT100/Y182) and... pyk2 pathway, along with the increased... kinase 3b (GSK3b (S9)) phosphorylation... an increase of G2/M phase in cells... control cells. Furthermore, GL-261 cells with... showed no significant change in cell... .

Commonly occurring malignant primary... tumors diagnosed with GBM is less than 5%... demonstrated that expression of the... with shorter patient survival. CCL5 is an... is CCR5³. The chemokine receptor CCR5... also serves as a co-receptor for HIV

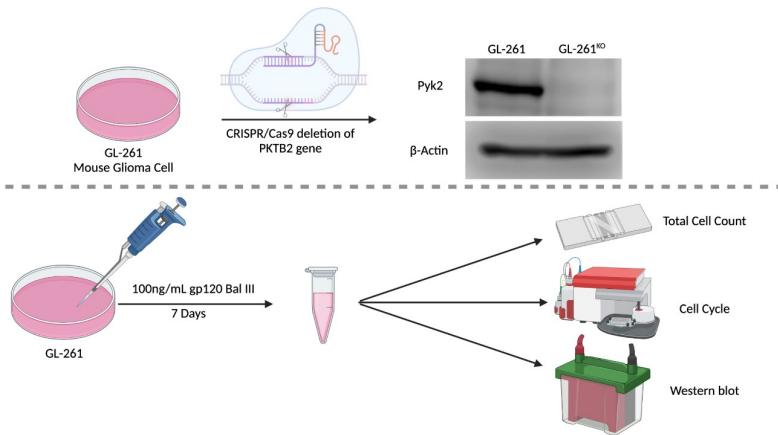
HIV-1 glycoprotein gp120 upregulates... in GBM tumors.⁴ Engagement of CCR5... r growth, induce extracellular matrix... port cancer stem cell expansion, enable... cytotoxicity of DNA-damaging agents...⁵ We hypothesize that gp120 interacts... signaling pathways that result in increased... and upregulated glycolysis.

Wolinsky, Y., ... & Barnholtz-Sloan, J. S. (2013).... system tumors diagnosed in the United States in...
... in the Treatment of Glioblastoma: Multisystem... 16, 505-517.
...eger, D., & Pestell, R. G. (2019). Recent Advances... cancer research, 79(19), 4801-4807.
...N. E., Pérez, J., Ortiz-Rivera, J., Inyushin, M.,...kli, N., & Kucheravykh, L. Y. (2018). HIV-1 Envelope...colysis in Glioma Cell. Cancers, 10(9), 301.

.../CCR5 Axis in Cancer Progression. Cancers, 12(7),



Methods



Results

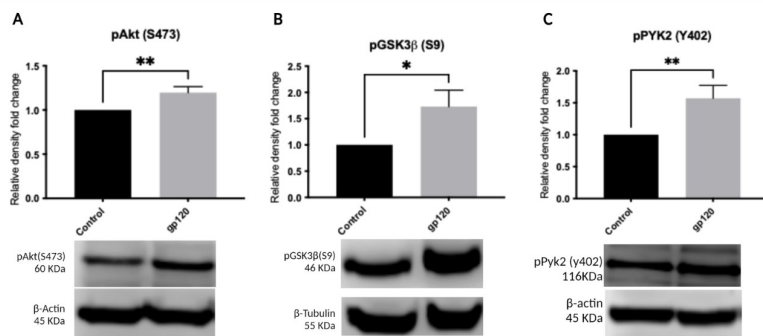


Figure 1: gp120 upregulates phosphorylation of Akt and GSK3β in GL-261 cells. Western blot and quantification of relative changes in phosphorylation of (A) pAkt (S473), (B) pGSK3β (S9) and (C) pPyk2 (Y402) for untreated and gp120-treated mice glioma cells. β-Actin Or β-Tubulin were used as loading controls. Results are presented as mean ± S.D. with significant difference from control (*) (p<0.05), (**) (p<0.005). An unpaired t-test was used to determine the significance between gp120-treated and untreated groups. Three independent experiments (n = 3) for each cell line were used for statistical analysis.

