Ataxia telangiectasia mutated (ATM) is a serine/threonine protein kinase that is recruited and activated by DNA double-strand breaks. It phosphorylates several key proteins that initiate activation of the DNA damage checkpoint, leading to cell cycle arrest, DNA repair or apoptosis. Several of these targets, including p53, CHK2, BRCA1, NBS1 and H2AX are tumor suppressors.

BRCA1-associated protein (BRAP) was first found to bind to the nuclear localization signal motifs of BRCA1.

Wei et al. from Tianjin, in a study, investigated the role of BRAP in gastric cancer. The cancer genome atlas(TCGA) data were obtained from UALCAN. They downregulated and upregulated the level of BRAP in gastric cancer cells by transfection with shRNAs and plasmids. Then, we evaluated the expression of BRAP by qRT-PCR and investigated the expression of important proteins by Western blot analysis. We conducted a microarray analysis to identify the function of BRAP in gastric cancer cells. Then, we investigated the effect of BRAP on proliferation and migration by CCK-8 assays, colony formation assays, wound healing assays and an extreme limiting dilution analysis. The analysis of TCGA data showed that BRAP was significantly overexpressed in gastric cancer tissues compared to that in normal gastric mucosal tissues ($P < 0.001$). A hybridization-based microarray assay was used to analyze MGC-803 cells and BRAP-downregulated MGC-803 cells. We found 22,199 protein-coding RNAs that were differentially expressed. The genes in the two groups were analyzed with the Kyoto Encyclopedia of Genes and Genomes (KEGG) database, and both the focal adhesion and MAPK pathways were significantly enriched. The results of Cell Counting Kit-8(CCK-8) assays, colony formation assays, wound healing assays and the extreme limiting dilution analysis showed that the knockdown of BRAP reduced gastric cancer cell proliferation and migration and inhibited the process of epithelial-mesenehymal transition (EMT). The overexpression of BRAP induced gastric cancer cell proliferation, migration and the process of EMT. To verify the function of the mitogen-activated protein kinase (MAPK) signaling pathway, we performed a Western blot analysis. The results showed that the downregulation of BRAP decreased the levels of p-ERK and p-Raf1, thereby decreasing the activity of the MAPK signaling pathway. The use of Honokiol increased the levels of p-ERK and p-Raf1, rescuing the function of BRAP downregulation in the MAPK pathway. Xenograft tumor transplantation experiments in nude mice further confirmed the role of BRAP in gastric cancer progression and metastasis [1].

1)
Wei X, Liu X, Liu H, et al. BRCA1-associated protein induced proliferation and migration of gastric cancer cells through MAPK pathway [published online ahead of print, 2020 Aug 14]. Surg Oncol. 2020;35:191-199. doi:10.1016/j.suronc.2020.08.007