Adherens Junctional Associated Protein-1 is a Negative Transcriptional Regulator of MAGEA2, Which Induces Cancer Cell Apoptosis and Inhibits Proliferation in GBM

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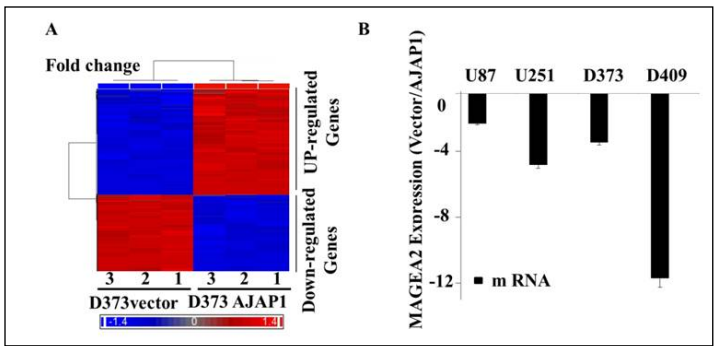
Introduction

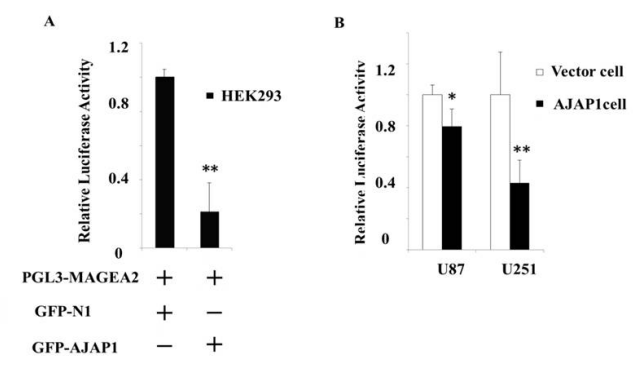
MAGEA2 is growth promoting through its interaction with the P53 pathway by increasing cellular proliferation, decreasing cell cycle arrest or resistance to apoptosis in many kinds of tumors. We recently discovered the loss of expression of Adherens Junctional Associated Protein-1 (AJAP-1) in GBM via genome-wide studies. AJAP1 is a transmembrane protein whose function is implicated in glioma cell migration by our prior work.

Method

We developed stable glioma transfections of AJAP1, verified by Western blot and Confocal Microscopy. Luciferase plasmid reporter constructs were designed to test transcriptional activity. TUNEL and other markers of apoptosis, cell death assays, and cell proliferation assays were utilized.



AJAP1 decreases activity of MAGEA2-promoter in HEK293, U87 and U251 glioma cells.



Results

Interestingly, AJAP1 protein disperses throughout the nucleus as well as the cell membrane when we overexpressed it in GBM cells. To investigate the possible transcriptional regulatory role of AJAP1 and its role on tumorigenesis, we identified ten candidate genes using Human Genome GeneChip array. Real-time PCR showed three genes in four different glioma cell lines which stably overexpressed AJAP1 matched gene chip results; MAGEA2 is one of them. Luciferase reporter analysis revealed AJAP1 directly down-regulated the expression of MAGEA2 in these glioma cells. Further study showed that AJAP1 expression decreased MAGEA2 protein which then induced cell apoptosis and inhibited proliferation in glioma cells.

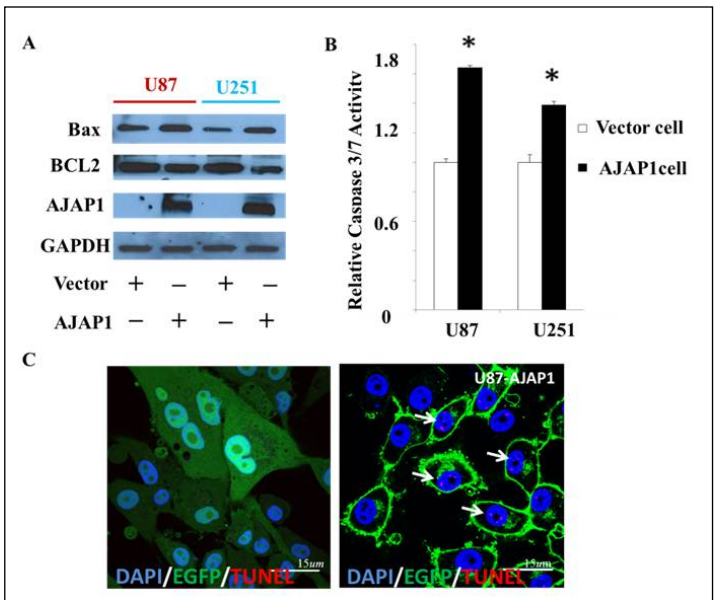


Fig3: **AJAP1 moderately induces apoptosis in GBM cells.**

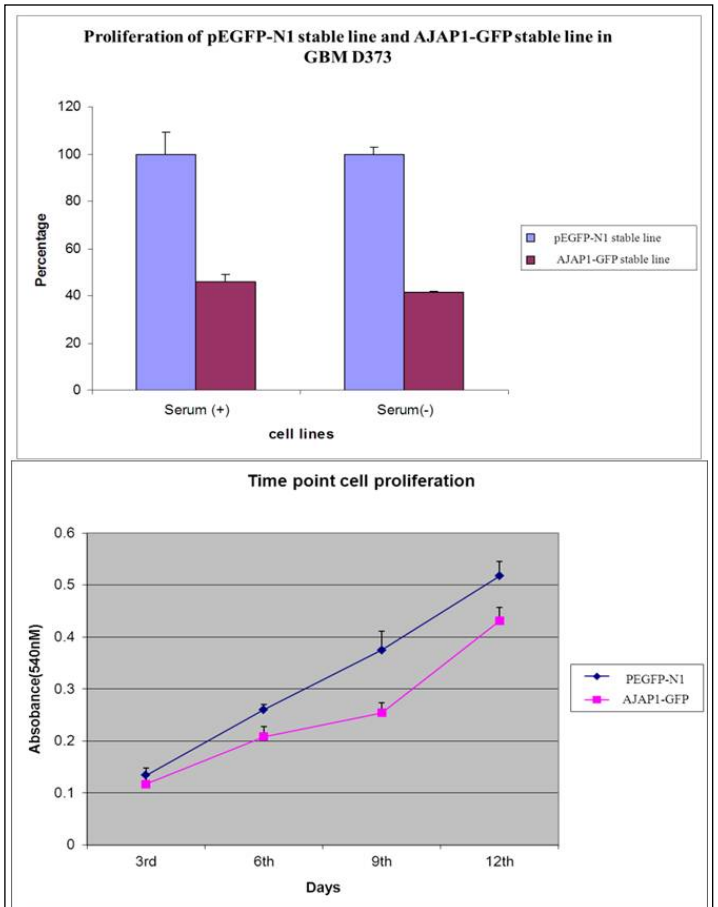


Fig4: **AJAP1 reduces cell proliferation in D373GBM cells.**

Learning Objectives

Novel transcription control of MAGEA2 in gliomagenesis.

Conclusions

Altogether, our results imply that AJAP1 may have a function in the induction of cell apoptosis and inhibition of cell proliferation in GBM through the transcriptional down-regulation of MAGEA2. This represents a novel finding for a new functional role for AJAP1 in gliomas.