

Bcl2L12

see [Bcl2L13](#).

Bcl2L12 as a new member of the [Bcl2 family](#), which contains a BH2 domain and shares a lower [amino acid](#) similarity with other Bcl2 family proteins. Bcl2L12 is reported to be involved in [apoptosis](#) regulation, but this role remains controversial in different [cancer](#) type. [Temozolomide](#) (TMZ) is currently used to intervene [glioblastoma multiforme](#) (GBM), but an acquired chemotherapeutic resistance maybe occurred due to undesired autophagy. Previous studies uncovered that Bcl2L12 may interact with [Bcl xL](#) and may harbor a BH3-like domain. Therefore, we investigated whether this BH3-like domain is responsible for the Bcl2L12 anti-apoptotic property. Moreover, we tested whether ABT-737, a BH3 mimetic agent, can be combined with TMZ to treat GBM. We aligned Bcl2L12 with Bcl2 family members, compared interacting pattern of BH3 domain and their protein 3D structure. We identified that Bcl2L12 interacts with Bcl-xL and Bcl2 in yeast two-hybrid system. Bcl2L12192-220 was a minimal region for Bcl2L12-Bcl-xL interaction. Five-point mutations with respect to hydrophobic and charge residues were generated to test whether they are the key residue of BH3-like domain. Our data showed that both h1 (L213) and h2 residue (L217) are essential for Bcl2L12 interacting with Bcl2 family proteins. Ectopically expressed h1 or h2 mutant in U87MG cell line resulted in reactivation of cleaved-PARP, caspase-3 and cytochrome c releasing compared to Bcl2L12 wt group. Implementing ABT-737 combined with TMZ provided a superior effect on apoptosis induction in Bcl2L12 wt group, which effectively reactivated apoptotic markers. Altogether, our findings indicated that Bcl2L12 retains a BH3-like domain, which is important for the Bcl2L12 anti-apoptotic property and TMZ-induced autophagy. These results basically support the idea of using ABT-737 to counteract the anti-apoptotic role of Bcl2L12 and sensitize drug response of the GBM cells to TMZ ¹⁾.

¹⁾

Yang MC, Loh JK, Li YY, Huang WS, Chou CH, Cheng JT, Wang YT, Lieu AS, Howng SL, Hong YR, Chou AK. Bcl2L12 with a BH3-like domain in regulating apoptosis and TMZ-induced autophagy: A prospective combination of ABT-737 and TMZ for treating glioma. *Int J Oncol*. 2015 Jan 13. doi: 10.3892/ijo.2015.2838. [Epub ahead of print] PubMed PMID: 25586056.

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