# Overcoming tumor resistance to anti-cancer agent TRAIL

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The TRAIL ligand is a promising anticancer agent that preferentially kills tumor cells without apparent damage to healthy cells. Many cancers exhibit resistance to TRAIL, however, thus limiting its therapeutic potential. According to a study in the March 22 issue of the *Journal of Cell Biology*, small molecules known to block Mcl-1 (induced myeloid leukemia cell differentiation protein) might represent a suitable means to overcome TRAIL resistance.

Researchers know that TRAIL-induced cell death entirely depends on the presence of Bax, which is a member of the proapoptotic Bcl-2 family of proteins and is often lost in tumor cells for various reasons. Despite the expression of Bak, another protein that promotes dell death, Bax-deficient cells are resistant to TRAIL-induced death.

Peter Daniel (Humboldt University, Germany) and colleagues investigate the role of two Bcl-2 proteins—Mcl-1 and Bcl-xL—that keep Bak in check. The team's findings show that blocking Mcl-1 but not Bcl-xL overcame resistance to TRAIL-induced cell death in bax-deficient cells and enabled TRAIL to activate Bak. Blocking Bak inhibitors like Mcl-1 appears to be a promising strategy in limiting the resistance of cancers to TRAIL.

**More information:** Gillissen, B., et al. 2010. J. Cell Biol. doi:10.1083/jcb.200912070

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