EGFL7 EXPRESSION PROFILE IN GLIOBLASTOMA IS ASSOCIATED WITH POOR PATIENT OUTCOME

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INTRODUCTION

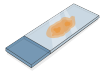
The average life span of patients with glioblastoma (GBM) is of 14 months despite the advances in GBM treatment. Thus, there is a need to identity biomarkers of prognostic and treatment response to be able to development new novel treatment strategies. *EGFL7* is a pro-angiogenic factor that might play a role in tumor progression through mediation of metastasis, proliferation, and angiogenesis. Also, we previously described the association of high EGFL7 expression and unfavorable outcome of pilocytic astrocytoma patients.

AIM

To analyze the biological processes and possible prognostic role of *EGFL7* in GBM, using immunohistochemistry and *in silico* approaches.

MATERIAL AND METHODS

Immunohistochemistry



Tissue microarray (n=78)

Intensity (I) – 0 to 3
Extension (E) – 0 to 3
0 – no reaction
1+ - until 25%
2+ - 25% - 50%
3+ - 50% -100%

Patient score (I+E)
0 to **2**: **negative** expression
3 to **6**: **positive** expression

Clinicopathological and molecular data from patients (age, gender, tumor location, KPS, and overall survival) were associated with the expression of each gene

Overall survival was analyzed in each dataset using log rank statistical analysis (p<0,005)

Bioinformatics

RNAseq TCGA GBM dataset
EGFL7 expression (n=152)

Z-score of EGFL7
- **LOW:** Z-score≤-2.0
- **NORMAL:** between -2.0 e 2.0
- **HIGH:** Z-score≥ 2.0

Diferentially expressed genes
fold change > 2,0 e FDR < 0,05

Enrichment analysis of **Gene Ontology** (GO) and **pahtway KEGG** on portal **DAVID**

RESULTS

Table 1– EGFL7 expression and its association with clinicopathological data.

			EGFL7 expression		
		N°	Low	High	P Value
Sex	Female	32	19 (48.7%)	13 (33.3%)	0.167
	Male	46	20 (51.3%)	26 (66.7%)	
Location	Frontal	22	13 (33.3%)	9 (23.1%)	0.227
	Parietal	16	11 (28.2%)	5 (12.8%)	
	Temporal	12	4 (10.3%)	8 (20.5%)	
	Occipital	3	1 (2.6%)	2 (5.1%)	
	Other	25	10 (25.6%)	15 (38.5%)	
Age group[a]	20-59 yo	49	28 (71.8%)	21 (53.8%)	0.101
	>59 yo	29	11 (28.2%)	18 (46.2%)	
KPS[b]	≤70	44	17 (43.6%)	27 (69.2%)	0.022
	>70	34	22 (55.4%)	12 (30.8%)	

[a] yo=years old; [b]Karnofsky Performance Status; [c]Number of patients;

Cox analysis showed that GBMs with high EGFL7 expression presented a 1.61-higher risk of death.

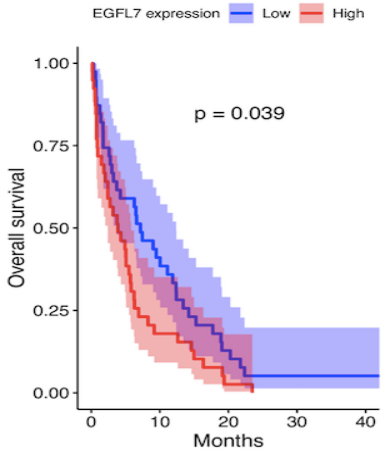


Fig. 1 – Overall survival curves of 78 GBM patients according to EGFL7 expression.

The *in silico* analysis found 78 genes strongly correlated to the expression of EGFL7. These genes were enriched in angiogenesis, cell adhesion process and PI3K-Akt, Notch and Rap1 signaling pathways.

CONCLUSION

This study gives insights regarding biological processes and signaling pathways related to EGFL7 expression as well the genes that are correlated with EGFL7, which should be further investigated in order to elucidate their role in glioblastoma biology and to develop new novel treatment strategies that will impact in the overall survival of GBM patients.

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