A Novel Splice Variant of BCAS1 That Promotes Glioblastoma Cell Proliferation and Migration via Dynein-Mediated Pathway

Meng-Ju Wu, Yu-Chi Wang, Ru-Huei Fu

***Abstract*—**Breast carcinoma amplified sequence 1 (*BCAS1*) is a candidate oncogene and forms stable homodimers. BCAS1 was found to be high relative transcript levels in brain, prostate, and some cancer cell lines. Glioblastoma (GBM) is incurable and the most aggressive primary brain tumor. Here, we identified a novel splicing variant of *BCAS1*, named BCAS1-SV1, with an in-frame addition of 202 bases (66 codons) including exon 6B and exon 12B, and deletion of 108 bases (36 codons) including the entire exon 8 and exon 10 of the *BCAS1* gene in GBM. Expression of BCAS1-SV1 is weak in normal brain cells but is high in GBM and some other cancer cells. BCAS1-AS1 can associated with BCAS1 to form homodimers or heterodimers. Overexpression of BCAS1-AS1 significantly increases proliferation and migration of GBM cells. RNAi-mediated knockdown of BCAS1-AS1 expression significantly decreases proliferation and migration of GBM cells. Using microarray analysis, data indicated > 50 genes to be differentially expressed in BCAS1-SV1-expressing compared with BCAS1-expression GBM cells. Moreover, we showed that dynein, a cytoskeleton-assocoated gene, to be required for the proliferation and migration phenotype of GBM cells, interact with BCAS1-AS1 but not with BCAS1 by yeast-two hybrid assay. Blocking expression of dynein completely abrogated effects of BCAS1-AS1 overexpression on proliferation and migration of GBM cells. This study provides the first evidence that a novel gain-of-function BCAS1 splice variant promotes proliferation and migration of GBM cells via dynein-mediated pathway and opens up a new research perspective on the role of the BCAS1 in malignancy.

***Keywords*—**Alternative cplicing, BCAS1, dynein, glioblastoma.

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