

Inhibition Of MTORC1 Through Amino Acid Transporter CD98 LAT1 Maintains The Stemness Of Glioma Stem Cell

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Purpose

Tumor stem cells (CSCs) are considered to be involved in tumor relapse. Mammalian Target of Rapamycin Complex 1 (mTORC1) plays an important role in tumor development and growing. However, the significance of mTORC1 in CSCs remains controversial. This study aims to provide more information for further understanding the mechanisms in down regulating mTORC1 activity in glioma stem cells (GSC).

Materials and Methods

GSC lines BTSC222, BTSC316 and BTSC1228 were used and their differentiated progenies DIFF222, DIFF316 and DIFF1228 were prepared. Expression levels of CD98/LAT1 in BTSCs and DIFFs were compared. Dynamic activation of mTORC1 and re-localization of CD98/LAT1 by stimulation mediums was examined in BTSCs and DIFFs. Further experiments were conducted on Hek293 and Hela cells to study the lysosomal CD98/LAT1 levels.

Results

Lower basic levels of mTORC1 in BTSCs than DIFFs were confirmed. Preliminary data revealed identical expression levels of amino acid transporter CD98/LAT1, the upper stream of mTORC1, in BTSCs and DIFFs. Interestingly, amino acid stimulation test showed slower and weaker activation of mTORC1 in BTSCs than DIFFs. And CD98/LAT1 could be localized onto lysosome membrane from cell membrane.

Conclusion

The different dynamic activations of mTORC1 in BTSCs and DIFFs were not due to the expression levels of CD98/LAT1, the amino acid upper stream in mTOR pathway. The re-localization of CD98/LAT1 from cell membrane to lysosome membrane after amino acid stimulation may contribute to the different activations in BTSCs and DIFFs. Our findings indicate new explanation and possible new target of the chemo-resistance in glioma stem cells.