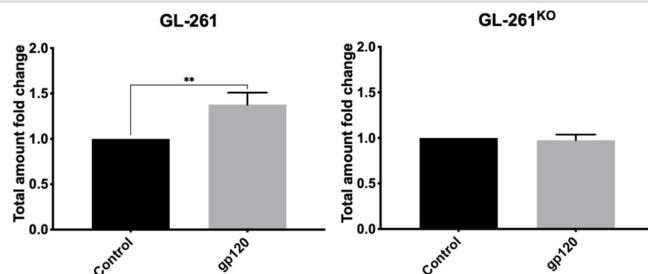


Figure 2: gp120 increases proliferation rate in GL-261 but not in GL-261^{KO}. Graphical representation of total amount of live cells after 7 day treatment with gp120 (100ng/μL). Change in total amount of cells represented in fold change compared to untreated cells. Results are presented as mean ± S.D. with significant difference from control (**) (p<0.005). An unpaired t-test was used to determine the significance between gp120-treated and untreated groups. Four independent experiments (n = 4) for each cell line were used for statistical analysis.

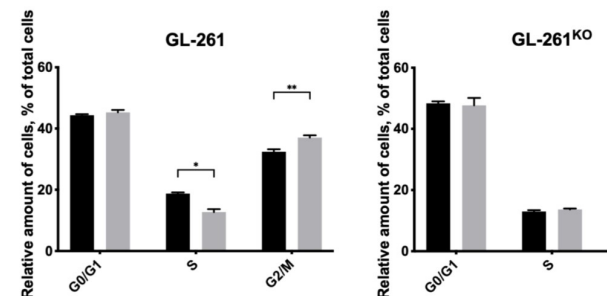


Figure 3: gp120 upregulates cell cycle progression in GL-261 but not in GL-261^{KO} cells. Graphical representation of cell cycle progression determined by flow cytometry. The percentage of cells in the G0/G1, S and G2/M phases was determined based on flow cytometry. The graphs represent the total distribution of cells at different phases of the cell cycle. The proportion is expressed as a percentage of the total number of cells. Mean ± S.D. and significant differences from control were used to determine the significance between groups. Three repeated experiments (n = 3) for each cell line were used for statistical analysis.

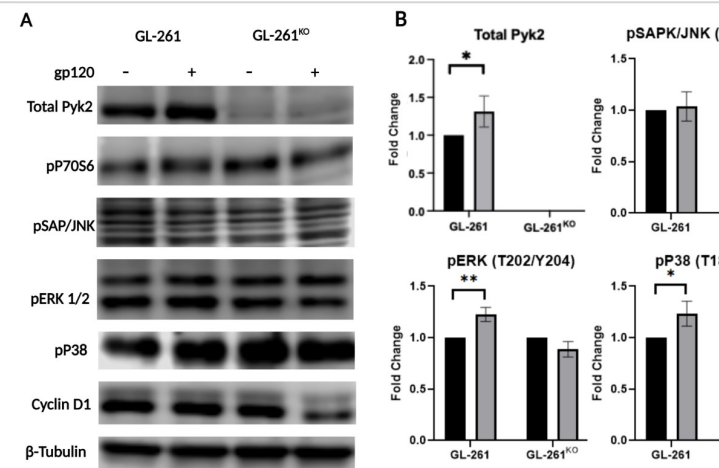


Figure 4: gp120 activates MAPK pathways through Pyk2. Western blot (A) and quantification of phosphorylation of SAPK/JNK (T183/Y185), ERK (T202/204), P38 (T180/182) and, upregulation of Cyclin D1 in untreated and gp120 treated GL-261 and GL-261^{KO}. β-Tubulin was used as loading control. Results are presented as mean ± S.D. with significant difference from control (*) (p<0.05), (**) (p<0.005). An unpaired t-test was used to determine the significance between gp120-treated and untreated groups. Three independent experiments (n = 3) for each cell line were used for statistical analysis.

Conclusions:

The HIV-1 glycoprotein gp120:

- Increases proliferation in GL-261 but not in GL-261^{KO}
- Mediates cell cycle progression through Pyk2 activation
- Leads to the phosphorylation of Akt (S473), GSK3β (S9) and Pyk2 (Y402)
- Activates the P38 and ERK MAPK pathways along with upregulation of Cyclin D1 and phosphorylation of SAPK/JNK

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